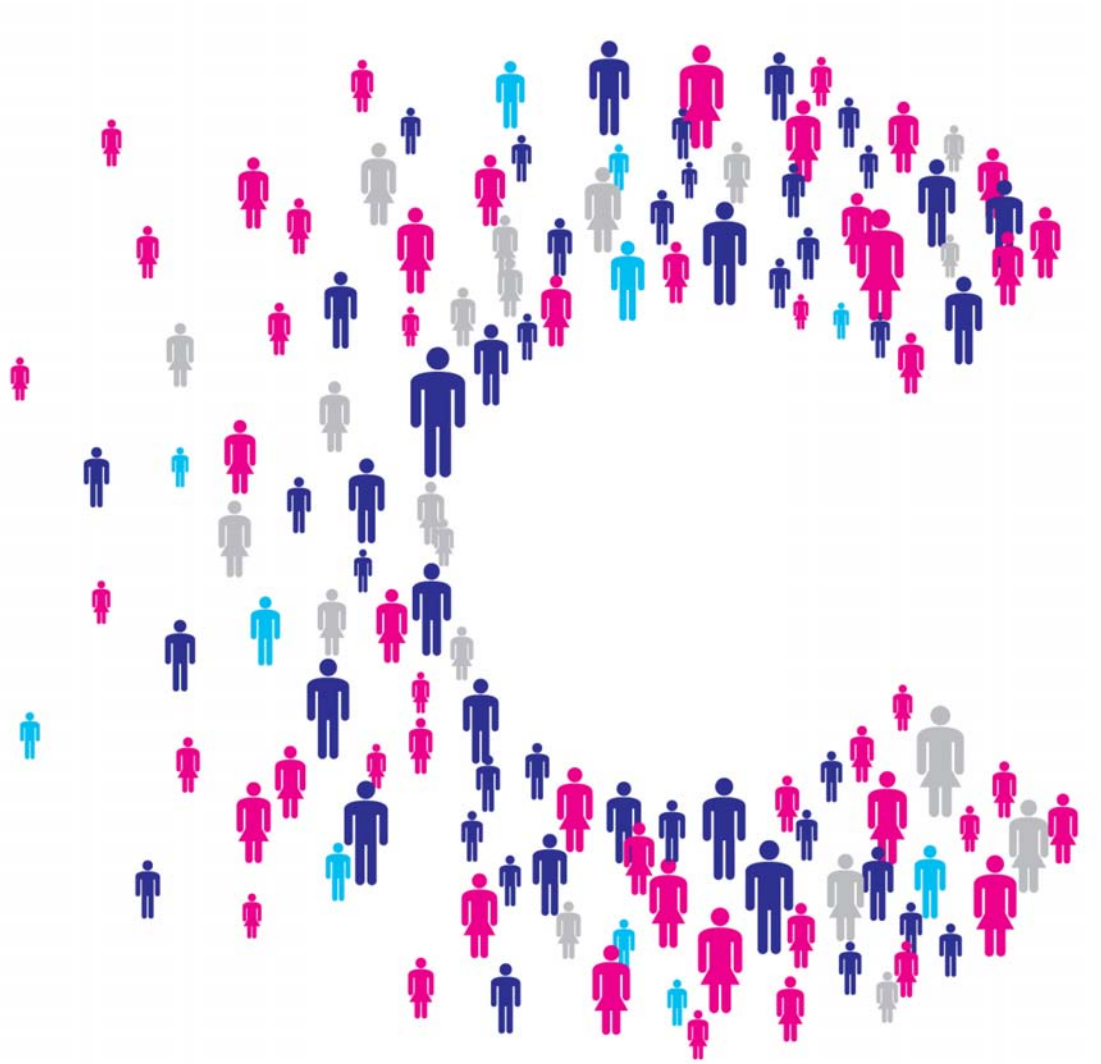

Cancer Research UK

Clinical Trials Catalogue

2014

CANCER RESEARCH UK

Catalogue Listings

ECMC Supported studies

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Bladder							
University of Birmingham	James	Tuxedo - Phase I/II feasibility study of cetuximab with or without cisplatin with concurrent radiotherapy in muscle invasive bladder cancer	2/45	2017		Yes	The optimum management strategy for the control of local disease (selective bladder preservation or radical cystectomy) remains to be determined. Improving bladder preservation will lead to an improved quality of life for many patients. The TUXEDO trial will assess the safety, feasibility and preliminary efficacy of a combination of radiotherapy with cetuximab and chemotherapy in muscle invasive bladder cancer; and to determine whether this treatment improves cystoscopic local control of advanced bladder cancer at three months after treatment. Results from TUXEDO, and other relevant studies, will be used in the design of an appropriate follow-on phase III trial supporting bladder preservation.
University College London	Kelly	HYMN: A Randomised controlled phase III trial comparing hyperthermia plus mitomycin to a second course of bacillus Calmette-Guerin in patients with recurrence of non-muscle invasive bladder cancer following induction or maintenance bacillus Calmette-Guerin therapy	104/242	2015		Yes	The HYMN trial together with another European randomised clinical trial will address the question whether hyperthermia with concurrent mitomycin is an effective treatment for non-muscle invasive bladder cancer after BCG failures. The HYMN trial together with another European randomised clinical trial will address the question whether hyperthermia with concurrent mitomycin is an effective treatment for non-muscle invasive bladder cancer after BCG failures.
University of Glasgow/Barts and the London NHS Trust	Jones/Powles	CRUKE/11/021: PLUTO - A randomised phase ii study investigating pazopanib versus paclitaxel in relapsed or locally advanced tcc of the bladder	46/140	2015			
EORTC and University of Leeds for UK	Chester	NCRI Bladder Trial EORTC 30994: Randomized phase III trial comparing immediate versus deferred chemotherapy after radical cystectomy in patients with pT3-pT4, and/or N+M0 transitional cell carcinoma (TCC) of the bladder	35/185	2013		Yes	Additionally the duration of effects on bone will be assessed and linked to the efficacy The number of patients recruited (284, world-wide) represents the largest randomised trial ever conducted for this indication. Although highly unlikely to generate a statistically significant result for its primary end-point, it should contribute substantially to a future updated meta-analysis.
EORTC and University of Leeds for UK	Chester	NCRI Bladder Trial EORTC 30994 Immediate versus deferred chemotherapy after radical cystectomy in patients with pT3-pT4, and/or N+M0 transitional cell carcinoma (TCC) of the bladder	35/185	2013		Yes	The number of patients recruited (284, world-wide) represents the largest randomised trial ever conducted for this indication. Although highly unlikely to generate a statistically significant result for its primary end-point, it should contribute substantially to a future updated meta-analysis. The number of patients recruited (284, world-wide) represents the largest randomised trial ever conducted for this indication. Although highly unlikely to generate a statistically significant result for its primary end-point, it should contribute substantially to a future updated meta-analysis.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Huddart (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Hall, ICR-CTSU)	CRUK/07/011: SPARE - Randomised trial of Selective bladder Preservation Against Radical Excision (cystectomy) in muscle invasive T2/T3 transitional cell carcinoma of the bladder – feasibility study	45 (trial closed early)/110	2013	PARAMASIVAN, S., et al. 2011. Key issues in recruitment to randomised controlled trials with very different interventions: a qualitative investigation of recruitment to the SPARE trial (CRUK/07/011). Trials, 12, 1-15. MOYNIHAN, C., et al. 2012. The Patient Deficit Model Overturned: a qualitative study of patients' perceptions of invitation to participate in a randomized controlled trial comparing selective bladder preservation against surgery in muscle invasive bladder cancer (SPARE, CRUK/07/011). Trials, 13, 228. HUDDART, R. A., et al. 2010. Life and Death of Spare (Selective Bladder Preservation against Radical Excision): Reflections on Why the Spare Trial Closed. BJU Int, 106, 753-755. HUDDART, R., et al. 2012. Results of the SPARE Feasibility Study – Selective Bladder Preservation Against Radical Excision in Muscle Invasive T2/T3 Transitional Cell Carcinoma of the Bladder (CRUK/07/011). Int J Radiat Oncol Biol Phys, 84, S119 #296. BRIGGS, K., et al. 2005. Involving consumers in trial design: experiences from the proposed SPARE Trial. NCRI National Cancer Conference, Birmingham. #P222. HUDDART, R., et al. 2012. Results of the SPARE Feasibility Study – Selective Bladder Preservation Against Radical Excision in Muscle Invasive T2/T3 Transitional Cell Carcinoma of the Bladder (CRUK/07/011). Int J Radiat Oncol Biol Phys, 84, S119 #296. (Oral presentation ASTRO) HUDDART, R., et al. 2012. SPARE feasibility study - selective bladder preservation against radical excision in muscle invasive T2/T3 transitional cell carcinoma of the bladder (CRUK/07/011). NCRI National Cancer Conference, Liverpool. A83.	No	The optimum radical treatment for muscle invasive bladder cancer patients has not been determined and there are no randomised data to suggest which treatment is best. SPARE is the first and only randomised trial comparing selective bladder preservation to surgery in this group of patients in the world, however it closed due to insufficient accrual in March 2010. Data relating to patient acceptance and clinical equipoise have informed the design of subsequent trials of complex interventions comparing dissimilar treatment strategies (eg. POUT). SPARE is unlikely to have great impact internationally given the small sample size resulting from the trial being unfeasible.
The Institute of Cancer Research	Kelly (University College London) (Hall, ICR-CTSU)	CRUK/07/004: BOXIT: A randomised phase III placebo-controlled trial evaluating the addition of celecoxib to standard treatment of transitional cell carcinoma of the bladder	472/475	2014/2015	MOSTAFID, A., et al. 2012. Compliance with intravesical therapy guidelines for intermediate and high risk non muscle invasive bladder cancer patients recruited into the BOXIT (CRUK/07/004) trial. BAUS Section of Oncology Annual Meeting, Belfast	Yes	BOXIT is the largest intervention trial in nonmuscle invasive bladder cancer undertaken and has successfully set up a network of oncologists/ urologists treating bladder cancer for future studies in this disease area. The results of BOXIT will contribute to the international knowledge base.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Birtle (Royal Preston Hospital) (Hall, ICR-CTSU)	CRUK/11/027: POUT: A phase III randomised trial of Peri-Operative chemotherapy versus sUrveillance in upper Tract urothelial cancer	38/345	2020	BIRTLE, A. 2012. Call for investigators to define international standard of care POUT: A phase III randomised trial of Peri-Operative chemotherapy versus surveillance in upper Tract urothelial cancer - CR-UK/11/027. European Urology Today, 24, 27. BIRTLE, A. J., et al, E. 2012. Lymphadenectomy at the Time of Nephroureterectomy for Upper Tract Urothelial Cancer. European Urology, 61, e16. BIRTLE, A., et al. 2012. Time to Define an International Standard of Postoperative Care for Resected Upper Urinary Tract Transitional Cell Carcinoma (TCC) – Opening of the Peri-Operative Chemotherapy Versus Surveillance in Upper Tract Urothelial Cancer (POUT) Trial. BJU International, 110, 919-921. BIRTLE, A., et al. 2012. Peri-operative chemotherapy or surveillance in upper tract urothelial cancer (POUT)-CRUK/11/027) - a new randomised controlled trial to define standard post-operative management. Annals Oncology, 23, ix292 #887. BIRTLE, A. et al. 2012. Peri-operative chemotherapy or surveillance in upper tract urothelial cancer (POUT)-CRUK/11/027) - a new randomised controlled trial to define standard post-operative management. Annals Oncology, 23, ix292 #887. (ESMO Conference, 2012.) BIRTLE, A., et al. 2012. Peri-operative chemotherapy or surveillance in upper tract urothelial cancer (POUT)-CRUK/11/027) - a new randomised controlled trial to define standard post-operative management. NCRI National Cancer Conference, A58. BIRTLE, A., et al. 2013. Peri-operative chemotherapy or surveillance in upper tract urothelial cancer (POUT)-CRUK/11/027) - a randomised controlled trial to define standard post-operative management. 28th Annual EAU Congress Poster presentation, Milan 15 March 2013 Abstracts (full bodies) are available on the EAU website to members.	Yes	If positive, POUT will define a new standard of care for this group of patients. The participation of centres across the UK will ensure all patients are discussed at MDT postnephroureterectomy, which was not occurring as standard at all sites when centres were surveyed about current practice during trial setup. This is the only phase III randomised trial in this disease setting. POUT is the only phase III randomised trial in this disease setting and it is internationally recognised that the outcome of the trial has the potential to define a new standard of care for these patients. The current version of the European Association of Urology guidelines for treatment of upper tract urothelial carcinoma highlights the importance of POUT, stating that existing data are insufficient to provide any recommendations regarding adjuvant chemotherapy.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Birmingham	James (University of Birmingham) AND Huddart (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Hall, ICR-CTSU)	CRUK/01/004: BC2001:A 2x2 factorial randomised phase III study comparing standard vs whole bladder radiotherapy with tumour boost+/- synchronous chemotherapy in muscle invasive bladder cancer	458/448	2011	JAMES, N. D., et al. 2012. Radiotherapy with or without Chemotherapy in Muscle-Invasive Bladder Cancer. N Engl J Med, 366, 1477-1488. HUDDART, R., et al. 2013. A randomized non-inferiority trial of reduced high dose volume versus standard volume radiotherapy for muscle-invasive bladder cancer: results of the BC2001 trial (CRUK/01/004). Int J Radiat Oncol Phys ,87(2), 261-269.	Yes	Synchronous chemotherapy with 5FU and mitomycin C combined with radiotherapy significantly improved locoregional control of muscleinvasive bladder cancer, compared with radiotherapy alone, with no significant increase in adverse events. Due to the comparison being underpowered, BC2001 could not formally conclude that reduced high dose volume radiotherapy resulted in noninferiority of locoregional control or a statistically significant reduction in late side effects compared to standard volume radiotherapy. Chemoradiotherapy treatment is a valid option for the treatment of muscle invasive bladder cancer. BC2001 is the largest trial of chemoradiation in bladder cancer worldwide. The chemoradiotherapy regimen has been incorporated into the TUXEDO trial (ISRCTN80733590) as a control arm. The low rate of toxicity in both reduced high dose volume and standard volume radiotherapy suggests there is scope to improve radiotherapy results by dose escalation using image guided techniques and/or by the incorporation of new systemic agents. The reduction In local recurrence should make chemoradiotherapy the new standard of care and it is being adopted as standard by many hospitals across the UK. In mainland Europe and the US cystectomy is the standard of care and in many countries RT is not offered to those considered unfit for surgery. The good toxicity profile, low risk of death and good functional outcomes demonstrated In BC2001 in an elderly group should result in many more patients being offered chemoradiotherapy worldwide.
The Institute of Cancer Research	Mostafid (Hampshire Hospitals NHS Foundation Trust) Hall (ICR-CTSU)	A phase II randomised feasibility study of Chemoresection and surgicAl management in Low rIsk non muscle invasive Bladder cancER (CALIBER)	unknown/174			No	CALIBER is a phase II study. If response to chemoresection meets predefined limits, it will progress to a phase III study investigating long term treatment efficacy. If this is positive, the trial results will enable patients to avoid inpatient surgical treatment of recurrent low risk non-muscle invasive bladder cancer. Patients will therefore not have to experience the risk of receiving a general anaesthetic and the inconvenience of being admitted to hospital, and there will be a consequent reduction in associated costs for the NHS. CALIBER is a phase II study which will contribute to the international knowledge base regarding chemoresection. If response to chemoresection meets predefined limits, it will progress to a phase III study investigating long term treatment efficacy. If this is positive, the trial results will enable patients to avoid inpatient surgical treatment of recurrent low risk non-muscle invasive bladder cancer.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Huddart (Royal Marsden Hospital NHS Foundation Trust) (Hall, ICR-CTSU)	HYBRID: A multicentre randomised phase II study of HYpofractionated Bladder Radiotherapy with or without Image guided aDaptive planning	unknown/62		HUDDART, R., et al. 2013. HYBRID - Evaluating New Radiation Technology in Patients with Unmet Needs. Clin Oncol (R Coll Radiol), 25, 546-8.	Yes	HYBRID offers the opportunity to standardise treatment for patients unfit for standard radical therapy of bladder cancer. It will also provide a quality assured environment to roll out adaptive bladder radiotherapy techniques at participating centres in the UK. HYBRID will provide prospective data on the toxicity profile and an indication of efficacy of hypofractionated bladder radiotherapy. This may provide evidence to define a new standard of care internationally for these patients who are unable to receive daily bladder radiotherapy. HYBRID will also investigate the value of adaptive radiotherapy techniques and whether they result in lower side effects than otherwise occur with hypofractionated radiotherapy treatment.
MRC	Parmar	CRUK/02/001: BA11: A randomised phase III study comparing paclitaxel/cisplatin/gemcitabine vs cisplatin/gemcitabine in patients with metastatic or locally advanced urothelial cancer.	626/700	2009	Bellmunt J et al. Randomized Phase III Study Comparing Paclitaxel/Cisplatin/ Gemcitabine and Gemcitabine/Cisplatin in Patients With Locally Advanced or Metastatic Urothelial Cancer Without Prior Systemic Therapy: EORTC Intergroup Study 30987. J Clin Oncol, 30(10): 1107-1113		Trial Closed, now in follow-up. The final year of funding for this trial, period April 09- Mar 10, has been surrendered voluntarily by the Trial Team. After a median follow-up of 4.6 years, the median OS was 15.8 months on PCG versus 12.7 months on GC (hazard ratio [HR], 0.85; P = .075). OS in the subgroup of all eligible patients was significantly longer on PCG (3.2 months; HR, 0.82; P = .03), as was the case in patients with bladder primary tumors. PFS was not significantly longer on PCG (HR, 0.87; P = .11). Overall response rate was 55.5% on PCG and 43.6% on GC (P = .0031). Both treatments were well tolerated. Conclusion: the addition of paclitaxel to GC provided a higher response rate and a 3.1 month survival benefit that did not reach statistical significance. Novel approaches are required to obtain major improvements in survival of incurable urothelial cancer.
The University of Birmingham	Cheng	CRUK/05/037: SELENIB - Randomised controlled trial of selenium and vitamin E in the recurrence and progression of non muscle invasive bladder cancer	185/515				
The University of Birmingham	Cheng	CRUK/05/28: BCPP - Bladder Cancer Prognosis Programme	1536/1562	2017	1. Zeegers MP et al., BJU Int. 2010 Mar;105(6):784-8. 2. van Roekel EH et al. Int J Cancer. 2013 Jul 15;133(2):446-54. 3. Bryan RT et al. BJU Int. 2013 Jul;112(2):169-75. 4. ShimwellNJ et al. Br J Cancer 2013 May 14;108(9):1854-61 5. Bryan RT et al. Br J Cancer. 2014 Feb 4;110(3):679-85.	No	This prospective study was designed to establish the role of lifestyle factors on recurrence and progression of non-muscle-invasive bladder cancer (NMIBC). The influence of cigarette smoking, diet, fluid intake and industrial exposure on prognosis have not yet been examined in detail and prospectively in NMIBC patients. There is therefore the potential to simply modify patients' behaviours to decrease their risks of recurrence and progression of disease. HRQoL has also been very much neglected in NMIBC patients, with the evdience-base focusing on MIBC. However, given the requirement for frequent surveillance episodes and interventions, these data are essential if we are to quantify the true impact and cost of this common disease. The panel of molecular markers being studied may better risk-stratify patients so that their surveillance and management can be better stratified, adding further biological sophistication to conventional grade and stage. Finally, the biospecimen collection linked to the cohort and outcome data provides and powerful resource for translational studies now and in

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
							the future. As per the UK - this study is of global significance, especially the biospecimen collection.
Barts and the London NHS Trust	Powles	CRUKE/09/002: LaMB: A randomised phase II, two-arm comparison of maintainence lapatinib versus placebo after first-line chemotherapy in patients with HER 1 and/or HER 2 overexpressing metastatic bladder cancer					
University of Southampton	King	CRUK/11/047: COAST (Cisplatin Ototoxicity attenuated by Aspirin Trial): A Phase II randomised controlled trial of aspirin in the preventative role of cisplatin induced ototoxicity.	9/88	2015		Yes	The COAST study aims to recruit 88 cisplatin-naïve patients who will be undergoing high dose cisplatin treatment for malignancy in order to assess whether aspirin can reduce hearing loss in this group of patients. Approximately 18,500 patients receive Cisplatin on an annual basis within the UK and 50% of the patients receiving a high dose regimen have a significant reduction in hearing loss following treatment which is both permanent and irreversible. As Cisplatin is usually given with a curative intent the treatment potentially leaves a patient with resulting deafness that results in considerable reduction in Quality of Life. In some patients the hearing loss may be restored by use of hearing aids however in others the hearing loss is so severe that they could only be considered for cochlear implantation. As well as the impact on the quality of life of the patient both hearing aids and cochlear implantation have important short and long term costs to the NHS. The outcome of this research could therefore have important implications both economically and for the quality of life of cancer patients worldwide
Cardiff University	Chester	CRUK/08/015: TOTEM: A Phase I/II single-arm trial to evaluate the combination of cisplatin and gemcitabine with the mTOR inhibitor temsirolimus as first-line treatment of patients with advanced transitional carcinoma of the urothelium	3/99	2015		No	This is a phase II trial. The result will be used to determine the experimental arm of a future phase III which, if positive, would lead to a change in clinical practice. Will contribute significantly to international knowledge base.
Cardiff University	Geldart	CRUK/07/044: SUCCINCT: A Phase II single-arm trial to evaluate cisplatin and gemcitabine chemotherapy in combination with sunitinib for first-line treatment of patients with advanced transitional carcinoma of the urothelium	63/63	2013		No	This is a phase II trial. The result will be used to determine the experimental arm of a future phase III which, if positive, would lead to a change in clinical practice. Will contribute significantly to international knowledge base.
Cardiff University	Jones	CRUKE/09/024: TOUCAN: A randomised phase II trial of carboplatin and gemcitabine +/- vandetanib in first line treatment of advanced urothelial cell cancer in patients who are not suitable to receive cisplatin.	40/122	2015		No	This is a randomsied phase II trial. The result will be used to determine the experimental arm of a future phase III which, if positive, would lead to a change in clinical practice. Will contribute significantly to international knowledge base.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Cardiff University	Kelly	CRUK/08/036: BOLERO: A study to determine the feasibility of randomisation to open versus minimal access cystectomy in patients with muscle invasive bladder cancer	72/72	2013		No	This is a feasibility study which includes a randomsied phase II trial. The result will be used to determine a future phase III which, if positive, would lead to a change in clinical practice. Will contribute significantly to international knowledge base.
Centre for Drug Development							
University of Nottingham	Bishop	CRUKD/01/020: A Phase I/II Trial of 67Cu-C595 Monoclonal Antibody in bladder cancer given as a single dose via intravesical instillation	5/25	2003	Murray A, Simms MS, Scholfield DP, Vincent RM, Denton G, Bishop MC, Price MR, Perkins AC. Production and characterization of 188Re-C595 antibody for radioimmunotherapy of transitional cell bladder cancer. J Nucl Med. 2001 May;42(5):726-32.		First time in patients for this radioimmunotherapy treatment. Trial did not complete recruitment due to drug supply issues. Too early in development to assess clinical impact.
University of Wales College of Medicine	Chester	CRUKD/12/009: FIESTA: FGFR Inhibition in Epithelial Solid Tumours - AZD4547 in combination with gemcitabine and cisplatin: a phase Ib trial in advanced bladder cancer and other solid tumours	4/44	2015			First time for this combination in this group of patients. This trial forms part of the Combinations Alliance, with the potential to make AZD4547 more rapidly and more widely available to patients in a broader range of clinical indications. The predictive biomarker studies proposed have the potential to spare un-necessary palliative and/or neoadjuvant chemotherapy to patients with bladder cancer, thereby achieving health economic benefits to the NHS, as well as personal benefits to the individual patients. This trial forms part of the Combinations Alliance, with the potential to make AZD4547 more rapidly and more widely available to patients in a broader range of clinical indications. The predictive biomarker studies proposed have the potential to spare un-necessary palliative and/or neoadjuvant chemotherapy to patients with bladder cancer, thereby achieving health economic benefits to the NHS, as well as personal benefits to the individual patients.
University of Wales College of Medicine	Mason	CRUKD/01/022: A Phase II Study of Cis-Amminedichloro(2-methylpyridine)Platinum(II) (ZD0473) administered every Three Weeks via Intravenous Infusion over One Hour in Patients with Recurrent and/ or Metastatic Transitional Cell Carcinoma of the Urinary Tract	10/45	2003			First time in this indication for this platinum agent. Follow up trial to CRUKD/97/015. Trial closed early due to lack of drug supply. Agent in Phase III development. Too early in development to assess clinical impact.
University of Oxford	Harris	CRUKD/00/018: A Phase I trial of intravesical Suramin in recurrent superficial transitional cell bladder carcinoma.	24/24	2004	Ord JJ, Streeter E, Jones A, Le Monnier K, Cranston D, Crew J, Joel SP, Rogers MA, Banks RE, Roberts IS, Harris AL. Phase I trial of intravesical Suramin in recurrent superficial transitional cell bladder carcinoma. Br J Cancer. 2005 Jun 20;92(12):2140-7.		First time for this agent in this group of patients. Trial completed. Development discontinued due to inadequate potency. Too early in development to assess clinical impact.
Brain							

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
MRC	Brada	CRUK/01/010: BR 12 Randomised trial of temozolomide vs PCV chemotherapy for recurrent high grade glioma	447/500	2009	Brada M et al., Temozolomide versus Procarbazine, Lomustine and Vincristine (PCV) in Recurrent High Grade Glioma. J Clin Oncol. 2010: 28(30);4601-8. ESMO presidential symposium, Stockholm September 2008 (oral presentation of primary results by S Ming Lee); EANO Barcelona, September 2008 (oral presentation of primary results by Michael Brada (September 2008); ASCO 2010 (poster presentation of translational study results by M Brada)	Yes	Trial now closed Results showed no clear evidence of survival benefit to Temozolomide over PCV. However,TMZ patients were sub-randomised to the 5 day (standard) or 21 day schedule, and the latter unexpectedly proved inferior with respect to progression free and possibly overall survival. These results question the basis of increasing TMZ 'dose intensity' by prolonged scheduling. Results presented at ASCO in 2010 showed IDH1 mutation and MGMT methylation to be strong, independent prognostic factors. Initial analysis suggests a prognostic but not predictive role for methylation status in this setting. Likely to stop the move towards longer schedules at least in the recurrent setting and possibly in the adjuvant setting, pending results of an ongoing intergroup primary treatment study.
MRC	Erridge	CRUK/07/028: BR14/CATNON (TATA): A randomised controlled trial of temozolomide as adjuvant and/or concurrent treatment in anaplastic (WHO grade III) glioma	57/Overall target 748	2017		Yes	Originally it was anticipated that the 748 randomised patients required could be obtained from ~830 registered patients. However the ineligibility rate has been higher than anticipated, and the total number of registrations has now been increased to 1360; the number of randomised patients required remains unchanged. Note this is an EORTC-led trial, CTAAC funding supports UK intergroup collaboration coordinated through the MRC CTU. Aim to optimize the treatment strategy in newly diagnosed anaplastic glioma patients without combined 1p/19q loss. The primary objective is to assess whether radiotherapy with concurrent and/or adjuvant temozolomide chemotherapy improves overall survival as compared to no concurrent/adjuvant temozolomide in non 1p/19q deleted anaplastic glioma. The outcome of this trial will guide the treatment of future patients with grade III glioma and, indirectly, inform the optimum use of adjuvant and/or concurrent temozolomide in patients with GBM in whom the separate contribution of adjuvant and concurrent treatment has not been evaluated.
University College London	Mulholland	CRUKE/10/044: Multi-centre, randomised, double-blind phase II study comparing cediranib (Recentin, AZD2171) plus gefitinib (Iressa, ZD1839) with cediranib plus placebo in subjects with recurrent/progressive glioblastoma	38/112	2014	Poster at SNO 2014	No	
University College London	Watts	CRUK/10/009: GALA-5 TRIAL: An Evaluation of the Tolerability and Feasibility of combining 5-Amino-Levulinic Acid (5-ALA) with Carmustine Wafers (Gliadel) in the Surgical Management of Primary Glioblastoma.	59/60	2014	British Neuro-oncology society education day, Liverpool, 9 July 2014	Yes	
University College London	Short	CRUK/11/057: HCQ: A randomised phase 2 trial investigating the additional benefit of hydroxychloroquine to short course	17/55	2016			

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
		radiotherapy in patients aged 70 years and older with high grade gliomas					
University College London	Whitfield	CRUK/13/017: HIPPO: A randomized phase II trial of Hippocampal Sparing versus Conventional Whole Brain Radiotherapy after surgical resection or radiosurgery in favourable prognosis patients with 1-4 brain metastases	0/84	2016/2017	British Neuro-oncology society education day, Liverpool, 9 July 2014, Royal college of Radiologists: Quality Improvement and Audit - Clinical Oncology Audit Forum, Royal College of Radiologists "Neuro-oncology meeting", 10 March 2015, Leeds	Yes	
University College London	Watts	InGala: An investigation into the efficacy of combining Giladel Wafers (Carmustine) with Gliolan (5-aminolevulinic acid 5-ALA) in the surgical management of primary Glioblastoma)					N/A - study abandoned prior to grant approval N/A - study abandoned prior to grant approval N/A - study abandoned prior to grant approval
Centre for Drug Development							
Beatson West of Scotland Cancer Centre	Chalmers	CRUKD/11/006: OPARATIC - A Cancer Research UK Phase I trial of olaparib (AZD2281), an oral PARP Inhibitor, in combination with extended low-dose oral temozolomide in patients with relapsed glioblastoma	10/30	2016			First time in patients for this combination. Trial planned. Aims to assess whether the drug crosses the blood brain barrier, safety, tolerability, efficacy, pharmacokinetics, pharmacodynamics and identify the MTD of the combination and dose for further evaluation. Too early in development to assess clinical impact. This trial may have significant impact both within the UK and internationally both in the treatment of Glioblastoma but also more widely in terms of the ability of drugs of this nature to cross the blood brain barrier This trial may have significant impact both within the UK and internationally both in the treatment of Glioblastoma but also more widely in terms of the ability of drugs of this nature to cross the blood brain barrier
University of Glasgow	Rampling	CRUKD/10/045: A Cancer Research UK Phase I trial of IMA950 (a novel multi-peptide vaccine) plus GM-CSF in patients with newly diagnosed glioblastoma	45/45	2013	EANO Sep-12 (oral presentation); ESMO Oct-12 (poster); AACR Apr-13 (oral presentation); MASIR May-13 (oral presentation); CIMT May-13 (poster and oral presentation		First time for this peptide vaccine in brain cancer. Investigating the safety and immunogenicity of the combination. Too early in development to assess clinical impact. Provided that IMA950 is successfully developed and brought to market it will be incorporated into first line standard of care for glioblastoma patients. The expected benefit to glioblastoma patients is an increase in their progression free and overall survival Provided that IMA950 is successfully developed and brought to market it will be incorporated into first line standard of care for glioblastoma patients. The expected benefit to glioblastoma patients is an increase in their progression free and overall survival

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Birmingham	Cruickshank	CRUKD/07/062: A Cancer Research UK pharmacokinetic trial of BPA (boron phenyl alanine) in patients with glioma to assess uptake parameters prior to a clinical trial of boron neutron capture therapy	10/15	2013	Schmidt E, et al. J Pharm Sci. 2012 Jan;101(1):223-32. Dick L, et al. J Pharm Biomed Anal. 2011; 56(3):633-6. Schmidt E, Dooley N et al. JPharmacy & Pharmacology. 2010. 62 (10): 1428-1429. D.G. Ngoga, G. Cruickshank, et al. Neuro-Oncology. 2010. 12:62-62 Cruickshank GS, et al. A Cancer Research UK pharmacokinetic study of BPA-mannitol in patients with high grade glioma to optimise uptake parameters for clinical trials of BNCT. Appl Radiat Isot. 2009 Jul;67(7-8 Suppl):S31-3.		If the trial is successful BPA could be used with BNCT to potentiate radiotherapy in brain cancer. Trial ongoing. Looking at diffferent methods of administration, dose levels and how the drug is metabolised. Too early in development to assess clinical impact.
Charing Cross Hospital	Newlands	CRUKD/92/008: Multicentre CRC phase II trial of temozolomide (Temodal) in recurrent or progressive high-grade glioma.	116/116	1996	Bower M, Newlands ES, Bleehen NM, Brada M, Begent RJ, Calvert H, Colquhoun I, Lewis P, Brampton MH. Multicentre CRC phase II trial of temozolomide in recurrent or progressive high-grade glioma. Cancer Chemother Pharmacol. 1997;40(6):484-8.		Follow up Phase II study in glioma following activity seen in glioma patients in Phase I trial CRUKD/87/003. Drug was developed by Malcolm Stevens' CR-UK funded research group at Aston Unversity. Trial completed. Drug registered for clinical use in brain cancer as Temodal. First trial in glioma patients of a drug developed from CR-UK funded research. Drug now licensed worldwide to treat brain cancer.
MRC	Rees	CRUK/07/032: BR13: Primary chemotherapy with temozolomide vs radiotherapy in patients with low-grade gliomas after stratification for genetic 1p loss: a phase III study (EORTC 22033-26033)	15/Overall target 466	2013	EORTC abstract accepted for oral presentation at ASCO 2013.	Yes	Note this is an EORTC-led trial, CTAAC funding supports UK intergroup collaboration coordinated through the MRC CTU. Registration and randomisation is now closed. Aim to evaluate temozolomide as an alternative to radiotherapy for the treatment of low grade glioma. The outcome of this trial will determine whether radiotherapy can be replaced by temozolomide.
Breast							
University of Birmingham	Spooner	BR3002: Adjuvant radiotherapy and tamoxifen in conservative management of early breast cancer	707/700	1995	D. SPOONER, D.D. STOCKEN Y, S. JORDAN, S. BATHERS, J.A. DUNN Z, C. JEVONS, L. DODSON, J.M. MORRISON, G.D. OATES, R.J. GRIEVE on behalf of the West Midlands Oncology Breast Cancer Group (2012) A Randomised Controlled Trial to Evaluate both the Role and the Optimal Fractionation of Radiotherapy in the Conservative Management of Early Breast Cancer Clinical Oncology 24 p.697:706 SPOONER et al., 2009 A Randomised Controlled Trial to Evaluate both the Role and Optimal Fractionation of Radiotherapy in the Conservative Management of Early Breast Cancer. Cancer Res 69: Abstract 5125		With a median follow-up of 17 years, this study confirms the benefit for patients with early breast cancer of radiotherapy. The 40 Gy in 15 fractions radiotherapy schedule continues to be a safe , efficient and effective regime at least as good as the international conventional regime of 50 Gy in 25 fractions.
University of Birmingham	Poole/Earl	NEAT: A Phase III randomised trial of CMF v sequential epirubicin followed by CMF in women receiving adjuvant chemotherapy for early breast cancer	2028/2000	2006	POOLE CJ, EARL HM, HILLER L, DUNN JA, BATHERS S, GRIEVE R, SPOONER D, AGRAWAL RK, FERNANDO IN, BRUNT AM, O'REILLY SM, CRAWFORD SM, REA DW, SIMMONDS P, MANSI JL, STANLEY A, HARVEY P, MCADAM K,		Relapse-free and overall survival rates were significantly higher in the epirubicin–CMF group than in the CMF-alone group. The overall incidence of adverse effects was significantly higher with epirubicin plus CMF than with CMF alone but did not significantly affect the delivered-dose

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
					FOSTER L, LEONARD RCF, TWELVES CJ, FOR THE NEAT INVESTIGATORS AND THE SCTBG (2006) Epirubicin and Cyclophosphamide, Methotrexate, and Fluorouracil as Adjuvant Therapy for Early Breast Cancer. New England Journal of Medicine; 355:p.1851-62 EARL HM , HILLER L, DUNN JA, BATHERS S, HARVEY P, STANLEY A, GRIEVE RJ, AGRAWAL RK, FERNANDO IN, BRUNT AM, MCADAM K, O'REILLY S, REA DW, SPOONER D AND POOLE CJ ON BEHALF OF THE NEAT INVESTIGATORS (2008) NEAT: National Epirubicin Adjuvant Trial – toxicity, delivered dose intensity and quality of life. Br J Cancer 99: p.1226- 1231 CAMPBELL HE, EPSTEIN D, BLOOMFIELD D, GRIFFIN S, MANCA A, YARNOLD J, BLISS J, JOHNSON L, EARL H, POOLE C, HILLER L, DUNN J, HOPWOOD P, BARRETT-LEE P, ELLIS P, CAMERON D, HARRIS AL, GRAY AM, SCULPHER M (2011) The cost-effectiveness of adjuvant chemotherapy for early breast cancer: a comparison of no chemotherapy and first, second, and third generation regimens for patients with differing prognoses. Eur J Cancer ;47(17):p.2517-30. EARL HM, HILLER L, DUNN JA, VALLIER A, BOWDEN SJ, JORDAN SD, BLOWS F, MUNRO A, BATHERS S, GRIEVE R, SPOONER DA, AGRAWAL R, FERNANDO I, BRUNT AM, O'REILLY SM, CRAWFORD SM, REA DW, SIMMONDS P, MANSI JL, STANLEY A, MCADAM K, FOSTER L, LEONARD RCF, TWELVES CJ, CAMERON D, BARTLETT JMS, PHAROAH P, PROVENZANO E, CALDAS C, AND POOLE CJP FOR THE NEAT INVESTIGATORS AND THE SCTBG (2012) Adjuvant Epirubicin followed by Cyclophosphamide, Methotrexate and Fluorouracil (CMF) versus CMF in early breast cancer: Results with over seven years median follow-up from the randomised phase III NEAT/BR9601 trials. British Journal of Cancer 9;107(8):p.1257-67 BARTLETT JM, MUNRO AF, DUNN JA, MCCONKEY C, JORDAN S, TWELVES CJ, CAMERON DA, THOMAS J, CAMPBELL FM, REA DW, PROVENZANO E, CALDAS C, PHAROAH P, HILLER L, EARL H, AND POOLE CJ (2010). Predictive markers of anthracycline benefit: a prospectively planned analysis of the		intensity or the quality of life. The results of the NEAT trial were initially presented in 2003, as a result anthracycline containing chemotherapy became standard in the UK and E-CMF became the control arm for the next national adjuvant breast cancer trial.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
					UK National Epirubicin Adjuvant Trial (NEAT/BR9601). Lancet Oncol 11(3):p.266-74. DI LEO A, DESMEDT C, BARTLETT JMS, PIETTE F, EJLERTSEN B, PRITCHARD KI, LARSIMONT D, POOLE C, ISOLA J, EARL H, MOURIDSEN H, O'MALLEY FP, CARDOSO F, TANNER M, MUNRO A, TWELVES CJ, SOTIRIOU C, SHEPHERD L, CAMERON D, PICCART MJ, BUYSE M FOR THE HER2/TOP2A META-ANALYSIS STUDY GROUP (2011) HER2 and TOP2A as predictive markers for anthracycline containing chemotherapy regimens as adjuvant treatment of breast cancer: a meta-analysis of individual patient data. Lancet Oncol 12: p.1134–42		
University of Birmingham	Poole	tAnGo: A phase III randomised trial of gemcitabine in paclitaxel-containing epirubicin-based adjuvant chemotherapy for ER/PgR-poor early stage breast cancer	3152/3000	2008	WARDLEY A, et al. (2008) British Journal of Cancer 99: 597-603	Yes	The tAnGo interim analysis confirmed that the addition of Gemcitabine showed no therapeutic advantage for women with higher risk early stage breast cancer. The tango safety sub study clearly demonstrated that the addition of Gemcitabine to paclitaxel after epirubicin and cyclophosphamide for treatment of early breast cancer is safe. This large randomised trial assessed the addition of gemcitabine (G) to paclitaxel (T), following epirubicin (E) and cyclophosphamide (C) in women with invasive higher risk early breast cancer. The tolerability of the tAnGo regimens were critical endpoints and both regimens were found to be tolerable and deliverable despite expected differences in acute toxicities. The addition of Gemcitabine to adjuvant chemotherapy with EC-T at this dose and schedule confers no therapeutic advantage for women with higher risk early stage breast cancer.
University of Birmingham	Rea	aTTom: Adjuvant Tamoxifen Treatment - offer more? Follow-up, Data Cleaning and Analysis.	8862/8000	2008	FERGUSON MJ et al. 2002 Eur J Cancer 38(14): 1857-1859. GRAY RG, et al. 2008, J Clin Oncol 26: (May 20 suppl) Abstract 513. GRAY et al. (2013) GRAY RG, REA R, HANDLEY K, BOWDEN SJ, PERRY P, EARL HM, POOLE CJ, BATES T, CHETIYAWARDANA S, DEWAR JA, FERNANDO IN, GRIEVE R, NICOLL J, RAYTER Z, ROBINSON A, SALMAN A, YARNOLD J, BATHERS S, MARSHALL A, LEE M, AND ON BEHALF OF THE ATTOM COLLABORATIVE GROUP (2013) aTTom: Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years in 6,953 women with early breast cancer. Journal of Clinical Oncology 31(15) Suppl: Abstract 5 ASCO 2013, British Breast Group 2013, NCRI National Breast Cancer Meeting		Longer tamoxifen is associated with a statistically significant reduced risk of breast cancer recurrence and a numerical reduction in breast cancer deaths. Endometrial cancer risk is increased but associated with a very small increase in endometrial cancer deaths. Results are consistent with updated data from the ATLAS trial. Combined data confirm a reduction in breast recurrence and breast cancer deaths with longer tamoxifen. Tamoxifen beyond 5 years is now a firmly evidence based treatment option for women with ER positive breast cancer completing 5 years of tamoxifen. This is likely to be particularly important in pre-menopausal women and in women where aromatase inhibitors are contraindicated or poorly tolerated. The results of aTTom and ATLAS indirectly support the continuation of hormone therapy irrespective of the agents used in the first 5-years after diagnosis. The results of aTTom are already being implemented in routine clinic practice with many clinicians recommending extended adjuvant endocrine therapy beyond 5-years. These results will undoubtedly impact on national and international guidelines. Results are consistent with updated

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
							data from the ATLAS trial. Combined data confirm a reduction in breast recurrence and breast cancer deaths with longer tamoxifen. Tamoxifen beyond 5 years is now a firmly evidence based treatment option for women with ER positive breast cancer completing 5 years of tamoxifen. This is likely to be particularly important in pre-menopausal women and in women where aromatase inhibitors are contraindicated or poorly tolerated. The results of aTTom and ATLAS indirectly support the continuation of hormone therapy irrespective of the agents used in the first 5-years after diagnosis. The results of aTTom are already being implemented in routine clinic practice with many clinicians recommending extended adjuvant endocrine therapy beyond 5-years. These results will undoubtedly impact on national and international guidelines.
University of Birmingham	Rea	TEAM: Tamoxifen and Exemestane Adjuvant Multicentre trial	1138/1240	2009	van de Velde, C. J. et al. (2011) Adjuvant tamoxifen and exemestane in early breast cancer (TEAM): a randomised phase 3 trial. Lancet, 377 (9762). p.321-331; BARTLETT, J. M. et al. (2011) Estrogen receptor and progesterone receptor as predictive biomarkers of response to endocrine therapy: a prospectively powered pathology study in the Tamoxifen and Exemestane Adjuvant Multinational trial. J Clin Oncol. 29 (12). p.1531-1538. BARTLETT, J. M. et al. (2011) Quantification of hormone receptors to guide adjuvant therapy choice in early breast cancer: better methods required for improved utility. J Clin Oncol. 29 (27). p.3715-3716. BARTLETT, J. M. (2012) Mammostrat as an immunohistochemical multigene assay for prediction of early relapse risk in the tamoxifen versus exemestane adjuvant multicenter trial pathology study. J Clin Oncol. 30 (36). p.4477-4484. FONTEIN, D. B. (2013) Specific Adverse Events Predict Survival Benefit in Patients Treated With Tamoxifen or Aromatase Inhibitors: An International Tamoxifen Exemestane Adjuvant Multinational Trial Analysis. J Clin Oncol. 31 (18). p.2257-2264. SABINE, V. S. (2012) PIK3CA mutations are linked to PgR expression: a Tamoxifen Exemestane Adjuvant Multinational (TEAM) pathology study. San Antonio Breast Cancer Symposium. Cancer Research. 72 (24 supp). p.S1-5.	Yes	Establishes the validity of both aromatase inhibition at diagnosis or introduced after 2-3 years as a planned sequence as equally effective treatments for the whole population and establishes the prognostic importance of quantitative steroid hormone receptor measurement. The trial also has demonstrated HER1-3 over expression is a marker of relative hormone resistance with no differential sensitivity to endocrine agents in preventing early relapse. In contract to HER1-3 negative tumours where early relapse is reduced by the use of exemestane particularly in the context of other high risk indicators. This trial has legitimised an upfront sequential approach as evidence based effective treatment option and has been implemented in many breast units as routine standard practice. This trial has legitimised an upfront sequential approach as evidence based effective treatment option and has been implemented in many breast units as routine standard practice.
University of Birmingham	Fernando	SECRAB: A phase III study of sequential V synchronous chemotherapy and radiotherapy in	2298/2500	2010	FERNANDO IN (2000) Clin Oncol, 12(3): 158-165. BOWDEN SJ et al. 2006 Clin Oncol (R Coll Radiol), 18(3); 247-256. The SECRAB	Yes	The SECRAB trial demonstrated a significant benefit for synchronous treatment with an 35% reduction in the relative risk of local in-field recurrence with an absolute reduction in

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
		the adjuvant treatment of early breast cancer			Cosmesis study was presented at ESMO: FERNANDO IN et al (2012) SECRAB (Sequencing of Chemotherapy and Radiotherapy in Adjuvant Breast cancer) Trial Cosmesis Results. Annals of Oncology 23 (Suppl 9) Abstract 253PD		5-year local recurrence rates of 2.3% (sequential 5.1% vs. synchronous. 2.8%). Reducing local recurrence is important as reduction in local recurrence is known to impact on breast cancer survival. The improvement in local recurrence rates reported in SECRAB is modest but similar to the practice changing 3% improvement reported for the addition of a tumour site boost. The SECRAB trial results have practice changing implications for the delivery of multimodality adjuvant treatments for early breast cancer.
University of Birmingham	Francis	NEO-EXCEL - Neoadjuvant trial of pre-operative exemestane or letrozole +/- celecoxib in the treatment of ER positive (+ve) postmenopausal early breast cancer	240/256	2019			Positive results will have clear and immediate implications for clinical management of large ER rich cancers and will have major implications for future direction of research into clinical applications of Cox 2 inhibition in cancer therapy biology.
University of Birmingham	Rea	ROSCO: Response to Optimal Selection of neo-adjuvant Chemotherapy in Operable breast cancer	unknown/1050	2019		Yes	If positive this trial will have a significant bearing on chemotherapy selection for all patients undergoing neo-adjuvant chemotherapy. If positive this trial will have a significant bearing on chemotherapy selection for all patients undergoing neo-adjuvant chemotherapy.
University of Cambridge	Earl	Neo-tAnGo: Neoadjuvant study of sequential epirubicin/cyclophosphamide and paclitaxel +/- gemcitabine in the treatment of poor risk early breast cancer with molecular profiling	831/800	2009	WARREN R et al., 2004 Br J Cancer 5;90(7):1349-60. Abraham J et al., 2006 Biochim Biophys Acta 1766(2):168-83. PINDER S et al., 2007 Histopathology 50(4): 409-17. ISMAIL A et al., 2010 Plast Reconstr Surg 126(1):1. GOUNARIS I et al., 2010 European Journal of Cancer Suppl 8(6):12. Gounaris I et al., 2011 Breast Cancer Res Treat 127(2):459-69	Yes	The Neo-tAnGo results confirmed those of the adjuvant tAnGo trial in terms of gemcitabine effect. However the sequence of T+G-first has demonstrated a significant advantage in pCR compared with the more conventional anthracycline-first sequencing. Neo-tAnGo has had practice changing impact with regard to chemotherapy sequencing of anthracyclines and taxanes as neoadjuvant treatment for breast cancer. Such that scheduling of docetaxel is ahead of anthracyclines in the control arm of the successor trial ARTEMIS.
Greater Glasgow and Clyde Health Board	Canney	CRUK/07/002: HER-PCI: Prospective randomised clinical trial testing the role of prophylactic cranial irradiation in patients treated with Trastuzmamb (Herceptin) for metastatic breast cancer.	51/390	2011	Final manuscript about to be submitted to Lancet Canney PA et al., Neurocognitive Function and Quality of Life of Patients Treated within a Prospective Randomised Clinical Trial Testing the Role of Prophylactic Cranial Radiotherapy (PCI) in Patients Treated with Trastuzumab for Metastatic Breast Cancer. The Anglo Celtic VII Trial. Cancer Research 2010; 70:24s (abstr P4-11-22).	Yes	As the study was closed early because of poor recruitment but nevertheless it has provided valuable evidence that PCI can be safely delivered in this group of patients and an indication that it may have an effect in reducing the effect of brain metastases. There was an associated translational study funded, but the trial was closed before this could be implemented. As the study did not reach its recruitment target it can't be the basis for a change in clinical practice As the study did not reach its recruitment target it can't be the basis for a change in clinical practice
Beatson West of Scotland Cancer Centre	Canney	CRUKE/10/033:SOLD: The Synergism Or Long Duration (SOLD) Study	282/300	Unknown		Yes	Twelve months of adjuvant trastuzumab is considered as the standard treatment for HER2-positive early breast cancer, although the optimal duration of trastuzumab administration is not known. The FINHER trial results have suggested that the combination of docetaxel plus 9-week concomitant trastuzumab is effective and well tolerated in the treatment of HER2-positive breast cancer, with hazard ratios similar to the trials using 1 year of adjuvant Trastuzumab. The primary objective of this trial is to compare disease-free survival of women treated with the FINHER regimen to that of women treated with the same regimen followed by single-agent

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
							trastuzumab for 1 year.
Leeds Teaching Hospitals NHS Trust	Stein	CRUKE/04/019: GBG26 TBP. A multicentre randomised phase III study to compare capecitabine alone or in combination with trastuzumab in patients with HER2 positive metastatic breast cancer and progression after previous treatment with trastuzumab (Treatment Beyond Progression, TBP)	3/100	2008	von Minckwitz G, du Bois A, Schmidt M, et al. (2009) Trastuzumab beyond progression in human epidermal growth factor receptor 2–positive advanced breast cancer: A German Breast Group 26/Breast International Group 03-05 study. J Clin Oncol 27:1999–2006 OS analysis: von Minckwitz G et al. (2011) Trastuzumab beyond progression: overall survival analysis of the GBG 26/BIG 3-05 phase III study in HER2-positive breast cancer. Eur J Cancer. 2011 Oct;47(15):2273-81	Yes	Recruitment closed early due to poor accrual. PA performed and published. This is the first evidence from a RCT that continuation of trastuzumab treatment for metastatic breast cancer beyond progression is beneficial. It is likely to influence the NICE guidance for the management of advanced breast cancer (out for consultation) although the precise effect will depend on the outcome of the NICE STA for lapatinib in combination with capecitabine for a similar patient population
University of Sheffield	Coleman	CRUKE/03/017: AZURE. Does Adjuvant Zoledronic acid redUce REcurrence in patients with high-risk, localised breast cancer?	2710/3300	2013	Coleman RE et al., In reply to "Breast-Cancer Adjuvant Therapy with Zoledronic Acid" by Hans J van der Vliet and Henk MW Verheul. New England Journal of Medicine 2012; 366(2):188-189. Oral presentation at 35th Annual San Antonio Breast Cancer Symposium, December 2012. Oral presentation planned at ECCO/ESMO, Amsterdam September 2013	Yes	Closed to accrual, in Follow-up phase. Second interim analysis in October 2010 did not have a positive result aside from on a sub-set of patients who are post - menopausal. Full primary analysis was carried out in April 2013. Results of the analysis will be presented at ECCO/ESMO in September 2013 with publication expected within the next year. As the largest trial addressing this question, the result could potentially affect clinical practice in the UK. Not known until the primary analysis is carried out and the results are known.
University of Sheffield	Coleman	CRUKE/09/036: AZURE - Bone Health Sub-protocol: Bone health in breast cancer survivors following adjuvant bisphosphonate treatment	229/244	2013		No	Planned analysis of data up to 2 year primary endpoint expected to take place in late autumn 2013. Long term effects of zoledronic acid on bone health through measurement of BMD and bone biomarkers in a sub-set of patients taking part in the AZURE study Additionally the duration of effects on bone will be assessed and linked to the efficacy and fracture data within the main study. n/k

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Sheffield	Coleman	CRUK/05/18: BISMARK Trial (Effective use of BISphosphonates in metastatic bone disease - a comparison of bone MARKer directed zoledronic acid therapy to a standard schedule).	289/1500	2011	Randomized trial of marker-directed versus standard schedule of zoledronic acid for bone metastases from breast cancer. RE Coleman, J Wright, S Houston, R Agrawal, OP-K Purhoit, L Hayward, P Simmonds, A Waterhouse, H Marshall, on behalf of the BISMARK investigators. Saturday 2 June 2012, 1:15-5:15pm, Breast Cancer – HER2/ER poster discussion session, abstract number 511(99595), Room E450a; Board1 The study investigators will be informed of the results and are responsible for disseminating them to patients. Results of the primary and secondary endpoint analyses will aim to be published in a peer-reviewed journal and presented at other appropriate meetings. Primary publication at the 2012 ASCO annual meeting Poster discussion RE Coleman, J Wright, S Houston, R Agrawal, OP-K Purhoit, L Hayward, P Simmonds, A Waterhouse, H Marshall, on behalf of the BISMARK investigators. Saturday 2 June 2012, 1:15-5:15pm, Breast Cancer – HER2/ER poster discussion session, abstract number 511(99595), Room E450a; Board1	No	Trial closed early due to poor accrual. End of trial report submitted July 2012 The study was underpowered to demonstrate non-inferiority in SRE outcome between the treatment strategies. However, the results do suggest that the adjustment of zoledronic acid schedule based on NTX values alone may represent suboptimal management. 3-4 weekly zoledronic acid appears to be needed following an SRE as well as when bone resorption markers are elevated. Expected impact on clinical practice is now minimal due to the lower than proposed recruitment leading to under-powered analyses n/a
Hoffman La Roche Ltd	Cameron (Global PI), Ellis (UK PI)	CRUKE/07/046: BEATRICE: An international multi-centre open-label 2-arm phase III trial of adjuvant bevacizumab in triple negative breast cancer.	175/unknown target	2012	Primary publication submitted to Lancet Oncology by Roche In June 2013 Cameron D, Brown J, Dent R, et al. Primary results of BEATRICE, a randomized phase III trial evaluating adjuvant bevacizumab-containing therapy in triple-negative breast cancer. Presented at: 2012 CTRC-AACR San Antonio Breast Cancer Symposium; December 4-8, 2012; San Antonio, Texas. Abstract S6-5.	Yes	Based on the IDFS results at the prespecified primary analysis, bevacizumab is not recommended as adjuvant treatment in unselected patients with triple-negative breast cancer. The suggestion of a benefit from bevacizumab in subsets of patients with high baseline plasma VEGFR-2 requires prospective validation. Further follow-up is required to assess the potential impact of bevacizumab on OS.Pre-Planned Overall Survival Analysis in 2014 This trial was the first randomised phase III trial looking specifically at early triple-negatice disease. The lack of positive effect in this trial highlights the need for futher follow-up to assess the impact of Bevacizumab on overall survival (planned 2014) and when results of the protocol specified biomarker analysis are known (analyses ongoing) this may lead to further investigation into subtypes of triple-negative breast cancers. as for the UK Impact
Leeds Teaching Hospitals NHS Trust	Dodwell	CRUKE/10/046: LANTERN: A randomised phase II screening trial with functional imaging and patient reported toxicity sub-studies	8/130	2014		Yes	Primary objective to investigate the effect of lapatinib plus capecitabine compared with trastuzumab plus capcitabine on time to progression of CNS metastases as measured by RECIST. Feasibility trial hoping to gain fruther information regarding the patient population to see whether a large phase III trial is feasible. Will contribute significantly to international knowledge base.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Joint Sponsors: The University of Sheffield and The University of Leeds	Wyld/ Reed	CRUK/06/010: ESTEeM Endocrine +/- Surgical Therapy for Elderly women with Mammary Cancer. A randomised, multi-centre, controlled, open label, prospective, parallel group, 2-arm, non-inferiority clinical trial, with equal randomisation, to determine whether Arimidex alone is non-inferior for anticancer efficacy compared to surgery plus adjuvant AI therapy.	9/1200			Yes	Trial closed due to poor recruitment and withdrawal of CRUK funding. The impact data relates to the impact the trial would have had, if sufficient patients had been recruited. n/a n/a
The Institute of Cancer Research	Yarnold (The Institute of Cancer Research and Royal Marsden Hospital NHS Foundation Trust) (Bliss, ICR-CTSU)	CRUK/00/003: UKCCCR Adjuvant Breast Cancer Trial (ABC)	2394/4000	2005	Adjuvant Breast Cancer Trials Collaborative Group. Ovarian ablation or suppression in premenopausal early breast cancer: results from the international adjuvant breast cancer ovarian ablation or suppression randomized trial. J Natl.Cancer Inst 2007;99(7):516-25. Adjuvant Breast Cancer Trials Collaborative Group. Polychemotherapy for early breast cancer: results from the international adjuvant breast cancer chemotherapy randomized trial. J Natl.Cancer Inst 2007;99(7):506-15. PINHEL, I., et al. 2012. ER and HER2 expression are positively correlated in HER2 non-overexpressing breast cancer. Breast Cancer Res, 14, R46. CAMPBELL, H. E., et al.,2011. The cost-effectiveness of adjuvant chemotherapy for early breast cancer: A comparison of no chemotherapy and first, second, and third generation regimens for patients with differing prognoses. Eur J Cancer, 47, 2517-30. PERREN, T. J. 1995. Adjuvant therapy for operable breast cancer; more answers, new questions. Br J Cancer, 71, 1142-4. BARRETT-LEE, P., et al. 2013. Late recurrence in Oestrogen Receptor (ER) positive early breast cancer patients in the ABC Trial following the first 5 years of endocrine treatment: Can we predict those at risk? British Breast Group, Manchester, June 2013	Yes	Compared with no chemotherapy, chemotherapy in combination with 5 years of tamoxifen treatment produced modest improvements in relapsefree and overall survival. Relapse free survival benefits emerged early and were maintained, whereas overall survival benefits did not emerge for at least 5 years, reinforcing the need for longterm followup in chemotherapy trials. Given a background of 5 years tamoxifen, no added effect of ovarian ablation or suppression was seen on relapsefree survival or overall survival of premenopausal women who were treated for earlystage breast cancer. However, the role of ovarian ablation or suppression in young (<40 years) women with ERpositive tumours, especially those not receiving chemotherapy, requires further study. ABC was the first truly national breast cancer trial of systemic therapy which led to a network of centres (some of which were new to RCT participation) who have subsequently contributed to other breast cancer trials including TACT, NEAT, TACT2 and POETIC. The trial facilitated development of the "hub and spoke" model for coordinating RCT's in breast cancer in the UK. This was the first UK breast cancer trial to have a prospective sample collection for use in driving/testing biomarker hypotheses. The trial confirmed longterm effects of combined chemoendocrine therapy in early breast cancer on background of current standard of 5 years endocrine treatment.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Johnston (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Bliss, ICR-CTSU)	CRUKE/06/039: MAPLE - Double blind short term pre-surgical study to assess the molecular antiproliferative predictors of lapatinib's effects in primary breast cancer	121/120	2012	Primary publication paper in preparation EVANS, A. et al. 2012. Lapatinib has antiproliferative effects in both HER2 positive (+) and HER2 negative (-) breast cancer (BC): results from the MAPLE short-term pre-surgical trial (CRUK E/06/039). Proc of AACR Cancer Res, 72, (Suppl 1) #LB222. DOWSETT, M., et al. 2012. Prediction of antiproliferative response to lapatanib by HER3 in an exploratory analysis of HER2-non-amplified (HER2-) breast cancer in the MAPLE pre-surgical study (CRUK E/06/039). Cancer Research, 72, PD07-07. DOWSETT, M., et al. 2012. Prediction of antiproliferative response to lapatanib by HER3 in an exploratory analysis of HER2-non-amplified (HER2-) breast cancer in the MAPLE pre-surgical study (CRUK E/06/039). Cancer Research, 72, PD07-07. (San Antonio Breast Cancer Symposium, 2012.)	No	A short term presurgical study for an agent such as lapatinib where the main endpoint is molecular rather than clinical, is feasible & safe. Whilst lapatinib is currently used exclusively in HER2+ disease, MAPLE has shown it also has antiproliferative effects in a subset of HER2 negative breast cancer. This study has helped to identify subsets of patients not currently treated with lapatinib but who may benefit from such treatment in the future, and to understand the factors which may determine response to lapatinib. MAPLE has identified a small group of HER2-negative tumours that can respond to lapatinib, and created a hypothesis that this may be related to HER2-HER3 heterodimers, which requires validation in other studies.
The Institute of Cancer Research	Leonard (Imperial College London) (Bliss, ICR-CTSU)	CRUK/06/002: ACTION: Adjuvant chemotherapy in older women versus no treatment	4 (trial closed early)/1000	2011	LEONARD, R., et al. 2011. Adjuvant chemotherapy in older women (ACTION) study - what did we learn from the pilot phase? Br J Cancer, 105, 1260-1266. LEONARD, R., et al. 2011. Adjuvant chemotherapy in older women (ACTION) study - what did we learn from the pilot phase? Br J Cancer, 105, 1260-1266. REED, M. W., et al. 2009. Breast cancer in older women: trials and tribulations. Clinical Oncology (Royal College of Radiologists), 21, 99-102. JOHNSON, L., et al. 2007. Adjuvant cytotoxic chemotherapy in older women (ACTION). Oncology Hematology, 64, S41 #P18.	No	There is a paucity of data on the efficacy of chemotherapy in the 70+ age group. This study aimed to determine whether high risk patients in this age group benefit from AC/EC chemotherapy in addition to other routine treatment. However, despite widespread support at several public meetings, input from patient groups including representation on the Trial Management Group, the trial failed to recruit. The trial provides evidence to assist researchers and funders alike when developing future studies of this kind in this patient group. ACTION's paper (Br J Cancer, 2011) recently evaluated and ranked as a recommended read by the Faculty 1000 post publication peer reviews.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Royal Marsden NHS Foundation Trust	Smith (Royal Marsden Hospital NHS Foundation Trust) (Bliss, ICR-CTSU and Peto, London School of Hygiene and Tropical Medicine)	CRUK/93/006: TOPIC - Trial of Primary Innovative Chemotherapy in patients with large breast tumours and TOPIC2 - Randomised Phase III trial of navelbine/epirubicin vs adriamycin/cyclophosphamide as pre-operative chemotherapy in patients with greater than or equal to 3cm diameter early breast cancer	TOPIC = 426 TOPIC2 = 451/TOPIC = 400 TOPIC2 =400	2000, 2012	SMITH, I. E., et al. 2004. A novel continuous infusional 5-fluorouracil-based chemotherapy regimen compared with conventional chemotherapy in the neo-adjuvant treatment of early breast cancer: 5 year results of the TOPIC trial. Ann Oncol, 15, 751-758. SMITH, I. E., et al. 2000. Preoperative continuous infusional ECISF (Epirubicin, Cisplatin and Infusional 5FU) vs conventional AC chemotherapy for early breast cancer: A phase III multicentre randomised trial by the Topic Trial Group. Proc Am Soc Clin Oncol, 19, #320. SMITH, I. E. 1994. Intensive primary infusional chemotherapy for large early breast cancer. Br J Cancer Supplements, 22, 5 #S9. CHUA, S., et al. 2005. Neoadjuvant vinorelbine/epirubicin (VE) versus standard adriamycin/cyclophosphamide (AC) in operable breast cancer: analysis of response and tolerability in a randomised phase III trial (TOPIC 2). Ann Oncol, 16, 1435-1441. SMITH, I. E., et al. 2003. A randomised neoadjuvant chemotherapy trial of vinorelbine/epirubicin (VE) vs standard adriamycin/cyclophosphamide (AC) in patients with greater than 3cm diameter operable breast cancer (TOPIC 2). Proc Am Soc Clin Oncol, 22, #83.	No	TOPIC: Preoperative continuous infusional 5FUbased chemotherapy is no more active than conventional AC for early breast cancer; with a median 5 year followup, the infusionbased schedule showed a nonsignificant trend towards improved survival. TOPIC2 : Neoadjuvant Vinorelbine and Epirubicin is as effective as AC in terms of clinical response in early breast cancer and was better tolerated except for thrombophlebitis and neuropathy.
The Institute of Cancer Research	Smith (Royal Marsden Hospital NHS Foundation Trust) (Bliss, ICR-CTSU and Peto, London School of Hygiene and Tropical Medicine)	CRUK/95/007: TRAFIC - Trial of adjuvant 5FU infusional chemotherapy	348/400	2009	SIROHI, B., et al. 2010. A randomised comparative trial of infusional ECisF versus conventional FEC as adjuvant chemotherapy in early breast cancer: the TRAFIC trial. Ann Oncol, 21, 1623-1629.	No	TRAFIC found no evidence of a clinically worthwhile benefit for infusional 5FU with Epirubicin and Cisplatin (ECF) treatment compared with standard FEC treatment in patients with early breast cancer. This trial better informed the design of subsequent studies.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Royal Marsden NHS Foundation Trust	Smith (Royal Marsden Hospital NHS Foundation Trust) (Bliss, ICR-CTSU)	CRUKE/01/012: HERA - A randomised three-arm multi-centre comparison of 1 year and 2 years of Herceptin versus no Herceptin in women with HER2-positive primary breast cancer who have completed adjuvant chemotherapy.	519/unknown target	2005	PICCART-GEBHART, M.J., et al. 2005. Trastuzumab after Adjuvant Chemotherapy in HER2-Positive Breast Cancer. N Engl J Med.353(16):1659-72. SMITH, I., et al. 2007. 2-year follow-up of trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer: a randomised controlled trial. Lancet, 369, 29-36. GIANNI, L., et al. 2011. Treatment with trastuzumab for 1 year after adjuvant chemotherapy in patients with HER2-positive early breast cancer: a 4-year follow-up of a randomised controlled trial. Lanc Oncol.12(3):236-44. SUTER, T.M., et al. 2007. Trastuzumab-associated cardiac adverse effects in the herceptin adjuvant trial. J Clin Oncol,25(25):3859-65. PROCTER, M., et al. 2010. Longer-term assessment of trastuzumab-related cardiac adverse events in the Herceptin Adjuvant (HERA) trial. J Clin Oncol,28(21):3422-8. UNTCH, M., et al. 2008. Estimating the magnitude of trastuzumab effects within patient subgroups in the HERA trial. Ann Oncol,19(6):1090-6	Yes	The updated analysis showed 1 year of treatment with trastuzumab after adjuvant chemotherapy had a continuing benefit compared with observation after a median followup of 4 years in patients with HER2 positive early breast cancer. The substantial selective crossover of patients in the observation group to trastuzumab was also associated with improved outcomes for this cohort. Groundbreaking results, confirmed benefits of trastuzumab. Led to early NICE approval (Early breast cancer guidelines trastuzumab, 2006) and early international regulatory approval (FDA, EMEA and MHRA, 2006) for use of trastuzumab in early breast cancer Other trials (e.g. Persephone and ALTTO) now use 1 year of Trastuzumab as the standard comparator. One year of trastuzumab is now standard in HER2 positive patients. This was the first BIG registration trial where ICRCTSU acted as a hub to facilitate UK recruitment. This model has now extended to ALTTO and APHINITY.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Cameron (University of Edinburgh and NHS Lothian) (Bliss, ICR-CTSU)	CRUK/05/019: TACT2: Trial of accelerated adjuvant chemotherapy with capecitabine in early breast cancer.	4391/4400	2012, 2013	CAMERON, D., et al. 2012. The UK TACT2 Trial: comparison of standard vs accelerated epirubicin in patients requiring chemotherapy for early breast cancer (EBC) (CRUK/05/019). Cancer Research: Volume 72, Issue 24, Supplement 3. CANNEY, P., et al., 2012. TACT2 trial in early breast cancer (EBC): Differential rates of amenorrhea in postmenopausal women following adjuvant epirubicin (aE) followed by capecitabine (X) or CMF (CRUK/05/019). Eur. J. Cancer; 48(Suppl 1):S102 #200. CAMERON, D., et al., 2010. TACT2 Randomised Adjuvant Trial in Early Breast Cancer (EBC): Tolerability and Toxicity of Standard 3 Weekly Epirubicin (E) Versus Accelerated Epirubicin (aE) in 129 UK Hospitals (4391 Patients) (CRUK/05/019). Cancer Res.;70(24 Suppl):#P5-10-06. BLISS, J., et al., 2010. TACT2 Randomised Adjuvant Trial in Early Breast Cancer (EBC): Tolerability and Toxicity of Standard 3 Weekly Epirubicin (E) Versus Accelerated Epirubicin (aE) Followed by Capecitabine (X) or CMF in 129 UK Hospitals (CRUK/05/019). Cancer Res.;70(24 Suppl):#P5-10-07. JOHNSON, L., et al. 2007. Improving adjuvant chemotherapy in breast cancer -- can we get more for less with TACT2? Clin Oncol (R.Coll.Radiol.), 19, 593-595. CAMERON, D., et al. 2012. The UK TACT2 Trial: comparison of standard vs accelerated epirubicin in patients requiring chemotherapy for early breast cancer (EBC) (CRUK/05/019). Cancer Research: Volume 72, Issue 24, Supplement 3.	Yes	No evidence of an improvement in disease outcome was observed for patients receiving accelerated compared with standard epirubicin. Serious CTCAE toxicity was less common with accelerated epirubicin compared with standard epirubicin, however patients report poorer global QL, fatigue & role function which does not appear to be explained by impact on daily activities due to individual side effects. Capecitabine has preferential side effect profile and global QL compared to CMF, including a lower rate of chemotherapy induced amenorrhea in pre-menopausal women, with no evidence that prior accelerated epirubicin compromised treatment delivery. Dose delivery data are consistent with advanced disease observations that for some patients, 2000mg/m2/day may be correct dose. TACT2 is the largest adjuvant trial comparing standard versus accelerated epirubicin and CMF versus capecitabine in early breast cancer. This study has the potential to reduce the burden of chemotherapy both in terms of service delivery with the NHS, and to the patient in terms of overall treatment duration, severity of toxicity and economic impact of receiving chemotherapy treatment. The high quality integrated sample collection enables linkage with clinical data to perform exploratory retrospective/prospective biomarker analyses The results from the comparison of standard and accelerated epirubicin will be considered in conjunction with other trials such as CALGB9741 in which an improved disease outcome was observed in patients receiving dose-dense chemotherapy. Results relating to the non-inferiority comparison of CMF vs. Capecitabine will provide new evidence to add to previous studies of Capecitabine in early breast cancer: and if non-inferiority is proven, this may offer a less toxic alternative therapy for women.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Marsden (King's College Hospital) (Bliss, ICR-CTSU)	CRUK/01/002: HRT: UK Randomised trial of hormone replacement therapy (HRT) in women with a history of early breast cancer	197 (trial closed early)/3000	2012	MARSDEN, J., et al., 2006. Efficacy of HRT in treating oestrogen deficiency symptoms in women taking concomitant tamoxifen: the UK HRT trial experience. Eur. J. Cancer Supplements; 4(2):118. DAWSON, C., et al., 2005. Patient satisfaction with information and support received during the UK randomized trial of hormone replacement therapy in women with a history of early-stage breast cancer: results of a postal survey. J Br Menopause Soc;11 (4):182. PARMAR, J., et al., 2005. Use of alternatives to hormone replacement therapy for the relief of estrogen deficiency symptoms in breast cancer survivors. J Br Menopause Soc; 11(4):184. MARSDEN, J., et al., 2002. The national randomised trial of hormone replacement therapy in women with a history of early stage breast cancer: an update. J Br Menopause Soc; 8 (4):129. HALL, E., et al., 2002. The UK randomized trial of hormone replacement therapy (HRT) in women with a history of early stage breast cancer. Clin. Oncol. (R. Coll. Radiol); 12:S31 #96	No	With the premature closure of the HRT trial, it is unlikely that the safety results of the HRT trial will alter clinical practice. However, the quality of life aspects of this trial may provide useful randomised quantitative evidence on the effect of HRT.
The Institute of Cancer Research	Smith (Royal Marsden Hospital NHS Foundation Trust) (Bliss, ICR-CTSU)	CRUK/07/015: POETIC: Trial of Perioperative Endocrine Therapy - Individualising Care	4397/4400	2015/2016	DOWSETT, M., et al. 2011. Endocrine therapy, new biologicals, and new study designs for presurgical studies in breast cancer. J Natl Cancer Inst Monogr, 120-3. SMITH, I., et al. 2011. Trial of perioperative endocrine therapy: Individualizing care (POETIC). J Clin Oncol, 29, 11s #TPS117. BLISS, J., et al. 2011. A Trial Model for the Future in the Search for Personalised Medicine - The UK POETIC and EPHOS-B Perioperative Trials Experience. Cancer Res, 71, OT2-03-04.	Yes	Novel perioperative clinical trial introducing new clinical trial procedures for UK breast centres (e.g. availability of ER at diagnosis). POETIC's perisurgical setting presents challenges for centres that have not arisen in earlier adjuvant studies. With its pragmatic design and broad appeal, POETIC is an ideal vehicle for overcoming these challenges, thus paving the way for more complex future studies (e.g. EPHOSB and RIO). The trial has biological markers as key endpoints - new in large RCTs. POETIC achievements include; -Allowing multiple pathways to accommodate patients approached at different times -Promotion of GCP training for surgeons. -Reaching an agreement with the HTA to better define "tissue in transit" to allow flexibility and time for patients to consent. - Encouraging local centres to consider fast tracking ER testing, and engaged with pathologists to find out centrespecific issues (e.g. delay in results reaching PI), discouraged batching and outsourcing of samples. - Obtaining clarification from National Cancer Action Team that entry into a trial like POETIC counts as first treatment for the purpose of cancer wait times. POETIC has the potential to identify more accurate prognostic factors, and therefore those patients with most to gain from additional adjuvant treatment. It may also lead to 2 weeks preoperative endocrine therapy becoming standard management for postmenopausal women with

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
							ER+ve cancers. Same as for UK Clinical Practice.
South Manchester University Hospital	Bundred (University Hospital South Manchester NHS Foundation Trust) (Bliss, ICR-CTSU)	CRUK/08/002: EPHOS-B: Effect of Perioperative anti-HER2 therapy on early breast cancer study -biological phase	132/250	2015	BLISS, J., et al. 2011. A Trial Model for the Future in the Search for Personalised Medicine - The UK POETIC and EPHOS-B Perioperative Trials Experience. Cancer Res, 71, OT2-03-04.	Yes	EPHOSB, in patients with HER2 positive breast cancer, builds on perioperative clinical trial model used in POETIC. EPHOSB has worked nationally to identify and resolve the issues specific to the trial including: • highlighting to all participating centres the requirement for the HER2 results to be available for review at MDT meetings. • working in close collaboration with the Breast CSG, its Translational Subgroup and the NCRI Breast CSG pathologist to ascertain the reasons for the delay in HER2 testing in order to improve delivery of portfolio trials which require timely HER2 results. • organising, with the Breast CSG Translational Subgroup, a NCRI workshop (Februray 2012). EPHOS has the potential to determine whether significant biological changes can be achieved with short pre-operative anti HER2 therapy. Same as for UK Clinical Practice.
The Royal Marsden NHS Foundation Trust	Smith (Royal Marsden Hospital NHS Foundation Trust) (Bliss, ICR-CTSU)	CRUKE/07/045: ALTTO: Adjuvant Lapatinib and/or Trastuzumab Treatment Optimisation Study	240/400	2014		No	Lapatinib may have a lower incidence of cardiac dysfunction, better CNS penetration and its oral route of administration would offer NHS resource savings over the iv infusion administration of trastuzumab.
The Institute of Cancer Research	Earl (Addenbrookes Hospital)	CRUKE/03/023: TEXT - Tamoxifen and Exemestane Trial	4/300	2013	RABAGLIO, M., et al., 2010. Death due to liver failure during endocrine therapy for premenopausal breast cancer. Acta Oncol 49(6):874-6. REGAN, M.M., et al., 2008. Premenopausal endocrine-responsive early breast cancer: who receives chemotherapy? Ann Oncol;19(7):1231-41. PRICE, K.N., et al., 2005. Clinical trial update: International Breast Cancer Study Group. Breast Cancer Res;7(6):252-4. FRANCIS, P., et al., 2003. Tailored treatment investigations for premenopausal women with endocrine responsive (ER+ and/or PGR+) breast cancer: The SOFT, TEXT, and PERCHE trials. The Breast;12, Supplement 1(0):S44. GELBER, R.D., et al., 2003. A. Tailored treatment investigations for premenopausal women with endocrine responsive (ER+ and/or PgR+) breast cancer: The open questions. The Breast;12, Supplement 1(0):S43-S44	Yes	Breast International Group trial co-ordinated by International Breast Cancer Study Group trial - ICR-CTSU is the UK CTU. Part of a suite of trials aiming to refine the role of ovarian suppression in premenopausal women with breast cancer.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Coleman (Weston Park Hospital)	CRUKE/03/022: SOFT - Suppression of Ovarian Function Trial	74/748	2013	RABAGLIO, M., et al. 2010. Death due to liver failure during endocrine therapy for premenopausal breast cancer. Acta Oncol, 49, 874-6. FLEMING, G., et al. 2007. Adjuvant goserelin in pre-menopausal patients with early breast cancer: Results from the ZIPP study. Breast Diseases: A Year Book. PRICE, K. N., et al. 2005. Clinical trial update: International Breast Cancer Study Group. Breast Cancer Res, 7, 252-4. FRANCIS, P., et al. 2003. Tailored treatment investigations for premenopausal women with endocrine responsive (ER+ and/or PGR+) breast cancer: The SOFT, TEXT, and PERCHE trials. The Breast, 12, S44 #P104. GELBER, R. D., et al. 2003. Tailored treatment investigations for premenopausal women with endocrine responsive (ER+ and/or PgR+) breast cancer: The open questions. The Breast, 12, S43-S44 #P103.	Yes	Breast International Group trial (n= 3066) co-ordinated by International Breast Cancer Study Group trial - ICR-CTSU is the UK CTU. The UK contribution was 75 patients. Part of a suite of trials aiming to define the role of ovarian suppression in addition to tamoxifen or an aromatase inhibitor for premenopausal women with breast cancer. Will clarify the role of ovarian suppression in young women receiving adjuvant chemotherapy and tamoxifen. If outcome improved then women continuing menstruation after adjuvant chemotherapy will be recommended to undergo ovarian suppression or oophorectomy. Alternatively, if no benefits are shown, this will reassure clinicians that they do not need to recommend ovarian suppression with the associated adverse effects of premature menopause. Same as for UK Clinical Practice.
The Institute of Cancer Research	Thompson (University of Dundee) (Bliss, ICR-CTSU)	CRUK/11/034: MA32: A Phase III Randomised Trial of Metformin versus Placebo on Recurrence and Survival in Early Stage Breast Cancer	137/200	2016	PARULEKAR, W., et al. 2011. A phase III randomized trial of metformin versus placebo on recurrence and survival in early-stage breast cancer (BC) (NCIC Clinical Trials Group MA.32). J Clin Oncol, ASCO Annual Meeting ProceedingsVol 29, No 15_suppl (May 20 Supplement) GOODWIN, P., et al. 2013. Effect of metformin versus placebo on weight and metabolic factors in initial patients enrolled onto NCIC CTG MA.32, a multicenter adjuvant randomized controlled trial in early-stage breast cancer (BC). J Clin Oncol 31, (suppl; abstr 1033)	Yes	The study aims to compare invasive disease free survival between breast cancer patients treated with metformin versus placebo in addition to standard adjuvant therapy. Evidence for efficacy of adjuvant metformin in ER positive breast cancers and ER negative cancers (where no long term oral adjuvant treatment exists) with an oral, widely available, low cost drug with few side effects could impact breast cancer in a way not seen since the advent of tamoxifen. Operationally the study is laying the foundations for future international collaboration between North America and the UK, in particular in terms of governance, complex IMP arrangements and tissue substudy management. The clinical impact described in column AO is internationally applicable.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Johnston (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Bliss, ICR-CTSU)	CRUK/09/007: SoFEA - Study of Faslodex with or without concomitant Arimidex vs exemestane following progression on non-steroidal Aromatase Inhibitors	698/750	2012	JOHNSTON, S. R., et al. 2013. Fulvestrant plus anastrozole or placebo versus exemestane alone after progression on non-steroidal aromatase inhibitors in postmenopausal patients with hormone-receptor-positive locally advanced or metastatic breast cancer (SoFEA): a composite, multicentre, phase 3 randomised trial. Lancet Oncol. DOI: 10.1016/S1470-2045(13)70322-X JOHNSTON, S., et al. 2012. Fulvestrant alone or with concomitant anastrazole vs exemestane following progression on non-steroidal aromatase inhibitor - First results of the SoFEA Trial (CRUKE/03/021 & CRUK/09/007) (ISRCTN441957747). Eur J Cancer, 48, S2 #2LBA. JOHNSTON, S., et al. 2012. Fulvestrant vs exemestane for treatment of metastatic breast cancer in patients with acquired resistance to non-steroidal aromatase inhibitors – a meta-analysis of EFECT and SoFEA (CRUKE/03/021 & CRUK/09/007). Cancer Research, 72, P2-14-01. DODWELL, D., et al. 2008. Combining fulvestrant (FaslodexTM) with continued oestrogen suppression in endocrine sensitive advanced breast cancer: The SoFea trial. Clinical Oncology, 20, 321-324. COOMBES, G., et al. 2004. Is faslodex more effective used alone or in combination with arimidex for treating postmenopausal women who have locally advanced/metastatic breast cancer following progression on non-steroidal aromatase inhibitors such as arimidex or letrozole? Clin Oncol (R Coll Radiol), 16, S24 #P1.02. JOHNSTON, S., et al. 2012. Fulvestrant vs exemestane for treatment of metastatic breast cancer in patients with acquired resistance to non-steroidal aromatase inhibitors – a meta-analysis of EFECT and SoFEA (CRUKE/03/021 & CRUK/09/007). Cancer Research, 72, P2-14-01. (San Antonio breast Cancer Symposium, 2012.)	No	SoFEA provides no evidence that the combination of fulvestrant and anastrozole (with a fulvestrant loading dose) is more effective than fulvestrant alone nor fulvestrant alone better than exemestane in patients with acquired resistance to a nonsteroidal aromatase inhibitor (NSAI). Median progression free survival in SoFEA is similar to the EFECT trial and lack of added benefit for the combination of fulvestrant and anastrozole is consistent with the FACT trial. SoFEA is the largest study investigating fulvestrant activity in patients with metastatic breast cancer. The trial has enabled a better understanding of the biology of endocrine resistance and helped to define the role of further endocrine therapy for this group of patients. In particular, it has confirmed that despite encouraging pre-clinical data, in clinical practice double endocrine therapy using fulvestrant combined with aromatase inhibition with exemestane is no more effective than either therapy alone in patients with acquired resistance to non-steroidal aromatase inhibitors (NSAI). A subsequent meta-analysis with the EFECT study has provided definitive clinical information on patients' response to fulvestrant at the 250mg dose used in these studies, and overall patients with acquired resistance to NSAI have limited clinical benefit from further endocrine therapies (median PFS 3-4 months). The SoFEA study adds to the body of international evidence on the efficacy of different endocrine therapies in metastatic breast cancer.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Tutt (Kings College London) (Bliss, ICR-CTSU)	CRUK/07/012: TNT: Triple Negative breast cancer Trial: A randomised phase III trial of carboplatin compared to docetaxel for patients with metastatic or recurrent locally advanced ER-, PR- and HER2- breast cancer.	353/370	2014/2015	ROBERTSON, L., et al. 2012. BRCA1 testing should be offered to individuals with triple-negative breast cancer diagnosed below 50 years. Br J Cancer, 106, 1234-8. KILBURN, L. S., et al. 2009. Treatment options for locally advanced or metastatic triple negative breast cancer: a survey of current UK practice. The Breast, 18, S65. [promotional only, poster presentation] Tutt, A., et al 2013 Trial in progress: Triple Negative breast cancer Trial (TNT). CRUK/07/012. Breakthrough Breast Cancer Triple Negative Breast Cancer Conference 2013. [promotional only, presentation] Tutt, A., et al 2012 Trial in progress: Triple Negative breast cancer Trial (TNT). CRUK/07/012. Cancer Genetics Group Meeting, Winter 2012.	Yes	The TNT trial tests a mechanistically driven therapeutic approach in a group of patients for whom no mechanism based therapeutic approach is currently available outside of clinical trials. There is still no effective licensed, targeted therapy or chemotherapy combination for TNBC. As the largest and only non commercial trial of triple negative breast cancer in the UK the TNT tissue resource is unique and invaluable for the future study of potential subgroups within TNBC. The increased prevalence of triple negative breast cancer within the AfroCaribbean population has meant such patients are more likely to be invited to join TNT, enabling better access to treatment and providing a vehicle for education and information about cancer and access to NHS resources. TNT blood samples used in the analysis presented in the paper published by Robertson et al have contributed to calls for a change in the guidelines for BRCA testing, to allow women <50 years old to be offered testing for faults in the BRCA1 gene. The NICE guidelines for familial breast cancer are being revised this year. Results from the TNT trial, its tissue resource and associated correlative biology program is eagerly awaited and often quoted by the international community. We therefore anticipate the results of the trial to have a similar impact internationally as for the UK.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Yarnold (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Bliss, ICR-CTSU)	CRUK/96/001: START pilot study: Randomised trial comparing fraction regimens after local excision in women with early breast cancer	1410/1400	2004	OWEN, J. R., et al. 2006. Effect of radiotherapy fraction size on tumour control in patients with early-stage breast cancer after local tumour excision:long-term results of a randomised trial. Lancet Oncol, 7, 467-471. HAVILAND, J. S., et al. 2008. Evaluation of a method for grading late photographic change in breast appearance after radiotherapy for early breast cancer. Clin Oncol (R Coll Radiol), 20, 497-501. YARNOLD, J., et al. 2005. Fractionation sensitivity and dose response of late adverse effects in the breast after radiotherapy for early breast cancer: long-term results of a randomised trial. Radiother Oncol, 75, 9-17. YARNOLD, J., et al. 2004. Radiotherapy fractionation: results of a pilot study to the NCRI Standardisation of Radiotherapy (START) Trial. Br J Cancer, 91, S19 #6.8. MARTIN, S., et al. 2010. Test of association between variant tg[beta]1 alleles and late adverse effects of breast radiotherapy. Radiother Oncol, 97, 15-18. HERSKIND, C., et al. 2010. Radiation-induced Gene Expression and Differentiation Status of Fibroblast Cultures from Breast Cancer Patients with and without Late Reaction to Radiotherapy. Int J Radiat Oncol Biol Phys, 78, S52 #110. GUJRAL, D. M., et al. 2011. Ipsilateral breast tumor relapse: local recurrence versus new primary tumor and the effect of whole-breast radiotherapy on the rate of new primaries. Int J Radiat Oncol Biol Phys., 79, 19-25.	Yes	It had previously been assumed that breast cancer should be treated with a large number of small fractions, as per the international standard schedule of 50Gy in 25 fractions of 2Gy. The results of the trial suggested that breast tumours might be as sensitive to fraction size as the latereacting normal tissues of the breast, and so could potentially be treated with fewer larger fractions. This was the pilot study to the NCRI UK START trials, and the first large randomised trial of hypofractionated wholebreast radiotherapy. The primary endpoint of the pilot study was late normal tissue effects; the design informed the START trials, which further tested the hypothesis with tumour control as the primary endpoint. Together with the START trials, results have contributed significantly to international knowledge base of radiobiology of breast cancer, and have led to new guidelines regarding wholebreast radiotherapy for early breast cancer.
The Institute of Cancer Research	Yarnold (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Bliss, ICR-CTSU and Peto, London School of Hygiene and Tropical Medicine)	CRUK/97/008: Breast Dosimetry: Randomised trial of standard 2D radiotherapy (RT) versus intensity modulated radiotherapy (IMRT) in patients prescribed breast radiotherapy	306/302	2006	DONOVAN, E., et al. 2007. Randomised trial of standard 2D radiotherapy (RT) versus intensity modulated radiotherapy (IMRT) in patients prescribed breast radiotherapy. Radiother Oncol, 82, 254-264. MARTIN, S., et al. 2010. Test of association between variant tg[beta]1 alleles and late adverse effects of breast radiotherapy. Radiother Oncol, 97, 15-18.	Yes	Minimisation of unwanted radiation dose inhomogeneity in the breast reduces late adverse effects. IMRT had been introduced in many RT centres in the UK before it had been proved effective. This trial demonstrated that IMRT does indeed reduce normal tissue effects in breast cancer. Most downloaded article from Radiotherapy and Oncology in first quarter of 2007 Established IMRT safe and effective in this population

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Bundred (University Hospital South Manchester NHS Foundation Trust) (Bliss, ICR-CTSU)	CRUK/05/005: BASO DCIS II: Randomised trial testing observation against radiotherapy in women with low-risk completely excised ER +ve ductal carcinoma in situ (DCIS) of the breast on adjuvant endocrine therapy.	63 - trial closed early/2000	2013	YARNOLD, J., et al. 2004. DCIS II Trial: A randomised trial testing observation (no radiotherapy) against radiotherapy in women with low-risk completely excised oestrogen receptor (ER) positive ductal carcinoma in situ (DCIS) of the breast on adjuvant endocrine therapy. Clin Oncol (R Coll Radiol), 16(6), S25 #P1.03. MILLS, J., et al. 2009. The psychological impact of the diagnosis and treatment of DCIS. Psycho-Oncology, 18, S163-S164. MILLS, J., et al. The Psychological impact of the diagnosis and treatment of DCIS (BASO-DCISII CR UK 05/0005). NCRI National Cancer Conference, 2009 Birmingham, UK. NCRI, 105 #B43.	No	Confirmed challenges of recruiting to trials with substantially different treatment options Has informed trial design of recent submission of DCIS trial to NIHR themed call for surgical trials.
The Institute of Cancer Research	Yarnold (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Bliss, ICR-CTSU)	CRUK/06/003: IMPORT HIGH: Randomised trial testing dose-escalated intensity modulated partial organ radiotherapy.	1404/2568	2018	DONOVAN, E. M., et al. 2011. Planning with intensity-modulated radiotherapy and tomotherapy to modulate dose across breast to reflect recurrence risk (IMPORT High trial). Int J Radiat Oncol Biol Phys, 79, 1064-72. JAMES, H., et al. 2008. The IMPORT high planning study: Defining dose constraints. Radiother Oncol, 88, S423 #1330. JAMES, H. V. 2007. A Practical, Inverse-planned IMRT Solution for Partial Breast Radiotherapy in the IMPORT HIGH Trial. Clin Oncol, 19, S17 #37. CONWAY, L., et al. 2007. A forward-planning solution for the IMPORT HIGH Breast IMRT Trial. Clin Oncol (R Coll Radiol), 19, S15 #31.	Yes	Many UK RT centres are acquiring new equipment which facilitates IMRT and IGRT which enable planned RT dose gradients to be delivered and verified for geometric accuracy in real-time. IMPORT HIGH requires the utilisation of both of these techniques. The comprehensive trial planning pack and Quality Assurance processes have been largely responsible for enabling UK RT centres to acquire expertise in these techniques. The IMPORT trials will particularly contribute to the understanding of the volume effect in breast radiotherapy, as well as add to knowledge of dose response effects of radiotherapy. The two IMPORT trials have significantly contributed to technical improvements in the accuracy of treatment planning and delivery of radiotherapy for patients with breast cancer in the following ways: • Enabled centres to use intensitymodulated radiotherapy (IMRT) for breast radiotherapy; increasing the number of RT centres moving from 2D to 3D planning and using 3D compensation. • The use of surgical clips to mark the tumour bed which not only improves the accuracy of partial breast radiotherapy but also whole breast radiotherapy. A change in surgical practice was needed at many centres to ensure the clips were inserted into the tumour bed for all breast cancer patients in order to accurately plan partial breast RT. This practice has now been endorsed by Association of Breast Surgery at BASO (Surgical Guidelines for the Management of Breast Cancer. Eur. J Surg. Oncol. 2009; 35: S1 – S22) as best practice and is being implemented across the country•

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Yarnold (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Bliss, ICR-CTSU)	CRUK/06/003: IMPORT LOW: Randomised trial testing intensity modulated radiotherapy and partial breast radiotherapy for early breast cancer.	2018/1935	2015	KIRBY, A., et al. 2011. IMPORT LOW partial breast outlining study: use of a training protocol to improve inter-observer concordance. Radiotherapy and Oncology, 99, S156 #394. CIURLIONIS, L., et al. Interim analysis of treatment plans in the IMPORT LOW Trial. NCRI National Cancer Conference, 2010 Liverpool.. COLES, C., et al. IMPORT LOW re-visited: How strategic trial management has increased average monthly accrual. NCRI National Cancer Conference, 2009 Birmingham. MILLS, J., et al. The IMPORT LOW Quality of Life Study: What we have learnt from the START Trial. NCRI National Cancer Conference, 2008 Birmingham. TSANG, Y., et al. Moving UK breast radiotherapy forward in the IMPORT LOW Trial - enabling safe change of practice through quality assurance (QA). NCRI National Cancer Conference, 2008 Birmingham.	Yes	IMPORT LOW has significantly contributed to technical improvements in the accuracy of treatment planning and delivery of radiotherapy for patients with breast cancer. Issues with limitations of physics resources common to all UK radiotherapy trials have been highlighted at a national level and submitted for inclusion in a review of the implementation of new techniques in the NHS. Results of the IMPORT LOW (partial breast) and IMPORT HIGH (whole breast) trials will eventually integrated with the results of the UK FAST Forward trial that is currently underway. The two IMPORT trials have significantly contributed to technical improvements in the accuracy of treatment planning and delivery of radiotherapy for patients with breast cancer in the following ways: • Enabled centres to use intensitymodulated radiotherapy (IMRT) for breast radiotherapy; increasing the number of RT centres moving from 2D to 3D planning and using 3D compensation. • The use of surgical clips to mark the tumour bed which not only improves the accuracy of partial breast radiotherapy but also whole breast radiotherapy. A change in surgical practice was needed at many centres to ensure the clips were inserted into the tumour bed for all breast cancer patients in order to accurately plan partial breast RT. This practice has now been endorsed by Association of Breast Surgery at BASO (Surgical Guidelines for the Management of Breast Cancer. Eur. J Surg. Oncol. 2009; 35: S1 – S22) as best practice and is being implemented across the country
University of Bristol	Winters (University of Bristol) (Bliss, ICR-CTSU)	CRUK/08/027: QUEST: A multi-centre randomised trial to assess the impact of the type and timing of breast reconstruction of quality of life following mastectomy.	25/110	2013	WINTERS, Z., et al. 2011. QUEST Perspective Study (QPS) to measure the understanding by patients and healthcare professionals of surgical breast reconstruction clinical trials: QUEST Trials A & B. Trials, 12, #A105. MILLS, J., et al. 2011. The development of a DVD to aid patients' understanding of surgical breast reconstruction clinical trials: QUEST A & B. Trials, 12, #A85. WINTERS, Z., et al. 2010. The QUEST Trial (CRUK/08/027): A multi-centre randomised trial to assess the impact of the type and timing of breast reconstruction on quality of life following mastectomy. Eur J Cancer Supplements, 8, 142 #289. WINTERS, Z., et al. 2010. The development of an EORTC breast reconstruction questionnaire to assess the quality of life of patients undergoing breast reconstruction. Eur J Surg Oncol, 36, 1115 #P34. MILLS, J., et al. 2010. The development of a DVD to aid patients' understanding of surgical breast reconstruction clinical trials: QUEST A & B. Eur J Surg Oncol, 36, 1123.	Yes	Despite extensive efforts to overcome barriers to recruitment it was not possible to reach target recruitment in a timely manner within the constraints of a feasibility study. Patient preference for breast reconstruction type and timing was the main barrier to recruitment. Both trials were closed to recruitment in December 2012 following the recognition of the challenges of recruiting the target number within a timely manner. The experience of QUEST trialists will help inform surgeons when designing future quality of life studies in breast reconstructive surgery. The trials increased the trials expertise and involvement by centres in surgical randomised controlled trials. An abstract has been accepted as a presentation at the San Antonio Breast Symposium 2013 entitled 'Quality of life following mastectomy and breast reconstruction (QUEST): learning from the feasibility randomisation trials. The presention and subsequent publication will inform the design of any future quality of life studies in breast reconstruction both in the UK and internationally.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Yarnold (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Bliss, ICR-CTSU)	CRUKE/04/015: FAST - Randomised Trial testing 5.7 Gy and 6.0 Gy fractions of whole breast radiotherapy in terms of late normal tissue response and tumour control	915/900	2011	The FAST Trialists, 2011. First results of the randomised UK FAST Trial of radiotherapy hypofractionation for treatment of early breast cancer (CRUKE/04/015). Radiother. Oncol. 2011;100(1):93-100. GOLDSMITH, C., et al. 2011. Large breast size as a risk factor for late adverse effects of breast radiotherapy: Is residual dose inhomogeneity, despite 3D treatment planning and delivery, the main explanation? Radiother Oncol, 100, 236-240. TSANG, Y. M., et al. 2007. Interim analysis of treatment plans in the FAST Trial. Clin Oncol (R Coll Radiol), 19, S16 #34. TSANG, Y. M., et al. Interim quality assurance (QA) analysis of treatment plans in the 'Faster Radiotherpay for Breast Cancer patients' (FAST) Trial. NCRI National Cancer Conference, 2006 Birmingham. SYDENHAM, M., et al. Further testing of radiotherapy hypofractionation (fewer, larger fractions) in early breast cancer - The FAST Trial. NCRI National Cancer Conference, 2006 Birmingham. DONOVAN, E., et al. Acute normal tissue reaction (moist desquamation) in patients with early breast cancer treated with 30Gy in 6 fractions over 15 days: Results of a pilot study. NCRI National Cancer Conference, 2006 Birmingham. #521. MARTIN, S., et al. 2006. Acute normal tissue reaction (moist desquamation) in patients with early breast cancer treated with 30Gy in 6 fractions over 15 days: Results of a pilot study. Radiother Oncol, 81, S276 #675. YARNOLD, J., et al. 2004. Prospective randomised trial testing 5.7 Gy and 6.0 Gy fractions of whole-breast radiotherapy in women with early breast cancer (FAST Trial). Clin Oncol (R Coll Radiol), 16, S30 #P3.02. National Cancer Research Institute (NCRI) National Cancer Conference, 2011. European Society for Radiotherapy and Oncology (ESTRO) Conference, 2010 (Radiother Oncol. 2010;96(Suppl 1):S36). European Cancer Organisation (ECCO) 15 and European Society for Medical Oncology (ESMO) Conference, 2009 (Eur J Cancer Supplements, 2009;7(3):2 #LBA 7)	Yes	Followed on from the START trials, to further test the limits of hypofractionation in breast radiotherapy. 2year results indicated that a 5fraction regimen was as safe (in terms of the latereacting normal tissues of the breast) as the international standard schedule of 50Gy in 25 fractions. An analysis of dosimetry data suggested that breast size remained a significant predictor of late toxicity even after allowing for dose inhomogeneity. FAST trial is the pilot study to the NIHR HTAfunded FAST Forward trial, which tests a 5fraction schedule delivered in 1 week. Further contributes to the knowledge of the effects of breast radiotherapy delivered in fewer larger fractions. Implementation of 3D planning of whole breast radiotherapy (more uniform distribution of dose) was adopted as standard for breast RT following the FAST trial. Introduction of simple forwardplanned intensity modulated RT (IMRT) via multiple static fields to almost half of UK RT centres.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Yarnold (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Bliss, ICR-CTSU)	CRUK/96/001: START Trials A and B - Randomised trials comparing fraction regimens after local excision or mastectomy in women with early breast cancer START Trial A: A randomised trial comparing 50 Gy in 25 fractions over 5 weeks (control schedule) with 41·6 Gy in 13 fractions over 5 weeks and 39 Gy in 13 fractions over 5 weeks (experimental schedules) START Trial B: A randomised trial comparing 40 Gy in 15 fractions in 3 weeks (experimental schedule) with 50 Gy in 25 fractions over 5 weeks (control schedule)	4451/3850	2007, 2012	START Trialists' Group. The UK Standardisation of Breast Radiotherapy (START) Trial B of radiotherapy hypofractionation for treatment of early breast cancer: a randomised trial. Lancet 2008;371(9618):1098-1107. START Trialists' Group. The UK Standardisation of Breast Radiotherapy (START) Trial A of radiotherapy hypofractionation for treatment of early breast cancer: a randomised trial. Lanc. Oncol. 2008;9(4):331-341. HAVILAND, J. S., et al. 2013. The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials. Lanc Oncol. doi:10.1016/S1470-2045(13)70386-3 HOPWOOD, P., et al. 2010. Comparison of patient-reported breast, arm, and shoulder symptoms and body image after radiotherapy for early breast cancer: 5-year follow-up in the randomised Standardisation of Breast Radiotherapy (START) trials. Lancet Oncol, 11, 231-240. HOPWOOD, P., et al. 2010. The course of anxiety and depression over 5 years of follow-up and risk factors in women with early breast cancer: results from the UK Standardisation of Radiotherapy Trials (START). Breast, 19, 84-91. HOPWOOD, P., et al. 2007. The impact of age and clinical factors on quality of life in early breast cancer: An analysis of 2208 women recruited to the UK START Trial (Standardisation of Breast Radiotherapy Trial). Breast, 16, 241-251. CHUA, M. L., et al. 2011. Residual DNA and chromosomal damage in ex vivo irradiated blood lymphocytes correlated with late normal tissue response to breast radiotherapy. Radiother Oncol, 99, 362-6. HAVILAND, J., et al. 2012. The UK START (Standardisation of Breast Radiotherapy) Trials; 10-year follow-up results. Cancer Res, 72, S4-1. (San Antonio Breast Cancer Symposium, 2012.) NAVA RODRIGUES, D., et al. 2012. Test of the association between Ki67 index of breast cancer and local relapse after adjuvant hypofractionated radiotherapy. Cancer Res, 72, P3-06-09. (San Antonio Breast Cancer Symposium, 2012.)	Yes	Following on from the START pilot study, the START trials have shown that: A lower total dose delivered in fewer fractions appears to be as safe and effective as the international standard fractionation schedule for wholebreast radiotherapy of 50 Gy in 25 fractions. Ratings by patients strengthen evidence in favour of hypofractionated regimens, with a potential for fewer adverse effects on the normal breast tissues. Breast tumours are as sensitive to fraction size as the latereacting normal tissues. Work on normal tissue effect assessments has also investigated the concordance between assessment methods (ESTRO 2012). Translational research collaborations include TransFRACTION testing for an association between Ki67 and fractionation sensitivity of breast cancer and GENEPI lowRT. These findings have important implications for radiotherapy practice with benefits to patients (including fewer hospital visits) and the NHS (reduced costs associated with fewer fractions). START trials have informed practice in UK and internationally (ASTRO guideline 2011) and led to a change in the recommended standard treatment schedule in the UK for wholebreast radiotherapy (UK NICE Guidance 2009). Patient reported outcomes in START have proved an invaluable resource to assess radiotherapy toxicity and have informed a decision to focus PROMS in future breast radiotherapy trials on normal tissue effects. The START has informed practice internationally (ASTRO guideline 2011) particularly in Europe and Canada.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Ellis (Guy's and St Thomas's NHS Foundation Trust) (Bliss, ICR-CTSU)	CRUK/01/001: TACT Trial - Taxotere as Adjuvant Chemotherapy	4162/4000	2007, 2012	ELLIS, P., et al., 2009. Sequential docetaxel as adjuvant chemotherapy for early breast cancer (TACT): an open-label, phase III, randomised controlled trial. Lancet; 373(9676):1681-92. BARTLETT, J. M., et al. 2013. Phosphorylation of AKT pathway proteins is not predictive of benefit of taxane therapy in early breast cancer. Breast Cancer Res Treat, 138, 773-81. CAMPBELL, H. E., et al. 2011. The cost-effectiveness of adjuvant chemotherapy for early breast cancer: A comparison of no chemotherapy and first, second, and third generation regimens for patients with differing prognoses. Eur J Cancer, 47, 2517-30. JOHNSON, L., et al. 2008. How do patients want to learn of results of clinical trials? - Results of a survey of 1431 breast cancer patients taking part in the TACT trial. Br J Cancer, 98, 34-38. BARTLETT, J. M. S., et al. 2007. Human epidermal growth factor receptor 2 status correlates with lymph node involvement in patients with estrogen receptor (ER) negative, but with grade in those with ER-positive early-stage breast cancer suitable for cytotoxic chemotherapy. . J Clin Oncol, 25, 4423-4430. TUTT, A., et al. 2009. Microtubule Associated Protein Tau Expression as a Predictive and Prognostic Marker in a Trial Assessing Sequential Docetaxel as Adjuvant Chemotherapy for Early Breast Cancer (TACT). Cancer Res, 69, 607. KILBURN, L. et al. 2012. Results of a retrospective linkage of TACT (CRUK 01/001) breast cancer trial data and the National Cancer Data Repository. NCIN/UKACR conference, Birmingham. BARRET, S., et al. 2012. Can linkage to routinely collected health records substitute for active follow-up of clinical trial participants? Annual Conference of the International Association of Cancer Registries, Cork, Ireland. BLISS, J. M., et al. 2012. Mature analysis of UK taxotere as adjuvant chemotherapy (TACT) trial (CRUK 01/001); effects of treatment and characterisation of patterns of breast cancer relapse. Cancer Res, 72, P1-13-03. (San Antonio Breast Cancer Symposium, 2012.)	No	TACT, the largest of the primary adjuvant taxane trials, did not show significant overall gain from the addition of docetaxel every 3 weeks to standard anthracycline chemotherapy of similar duration. Additionally, the anthracyclinedocetaxel sequential schedule was associated with a higher frequency of adverse events and transiently poorer quality of life than the nontaxane control regimen. Data from TACT, however, was consistent with findings from CALGB9344 trial suggesting that taxane benefit was most apparent in patient with ER negative, HER2 positive tumours with other subgroups deriving lesser or no apparent benefit. The trial was recognised internationally for its strong design features in that the taxane treatment was compared with a control regimen of similar duration and for its pragmatism in allowing use of a choice of control to enable widespread UK participation. The little apparent benefit for substituting a taxane in place of longer duration standard anthracycline treatment rekindled the debate on taxane use in early breast cancer and anecdotal evidence suggests a reduction in UK use of taxanes in this context. It seems also that over time one of the unexpected impacts of the TACT trial has been the reduced use of the ECMF regimen in the UK. Integral prospective specimen collection in TACT enabled phenotypic specific results to be presented alongside the overall clinical results and has meant that retrospectiveprospective biomarker analyses can be conducted. The TACT paper was cited by The Lancet as being an exemplar of how to publish large contemporary randomised trials within the context of the worldwide evidence base. The TACT trial has been hugely cited and is recognised around the globe. It was also quoted specifically during the most recent EBCCTG process where the conclusion that in trials of equivalent duration therapy in the control arm the impact of taxanes was modest at best. Taxane usage has almost certainly reduced in many parts of the world particularly in health economies with scarce resources.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Yarnold (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Bliss, ICR-CTSU)	FAST Forward: Prospective randomised clinical trial testing 5.7Gy and 6.0Gy fractions of whole breast radiotherapy in terms of local tumour control, late normal tissue responses and QL	2715/4000	2021		Yes	The recruitment rate into FAST FORWARD is far exceeding original estimates although some centres have reported that payment by results has resulted in delays obtaining R&D approval and/or a restriction in monthly recruitment. A report regarding payment by results was submitted to the National Institute for Health Research Clinical Research Network (NIHR CRN) Coordinating Centre as part of a wider report compiled for a Performance Review with the NIHR Cancer Research Network (NCRN) Executive. The contents and findings of which were discussed in July 2013 and Dr Jonathan Sheffield, Chief Executive of NIHR CRN, has indicated that he intends to act on the contents. A plan for escalation to DH and NHS England has been agreed Following on from START and FAST this trial further contributes to the knowledge of the effects of breast radiotherapy delivered in fewer larger fractions. The current proposal aims to test 5-fraction schedules delivered over 5 weeks and over 1 week. A schedule of curative radiotherapy involving 5 fractions would address serious shortages in NHS radiotherapy resources. As a large phase III study FAST FORWARD will make a significant contribution to the interanational knowledge base.
The Institute of Cancer Research	Turner (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Bliss, ICR-CTSU)	Rucaparib Window of Opportunity study in patients with primary triple negative or BRCA1/2 related breast cancer (RIO)	unknown/94	2016		No	The RIO study application for endorsement was submitted to CTAAC alongside completion of Phase I dose escalation studies of the oral re-formulation of rucaparib. As described in detail in the application, the study will not commence until the recommended phase II dose (RP2D) is established, and sufficient safety data at this dose is collated. The RP2D is now estabilised at 600mg BID and the required safety data will be available by Q1 2014. Parallel submission for endorsement was favoured so that regulatory submissions can be made as soon as the relevant information is confirmed. The lack of targeted therapy for TNBC is an unmet clinical need, RIO will investigate the biological response to rucaparib in this poor prognosis group of patients. The aim of the study is to identify biomarkers to identify subsets of TNBC that are sensitive to rucaparib that will then allow subsequent randomised trials. As the UK is uniquely placed to deliver trials in the peri-operative setting, the clinical impact described for the UK also applies internationally.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Cameron, UK CI (University of Edinburgh and NHS Lothian) (Bliss, ICR-CTSU)	UNIRAD - Randomised, double-blind, multicentre phase III trial evaluating the safety and benefit of adding everolimus to adjuvant hormone therapy in women with poor prognosis, ER+ and HER2- primary breast cancer who remain free of disease after receiving 3 years of adjuvant hormone therapy	unknown/750	2020		Yes	Everolimus treatment is associated with a number of expected side effects, which can be severe in nature. Therefore, a key consideration for the management of these patients is regular safety monitoring. Additional safety visits and follow up telephone calls have been added specifically for the UK trial population. Patients with ER+ve breast cancer with ≥4 involved nodes at the time of diagnosis are at a particularly high risk of disease relapse while receiving or following endocrine therapy. Recent advances in our understanding of endocrine therapy resistance pathways and mechanisms of action of novel agents such as everolimus, provide the first new approach to treatment of ER+ve/HER2-ve breast cancer patients at high risk of relapse for over a decade. Therefore if this trial is "positive" it has the potential to change clinical practice, particularly as the agent being tested will become generic around the time this trial is likely to report, reducing its potential cost to the NHS. The clinical impact described for the UK also applies internationally. The study is being led by the French UNICANCER group, therefore this study also establishes new working collaborations between the UK and French cancer research communities.
The Institute of Cancer Research	Schmid (Brighton & Sussex University Hospitals Trust, University of Sussex) (Bliss, ICR-CTSU)	ICORG 11-10: A phase III randomized study of PH (Paclitaxel and Trastuzumab) versus PHL (Paclitaxel, Trastuzumab and Lapatinib) in first line treatment of HER2 positive metastatic breast cancer.	unknown/30	2017/18		Yes	When this study was initiated, the combination of taxane and trastuzumab was the treatment of choice for patients with HER2+ve metastatic breast cancer. However, in April 2013 the therapeutic landscape for these patients changed in England, when pertuzumab became available via the cancer drugs fund. Dual blockade of the HER2 receptor via pertuzumab and trastuzumab in combination with docetaxel has now become one of the main therapeutic standards in England. As such, ICORG 11-10 will proceed in Wales and Scotland only, where pertuzumab is not currently available. Despite the significant progress made in the treatment of HER2-positive breast cancer, resistance to trastuzumab therapy remains a major clinical challenge and dual blockade of HER2 has shown positive results. As the patent of lapatinib will shortly expire (~2017), and biosimilar trastuzumab is also expected to be available within a couple of years, should the results of the ICORG 11-10 trial be positive, the combination of trastuzumab, lapatinib and paclitaxel may provide a cost effective dual blockade therapy for HER2 positive metastatic breast cancer. The clinical impact described for the UK is also applicable internationally. The international interest in this question is confirmed by the extent of international participation in the trial.
MRC	Moss	CRUK/95/016: FREQUENCY: 1 year versus 3 years mammography			Breast Cancer Research 2005, 7:230-234, 1: Eur J Cancer. 2002 Jul;38(11):1458-64		At 3 years of follow-up (that is, when both arms had been reinvited) a non-significant increase in breast cancers of 19% (13% invasive) was observed in the annual screening arm. Therefore the screening interval in the Breast Screening Programme will remain at three years.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
MRC	Langley	Add-Aspirin Trial: A phase III double-blind placebo-controlled randomized trial assessing the addition of aspirin after standard primary therapy in early stage common solid tumours	0/8250	2024	Langley, R. E., Burdett, S., Tierney, J. F., et al. 2011. Aspirin and cancer: has aspirin been overlooked as an adjuvant therapy? Br J Cancer, 105, 1107-13; Langley, R. E. & Rothwell, P. M. 2013. Potential biomarker for aspirin use in colorectal cancer therapy. Nat Rev Clin Oncol, 10, 8-10; Langley, R. E. 2013. Clinical evidence for the use of aspirin in the treatment of cancer. Ecancermedicalscience, 7, 297; Phillips, I., Langley, R., Gilbert, D. & Ring, A. 2013. Aspirin as a treatment for cancer. Clin Oncol (R Coll Radiol), 25, 333-5. Poster presentation (on the background/rationale and design of the trial) at the 1st World Congress on Controversies in Gastroenterology (CIGI), Berlin, Germany, June 2013	Yes	Aspirin is an inexpensive, easily administered agent which is widely available. If it is shown to be beneficial as an adjuvant therapy, it could be implemented quickly and on a broad scale across the UK as well as internationally, and would have a huge impact on cancer outcomes. If aspirin is shown to be beneficial as an adjuvant therapy, it could be implemented in both resource rich and resource poor countries and would have a huge impact, improving cancer outcomes worldwide.
KCL	Hunter	CRUK/08/028: MENOS 1 - A randomised controlled trial of a cognitive behavioural intervention for women who have menopausal symptoms following breast cancer	65/96		Hunter MS et al., Maturitas. 2009 Aug 20;63(4):336-40. Hunter MS, et al., Psychooncology. 2009 May;18(5):560-3.		
Quuen Mary University of London	Tony Howell	CRUK/04/032/033: International Breast Cancer Intervention Studies (IBIS II)	3078/unknown target	2014	Cuzick, J et al (2008). IBIS II: a breast cancer prevention trial in postmenopausal women using the aromatase inhibitor anastrozole. Expert Rev Anticancer Ther. Sep;8(9):1377-85. Singh, S et al (2011). Effect of baseline serum vitamin D levels on aromatase inhibitors induced musculoskeletal symptoms: results from the IBIS-II, chemoprevention study using anastrozole. Breast Cancer Res Treat. DOI 10.1007/s10549-011-1911-6. Singh S, Cuzick J, Mesher D, Richmond B, Howell A (2012).Effect of Baseline Serum Vitamin D levels on aromatase inhibitors induced musculoskeletal symptoms: results from the IBIS II, chemoprevention study using anastrazole. Breast Cancer Res Treat. Apr;132(2):625-9.	Yes	To determine if anastrozole is effective in preventing breast cancer in post-menopausal women in high risk and to determine if anastrozole is at least as effective than tamoxifen in preventing breast cancer in women who have had a DCIS. Could mean that anastrozole could be prescribed as a preventive measure rather than only for treatment. Side effects appear to be fewer with the aromatase inhibitors, with no excess of gynecologic (including endometrial cancer) or thromboembolic events, but an increase in fracture risk and joint symptoms does occur. The trial could mean that women at high risk of breast cancer could be prescribed anastrozole as a preventative treatment. It could mean that DCIS patients be prescribed anastrozole to prevent recurrence and/or breast cancer development.
Barts and the London NHS Trust	Cuzick	CRUK/08/035: LATTE (previously LT-ATAC): Long-term Anastrozole vs. Tamoxifen Treatment Effects	1051/1307		Cuzick J, Sestak I, Baum M, Buzdar A, Howell A, Dowsett M, Forbes JF; ATAC/LATTE investigators.. (2010). Effect of anastrozole and tamoxifen as adjuvant treatment for early-stage breast cancer: 100-month analysis of the ATAC trial. The Lancet Oncology. 9 (1), 45-53. Forbes, J.F., et al., Effect of anastrozole and tamoxifen as adjuvant treatment for early-stage breast cancer: 100-month analysis of the ATAC trial. Lancet Oncol, 2008. 9(1): p. 45-53	Yes	The aims of the LATTE study are to collect long term follow-up information after this point, and for at least another 5 years in terms of additional efficacy data and safety data. AIs have been shown to significantly improve survival in women with early breast cancer when compared to tamoxifen, the previous standard for adjuvant therapy. However, no data exist on the long term safety and efficacy of AIs. This is a key question for the treatment of early breast cancer because five-year survival with AIs is so good and tamoxifen is known to have minimal side effects. Ultimately, results from this work will enable patients and clinicians to make more informed decisions about the overall risks and benefits of AI therapy including long-term consequences of treatment for women with early breast cancer, particularly when it comes to choosing between

Key:	Trials that are currently in set-up		Trials that are currently open			Trials that have closed, suspended, or withdrawn during set up	
Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
							anastrozole and tamoxifen.
Barts and the London NHS Trust	Cuzick (Sasieni)	CRUK/04/026: IBIS I	7152/7000	2002	Cuzick, J., et al. (2002). "First results from the International Breast Cancer Intervention Study (IBIS-I): a randomised prevention trial." Lancet 360(9336): 817-824. Palva, T., et al. (2012). "A double-blind placebo-controlled study to evaluate endometrial safety and gynaecological symptoms in women treated for up to 5 years with tamoxifen or placebo - A substudy for IBIS I Breast Cancer Prevention Trial." European journal of cancer. Sestak, I. et al. (2012). "Relationships between CYP2D6 phenotype, breast cancer and hot flushes in women at high risk of breast cancer receiving prophylactic tamoxifen: results from the IBIS-I trial." British journal of cancer 107(2): 230-233. Cuzick, J., J. et al. (2011). "Tamoxifen-induced reduction in mammographic density and breast cancer risk reduction: a nested case-control study." Journal of the National Cancer Institute 103(9): 744-752. Cuzick, J., et al. (2004). "Tamoxifen and breast density in women at increased risk of breast cancer." Journal of the National Cancer Institute 96(8): 621-628. Stone, J., et al. (2009). "Determinants of percentage and area measures of mammographic density." American journal of epidemiology 170(12): 1571-1578. Warwick, J., et al. (2003). "Breast density and breast cancer risk factors in a high-risk population." Breast 12(1): 10-16. The first formal presentation of the IBIS-I results was at the Breast Cancer Conference, Barcelona 2002. The data has been presnted formally on numerous occasions since.	Yes	IBIS-I has been an important source of information about the role of tamoxifen in breast cancer prevention & identification of the risk factors for developing breast cancer. In addition it has demonstrated the preventive effect of tamoxifen is sustained after 10 years of follow up , i.e. 5 years after completing treatment. As a result NICE has recommended that women in England and Wales who are aged over 35 and at "moderate" or "high" risk of breast cancer as a result of their family history or genes should be considered for preventative drug therapy. It is hoped that long-term follow-up of the IBIS-I participants will indicate how long these benefits last, whilst allowing us to monitor any late side effects, such as endometrial cancer where the current evidence on late occurrence is inconclusive. Furthermore, we have observed that changes in mammographic density are predictive of the effectiveness of tamoxifen in the short term. Again, long-term follow-up will allow us to see if this protection is sustained. Finally, the IBIS-I study provided the basis for its successor, the IBIS-II trial. As a result of the study results, NICE has recommended that women in England and Wales who are aged over 35 and at "moderate" or "high" risk of breast cancer as a result of their family history or genes should be considered for preventative drug therapy. The new guidelines from NICE are the first in Europe to recommend that healthy women are given drugs to prevent breast cancer. It is unclear how this may impact on International health policy. However, outside of England & Wales, it is likely that Northern Ireland will soon follow suit. In addition, the Scottish government says women with two or more family members who have had breast cancer will be offered the treatment for five years.
QMUL	Roylance	CRUK/08/046: ICICLE - A study to Investigate the genetiCs of In situ Carcinoma of the ductaL subtypE	1320/6000				
QMUL	Roylance	GLACIER - A study to investigate the Genetics of LobulAr Carcinoma In situ in EuRope	1520/2000		Cuzick, J., J. F. Forbes, et al. (2007). "Long-term results of tamoxifen prophylaxis for breast cancer--96-month follow-up of the randomized IBIS-I trial." Journal of the National Cancer Institute 99(4): 272-282.		
QMUL	Wald	CRUK/95/015: UKCCCR multicentre randomised controlled trial of one and two view mammography in breast cancer screening	40/163		Clin Radiol 2005 Jun;60(6):674-80; BMJ 1995;311:1189-1193 (4 November),		The effect of changing to two view mammography was a 20% increase in overall cancer detection rate. As a result of these findings the screening programme was changed to incorporate two view mammography.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Queen Mary, University of London	Jones/Eccles	Prospective Study of Outcomes in Sporadic versus Hereditary (POSH) breast cancer: Pathology Biomarker Study			Evans DG, Howell A, Ward D, Lalloo F, Jones JL, Eccles DM. Prevalence of BRCA1 and BRCA2 mutations in triple negative breast cancer. J Med Genet 2011; 48(8):520-522: Wilson JR, Bateman AC, Hanson H, An Q, Evans G, Rahman N et al. A novel HER2-positive breast cancer phenotype arising from germline TP53 mutations. J Med Genet 2010; 47(11):771-774: Haiman CA, Chen GK, Vachon CM, Canzian F, Dunning A, Millikan RC et al. A common variant at the TERT-CLPTM1L locus is associated with estrogen receptor-negative breast cancer. Nat Genet 2011; 43(12):1210-1214. Copson E et al, Presented at British Breast Group meeting January 2013. Ethnic minorities with young onset breast cancer show clear differences in breast cancer characteristics and prognosis when compared to age matched white caucasian patients:		This will be a major focus for the translational studies for this cohort study for the near future. Will demonstrate whether current clinical prognsotic tools appropriate in this age group and whether BRCFA status has prognsotic significance independent of tumour subtype and age effect.
Velindre NHS Trust	Barrett-Lee	CRUKE/04/022: ZICE: Zoledronate versus Ibandronate comparative evaluation	1404/1400	2012	San Antonio Breast Cancer Symposium, December 2012: Zoledronate versus ibandronate comparative evaluation (ZICE) trial - first results of a UK NCRI 1,404 patient phase III trial comparing oral ibandronate versus intravenous zoledronate in the treatment of breast cancer patients with bone metastases.	No	Since starting ZICE, it has been demostrated in another trial that a new treatment, denosmab, is superior to zoledronate. However, this trial will still be of value for patients who are not suitable for treatment with denosomab. Denosomanb is not standard treatment in all countries outside of the UK, so the results of this trial will be of interest internationally.
Cardiff University	James	CRUKE/09/039: PLANET - A randomised Phase II study of carboplatin with or without the addition of the ETAR inhibitor ZD4054 as treatment for patients with metastatic breast cancer.	0/132	2013		No	N/A Study shelved N/A Study shelved
Velindre NHS Trust	Howell and Jones	CRUK/12/044:FAKTION - A randomised double blind placebo controlled Phase I/II study of Fulvestrant with or without the addition of the Akt inhibitor AZD5363 as treatment for patients with metastatic breast cancer resistant to aromatase inhibitor therapy.	0/150	2017		Yes	Will potentially change clinical practice. Will contribute significantly to international knowledge base.
Cambridge University	Earl	CRUK/08/037: ARTemis: Avastin Randomised Trial with neo-adjuvant chemotherapy for patients with early HER 2 negative breast cancer	800/800	2014	1/ Earl, Hiller et al. ARTemis: A randomised trial of bevacizumab with neo-adjuvant chemotherapy (NACT) for patients with HER2-negative early breast cancer: The primary endpoint results- pathological complete response (pCR). American Society of Clinical Oncology meeting. Chicago, Illinois, USA. June 2014. 2/ Hiller, Dunn et al. The challenges of using radiological 'tumour response' as an outcome: Lessons learned from Neo-tAnGo	Possibly	Bevcizumab in addition to neo-adjuvant chemotherapy significantly increases pathCR rates This study will contribute to findings of the Geparquinto and NSABP-B40 results on the use of Bevacizumab in the treatment of early breast cancer This study will contribute to findings of the Geparquinto and NSABP-B40 results on the use of Bevacizumab in the treatment of early breast cancer

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
					and ARTemis, two neo-adjuvant chemotherapy breast cancer trials. UK Clinical Trials Methodology Conference, Edinburgh Nov 2013. P75		
University College London and Birmingham University	Baum	CRUK/95/002: ZIPP: Adjuvant GnRHa in premenopausal women with early breast cancer.	2106/2106		Baum M et al. Adjuvant Zoladex in premenopausal patients with early breast cancer; results from the ZIPP trial. The Breast 2001;10:(Suppl 1)P64, S32-S33. Baum M,et al. Adjuvant goserelin in premenopausal patients with early breast cancer: results from the 'Zoladex' in premenopausal patients (ZIPP) trial. Eur J Cancer 2006;42:895-904. Hackshaw et al Long-term effectiveness of adjuvant Goserelin in premenopausal women with early breast cancer; JNCI, Vol 101, No. 5, March 2009, pp 341-349		Together with other trials of complimentary design it is now standard of care to offer zoladex for women <50 with ER+ breast cancer either in addition to chemotherapy or as an alternative.
University College London and Birmingham University	Baum (Smith, Cuizick & Sasieni)	CRUK/95/003: ATAC: Comparing an aromotase inhibitor with tamoxifen in first line adjuvant endocrine therapy for post-menopausal women with early breast cancer.	9366/unknown target		Buzdar A et al Lancet Oncol. 2006 Aug;7(8):633-43,Eastell R et al Bone Miner Res. 2006 Aug;21(8):1215-23, Buzdar AU et al, Cancer. 2006 Aug 1;107(3):472-80. Erratum in: Cancer. 2006;107(9 No 1):2314. Dowsett M et al Clin Oncol. 2005 Oct 20;23(30):7512-7. Breast Cancer Res Treat. 2004;87 Suppl 1:S11-8. Duffy S et al Hum Reprod. 2006 Feb;21(2):545-53,Hum Reprod. 2006 Feb;21(2):545-53. Obstet Gynecol. 2004 Dec;191(6):1921-7.Howell A et al Lancet. 2005 Jan 1-7;365(9453):60-2.		The recent NICE report accepts front line anastrozole as an alternative for tamoxifen and this is rapidly becoming standard of care.
University College London and Birmingham University	Baum	CRUK/70/001: CRC King's Cambridge Trial (CRC I): a phase III trial to evaluate the role of prophylactic radiotherapy following simple mastectomy for early breast cancer	2800/2800		Elston CW et al The Lancet 1980; 55-60. Brinkley D et al. BJC 1982;45:655. Haybittle JL et al British Journal of Radiology 1984;57:309-316 Berstock DA et al World journal of Surgery 1985; 9: 667-670 Haybittle JL et al British Medical Journal 1989; 298: 1611-1614 Cuzick J Journal of Clinical oncology 1994; 12 (3); 447-453 Haybittle J et al british Journal of Cancer 1997; 75 (5): 729-733. Long term follow up paper in preparation.		Established principles of statistical power, rapid recruitment and mature follow up. Showed that failure to treat the chest wall and axillary nodes had significant impact on reduction of local recurrence but only had a modest impact on the regional recur
University College London and Birmingham University	Baum	CRUK/95/005: Nolvadex adjuvant tamoxifen trial (NATO): a phase III trial to determine whether adjuvant tamoxifen treatment for two years prolongs survival and relapse-free survival	1285/1285		Baum M et al., Controlled trial of tamoxifen as adjuvant management of early breast cancer. The Lancet 5 February 1983; 257-260. Baum M et al., Controlled trial of tamoxifen as single adjuvant agent in management of early breast cancer The Lancet 13 April 1985; 836-839		First study to report the survival advantage of adjuvant tamoxifen which has now become standard of care (trial was mostly funded by ICI and CRC, and later CRUK funded the infrastructure and translational research which has lead to a better understanding
University College London and Birmingham University	Baum	CRUK/95/006: CRC II	2230/2230		Cuzick J, Baum M. Tamoxifen and contralateral breast cancer. The Lancet 1985; 282 Houghton J, et al Long-term tamoxifen for breast cancer. Ed Jordan VC. Pub. university of Wisconsin Press 1994:93-112 Houghton J, et al. Is there a role for perioperative adjuvant cytotoxic therapy in the treatment of early		Repeated NATO and additionally assessed a short course of perioperative chemotherapy and added considerably to the power of the first EBCTCG overview of adjuvant tamoxifen.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
					breast cancer? Rec Results Cancer Res 1989; 115: 54-61		
University College London and Birmingham University	Baum	CRUK/86/001: Over 50s: Cancer Research Campaign Adjuvant Breast trial for patients over the age of 50	3979/3979		Preliminary results from the Cancer Research Campaign trial evaluating tamoxifen duration in women aged fifty years or older with breast cancer. JNCI 1996; 88: 1834 - 1839. Potyka I, et al Duration of tamoxifen therapy in women with early, operable breast cancer over the age of fifty. The Breast 1997;6:254. Hackshaw A, et al. Long-term benefits of 5 years of tamoxifen: 10 year follow up of a large randomised trial in women aged at least 50 years with early breast cancer. Submitted JCO 2010.		Our results suggest that 5 years may be better than 2 years of tamoxifen therapy, but more evidence regarding the optimal duration of tamoxifen therapy must be obtained.
University College London and Birmingham University	Baum	CRUK/87/002: Under 50's: Cancer Research Campaign Adjuvant Breast trial for patients under the age of 50	1191/1191		Allan Hackshaw et al. JNCI, Vol 101, No. 5, March 2009, pp 341-349. Swerdlow AJ et al Cancer Inst 99 [3]: 206-214. Mudie NY et al Clin Oncol 24: 1568-1574 Baum M et alThe Breast 2001;10:(Suppl 1)P64, S32-S33. Baum Met al Eur J Surgery 2006;42:895-904.		Two years of goserelin treatment was as effective as 2 years of tamoxifen treatment 15 years after starting therapy. In women who did not take tamoxifen, there was a large benefit of goserelin treatment on survival and recurrence, and in women who did take tamoxifen, there was a marginal potential benefit on these outcomes when goserelin was added.
University College London and Birmingham University	Robertson (Baum)	CRUK/89/001: CRC Elderly Trial	455/455		Latteier J et al The Breast 1997;6:244 Houghton J et al Programme / Proc Am Soc Clin Oncol 1999;18:576A. Bates TBr et al J Surg 2001;88:41. Bates T et al Eur J Cancer 2001;37(S5): Fennessy M et al British Journal of Surgery. 91 (6): 699-704 Jun 2004 Tom Bates et al ASCO; 2001		Demonstrated that primary surgery has a significant effect on long term local control of the disease and a modest effect on survival. It is now standard of care not to compromise on adequate surgical control based on age alone.
Barts and the London NHS Trust	Cuzick (Joslin)	CRUK/90/002: UKCCCR DCIS Trial: Protocol of the UK randomised trial for the management of screen-detected ductal carcinoma in situ (DCIS) of the breast	1701/1701		Radiotherapy and tamoxifen in women with completely excised ductal carcinoma in situ of the breat in the UK, Australia, and New Zealand: randomised controlled trial. The Lancet, Vol 362, 12 July 2003, 95-10. Pinder SE, et al. A new pathological system for grading DCIS with improved prediction of local recurrence: results from the UKCCCR/ANZ DCIS trial. Br J Cancer. 2010;103(1):94-100. Houghton J et al, The Breast 1997;6:229. Cuzick J, George WD, Houghton J. Br J Cancer 2001;85:(S1):2. Cuzick J, et al. Cancer Res. 2009;69(24 Supp 3):493S-493S.		Radiotherapy useful for women with DCIS after surgery, but tamoxifen was not useful
Guy's & St Thomas's NHS Foundation Trust	Tutt	CRUKE/11/044: Neptune: NEo-adjuvant PARP Inhibitor Trial in Unilateral Triple NEgative Breast Cancer					

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University College London	Tutt	CRUK/04/011: BRCA: Breakthrough Breast Cancer & Cancer Research UK phase II trial of carboplatin versus docetaxel in patients with metastatic genetic breast cancer	23/148	2015			Trial closed early to recruitment and has been merged with the TNT breast trial run by ICR
Centre for Drug Development							
Imperial College London	Seckl	CRUKD/11/004: RADICAL a First in Man Phase I/IIa study of AZD4547, an FGFR inhibitor, in combination with a non-steroidal aromatase inhibitor (anastrozole or letrozole) in ER+ advanced breast cancer patients	6/50	2015			Trial aims to assess safety and efficacy of combination, MTD of drug, if combination can overcome reisistance to aromatase inhibitors and identify dose for further evalauation. First time in patients for this novel combination of an FGFR inhibitor and an aromatase inhibitor. If positive will lead to larger Phase III randomised trials of the FGFRI either as a single agent or in combination with AIs versus exemestane in AI resistant breast cancer. A subsequent positive phase III study which could potentially change the standard of care for a significant proportion of breast cancer patients in the UK and internationally. Additionally if reversal of hormonal resistance is demonstrated this could have implications for treatment of other FGFR expressing tumour e.g. prostate. First time in patients for this novel combination of an FGFR inhibitor and an aromatase inhibitor. If positive will lead to larger Phase III randomised trials of the FGFRI either as a single agent or in combination with AIs versus exemestane in AI resistant breast cancer. A subsequent positive phase III study which could potentially change the standard of care for a significant proportion of breast cancer patients in the UK and internationally. Additionally if reversal of hormonal resistance is demonstrated this could have implications for treatment of other FGFR expressing tumour e.g. prostate.
Institute of Cancer Research/Royal Marsden Hospital	de Bono	CRUKD/08/044: A CR-UK Phase I/II trial of abiraterone acetate (CB7630) in patients with ER+, PR+ or AR+ refractory metastatic breast cancer	69/83	2015	B. Basu, et al. Phase I study of abiraterone acetate (AA) in patients (pts) with estrogen receptor– (ER) or androgen receptor (AR) – positive advanced breast carcinoma resistant to standard endocrine therapies. J Clin Oncol 29: 2011 (suppl; abstr 2525) ASCO 2011		First trial in patients with breast cancer for this agent targeting CYP17. Drug was developed at the Institute of Cancer Research by Mike Jarman part funded by Cancer Research UK. First trials were in prostate: CRUKD/96/014, CRUKD/98/007 & CRUKD/98/008. Trial ongoing. Aims to identify a suitable dose, look at side effects, PK/PD and efficacy in breast cancer. Agent registered by the FDA in 2011 for prostate cancer. Too early in development to assess clinical impact.
University of Newcastle	Plummer	CRUKD/08/042: A CR UK Phase II trial of PARP inhibitor AG014699 in metastatic breast & ovarian cancer with known BRCA1 or BRCA2 mutation	78/114	2015	Drew Y, et al. J Natl Cancer Inst. 2011 Feb 16;103(4):334-46 Y. Drew, et al. J Clin Oncol 29: 2011 (suppl; abstr 3104) ASCO 2011		First trial with this agent in patients with BRCA mutations. Follow on trial to CRUKD/03/042. Trial ongoing. Aims to look at efficacy, side effects and PK/PD. Representative of a new class of anti cancer treatment for patients with BRCA related breast and ovarian cancer.
University of Oxford	Harris	CRUKD/08/043: A CR-UK Phase II trial of copper-binding agent ATN224 in combination with exemestane versus exemestane alone in postmenopausal women with	1/45	2008			Follow up Phase II trial to CRUKD/04/039. Trial did not complete recruitment. Agent was withdrawn for financial reasons. Too early in development to assess clinical impact.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
		recurrent/advanced oestrogen/progesterone receptor positive breast cancer					
Imperial College	Coombes	CRUKD/03/038: A Cancer Research UK Phase I trial of 667-Coumate (a sulphatase inhibitor) administered to postmenopausal women with locally advanced or metastatic breast cancer	14/14	2005	Stanway SJ, Purohit A, Woo LW, Sufi S, Vigushin D, Ward R, Wilson RH, Stanczyk FZ, Dobbs N, Kulinskaya E, Elliott M, Potter BV, Reed MJ, Coombes RC. Phase I study of STX 64 (667 Coumate) in breast cancer patients: the first study of a steroid sulfatase inhibitor. Clin Cancer Res. 2006 Mar 1;12(5):1585-92.		First time in patients for this second generation steroid sulphatase inhibitor. Trial completed. Agent in Phase II development. Too early in development to assess clinical impact. Led on to Phase II evaluation.
University of Newcastle	Calvert	CRUKD/02/024: A Phase II Trial of CT2103 given every 21 days via a 10 minute intravenous infusion in patients with metastatic breast cancer	25/25	2004			First trial in breast cancer with this agent. Follow up Phase II trial to CRUKD/00/016. Trial did not complete recruitment due to toxicity. Agent in Phase III development. Too early in development to assess clinical impact.
Institute of Cancer Research/Royal Marsden Hospital	Sacks	CRUKD/97/017: The use of Radioimmunoscintigraphy with blood clearance as a method of determining the axillary lymph node status of patients with breast cancer		1997	Spillane AJ, Sacks NP. Swiss Surg. 1999;5(5):205-13. Smellie WJ, et al. Cancer Res. 1995 Dec 1;55(23 Suppl):5842s-5846s. Allan SM et al. Br J Cancer. 1993 April; 67(4): 706–712. Tjandra JJ, Sacks NP, Thompson CH, et al: Br J Cancer 59:296-302,1989.		Agent to improve staging and hence management of breast cancer patients. Development discontinued during Phase I due to problems with manufacture. Too early in development to assess clinical impact.
University of Glasgow	Twelves	CRUKD/97/016: A CRC Phase II study of PK1 [N-(2-hydroxypropyl) methacrylamide copolymer doxorubicin] in women with advanced breast cancer	17/17	2008	Seymour LW, Ferry DR, Kerr DJ, Rea D, Whitlock M, Poyner R, Boivin C, Hesslewood S, Twelves C, Blackie R, Schatzlein A, Jodrell D, Bissett D, Calvert H, Lind M, Robbins A, Burtles S, Duncan R, Cassidy J. Phase II studies of polymer-doxorubicin (PK1, FCE28068) in the treatment of breast, lung and colorectal cancer. Int J Oncol. 2009 Jun;34(6):1629-36.		Follow on Phase II trial to CRUKD/94/007 and companion trial to CRUKD/97/011 & CRUKD/97/014. Important because these trials were the first large scale trials of a polymer targeted agent in humans. The trials came from lab work supported by CRUK. Unlikely this would have been done by industry alone. Trial completed. One patient had a PR. PK1 shown to have some activity in lung and breast cancer, not felt to be sufficient to take forward into phase III evaluation. Development discontinued after Phase II due to insufficient activity. Demonstrated safety of polymer-based anticancer agents now widely employed in cancer therapeutics.
Charing Cross Hospital	Coombes	CRUKD/95/018: A Cancer Research (UK) randomized phase II study of idoxifene in patients with locally advanced and/or metastatic breast cancer resistant to tamoxifen.	56/56	2003	Johnston SR, Gumbrell LA, Evans TR, Coleman RE, Smith IE, Twelves CJ, Soukop M, Rea DW, Earl HM, Howell A, Jones A, Canney P, Powles TJ, Haynes BP, Nutley B, Grimshaw R, Jarman M, Halbert GW, Brampton M, Haviland J, Dowsett M, Coombes RC; Cancer Research UK Phase I/II Committee. A cancer research (UK) randomized phase II study of idoxifene in patients with locally advanced/metastatic breast cancer resistant to tamoxifen. Cancer Chemother Pharmacol. 2004 Apr;53(4):341-8.		Randomised evaluation of a 2nd generation tamoxifen analogue. Trial completed. Development discontinued after Phase II due to oestrogenic side effects. Too early in development to assess clinical impact.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Colorectal							
University of Birmingham	Kerr/Gray	QUASAR 1: A UKCCCR study of adjuvant chemotherapy for colorectal cancer. All eligible patients with resected colorectal cancer, no distant metastases and a definite-indication for chemotherapy will be randomised to high or low dose folinic acid, with or without additional levamisole	3239/2500	2007	QUASAR Collaborative Group 2007 Lancet 370: 2020-2029,	Yes	Chemotherapy with fluorouracil and folinic acid provides a small but significant improvement in survival for patients with node negative stage II colorectal cancer. This is important in guiding clinical decisions on treatment options for individual patients (e.g. probably not advisable for the over 70s) This is important in guiding clinical decisions on treatment options for individual patients (e.g. probably not advisable for the over 70s)
University of Birmingham	Bach	TREC: Transanal endoscopic microsurgery (TEM) and radiotherapy in early rectal cancer.	34/46	2014		Yes	Ongoing This is a fesability study with the aim to lead onto ta full scale phase III trial. This will impact on the treatment guidelines for early rectal cancer This is a fesability study with the aim to lead onto ta full scale phase III trial. This will impact on the treatment guidelines for early rectal cancer
Royal Surrey County Hospital NHS Trust	Middleton	CRUKE/10/042: A prospective, phase II, controlled, multicentre, randomized double-blind clinical trial comparing combination FOLFIRI and AZD7762 therapy with FOLFIRI therapy alone in advanced colon cancer	0/140	2013			The study drug was withdrawn by Astra Zeneca beforethe study could open.
Greater Glasgow and Clyde Health Board & University of Glasgow	Tim Iveson	SCOT - Short Course Oncology Therapy	4964/6400	2015		Yes	The aim is to determine whether the duration of adjuvant treatment in ths setting without signifícnatly undermining efficacy. If this were to be the case those would have a tremendous impact both on patient morbidity and the cost of treatment.The results of SCOT have the potential to change the global standard of care in adjuvant therapy in colorectal cancer This depends on the result. Potentially could change duration of adjuvant treatment both in the UK and worldwide. This depends on the result. Potentially could change duration of adjuvant treatment both in the UK and worldwide.
University of Oxford	Kerr	CRUKE/00/007: VICTOR: Phase III randomised, double blind, placebo controlled study of rofecoxib in colorectal cancer patients following potentially curative therapy	2434/7000	2010	JCO October 20, 2010 vol. 28 no. 30 4575-4580 Kerr DJ et al. Rofecoxib and cardiovascular adverse events in adjuvant treatment of colorectal cancer. N Engl J Med (2007); 357: 360-9 First Efficacy Data poster presented by Rachel Midgley at ASCO 2008, Chicago & ESMO 2008, Stockholm		On 30th September 2004 Merck &. Co., Inc. announced a voluntary worldwide withdrawal of VIOXX (rofecoxib). This trial is now closed to recruitment, but not to follow-up.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Oxford	Kennedy	CRUK/07/019: EnROL: Conventional versus laparoscopic surgery for colorectal cancer within an Enhanced Recovery Programme (supported by the Bobby Moore fund)	204/202	2012	EnROL: A multicentre randomised trial of conventional versus laparoscopic surgery for colorectal cancer within an enhanced recovery programme. BMC Cancer 2012, 12: 181 Planned for 2013	Yes	EnROL is the first multicentre trial of open versus laparopsopic surgery for colorectal cancer when both techniques have been optimised within an Enhanced Recovery Programme. It aims to examine the hypothesis that laparoscopic surgery within an enhanced recovery programme will provide superior postoperative outcomes when compared to conventional open resection of colorectal cancer within the same programme. Analysis of results currently underway. Potential to change practice so laparoscopic surgery becomes standard, replacing open surgery, in elective resections for bowel cancer. Potential to change practice so Enhanced Recovery Programme becomes widely implemented, replacing current post-surgical care (benefits beyond bowel cancer surgery). Planned
University of Oxford	Kerr	CRUKE/02/017: QUASAR 2: Adjuvant chemotherapy trial in colorectal cancer	1529/2240	2014	Presentations about recruitment etc at the annual NCRI Colorectal Meetings. Poster discussion of safety data at ESMO 2012		The main study objective is to compare the efficacy of the two regimens If the trial shows an improvement in disease free survival and overall survival then avastin could be adopted for wider use in the adjuvant setting.
University of Oxford	Sharma	CRUK/07/030: FOXFIRE: Randomised phase II-III trial of 5-Fluorouracil, Oxaliplatin, Folinic acid +/- Interventional Radio-Embolisation with yttrium-90 SIR-Spheres in metastatic colorectal cancer (supported by the Bobby Moore fund)	240/320	2016	Sharma RA et al., FOXFIRE: A Phase III Clinical Trial of Chemo-radio-embolisation as First-line Treatment of Liver Metastases in Patients with Colorectal Cancer. Clin Oncol 2008, 20: 261-263. FOXFIRE trial update side meeting, NCRI conference Birmingham, October 2009 FOXFIRE trial upadte side meeting, NCRI conference Liverpool, November 2010		If this trial shows an improvement in overall survival for this patient group, radioembolisation will be incorporated into the first-line treatment for metastastic colorectal cancer. Other large randomised studies of this technology in the treatment of liver metastases from other cancers are likely to follow. The trial will also provide essential quality of life and healthcare economic data which will allow national bodies to make decisions regarding funding this treatment.
University of Leeds	Seymour	CRUK/05/016: PICCOLO Trial. Panitumumab, Irinotecan & Ciclosporin in COLOrectal cancer therapy. A randomised clinical trial of treatment for fluorouracil-resistant advanced colorectal cancer comparing standard single-agent irinotecan versus irinotecan plus panitumumab and versus irinotecan plus ciclosporin	1198/1324	2011	Seymour, M. et al, 2013. Panitumumab and irinotecan versus irinotecan alone for patients with KRAS wild-type, fluorouracil-resistant advanced colorectal cancer (PICCOLO): a prospectively stratified randomised trial. The LANCET oncology, Volume 14, Issue 8, July 2013, Pages 749–759. Currently in preparation. Ir vs IrCs comparison has been submitted for publication	No	Closed to accrual. Ir vs. IrCs 672 patients were randomised between Ir and IrCs. ITT analysis showed 179/335 (53.4%) patients to be progression-free at 12 weeks in the Ir arm and 159/337 (47.2%) in the IrCs arm. Ir vs. IrPan 696 patients were randomised between Ir and IrPan, 460 in the primary efficacy population (no previous anti-EGFR targeted therapy, KRAS wildtype status). Both regimens were well tolerated, though higher rates of diarrhoea, skin and haematological toxicity were seen with IrPan than Ir. Overall survival improvement with IrPan did not reach statistical significance (HR=0.91, 95% CI [0.73, 1.14], p=0.44). BMD and bone biomarkers in a sub-set of patients taking part in the AZURE study. Yes though quite hard to evidence this. We demonstrated harmful effect of panitumumab when given to patients with tumours wild-type for KRAS but with mutations in certain other genes (NRAS, BRAF, PIK3CA) and this information has now been corroborated in another study and is now widely used in patient selection. Some commercial testing kits now include these genes.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
MRC	Seymour	CRUK/03/003: FOCUS-2: Chemotherapy for metastatic colorectal cancer: optimum treatment choices when full-dose combination chemotherapy is not indicated	460/460	2007	Seymour MT et al., Chemotherapy options in elderly and frail patients with metastatic colorectal cancer (MRC FOCUS2): an open-label, randomised factorial trial. The Lancet 2011; 377:1749-59. Seymour MT et al., Chemotherapy options in elderly and frail patients with metastatic colorectal cancer (MRC FOCUS2): an open-label, randomised factorial trial. The Lancet 2011; 377:1749-59. First results were presented at ASCO 2007 in Chicago as a poster discussion. They have subsequently been presented at ECCO 2007, Barcelona as a plenary presentation. A poster was displayed at the NCRI conference in Birmingham October 2007 and there was a plenary presentation at SIOG in November 2007.	Yes	Unique study, largest cancer trial to specifically target elderly patients in colorectal cancer. The trial demonstrated that it is possible to dose reduce for elderly patients without causing reduced survival and that it is possible to dose increase these patients after 6 weeks without increased toxicity. The trial demonstrated that it is possible to dose reduce for elderly patients without causing reduced survival and that it is possible to dose increase these patients after 6 weeks without increased toxicity.
MRC	Maughan	CRUK/05/001: COIN: Phase III trial comparing continuous or intermittent palliative combination chemotherapy in first line treatment of metastatic colorectal cancer	2384/2421	2009	Maughan TS et al., Addition of cetuximab to oxaliplatin-based first-line combination chemotherapy for treatment of advanced colorectal cancer: results of the randomised phase 3 MRC COIN trial. Lancet, 2011; 377:2103-2114. Adams RA et al., Intermittent versus continuous oxaliplatin and fluoropyrimidine combination chemotherapy for first-line treatment of advanced colorectal cancer: results of the randomised phase 3 MRC COIN trial. Lancet Oncology,2011; 12:642-653. Adams RA et al., Toxicity associated with combination oxaliplatin plus fluoropyrimidine with or without cetuximab in the MRC COIN trial experience. Br. J. Cancer 2009; 100: 251–8. Adams, R et al., Cetuximab therapy in first-line metastatic colorectal cancer and intermittent palliative chemotherapy: review of the COIN trial. Expert Review of Anticancer Therapy, 8 (8): 1237-1245 Aug 2008. J Clin Oncol 25 (suppl 18): A-4070, 2007. Vale, CL, et al., Does anti-EGFR therapy improve outcome in advanced colorectal cancer? A systematic review and meta-analysis. Cancer Treatment Reviews 2012 38(6): 618-625 Maughan TS et al., Addition of cetuximab to oxaliplatin-based first-line combination chemotherapy for treatment of advanced colorectal cancer: results of the randomised phase 3 MRC COIN trial. Lancet, 2011; 377:2103-2114. Adams RA et al., Intermittent versus continuous oxaliplatin and fluoropyrimidine combination chemotherapy for first-line treatment of advanced colorectal cancer: results of the randomised phase 3 MRC COIN trial. Lancet Oncology,2011; 12:642-653.	Yes	COIN A vs B: COIN has not confirmed a benefit of addition of cetuximab to oxaliplatin-based chemotherapy in first-line treatment of patients with advanced colorectal cancer. Cetuximab increases response rate, with no evidence of benefit in progression-free or overall survival in KRAS wild-type patients or even in patients selected by additional mutational analysis of their tumours. The use of cetuximab in combination with oxaliplatin and capecitabine in firstline chemotherapy in patients with widespread metastases cannot be recommended. However, the trial showed the powerful effect of the presence of specific mutations (KRAS, BRAF and NRAS) in the tumour on prognosis and this should influence future clinical trials in bowel cancer. COIN A vs C: COIN did not show non-inferiority of intermittent compared with continuous chemotherapy for advanced colorectal cancer in terms of overall survival, chemotherapy-free intervals remain a treatment option for some patients with advanced colorectal cancer, offering reduced time on chemotherapy, reduced cumulative toxic effects, and improved quality of life. Subgroup analyses suggest that patients with normal baseline platelet counts could gain the benefits of intermittent chemotherapy without detriment in survival, whereas those with raised baseline platelet counts have impaired survival and quality of life with intermittent chemotherapy and should not receive a treatment break. The outcomes of this trial have already had major influence on the emerging international consensus that combinations of active agents can have paradoxiical disappointing or even negative effects.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
					Adams RA et al., Toxicity associated with combination oxaliplatin plus fluoropyrimidine with or without cetuximab in the MRC COIN trial experience. Br. J. Cancer 2009; 100: 251–8. Adams, R et al., Cetuximab therapy in first-line metastatic colorectal cancer and intermittent palliative chemotherapy: review of the COIN trial. Expert Review of Anticancer Therapy, 8 (8): 1237-1245 Aug 2008. J Clin Oncol 25 (suppl 18): A-4070, 2007. Vale, CL, et al., Does anti-EGFR therapy improve outcome in advanced colorectal cancer? A systematic review and meta-analysis. Cancer Treatment Reviews 2012 38(6): 618-625		
Oxford University/MRC	Maughan	Molecular selection of therapy in metastatic colorectal cancer: a molecularly stratified randomised controlled trial programme (FOCUS4)	0/1536	2018 (but there will be separate primary analyses at various times)	Kaplan et al. paper on design of FOCUS4, JCO in press 2013 Poster Presentation at ASCO 2013 - FOCUS4: A molecularly stratified randomised controlled trial programme for patients with metastatic colorectal cancer		New streamlined and efficient design for stratified trials Aim: To classify patients with stable metastatic colorectal cancer into molecular subgroups according to their biomarker profile and investigate the efficacy of targeted new novel agents against placebo in terms of progression-free-survival. The trial could possibly change practice.
University of Southampton	Primrose	CRUK/00/002: Perioperative chemotherapy in patients with resectable liver metastases of colorectal origin (EORTC Intergroup study 40983) and Pre and Post Operative Chemotherapy with Oxaliplatin 5-FU/LV vs surgery alone in resectable liver metastases from colorectal origin (EORTC Intergroup study 40983)	76/unknown target	2008	Nordlinger B, Sorbye H, Glimelius B, Poston GJ, Schlag PM, Rougier P, Bechstein WO, Primrose JN, et al (2008). Perioperative chemotherapy with FOLFOX4 and surgery versus surgery alone for resectable liver metastases from colorectal cancer (EORTC Intergroup trial 40983): a randomised controlled trial. Lancet 371, 1007-1016. PMID 18358928. Sorbye H et al., (2012) Predictive Factors for the Benefit of Perioperative FOLFOX for Resectable Liver Metastasis in Colorectal Cancer Patients (EORTC Intergroup Trial 40983). Ann Surg 2012; 255(3):534-539. Primrose J et al., EPOC Trial: EORTC liver metastases intergroup randomized phase III study 40983 - long-term survival results NCRI Cancer Conference, Liverpool 2012, Abstract Reference 345	Yes	Chemotherapy plus surgery likely to become standard of care. Likely to change NICE recommendations.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Southampton	Primrose	CRUK/06/031: New EPOC A: Peri-operative chemotherapy in patients with resectable colorectal liver metastases - does the addition of an anti-EGF receptor antibody improve progression free survival?	272/288	2018	A randomized clinical trial of chemotherapy compared to chemotherapy in combination with cetuximab in k-RAS wild-type patients with operable metastases from colorectal cancer: The new EPOC study J Clin Oncol 31, 2013 (suppl; abstr 3504)John Neil Primrose, Stephen Falk, Meg Finch-Jones, Juan W. Valle, David Sherlock, Joanne Hornbuckle, James Gardner-Thorpe, David Smith, Charles Imber, Tamas Hickish, Brian Davidson, David Cunningham, Graeme John Poston, Tim Maughan, Myrrdyn Rees, Louise Stanton, Louisa Little, Megan Bowers, Wendy Wood, John A. Bridgewater; Southampton General Hospital, Southampton, United Kingdom; Bristol Haematology and Oncology Centre, Bristol, United Kingdom; University Hospitals Bristol, Bristol, United Kingdom; University of Manchester, Manchester Academic Health Science Centre; Department of Medical Oncology, The Christie NHS Foundation Trust, Manchester, United Kingdom; Pennine Acute Hospitals NHS Trust, Manchester, United Kingdom; Weston Park Hospital, Sheffield, United Kingdom; Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom; Clatterbridge Centre for Oncology NHS Foundation Trust, Wirral, United Kingdom; University College London Hospitals NHS Foundation Trust, London, United Kingdom; Royal Bournemouth Hospital, Bournemouth, United Kingdom; University College London, London, United Kingdom; The Royal Marsden Hospital NHS Foundation Trust, London, United Kingdom; University Hospital Aintree, Liverpool, United Kingdom; Gray Institute for Radiation Oncology and Biology, University of Oxford, Oxford, United Kingdom; North Hampshire Hospital, Basingstoke, United Kingdom; University of Southampton Clinical Trials Unit, Southampton, United Kingdom; University College London Cancer Institute, London, United Kingdom	Yes	In patients with resectable liver metastases and K-RAS wt tumours the addition of cetuximab to chemotherapy is not beneficial May lead to change in NICE guidleines
University of Southampton	Primrose	CRUK/06/031: New Epoc B: A exploratory study to investigate the optimal scheduling of chemotherapy in patients with operable colorectal liver metastases	20/78	2014		No	Feasibility study demonstrated that a large phase III trial of this deisgn would not be possible.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Cardiff University	Gollins	CRUK/10/020: COPERNICUS: A stratified Phase II study of neoadjuvant chemotherapy with or without the addition of panitumumab given before SCPRT as treatment for patients with MRI-staged operable rectal cancer at high risk of metastatic relapse	34/62	2014		Maybe	This is a phase II trial. The result will be used to determine the experimental arm of a future phase III which, if positive, would lead to a change in clinical practice. COPERNICUS is the only trial which looks at the efficacy of treating patients with neo-adjuvant chemo and may potentially be compared to other UK trials such as RAPIDO, PROSPECT and FOXTROT
Cardiff University	Thomas	CRUKE/09/023: FOLFERA:A randomised phase II study of Irinotecan, 5-Fluorouracil and Folinic Acid (FOLFIRI) with or without the addition of an endothelin receptor antagonist in patients with metastatic colorectal cancer after failure of Oxaliplatin-containing chemotherapy	111/122	2013			Unlikely to have any impact due to lack of efficacy. Unlikely to have any impact due to lack of efficacy.
Cardiff University	Wilson	CRUKE/09/037: FOLFIRANIB: A randomised phase II study of Irinotecan, 5-Fluorouracil and Folinic Acid with or without the addition of cediranib in the first line treatment of patients with metastatic colorectal cancer.	0/132	2012		No	N/A Study shelved N/A Study shelved
Royal Free & University College Medical School	Poston	CRUK/03/002: UK Centres of EORTC CLOCC Trial: a randomised phase II EORTC trial evaluating the role of radiofrequency ablation in addition to chemotherapy in patients with unresectable colorectal liver metastases	7/390		Ruers, T; Van Coevorden, F; Pierie, J; et al. Radiofrequency ablation (RFA) combined with chemotherapy for unresectable colorectal liver metastases (CRC LM): Interim results of a randomised phase II study of the EORTC-NCRI CCSG-ALM Intergroup 40004 (CLOCC). Ann. Onc. 21: I41-I42 Suppl. 1 Apr 2010. Evrard, S. Intraoperative radiofrequency ablation of liver metastases: age of reason. Bull. Du. Can. 97 (1): 91-96 Jan 2010. Presented at ASCO 2010.		This phase III EORTC trial is the first study to test the efficacy of RFA in combination with chemotherapy in the treatment of unresectable colorectal liver metastases Final results were presented indicating that benefit in overall survival of adding RFA to chemotherapy is uncertain, and that longer follow-up is needed. First prospective study of this combination of therapies.
Royal Free & University College Medical School	Glynne-Jones	CRUK/03/009: CHRONICLE: Chemotherapy or no chemotherapy in clear margins after preoperative chemoradiation in locally advanced rectal cancer. A RCT of capecitabine plus oxaliplatin vs control	113/800		Results of a randomised phase III trial in locally advanced rectal cancer after neoadjuvant chemoradiation randomising postoperative adjuvant capecitabine plus oxaliplatin (Xelox) versus control. In press Glynne-Jones R, Meadows H, Wood W. Chemotherapy or no chemotherapy in clear margins after neoadjuvant chemoradiation in locally advanced rectal cancer: CHRONICLE. A randomised phase III trial of control vs. capecitabine plus oxaliplatin. Clin Oncol (R Coll Radiol). 2007 Jun;19(5):327-9. ESMO 2013	No	Trial was stopped early because of poor recruitment. The recruited patients are being followed up, and the MRC will perform a later analysis. - The Chronicle trial did not detect a significant difference in DFS or OS for adjuvant XELOX. No definitive conclusion can be drawn from a trial with inadequate numbers, poor compliance and insufficient statistical power. We remain unsure of the advantage of additional adjuvant chemotherapy following CRT, either in terms of 5FU alone or combined with oxaliplatin, and of specific subgroups who might benefit most/least. Although unable to provide a definitive result, this trial in terms of the hazard ratio of

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Royal Free & University College Medical School	Ledermann	CRUK/01/011: ACT II: The second UK phase III anal cancer trial: A trial of chemoradiation and maintenance therapy for patients with anal cancer.	940/950	2009	Mitomycin or cisplatin chemoradiation with or without maintenance chemotherapy for treatment of squamous-cell carcinoma of the anus (ACT II): a randomised, phase 3, open-label, 2x2 Lancet Oncol 2013; 14: 516–24 James, R; Meadows, H; Wan, S, ACT II: The second UK phase III anal cancer trial. Clinical Oncology, 17 (5): 364-366 Aug 2005. James R, Clin Oncol (R Coll Radiol), 2005; 17(5); 364-366. James R; Wan S; Glynne-Jones R et al. JCO, 27 (18): - Suppl. S Jun 20 2009 End Points in Anal Cancer: Hopes for a Common Language Published Ahead of Print on March 17, 2014 as 10.1200/JCO.2014.55.1515 - Prognostic factors for recurrence and survival in anal cancer: generating hypotheses from the mature outcomes of the ACT I trial. Cancer, Vol. 119, Issue 4 (article first published online 25/09/2012) - Tumor-related and treatment-related colostomy-free survival (CFS) following chemoradiation (CRT) using mitomycin (MMC) or cisplatin (CisP), with or without maintenance 5FU/CisP - Patient and tumor characteristics impacting on lymph node metastases rate (LNMR) in squamous cell carcinoma of the anal canal and margin (SCCA) using data from the NCRI randomized phase III ACT II trial: Implications for radiotherapy target volume. In pre Presented at ASCO 2003 and 2009. Oral presentation at ASCO 2012: J Clin Oncol 30, 2012 (suppl; abstr 4004) Poster presentation at ASCO 2012: J Clin Oncol 30, 2012 (suppl; abstr 4029) Poster presentation at NCRI 2013 and NCRI 2014	No	29% of pts not in CR at 11 weeks achieved CR at 26 weeks. Early surgical salvage would not have been appropriate for these pts. We recommend assessment at 26 weeks in future trials. In conclusion, we require consensus on unambiguous end point definitions.End points should be relevant to clinicians and patients and we recommend DFS as primary end point with other end points reported to provide datain this rare disease: response at 18 to 26weeks, CFS, cancer-specific survival, overall survival, acute toxicity including treatment-related deaths, late toxicity, and QoL. We hope this letter will prompt an international consensus statement, ensuring a broad and objective input from recognized experts. Mitomycin vs cisplatin randomization: No difference in colostomy rate. Maintenance randomization: No difference in RFS (3-years 75%) or OS. The ACT II trial results demonstrate a low rate of pelvic failure requiring surgical salvage In ACT II, neither the type of CRT (5FU/CisP vs. 5FU/MMC) nor maintenance chemotherapy improved CFS. 34% - Excellent CR rate at 6 months - 83% v 84% 27% of pts not in CR at 11 weeks achieved CR at 26 weeks. We recommend assessment at 26 weeks in future trials. In the ACT II trial for stages cT1 and cT2, the baseline risk of clinical nodal involvement is 21% and in stages cT3 or cT4 is 46%. We conclude ACT II field sizes were rationally applied . The introduction of magnetic resonance imaging (MRI) after 2005 may have influenced the baseline nodal staging, and its utility in intensity-modulated radiotherapy (IMRT) needs evaluation. Chemoradiotherapy (CRT) with 5-fluorouracil (5-FU) and mitomycin-C (MMC) is standard treatment for anal cancer. This trial addressed two questions: whether (i) replacing MMC with cisplatin (CDDP) improves the complete response (CR) rate, and (ii) two cycles of maintenance chemotherapy after CRT reduces recurrence. High CR (95%) and RFS (75% at 3 yrs) rates were achieved with this CRT. This excellent outcome may have been influenced by the absence of a gap in the RT schedule. There was no difference in CR rates between MMC and CDDP or in RFS rates with or without maintenance chemotherapy. 5-FU, MMC with RT remains the standard of care. N/K

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Royal Free & University College Medical School	Ledermann	CRUK/87/001: ACT I trial: a phase III trial to assess the impact on local failure of adding chemotherapy to radiotherapy in the primary management of anal carcinoma	585/585	1996	UKCCR Anal Cancer Trial Working Party. Epidermoid anal cancer: results from the UKCCCR randomised trial of radiotherapy alone versus radiotherapy, 5-fluorouracil, and mitomycin. UKCCCR Anal Cancer Trial Working Party. UK Co-ordinating Committee on Cancer Research. Lancet 1996 Oct 19;348(9034):1049-54. UKCCCR Anal Trial Working Party (1996) Epidermoid anal cancer:results from the UKCCCR randomised trial of radiotherapy alone versus radiotherapy, 5-fluorouracil and mitomycin. The Lancet, vol 348, No. 9034, 1049-1054. J Northover et al., Chemoradiation for the treatment of epidermoid anal cancer: 13-year follow-up of the first randomised UKCCCR Anal Cancer Trial (ACT I), British Journal of Cancer 102, 1123-1128 (16 March 2010), doi:10.1038/sj.bjc.6605605 Full Paper	N/K	Demonstrated an improvement in local treatment failure rate in patients receiving 5-FU and mitomycin C in addition to radiotherapy alone. First randomised trial to show benefit of chemoradiation over radiation. The protocol became the standard treatment N/K
University College London	Glynne-Jones	CRUK/10/003: BACCHUS: Bevacizumab And Combination CHemotherapy in rectal cancer Until Surgery A Phase II, Multicentre, Open-label, Randomised Study of Neoadjuvant Chemotherapy and Bevacizumab in Patients with MRI defined High-Risk Cancer of the Rectum	10/60	2017	Poster presented at GI ASCO May 2014 in the trials in progress session Abstract ID: #TPS3653		
University College London	Gollins	CRUK/07/043: EXCITE: Erbitux, Xeloda, Campto, Irradiation Then Excision for locally advanced rectal cancer. (North West Clinical Oncology Group-04 on behalf of the NCRI rectal cancer subgroup) (Supported by the Bobby Moore Fund).	82/80	2012	EXCITE: A PHASE II TRIAL OF PREOPERATIVE CETUXIMAB, IRINOTECAN AND CAPECITABINE PLUS RADIOTHERAPY (RT) IN MRI-DEFINED LOCALLY ADVANCED RECTAL CANCER (LARC) J Clin Oncol 32, 2014 (suppl 3; abstr 458) EXCITE: A PHASE II TRIAL OF PREOPERATIVE CETUXIMAB, IRINOTECAN AND CAPECITABINE PLUS RADIOTHERAPY (RT) IN MRI-DEFINED LOCALLY ADVANCED RECTAL CANCER (LARC) J Clin Oncol 32, 2014 (suppl 3; abstr 458) ASCO 2014		GI ASCO 2014
University College London	O'Bichere	CRUK/08/038: ISAAC: A randomised trial of Initial Surgery in Advanced Asymptomatic Colorectal cancer patients receiving chemotherapy for metastatic disease	24/500	N/K		No	Trial did not progress to full phase III. Publication planned to discuss the difficulties in carrying out surgical trials in this patient group. N/A N/A
University College London	Sebag-Montefiore	CRUK/08/032: ARISTOTLE: A phase III trial comparing standard versus novel CRT as pre-operative treatment for MRI defined locally advanced rectal cancer	253/916	2017	Quality assurance of target volume definition in the ARISTOTLE phase III rectal cancer trial - initial assessment Radiotherapy and Oncology, Volume 103, Suppliment 1, May 2012, Page S380 - The development of a conformal radiotherapy protocol for the phase III ARISTOTLE rectal cancer trial Radiotherapy	Yes	This RCT has the most advanced prospective radiotherapy QA programme ever in LARC. The early CI work shows promise as a potentially automated system for QA, useful for training/re-validation.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
					and Oncology, Volume 106, Suppliment 2 (2013), abstr EP-1307		
University College London	Glynne-Jones	XERXES: Examining the role of early neoadjuvant and synchronous Erbitux in preoperative chemoradiotherapy using Xeloda followed by excisional surgery	22/60	2012			
Centre for Drug Development							
University College London	Hochhauser	CRUKD/12/015: PANtHER a Phase I/II study of EGFR inhibitor AZD8931 in combination with FOLFIRI to determine the importance of schedule and activity in colorectal cancer	0/64	2017			First time for this combination in this group of patients. The outcome of this trial could inform future national treatment strategies for this patient population. The outcome of this trial could inform future national treatment strategies for this patient population.
University of Manchester/Christie Hospital	Saunders	CRUKD/10/013: Dual REctal Angiogenesis or MEK inhibition radioTHERAPY trial - DREAM Therapy - RT + AZD6244 (Selumetinib) or AZD2171 (Cediranib) in colorectal cancer	14/48	2014			This is the first chemoradiotherapy study in rectal cancer with these IMPs (AZD6244 and cediranib) targeting MEK and angiogenesis, with extensive associated translational research, designed to identify imaging or serological biomarkers that could be incorporated into subsequent phase II trials. Trial ongoing. If successful results will lead to Phase II and Phase III trials.
University of Manchester/Christie Hospital	Hawkins	CRUKD/07/064: A Cancer Research UK Phase I trial of Adoptive Transfer of Autologous Tumour Antigen-Specific T Cells (MFE-z T cells) with Pre-conditioning Chemotherapy and Intravenous IL2 in Patients with Advanced CEA Positive Tumours	16/16	2011	RD Guest, N Kirillova, S Mowbray, H Gornall, D G Rothwell, E J Cheadle, E Austin, K Smith, S M Watt, K Kuhlcke, N Westwood, F Thistlethwaite, R E Hawkins, D E Gilham.. Definition and application of Good Manufacturing Process-compliant production of CEA-specific Chimeric Antigen Receptor expressing T cells for Phase I/II clinical trial. Cancer Immunol Immunother; published on line 5 Nov 2013		First time in patients for this treatment using chimeric T cells. Trial recently closed to recruitment. Data being cleaned. Too early in development to assess clinical impact.
University of Southampton	Ottensmeier	CRUKD/06/053: A Cancer Research UK Phase I trial of anti-CEA DNA vaccine (ACVA) in patients with CEA expressing carcinoma	27/27	2013	ASCO Meeting Abstracts 2010 28: 2579		First time in patients for this vaccine. Trial is in closedown. The data show 1) vaccine works better in patients with low volume disease, 2) even in patients with end stage cancer the vaccine can stimulate the immune system in the desired way, 3) the immune effects appear to correlate with outcome (time on study); survival data under evaluation. The data will be used to develop a randomized phase II study in colorectal cancer. The endpoints will be time to disease progression and survival.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Manchester/Christie Hospital	Hawkins	CRUKD/04/040: A Cancer Research UK Phase II trial immunologically evaluating 5T4-MVA (TroVax) in patients undergoing surgical resection of colorectal liver metastases	20/20	2007	Elkord E, Dangoor A, Drury NL, Harrop R, Burt DJ, Drijfhout JW, Hamer C, Andrews D, Naylor S, Sherlock D, Hawkins RE, Stern PL. An MVA-based Vaccine Targeting the Oncofetal Antigen 5T4 in Patients Undergoing Surgical Resection of Colorectal Cancer Liver Metastases. J Immunother. 2008 Nov-Dec;31(9):820-9. Elkord E, Dangoor A, et al. Immune evasion mechanisms in colorectal cancer liver metastasis patients vaccinated with TroVax (MVA-5T4). Cancer Immunol Immunother 2009 Oct;58(10):1657-67. Dangoor A, Burt D, et al. A vaccinia-based vaccine (TroVax) targeting the oncofetal antigen 5T4 administered before and after surgical resection of colorectal cancer liver metastases: Phase II trial. J Clin Oncol 2006 24 18 Supp Pt 118S. ASCO Meeting Abstracts 2006 24: 2574		Translational research study demonstrating immunological effects of a novel antitumour vaccine. Trial completed. Agent in Phase III development. Too early in development to assess clinical impact.
Royal Free & University College Medical School	Begent	CRUKD/01/018: A CR-UK Phase I/II trial of ADEPT MFE23-CPG1 glycosylated fusion protein and ZD2767P in patients with advanced colorectal carcinoma & other CEA producing tumours	43/43	2005	Mayer A, Francis RJ, Sharma SK, Tolner B, Springer CJ, Martin J, Boxer GM, Bell J, Green AJ, Hartley JA, Cruickshank C, Wren J, Chester KA, Begent RH. A phase I study of single administration of antibody-directed enzyme prodrug therapy with the recombinant anti-carcinoembryonic antigen antibody-enzyme fusion protein MFECP1 and a bis-iodo phenol mustard prodrug. Clin Cancer Res. 2006 Nov 1;12(21):6509-16.		First time in patients for this novel combination of a fusion protein enzyme natibody fragment in ADEPT. Follow up trial to CRUKD/97/012. CR UK was involved in developing ADEPT and these agents. Trial completed. Too early in development to assess clinical impact.
University of Aberdeen	Cassidy	CRUKD/97/011: A CRC Phase II study of PK1 [N-(2-hydroxypropyl)methacrylamide copolymer doxorubicin]: in advanced colorectal cancer	16/16	2005	Seymour LW, Ferry DR, Kerr DJ, Rea D, Whitlock M, Poyner R, Boivin C, Hesslewood S, Twelves C, Blackie R, Schatzlein A, Jodrell D, Bissett D, Calvert H, Lind M, Robbins A, Burtles S, Duncan R, Cassidy J. Phase II studies of polymer-doxorubicin (PK1, FCE28068) in the treatment of breast, lung and colorectal cancer. Int J Oncol. 2009 Jun;34(6):1629-36.		Follow on Phase II trial to CRUKD/94/007 and companion trial to CRUKD/97/014 & CRUKD/97/016. Important because these trials were the first large scale trials of a polymer targeted agent in humans. Unlikely this would have been done by industry alone and also came from lab work supported by CRUK. Trial completed. PK1 shown to be inactive in colorectal cancer. Development discontinued after Phase II due to insufficient activity. Too early in development to assess clinical impact.
Royal Free Hospital	Begent	CRUKD/96/019: A phase I trial of Radioimmunoguided surgery (RIGS) with 125-iodine labelled genetically engineered single chain Fv antibody to carcinoembryonic antigen (CEA) in primary or recurrent colorectal and other CEA-producing carcinoma.	35/35	1999	Mayer A, Tsiompanou E, O'Malley D, Boxer GM, Bhatia J, Flynn AA, Chester KA, Davidson BR, Lewis AA, Winslet MC, Dhillon AP, Hilson AJ, Begent RH. Radioimmunoguided surgery in colorectal cancer using a genetically engineered anti-CEA single-chain Fv antibody. Clin Cancer Res. 2000 May;6(5):1711-9.		First in patient study of radioimmunoguided surgery with this agent developed by CR UK funded research. Trial completed. Too early in development to assess clinical impact.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Royal Free Hospital	Begent	CRUKD/97/012: A phase I trial of antibody directed enzyme prodrug therapy (ADEPT) in patients with advanced colorectal carcinoma or other CEA producing tumours	28/28	2001	Francis RJ, Sharma SK, Springer C, Green AJ, Hope-Stone LD, Sena L, Martin J, Adamson KL, Robbins A, Gumbrell L, O'Malley D, Tsiompanou E, Shahbakhti H, Webley S, Hochhauser D, Hilson AJ, Blakey D, Begent RH. A phase I trial of antibody directed enzyme prodrug therapy (ADEPT) in patients with advanced colorectal carcinoma or other CEA producing tumours. Br J Cancer. 2002 Sep 9;87(6):600-7.		First time in patients for this treatment. Trial completed. Led to optimised therapy in trial CRUKD/01/018.
University of Nottingham	Hardcastle	CRUKD/94/008: A randomized double-blind phase II survival study comparing immunization with the anti-idiotypic monoclonal antibody 105AD7 against placebo in advanced colorectal cancer	162/165	2000	Maxwell-Armstrong CA, Durrant LG, Buckley TJ, Scholefield JH, Robins RA, Fielding K, Monson JR, Guillou P, Calvert H, Carmichael J, Hardcastle JD. Randomized double-blind phase II survival study comparing immunization with the anti-idiotypic monoclonal antibody 105AD7 against placebo in advanced colorectal cancer. Br J Cancer. 2001 Jun 1;84(11):1443-6.		Follow on trial to CRUKD/92/007. Trial completed. Agent in Phase II development. Too early in development to assess clinical impact.
University of Nottingham	Hardcastle	CRUKD/92/007: Induction of anti-tumour responses in patients with primary colorectal carcinoma receiving human anti-idiotypic monoclonal antibodies	78/90	1993	Denton GW, Durrant LG, Hardcastle JD, Austin EB, Sewell HF, Robins RA. Clinical outcome of colorectal cancer patients treated with human monoclonal anti-idiotypic antibody. Int J Cancer. 1994 Apr 1;57(1):10-4.		Early trial of anti-idiotypic antibodies. Trial completed. Led to trials of 105AD7: a Phase II in colorectal cancer: CRUKD/94/008 and a paediatric osteosarcoma trial: CRUKD/98/009. Agent in Phase II development. Optimal antibody from this trial picked for randomised phase II trials in colorectal cancer and paediatric osteosarcoma.
Gynaecology							
University of Birmingham	Poole	NEO ESCAPE - Neoadjuvant Extended Sequential Chemotherapy with Adjuvant Postoperative treatment for Epithelial Ovarian Cancer	75/88	2012	POOLE CJ, MARSHALL A, HIGGINS H, FLETCHER J, WILLIAMS S, LO N, FERNANDO I, OSBORNE R, CRAWFORD M, RAFII S, GILL S, DUNN JA. (2012) Results from the phase II Neo-Escape trial of Neoadjuvant Extended Sequential Chemotherapy with Adjuvant Postoperative treatment for Epithelial non-mucinous advanced inoperable peritoneal malignancy. The National Cancer Research Institute Cancer Conference November, Liverpool, UK. POOLE CJ et al., (2012) ASCO (American Society of Clinical Oncology) Annual Meeting, Chicago, USA. Published in Journal of Clinical Oncology 30(suppl); abstract 5046.		Randomised phase II study looking a different sequencing and of existing drugs for this condition. The responses, toxicities and tolerability will inform new studies in this area. The results of this study will inform new trials in this area
University of Birmingham	Luesley	DESKTOP III: Randomised multicentre study to compare the efficacy of additional tumour debulking surgery versus chemotherapy alone for recurrent platinum sensitive ovarian cancer	0/100	2017		Yes	This pan European trial is of particular relevance to the UK where a paradigm shift in the radical approach to surgical intervention is a possibility. Could change clinical practice

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Glasgow and Greater Glasgow and Clyde Health Board	Kaye	CRUK/04/010: SCOTROC 4: A prospective multicentre randomised trial of carboplatin flat dosing vs intrapatient dose escalation in first line chemo. of ovarian, fallopian tube and peritoneal cancers	900/1000	2010	Banerjee S, Rustin G, Paul J, Williams C, Pledge S, Gabra H, et al. A multicenter, randomized trial of flat dosing versus intrapatient dose escalation of single-agent carboplatin as first-line chemotherapy for advanced ovarian cancer: an SGCTG (SCOTROC 4) and ANZGOG study on behalf of GCIG. Annals of Oncology. 2013;24(3):679-87. KAYE, S. B., VASEY, P., RUSTIN, G., PLEDGE, S., WILLIAMS, C., GABRA, H., SKAILES, G., LAMONT, A., LEWSLEY, L., PAUL, J. & SCOTTISH GYNAECOL CANC, T. 2009. Randomized trial of intrapatient dose escalation of single agent carboplatin as first-line treatment for advanced ovarian cancer: An SGCTG study (SCOTROC 4). Journal of Clinical Oncology, 27, 5537.	Yes	Study definitively demonstrated that intra-patient dose escalation of carboplatin does not improve efficacy. This should lead to the practice of dose escalatiion based on nadir blood counts being abandoned. This should lead to the practice of dose escalatiion based on nadir blood counts being abandoned.
University of Glasgow and Greater Glasgow and Clyde Health Board	Green	CRUK/07/029: CCC-1 : Randomised Phase III Trial of Paclitaxel plus Carboplatin (tc) therapy versus Irinotecan plus Cisplatin therapy (cpt-p) as First Line Chemotherapy for Clear cell Carcinoma of the Ovary (JGOG 3017)	7/50	2014		Yes	This is the first definitive RCT restricted to this histological sub-type; it thus could have a major impact on the treatment of these patients who do relatively badly on standard therapy. This study is being conducted with the Japanese Gynaecological Oncology Group. The results of the trial will be used to determine the most appropriate treatment for patients with clear cell carcinoma of the ovary The results of the trial will be used to determine the most appropriate treatment for patients with clear cell carcinoma of the ovary
University of Leicester	Symonds	CRUK/10/001: CIRRCa - Cediranib in recurrent cervical cancer.	66/80	2014			Phase II study determing whether or not Recentin is worth pursuing in the phase II setting in relapsed cervical cancer. Will also provide a preliminary inidcation of ist possible worth in the adjuvant setting. Results of this study may provide basis for phase II/III studies in patients with locally advanced disease receiving primary treatment by radiotherapy and cisplatin. Results of this study may provide basis for phase II/III studies in patients with locally advanced disease receiving primary treatment by radiotherapy and cisplatin.
Cambridge University Hospital	Hatcher	CRUK/11/051: A Phase III randomised trial of gemcitabine plus docetaxel followed by doxorubicin versus observation for uterus limited, high grade uterine leiomyosarcoma (International Rare Cancers Initiative study)	0/50	2020	Presented at British Sarcoma Group Conference, East Midlands Conference Centre, Nottingham 27th Feb 2013- 01st March 2013 by UK Chief Investigator - Dr Helen Hatcher	Yes	This is a phase III trial to assess whether adjuvantchemotherpay (SARC GT-D regimen) improves survival in high grade uterine LMS. This study is part of Interational Rare Cancer Initiative and is being led by the GOG in the USA. It has the potential to change the management of uterine sarcomas and the design may impact on the development of other rare sarcoma trials in an international collaboration It has the potential to change the management of uterine sarcomas and the design may impact on the development of other rare sarcoma trials in an international collaboration

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Edinburgh University	Gourley	CRUKE/12/028: LOGS Study- A randomised 2 arm phase III study to assess the efficacy of MEK inhibitor GSK1120212 in patients with recurrent or progressive low grade serous ovarian cancer following primary platinum based chemotherapy	0/100	2017	Presented a Joint Meeting between NCRI Ovarian Sub Group and Scottish Gynaecological Cancer Trials Group. Friday 08th February 2013 by UK Chief Investigator - Professor Charlie Gourley	Yes	Low grade serous ovarian cancer (LGSOC) has recently been identified as a distinct subtype of ovarian cancer. A recently performed US phase II study found a high response rate to a MEK inhibitor in LGSOC. This randomised phase III trial aims to determine the worth of this approach. This study is an international study and will potentially impact on the management of these patients worldwide. This study is an international study and will potentially impact on the management of these patients worldwide.
Greater Glasgow and Clyde Health Board	Glasspool	CRUKE/12/024: A randomised phase II study of BIBF 1120 compared to chemotherapy in patients with recurrent clear cell carcinoma of the ovary or endometrium.	0/60	2017	Presented 31May2013 at GCIG/ASCO meeting, Chicago by Dr Ros Glasspool, UK Chief Investigator	Yes	Clear cell carcinomas (CCC) make up 3-5% of endometrial and ovarian carcinomas. The prognosis is poor. Ovarian and endometrial CCC share marked molecular similarities with renal CCC. Inhibition of angiogenesis is an effective strategy in renal cell carcinomas. This randomised phase II study will provide preliminary evidence ons this approach in ovarian and endometrial CCC using BIBF 1120 (triple kinase inhibitor of VEGFR, PDGFR, and FGFR). This is an international study and will potentially impact on the management of these patients worldwide. This is an international study and will potentially impact on the management of these patients worldwide.
Newcastle University	Edmondson	CRUK/10/056: PARAGON: Phase II study of aromatase inhibitors in women with potentially hormone responsive recurrent/metastatic gynaecological neoplasms	45/150	2016	Presented a Joint Meeting between NCRI Ovarian Sub Group and Scottish Gynaecological Cancer Trials Group. Friday 08th February 2013 by UK Chief Investigator - Professor Richard Edmondson		A substantial proportion of gynaecological cancers express steroid hormone receptors, are potentially hormonally responsive and may therefore respond to treatment with an aromatase inhibitor. This study will investigate the response of patients with ER/PR + ve gynaecological cancer to treatment with an aromatase inhibitor. The design of the study will allow each tumour subgroup to be analysed independently, butthe single protocol reduces the administrative burden making a study in these relatively rare subgroups more feasible. This trial focuses on some rare groups of gynaecological tumours. Whilst rare, these tumours share some features including expression of steriod hormone receptors and therefore this trial design allows study of each of these rare tumour groups using a common protocol which minimise the administrative burden. This study is an initiative from ANZGOG(Australian and New Zealand Gynaecological Oncology Group) under the auspices of the GCIG (Gynaecological Cancer Intergroup). This type of international collaboration is an important model for doing effective research in rare cancers. This trial focuses on some rare groups of gynaecological tumours. Whilst rare, these tumours share some features including expression of steriod hormone receptors and therefore this trial design allows study of each of these rare tumour groups using a common protocol which minimise the administrative burden. This study is an initiative from ANZGOG(Australian and New Zealand Gynaecological Oncology Group) under the auspices of the GCIG (Gynaecological Cancer Intergroup). This type of international collaboration is an important model for doing effective research in rare cancers.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Eeles (The Institute of Cancer Research) Bliss (ICR-CTSU)	CRUK/91/003: AHT: UKCCCR Adjuvant Hormone Therapy Trial	151 - trial now closed, poor accrual/570	2010	EELES, R., et al. 1992. Should ovarian cancer patients receive hormone replacement therapy? AHT trial: an international randomized controlled trial. Proc of the Annual Meeting American Association of Cancer Researchers, 33, A1333.	No	
The Institute of Cancer Research	Banerjee (Royal Marsden Hospital NHS Foundation Trust) (Bliss, ICR-CTSU)	Cancer of the Ovary Abiraterone Study (CORAL)	unknown/47	2016		Yes	CORAL is the first trial designed to evaluate the clinical efficacy of abiraterone in patients with epithelial ovarian cancer (including fallopian tube and primary peritoneal). The adaptive nature of the study will also permit identification of sub-groups of patients who derive clinical benefit from abiraterone and baseline biomarkers that may identify such a sub-group. If the response rate reported is clinically meaningful, then a randomised, multi-centre, phase II/III trial of abiraterone in ovarian cancer will be warranted. The clinical impact described for the UK also applies internationally.
MRC	Kehoe	CRUK/07/009: CHORUS: A randomised trial to determine the impact of timing of surgery and chemotherapy in newly diagnosed patients with advanced epithelial ovarian, primary peritoneal or fallopian tube carcinoma	539/550	2013	ASCO 2013; oral presentation. Kehoe et al, Journal of Clinical Oncology, 2013 ASCO Annual Meeting Proceedings (Post-Meeting Edition). Vol 31, No 15_suppl (May 20 Supplement), 2013: 5500		CHORUS has shown that neo-adjuvant chemotherapy with delayed primary surgery is non-inferior to upfront surgery for women with advanced ovarian cancer. The results have been presented and a publication is in preparation. A meta-analysis with the EORTC 55971 trial is planned for 2014. Data from this trial, and that of the EORTC: 55971, wil influence clinical practice and provide alternative treatment strategies for women with ovarian cancer. CHORUS plus EORTC 55971 together may influence practice internationally, and prompt further surgical trials in ovarian cancer.
MRC	Ledermann	CRUK/07/025: ICON6: An international randomised trial of molecular targeted therapy with AZD2171 with Pt-based chemotherapy for patients with ovarian cancer relapsing more than 6 months following completion of first line Pt-based treatment	380/Overall target 470	2013 (now done)	To be presented ECCO Sept 2013 with manuscript to follow Initial toxicity assessment of ICON6: a randomised trial of cediranib plus chemotherapy in platinum-sensitive relapsed ovarian cancer. Raja FA et al., Br J Cancer. 2011 Sep 27;105(7):884-9. doi: 10.1038/bjc.2011.334. Epub 2011 Aug 30. Accepted for oral presentation at ECCO 2013		Closed early due to Astra Zeneca halting cediranib development programme. Redesigned with progression-free survival as primary outcome measure and target sample size 470. Aims to evaluate effects of treatment with a novel oral tyrosine kinase inhibitor (cediranib) and will contribute to knowledge about the role of angiogenesis inhibition in the treatment of recurrent ovarian cancer. If the results are positive and provide a pivotal trial outcome this may warrant submission to authorities for registration.
MRC	Clamp	CRUK/10/030: ICON 8: An international 3-stage randomised trial of dose-fractionated CT compared to standard 3-weekly CT, following immediate primary surgery or as part of delayed primary surgery, for women with epithelial ovarian cancer, primary peritoneal or fallopian tube cancer	690/1300	2015	NCRI conference; poster; Current delays in setting-up investigator-driven randomised controlled trials: the MRC ICON8 experience. Jane Hook, Suzanne Freeman, Monique Tomiczek, Sally Stenning, Iain McNeish, Jonathan Ledermann, Andrew Clamp; NCRI 2012 conference abstracts (online)	Yes	Opened to accrual in June 2011. Aim to evaluate the efficacy and safety of two dose-fractionated weekly chemotherapy regimens compared to standard 3-weekly carboplatin-paclitaxel in 1st-line treatment of ovarian cancer. If weekly treatment is shown to be superior to 3-weekly, it is likely to become standard of care for UK women with ovarian cancer. ICON8 is the 3rd international trial to investigate weekly chemotherapy in ovarian cancer. The first trial conducted in Japan showed a significant improvement in survival with weekly treatment. The results from the 2nd trial in the USA are awaited. ICON8 will make a significant contribution to the international evidence base and may contribute to a change in international practice.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
MRC	Perren	CRUKE/05/024: ICON 7: A randomised, multi centre phase III trial of carboplatin + paclitaxel vs carboplatin + paclitaxel + bevacizumab in first line treatment of patients with epithelial ovarian cancer	375/1520 overall	2013	1) A phase 3 trial of bevacizumab in ovarian cancer. Perren TJ et al., ICON7 Investigators. N Engl J Med. 2011 Dec 29;365(26):2484-96. Erratum in: N Engl J Med. 2012 Jan 19;366(3):284. 2) Standard chemotherapy with or without bevacizumab in advanced ovarian cancer: quality-of-life outcomes from the International Collaboration on Ovarian Neoplasms (ICON7) phase 3 randomised trial. Stark D et al., Lancet Oncology. 2013 March; 14(3): 236-43. ESMO 2010 Presidential Session (initial PFS results); ASCO 2011 (updated PFS and interim OS analysis); ESMO 2011 (quality of life data); EORTC QoL Conference 2012 (QoL results); ECCO 2013 (initial OS results)	Yes	The trial is now closed. OS results and updated PFS results are currently being analysed. Aims Primary - to determine whether the addition of bevacizumab to standard chemotherapy improves progression free survival (PFS) and Overall survival (OS) when compared to standard chemotherapy alone. Secondary - to evaluate whether the addition of bevacizumab to standard chemotheraoy will result in improved response rates, duration of tumour response and biological progression free interval. Other secondary aims include safety, quality of life and cost effectiveness assessments. First industry/academy collaboration on licensing trial for a novel agent. Results of ICON7 will inform the future standard first line treatment of women with ovarian cancer. The ICON7 is one of several trials that, in somewhat different settings, have confirmed the benefit of anti-angiogenic agents in advanced ovarian cancer. However it is the only one that suggests that that effect can be achieved with somewhat lower doses of bevacizumab. This is likely to have influence on the use of this type of therapy in many countries.
MRC	Hall	CRUKE/05/025: OVO7:A randomised multicentre phase III study of Erlotinib vs observation in patients with no evidence of progression after Pt-based chemotherapy for high risk stage I+II-IV epithelial ovarian primary peritoneal or fallopian tube	86/830 overall	2013	1. VERGOTE I, JOLY F, KATSAROS D, COENS C, REINTHALLER A, HALL M, STEER C, COLOMBO N, LESOIN A, CASADO A, PETRU E, GREEN J, BUCK M, RAY-COQUARD I, FERRERO A, FAVIER L, REED N, CURVE H, JIMENO A, PUJADE-LAURAINE E. Randomized phase III study of erlotinib versus observation in patients with no evidence of disease progression after first-line platin-based chemotherapy for ovarian carcinoma: A GCIG and EORTC-GCG study. 2012 ASCO Annual Meeting Oral Presentation, 2012 2. DESPIERRE E, YESILYURT B, PEUTEMAN G, LAMBRECHTS S, JOHNSON N, VERHEIJEN R, VAN DER BURG MEB, CASADO A, RUSTIN G, LEUNEN K, NEVEN P, AMANT F, LAMBRECHTS D, VERGOTE I. Epithelial ovarian cancer: rationale for changing the one-fits-all standard treatment regimen to subtype-specific treatment. IGCS 2012.	Yes	EORTC TRIAL 55041 - this is an EORTC-led trial, CTAAC funding supports UK intergroup collaboration coordinated through the MRC CTU. Aim: To assess the impact on progression-free survival of Erlotinib versus observation in patients with no evidence of disease progression after first line, platinum-based chemotherapy for high-risk Stage I and Stage II-IV ovarian epithelial, primary peritoneal, or fallopian tube cancer This trial will establish the maintenance standard for patients with no evidence of disease progression after first-line platin-based chemotherapy for ovarian carcinoma. Currently there is no established standard and the prevailing practice is not give any maintenance treatment but to continue wait-and-see observation. In addition, this trial aims to identify subgroups based on molecular markers which may benefit to a larger or lesser extent from Erlotinib treatment.
MRC and UCL	Cruickshank and Jacobs	CRUK/03/029: UKCTOCS Trial - Middlesborough Centre	204707/200000		Menon U et al., Lancet Oncol. 2009 Apr;10(4):327-40. Menon U, et al., BMJ. 2008 Nov 13;337:a2079.	Yes	A randomised controlled trial designed to assess the effect of screening on mortality, UKCTOCS randomised 202 638 post-menopausal women to no treatment (control); annual CA125 screening with transvaginal ultrasound scan as a second-line test; or annual screening with transvaginal ultrasound alone, in a 2:1:1 ratio. There was a significant difference in specificity but not sensitivity between the two screening groups for both primary ovarian and tubal cancers as well as primary epithelial invasive ovarian and tubal cancers. The prevalence screen has established that the screening strategies are feasible. Specificity was higher in the MMS than in the USS group, resulting in lower rates of

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
							repeat testing and surgery.
Barts and the London NHS Trust	Powell	CRUK/10/002: DEPICT - Dose Escalation Pelvic IMRT in Cervical Tumours (A Phase I/II dose escalation study of simultaneous integrated boost intensity-modulated radiotherapy for locally advanced cervical cancer)					Survival from cervical cancer is directly related to radiation dose, which is currently limited by the long-term complication risk. Intensity-modulated radiotherapy delivers complex curved treatments, reducing normal tissue doses while delivering boosts to selected areas. This trial assesses the feasibility of increasing tumour dose while maintaining acceptable toxicity using IMRT.
Cardiff University	Tristram	CRUK/06/024: RT3 VIN: A randomised phase II multi-centre trial of topical treatment in women with vulval intraepithelial neoplasia (Griffiths for sample collection)	181/168	2013		Maybe	This is a randomsied phase II trial. The result will be used to determine the experimental arm of a future phase III which, if positive, would lead to a change in clinical practice. Will contribute significantly to international knowledge base.
University College London (sponsor Leiden university)	Powell	CRUK/08/001: PORTEC-3: Randomised Phase III Trial Comparing Concurrent Chemoradiation and Adjuvant Chemotherapy with Pelvic Radiation Alone in High Risk and Advanced Stage Endometrial Carcinoma.	184/670	Expected 2015		yes	The results of this randomised controlled trial will inform decision making in women with endometrial cancer and provide clinicians with evidence as to the benefits of additional chemotherapy with regard to survival, local control and quality of life. It should establish whether patients with high-risk and advanced stage endometrial carcinoma should receive concurrent radiotherapy and chemotherapy, followed by adjuvant chemotherapy, or the standard of pelvic radiation alone, following surgery Same as for UK
University College London	Gore	CRUK/08/008: mEOC: A GCIG Intergroup multicentre trial of open label carboplatin and paclitaxel +/- bevacizumab compared with oxaliplatin and capecitabine +/- bevacizumab as first line chemotherapy in patients with mucinous epithelial ovarian cancer	34/332	Expected 2015		Yes	If the results of this trial demonstrate that treatment with oxaliplatin and capecitabine is significantly more effective than standard treatment with carboplatin and paclitaxel, then this could lead to changed in the standard chemotherapy regimens given to patients with mEOC. The application of efficacy of bortezomib can also be assessed in the trial, which may become a standard therapy for ovarian tumours if the results of the ICON-7 and GOG 218 trials are positive.
University College London	Gallagher	CRUK/09/015: PETROC - PEritoneal TReatment of Ovarian Cancer - PETROC (OV21): A Phase II/III study of intraperitoneal (IP) plus intravenous (IV) chemotherapy versus IV carboplatin plus paclitaxel in patients with epithelial ovarian cancer optimally dubulked at surgery	69/400	Expected 2021		Yes	The aim of the completed phase II part of this international trial was to identify whether cisplatin or carboplatin based chemotherapy is more effective in terms of 9 month progression and toxicity and so determine which should be used in the phase III part of the trial. The IDMC preliminary analysis of the phase II feasibility study showed that the comparison of IP and IV therapy was not futile, and that the Carboplatin arm was the preferred arm to take forward. The phase III results will answer the long-term question as to whether intraperitoneal chemotharapy is superior to intravenous. The trial will answer the question as to whether intraperitoneal chemotharapy is superior to intravenous for this group of patients. May provide new standard of care treatment for this group of patients. Same as UK

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University College London	Jacobs (Mackay)	CRUK/00/005: UKFOCSS: United Kingdom Familial Ovarian Cancer Screening Study (Extension)	5800/5000	2011	Br J Cancer. 2006 Oct 23;95(8):1124; author reply 1126-7.	Yes	Will recruit 5,000 patients identified as being at 'high-risk' due to family history. Women will be screened by using CA125 testing three times a year for up to 4 years. Results will demonstrate whether screening reduces mortality from ovarian cancer. The trial is currently ongoing so no impact yet. However if we show there is evidence for CA125 level-based risk assessments, we can develop an optimised screening procedure for ovarian cancer in high-risk women, to determine the physical morbidity, resource implications and feasibility of screening this high-risk population and to establish a serum bank for future assessment of novel tumour markers.
University College London (sponsor Boehringer Ingelheim)	Ledermann	CRUKE/05/020: BIBF: BIBF: A randomised placebo-controlled phase II study of continuous maintenance treatment with BIBF 1120 following chemotherapy in patients with relapsed ovarian cancer	83/80		Ledermann, JA et al. Randomized phase II placebo-controlled trial of maintenance therapy using the oral triple angiokinase inhibitor BIBF 1120 after chemoemotherapy for relapsed ovarian cancer (2011) J Clin Oncol 29, 3798-804 Ledermann JA et al, JCO, 27 (15): - 5501 Suppl. S May 20 2009. Oral presentation at ASCO 2009, and ESGO 2009 Presenter Professor J Ledermann. Preliminary findings	No	BIBF 1120 is well tolerated and is associated with a potential improvement in progression free survival. The observed treatment effect is sufficient to justify further study within a large phase III trial The trial suggests that maintenance BIBF 1120 could delay disease progression in OC pts who had previously responded to chemotherapy. A large phase III trial is needed to confirm the efficacy of this drug.
University College London	McNeish	CRUK/10/007: SaPPrOC (prev.AZD 0530): A randomised placebo-controlled trial of saracatinib (AZD0530) plus weekly paclitaxel in platinum resistant ovarian, fallopian tube or primary peritoneal cancer.	107/102	2014	Ann Oncol (2014) doi: 10.1093/annonc/mdu363 First published online: July 28, 2014 IA McNeish, JA Ledermann, L Webber et al. A randomized placebo-controlled trial of saracatinib (AZD0530) plus weekly paclitaxel in platinum-resistant ovarian, fallopian-tube, or primary peritoneal cancer. ASCO abstract number 5514	No	Saracatinib does not improve activity of weekly paclitaxel in platinum-resistant ovarian cancer. Taxane-free interval of <=6months/no prior taxane was associated with better outcome in both treatment arms. While saracatinib will not be investigated further in platinum-resistant ovarian cancer, SaPPrOC has shown that weekly paclitaxel trials using an additional novel agent can be run effectively and recruit well. There is scope to investigate other IMP using a similar trial design. Furthermore there is evidence that treatment with weekly paclitaxel in this population should be restricted to patients who have either not received paclitaxel before, or have not received paclitaxel for at least 6 months. Not known at present
University College London	McCormack	CRUK/11/024: C37815/A12832: INTERLACE: A phase II multicentre trial of weekly induction chemotherapy followed by standard chemoradiation versus standard chemoradiation alone in patient with locally advanced cervical cancer	40/770	2019		Yes	The results will show if the addition of a short-course, dose-dense course of chemotherapy prior to standard chemorariation improves survival in women with cervical cancer. The results will also have implications for large numbers of women in developing countries where cervical screening and vaccinations rates are low/non-existant. May provide new standard of care treatment for this group of patients Unknown at present
University College London	Michael	CRUKE/11/059: TRIOC - A Randomised Parallel Group Double-Blind Phase II Study to Assess the Activity of TroVax® (MVA-5T4) Versus Placebo in Patients with Relapsed Asymptomatic Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Cancer	10/100	2017		Yes	Unknown at this point

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University College London	McCormack	CxII: A phase II study of weekly neo-adjuvant chemotherapy followed by radical chemoradiation for locally advanced cervical cancer.	46/50	Published 2013	McCormack M et al. A phase II study of weekly neoadjuvant chemotherapy followed by radical chemoradiation for locally advanced cervical cancer. Br J Cancer (2013) 108, 2464-69	No	A good response is achieved by dose dense neo adjuvant chemotherapy with carboplatin and paclitaxel followed by radical chemoradiotherapy. The regimen is feasible as evidenced by the acceptable toxicity and high compliance to radiotherapy Results of this trial have led to a phase III trial being conducted None at present
University College London	Hall	CRUKE/11/024: METRO-BIBF: A Phase II, randomised, placebo controlled, multicentre, feasibility study of low dose (metronomic) cyclophosphamide with and without BIBF1120 in advanced ovarian cancer	11/16	Expected 2017		Yes	
University College London	Lanceley	Symptom Benefit Trial: Does Palliative Chemotherapy Improve Symptoms in Women with Recurrent Ovarian Cancer?	159/120	2016		No	This study aims to develop criteria for defining symptom benefit, to determine how many women obtain this benefit, and to investigate prognostic models for benefit, time to progression and survival for women who have platinum resistant/refractory epithelial ovarian, fallopian tube or primary peritoneal cancers. To develop a measure of symptom benefit that can be used as an endpoint in clinical trials of palliative chemotherapy. Same as UK
University College London	Tidy	SHAPE: A randomised phase III trial comparing radical hysterectomy and pelvic node dissection vs. simple hysterectomy and pelvic node dissection in patients with low-risk early-stage cervical cancer	0/200	2022		Yes	Sites at which Sentinel Node mapping is already in place or will be implemented in the future may be less likely to set up/recruit to SHAPE Best practice will be determined in this group of patients Best practice will be determined in this group of patients
University College London	Kristeleit	CRUK/13/008: PANDA: A single arm phase II trial of BMN 673 for inoperable, advanced endometrial cancer with retrospective PTEN, MSI and MRE11 analysis	0/100	2017		Yes	To trial will assess whether BMN 673 monotherapy is safe, tolerable and has therapeutic benefit in advanced endometrial cancer and whether status of PTEN, microsatellite instability (MSI), MRE11 or platinum-free interval predicts response This Phase II trial of BMN 673 could demonstrate activity that might lead to a new effective treatment for patients with inoperable, advanced, recurrent or metastatic endometrial cancer. This trial also has the potential to characterise a molecular subset of patients that may preferentially derive benefit from BMN 673. The identification of such biomarkers could also be extrapolated to other tumour types to predict their response to PARP inhibition. Not known at present
Centre for Drug Development							
Institute of Cancer Research/Royal Marsden Hospital	Banerji	CRUKDE/12/013: TAX-TORC A Phase I/II multi-centre trial of AZD2014 (dual mTORC1 and mTORC2 inhibitor) combined with weekly paclitaxel in patients with platinum-resistant ovarian, fallopian, or primary peritoneal cancer.	3/38	2015			First time for this combination in this group of patients. Current treatment strategies in platinum-resistant ovarian cancer achieve modest benefit and there remains an unmet clinical need to explore ways of adding novel targeted anticancer agents to existing treatment strategies to improve treatment outcomes in this setting. Global treatment strategies

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Glasgow	Cassidy	CRUKD/07/065: A Cancer Research UK Phase II trial of the DNA-hypomethylating agent decitabine (Dacogen) in combination with carboplatin in relapsed ovarian cancer (DACROC)	29/29	2008	R. M. Glasspool, M. Gore, G. Rustin, I. McNeish, R. Wilson, S. Pledge, J. Paul, M. Mackean, S. Halford, S. Kaye. Randomized phase II study of decitabine in combination with carboplatin compared with carboplatin alone in patients with recurrent advanced ovarian cancer. J Clin Onc, 2009; 27, (15S), 5562. Appleton K, Mackay HJ, et al. Phase I and pharmacodynamic trial of the DNA methyltransferase inhibitor decitabine and carboplatin in solid tumors. J Clin Oncol. 2007 Oct 10;25(29):4603-9.		Phase 2 development from CRUKD/02/023. Aimed to look at side effects and efficacy of the combination. The trial was based on the notion that hypermethylation was a valid target (ie using decitabine) as a means of reversing platinum resistance. The fact that the trial showed no sign of any benefit (as well as demonstrating the difficulties of this drug combination) is an important observation. Trial completed. Biomarker studies suggested the drug resistance phenotype was reversed by the combination. Trial was closed at the first interim analysis, due to problems with feasibility and concerns of reduced efficacy in the experimental arm. The company has not developed the combination further. The study illustrates the likely importance of a selective approach if demethylation were to be proposed in the future as a resistance-reversal strategy.
University of Manchester/Christie Hospital	Kitchener	CRUKD/00/021: A phase I trial to investigate the safety and immunogenicity of an HPV16 L1 vaccine in women with mild cervical dyskaryosis	23/23	2002	Davidson EJ, Sehr P, Faulkner RL, et al. Human papillomavirus type 16 E2- and L1-specific serological and T-cell responses in women with vulval intraepithelial neoplasia. J Gen Virol. 2003 Aug;84(Pt 8):2089-97. Stern PL, Faulkner R, et al. Best Pract Res Clin Obstet Gynaecol. 2001 Oct;15(5):783-99.		First time in patients for this vaccine. Trial completed. Development discontinued after Phase I due to lack of immunological activity. Too early in development to assess clinical impact.
University of Newcastle	Calvert	CRUKD/00/015: A Phase II study of BBR 3464 as treatment in patients with advanced ovarian cancer failing one platinum and taxane regimen	41/41	2003			First evaluation of the efficacy of a non cross resistant platinum complex in ovarian cancer. Companion trial to gastric trials: CRUKD/00/019 and CRUKD/00/020. Trial completed. Development discontinued after Phase II due to lack of activity. Too early in development to assess clinical impact.
University of Manchester/Christie Hospital	Jayson	CRUKD/99/012: A CRC Phase II trial of bryostatin-1 administered by weekly 24-hour infusion in recurrent epithelial ovarian carcinoma.	17/17	2002	Clamp AR, Blackhall FH, et al. A phase II trial of bryostatin-1 administered by weekly 24-hour infusion in recurrent epithelial ovarian carcinoma. Br J Cancer. 2003 Oct 6;89(7):1152-4.		First trial in ovarian cancer for this agent. Follow up Phase II trial to CRUKD/91/006, companion trial to CRUKD/99/011 & CRUK/99/013. Trial completed. Development discontinued after Phase II due to lack of efficacy. Too early in development to assess clinical impact.
Haematology							
University Hospital Birmingham NHS Foundation Trust	Cook	LenaRic: A phase II study of adjuvant use of lenalidomide in patients undergoing reduced intensity conditioning allogeneic transplantation for multiple myeloma	12/40	2015		Yes	This trial addresses the use of reduced intensity stem cell transplants in Multiple Myeloma patients and the high rate of relapse. The results from this trial will influence the post transplant treatment of these patients, using Lenalidomide to maintain a minimal disease state thus creating a platform for subsequent DLI. Potential to have similar impact as in UK clinical practice

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Liverpool	Pettitt	Randomised phase II trial of ofatumumab, dexamethasone and lenalidomide induction followed by lenalidomide maintenance versus no further treatment for high-risk CLL. (CLL2010)	16/101 (note 16 patients recruited to original regiment (containing alemtuzumab). 0/85 patients recruited to new regiment (cotaining ofatumumab)	2018		Yes	Following withdrawal of licence for alemtuzumab in August 2012, the study has been re-launched with an alternative monoclonal antibody (ofatumumab) included in the treatement regimen. 16 patients were recruited to the original (alemtuzumab containing) regimen, a further 85 will be recruited to the new (ofatumumab containing) regumen. Treatment options for patients with CLL and TP53 defects have hitherto been extremely limited owing to the poor results associated with chemotherapy. Recently, however, several non-chemotherapy drugs have been identified that are active in this setting, such as alemtuzumab (humanised rat anti-CD52 monoclonal antibody), ofatumumab (human anti-CD20), high-dose methylprednisolone (HDMP) and lenalidomide. However none of these drugs when used as monotherapy are capable of producing complete or durable remissions in a significant proportion of patients.
University of Liverpool	Pettitt	RIAltO: A Randomised Investigation of Alternative Ofatumumab-based regimens for less fit patients with CLL	101/670	2016-2017	RIAltO was presented at the Annual Leukaemia Trials Review 24/06/2013	Yes	To compare O-Chl and O-B in patients with CLL who are considered not fit enough for R-FC. To identify clinical features and biomarkers that predicts the efficacy and toxicity of O-Chl and O-B. Results may lead to changes in clinical practice.
Imperial College London	Gaskin	CRUK/03/004: MERIT MyEloma Renal Impairment Trial. A randomised controlled trial of adjunctive plasma exchange in patients with newly diagnosed multiple myeloma and acute renal failure.	79/286	2012	Currently in preparation	No	Closed to accrual Demonstrated the importance of early effective treatment of myeloma in preserving kidney function (irrespective of plasma exchange). n/k
University College London	Gillmore	CRUK/06/032: UKATT TRIAL. A randomised, multicentre feasibility trial in AL Amyloidosis, comparing CTD with SCT in patients with low risk of Treatment Related Mortality and CTD with Mel-Dex in patients in whom SCT would not be considered appropriate as first line therapy	27/48	2010	Gibbs, SDJ et al., In AL Amyloidosis, Both Oral Melphalan and Dexamethasone (Mel-Dex) and Risk-Adapted Cyclophosphamide, Thalidomide and Dexamethasone (CTD) Have Similar Efficacy as Upfront Treatment. BLOOD, 114 (22): 310-310 NOV 20 2009. Presented at ASH 2009	No	This trial is testing the feasibility of recruiting patients through the Department of Health UK National Amyloidosis Centre at the Royal Free Hospital in London The trial has cemented the UK NAC network throughout the participating centres within the UK n/a
Leeds Teaching Hospitals NHS Trust	Hillmen	CRUKE/04/018: CLL201 FCM/FCM-R. A randomised Phase II Trial of fludarabine, cyclophosphamide and mitoxantrone (FCM) with or without rituximab in previously treated chronic lymphocytic leukaemia	52/54	2008	A randomized phase II trial of fludarabine, cyclophosphamide and mitoxantrone (FCM) with or without rituximab in previously treated chronic lymphocytic leukaemia. Hillmen Pet al. BJH: 1365-2141 2010	No	The objective of CLL201 FCM/FCM-R is to assess the efficacy and safety of fludarabine, cyclophosphamide and mitoxantrone in combination with rituximab (FCM-R), and fludarabine, cyclophosphamide and mitoxantrone alone (FCM) in previously treated patients with chronic lymphocytic leukaemia (CLL). The FCMR arm of this trial will be used in the ADMIRE Trial None because this is a Phase II trial n/a
University of Leeds	Morgan	CRUK/09/014: Myeloma XI: Randomised comparisons, in myeloma patients of all ages, of thalidomide, lenalidomide, carfilzomib and bortezomib induction combinations, and of lenalidomide and combination lenalidomide vorinostat as maintenance	2485/1970	2018	Two oral presentations given by Dr Annamaria Brioli at EHA June 2013. Oral presentation given by Dr Charlotte Pawlyn at ASH Dec 2012.	Yes	The trial will demonstrate the effect of lenalidomide- and lenalidomide plus carfilzomib oontaining treatment compared to standard treatment, during induction and maintenance. It will also demonstrate whether bortezomib can improve responses in patients who do not respond to lenalidomide or thalidomide. Investigating prognostic factors. It will determine the standard of care for newly diagnosed myeloma patients in the UK n/k

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Leeds Teaching Hospitals NHS Trust	Cook	CRUK/06/018: Myeloma X Relapse (Intensive): a phase III study to determine the role of a second autologous stem cell transplant (ASCT) as consolidation therapy in patients with relapsed multiple myeloma following prior high-dose chemotherapy and autologous stem cell rescue.	297/460	2013	To be published autumn 2013 Oral presentation presented by Professor G Cook at BSH in Liverpool and at EBMT in London, both held in April 2013.	Yes	Will determine if there is merit in performing a second transplant at second relapse in terms of time to progression. Also, current practice is to store stem cells from first transplant harvest for use if needed at second transplant. This is very costly, so the results from this trial will inform whether this is worthwhile practice. Will determine the role of second autologous transplant as a relapse treatment option n/k
Leeds Teaching Hospitals NHS Trust	Hillmen	CRUKE/07/047: CLARET: A randomised, phase III study to assess alemtuzumab consolidation therapy in patients with CLL who have responded to previous therapy.	0/116	2018		No	CLARET intends to assess the effect on progression free survival (PFS) of subcutaneous alemtuzumab in B-CLL patients who have responded to previous chemotherapy. No - still in set-up n/a
Leeds Teaching Hospitals NHS Trust	Hillmen	CRUKE/09/016: ADMIRE. Does the ADdition of Mitoxantrone Improve REsponse to FCR chemotherapy in patients with CLL: A randomised phase II trial of fludarabine, cyclophosphamide and rituximab (FcR) with or without mitoxantrone (M) in previously untreated chronic lymphocytic leukaemia.	215/218	2013	Oral presention at EHA in June 2013. Poster presentation at IWCLL in September 2013.	No	Trial recruitment was slower than expected and the recruitment period was extended by 12 months. ADMIRE intends to compare the complete response rates of fludarabine, cyclophosphamide and rituximab (FCR) with or without mitoxantrone (M) in patients with previously untreated chronic lymphocytic leukaemia. No because this is a Phase II trial n/a
Leeds Teaching Hospitals NHS Trust	Bowen	CRUK/08/034: CMML201: A phase 2 study of 5-azacytidine in chronic myelomonocytic leukaemia (CMML)	32/30	2012	To be published autumn 2013 Poster presented by Dr Mark Drummond at EHA Jun 2012	NO	To assess the safety, tolerability and efficacy of azacitidine in patients with CMML None None
Leeds Teaching Hospitals NHS Trust	Hillmen	CRUKE/06/038*: CLL207: Eradication of minimal residual disease (MRD) in patients with chronic lymphocytic leukaemia (CLL) with alemtuzumab: A phase II study.	61/61	2011	Poster presented at IWCLL in September 2013	No	Closed to recruitment, in analysis. To assess whether alemtuzumab is effective and safe at treating patients with CLL who disease is present at a low level following conventional treatments. There will also be an investigation where patients whose CLL is below the level of detectability (known as MRD negative) are monitored and re-treated when necessary. No because this is a phase II trial n/a
Leeds Teaching Hospitals NHS Trust	Bowen	AML_LEN-5 A pilot safety / tolerability study of Lenalidomide administered as monotherapy and in combination with standard chemotherapy for Acute Myeloid Leukaemia / high-risk Myelodysplastic Syndrome with structural abnormalities of chromosome 5	14/39	2011	The manuscript has been accepted by Leukemia research reports and is in press Currently in press Poster presented at EHA 2011: A Phase 2 study of lenalidomide as monotherapy and in combination with cytarabine, daunorubicin and etoposide for high-risk MDS/AML with chromosome 5 abnormalities: the NCRI Len5 study	No	Trial met protocol defined stopping rule. Recruitment stopped. Lenalidomide monotherapy at a dose of 10mg daily is ineffective as induction therapy in MDS/AML patients with increased marrow blasts. Lenalidomide combined with ADE chemotherapy has predictable toxicity and has efficacy even in this particularly adverse patient cohort which warrants further investigation. n/a n/a

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Leeds Teaching Hospitals NHS Trust	Hillmen	COSMIC: Combination FC Plus Ofatumumab at Standard or Mega dose In CLL	14/82	2014		No	To assess the efficacy of standard dose and high (mega) dose Ofatumumab in combination with chemotherapy (Fludarabine and Cyclophosphamide) in relapsed B-CLL patients. The optimal anti-CD20 monoclonal antibody dose in CLL is unclear. This trial will demonstrate whether very high doses of anti-CD20 antibody are more effective than conventional doses and will inform future Phase III trials of chemo-immunotherapy. High doses of ofatumumab as monotherapy have been shown to be well-tolerated and effective in refractory CLL whereas this is not the case for rituximab N/A
University of Leeds	Hillmen	FLAIR (previously CLL10): Front-Line therapy in CLL: Assessment of Ibrutinib + Rituximab	0/754	2021		No	To compare the effect on progression free survival of ibrutinib + rituximab (IR) with that of fludarabine, cyclophosphamide and rituximab (FCR). This will be the first randomised trial in front line CLL of ibrutinib (or similar agents) and has the potential to lead to a paradigm shift in the treatment of CLL. N/k
University of Leeds	Hillmen	CRUK/11/040: CLL8 (previously CLARET): A randomised, phase II/III trial to assess GA-101 (obinutuzumab) consolidation therapy in patients with CLL who have responded to previous therapy	0/188	2021		No	The trial was recently amended to use GA-101 rather than alemtuzumab. Emerging chemotherapy resistance, mainly through p53 mutation, is the major reason for failure of therapy in CLL. Consolidation with monoclonal antibodies, which are independent of p53, appears to prevent relapses and the occurrence of chemotherapy resistance. Therefore this trial has the potential to fundamentally change the way CLL is treated. n/k
University of Newcastle	O'Brien	CRUKE/09/003: SPIRIT 2: a phase III, prospective randomised comparison of imatinib 400mg daily versus dasatinib 100mg daily in patients with newly-diagnosed chronic phase chronic myeloid leukaemia	814/810	2018			The trial results will increase knowledge of the use and effectiveness of dasatinib for newly diagnosed CML patients. It will inform clinical decision making with regard to which of the currently available therapies is most suitable for a patient based on efficacy, tolerability, cost effectiveness and effect on quality of life. It is also hoped that this data can be used to inform NICE when CML therapies are next reviewed. unknown
QMUL	Lister	CRUKE/05/022: Depocyte: A phase II Clinical study to determine the efficacy and safety of Depocyte					Will determine the efficacy and safety of Depocyte in the treatment of CNS relapse in adult patients with ALL.
Cardiff University	Burnett	CRUK/08/025: AML17: A Trial for Acute Myeloid Leukaemia and High Risk Myelodysplastic Syndrome in Younger Patients	2270/3000	2014		Yes	If positive, it would lead to a change in clinical practice. Will contribute significantly to international knowledge base.
University College London	Weckalekar	CRUK/09/027: REVEAL: A pilot study of relapsed or refractory patients using Velcade™ (Bortezomib)combination chemotherapy in AL amyloidosis.	7/52	2016		Yes	Ongoing The trial is anticipated to have an impact on the treatment (possibly a change or modification) on this group of patients The trial is anticipated to have an impact on the treatment (possibly a change or modification) on this group of patients
Kings college Hospital NHS Foundation Trust	Schey	CRUK/08/016: A phase I does escalation study of the combination of Lenalidomide (Revlimid), Dexamethasone and		2011			

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
		Cyclophosphamide in patients relapsing from stable disease with multiple myeloma					
University College London	Fielding	CRUK/09/006: UKALL14: An international randomised trial for adults with newly diagnosed acute lymphoblastic leukaemia.	423/720	2018		Yes	This trial will help to establish or refute a role of monoclonal B cell antibodies as additional therapy in B cell ALL and of nelarabine in T-cell ALL. These data will definitively inform as to whether a graft versus leukaemia effect can be exploited for the benefit of the general adult population with adult ALL. This study is expected to accrue more patients with adult ALL than any other study worldwide. It aims be able to answer these questions more rapidly and with a higher statistical power, making the results of the study highly influential. Will help to confirm the role of monoclonal B cell antibody therapy in B cell ALL, and nelarabine in T cell therapy. Unknown at present
University College London	Hough	RIC UCBT: Transplantation of umbilical cord blood from unrelated donors in patients with haematological diseases using a reduced intensity conditioning regimen aka Cord blood transplantation study	60/60	2015	American Society of Hematology 2013- Early multilineage chimerism predicts the wining unit in double cord blood transplantation American Society of Hematology 2013- Early multilineage chimerism predicts the wining unit in double cord blood transplantation		To validate the safety and efficacy of unrelated donor UCBT using a reduced intensity conditioning regimen.
University College London	Chakraverty	ProT4 - Prophylactic Transfer of CD4 lymphocytes. Multicentre randomised phase II study to evaluate the efficacy of prophylactic transfer of CD4 lymphocytes after T-cell depleted reduced intensity HLA-identical sibling transplantation for haematological ca	15/56	2016			
Christie NHS Foundation Trust	Radford	RAPID: PET Trial in Hodgkin's disease: A randomised phase III trial to determine the role of FDG-PET imaging in clinical stages IA/IIA Hodgkin's disease.	602/600		Submitted NEJM August 2014, not yet accepted/published Annals of Oncology 22: 739–745, 2011 (Establishment of a UK-wide network to facilitate the acquisition of quality assured FDG–PET data for clinical trials in lymphoma S. F. Barrington et al) The results of the trial were presented at the American Society of Hematology (ASH) Annual meeting in December 2012 in Atlanta and at the International Symposium on Hodgkin Lymphoma in Cologne in October 2013.	Yes	The main conclusion from the trial is that patients with a negative PET scan after 3 cycles ABVD have very good prognosis, both with and without consolidation radiotherapy, although the non-inferiority margin was just exceeded. These results support a more individualised approach to the treatment of early stage HL
University College London	Raj	UK-Haplo: A UK multicentre phase II study of haploidentical stem cell transplantation in patients with haematological malignancies	13/78	2018		yes	The trial has the ability to demonstrate the potential for the use of HLA mismatched related donors and the utility of high dose cyclophosphamide for immune tolerisation. Extensions of this protocol may result in its use outside the haploidentical setting.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University College London	Fielding	CRUK/11/028: UKALL60+: A Phase 2 study of older adults with Acute Lymphoblastic Leukaemia	39/148	Not yet known		Yes	This multicentre prospective study will test the safety, tolerability and efficacy of a standard 'backbone' chemotherapeutic regime for older patients with ALL thereby providing essential baseline data to inform the design of advanced phase II/III studies in ALL in which the activity and tolerability of novel agents/therapeutic approaches in this patient group will be assessed.
University College London	Kwee Yong	BCT: Phase II Study of bortezomib consolidation after high dose therapy and autologous stem cell transplantation for multiple myeloma	55/65	2015		Yes	
University College London	Amrolia	ICAT: Adoptive Immunotherapy with CD25/71 allodepleted donor T-cells to improve Immunity after Stem Cell Transplant. (Previously: Allodepletion Trial)	1/32	2018			Trial at early stage
University College London	Yong	CRUK/13/032: CARDAMON: Carfilzomib/Cyclophosphamide/Dexamethsasone with maintenance carilzomib in untreated transplant - eligible patients with symptomatic MM to evaluate the benefit of upfront ASCT	0/280	2021		Yes	1. To determine the response rate (very good partial response or better) to Carfilzomib, Cyclophosphamide and Dexamethasone (CarCyDex). 2. To investigate if patients who respond to a highly efficacious triplet regimen like CarCyDex need upfront autologous stem cell transplantation (ASCT). Demonstrate the utility and feasibility of using MRD status to direct threapy; determine whether ASCT is needed in patients who respond to highly efficacious triplet regimens Not known at present
University College London	Hough	MAC UCBT: Transplantation of umbilical cord blood from unrelated donors in patients with haematological diseases using a myeloablative conditioining regimen	11/60	n/a- study closed due to poor recruitment			To validate the safety and efficacy of unrelated donor UCBT using a myeloablative conditioning regimen.
University College London	Amrolia	CD19TPALL: Immunotherapy with CD19ζ gene-modified EBV-specific CTLs after stem cell transplant in children with high-risk acute lymphoblastic leukaemia	20/unknown target			yes	This study will be the first clinical study in man of chimeric TCR transfer for leukaemia The study aims establish the feasibility and safety of adoptive immunotherapy with CD19-specific T-cells, which may help prevent relapse in patients with high-risk ALL and has important broader implications for other cancers which may be targeted using a similar approach International trial
Centre for Drug Development							
Imperial College	Samson	CRUKD/01/021: A Phase I Trial of intravenous Anti-CD38-saporin (OKT10-Saporin) in Late Stage Myeloma	10/25	2003			First time in patients for this agent. Trial completed. Development discontinued after Phase I due to lack of efficacy. Too early in development to assess clinical impact.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Head and Neck							
University of Liverpool and Aintree University Hospitals NHS Foundation Trust	Shaw	HOPON: Hyperbaric Oxygen for the Prevention of Osteoradionecrosis. [Feasibility study followed by main Randomised Controlled Trial]	98/221	2018		Yes	To determine the benefit of hyperbaric oxygen (HBO) in the prevention of osteoradionecrosis (ORN) at the time of a surgical procedure to the irradiated jaw. If HBO is proven to be worthwhile in this indication, then the saving to the NHS will be quite significant in terms of avoidable major surgery for jaw osteoradionecrosis. Alternatively if not worthwhile on health economics grounds then avoiding hyperbaric oxygen treatment in the future will be a natural recommendation of the subsequent NICE guidelines. If HBO is proven to be worthwhile in this indication, then the saving to the health services will be quite significant in terms of avoidable major surgery for jaw osteoradionecrosis. Alternatively if not worthwhile on health economics grounds then avoiding hyperbaric oxygen treatment in the future will be a natural recommendation of the subsequent NICE guidelines.
University of Liverpool	Shaw	TITAN: Trial of Induction TPF Therapy in Advanced Head & Neck Cancer.	7/50	TBC	The 2nd One Day Translational Symposium (Run by University of Liverpool)	Yes	The study was determined not feasible for recruitment in the UK. Futhermore, a similiar trial in China had already reported negatively; however it should be stressed that there were certain differences between the populations groups
University of Liverpool	Jones	REALISTIC: A phase I, dose esclation trial of recombinant listeria moncytogenes (Lm)-based vaccine encoding human papilloma virus serotype 16 target antigens (ADXS11-001) in patients with HPV-16+ oropharyngeal SCC.	17 (REGISTERED)/36	TBC	The 2nd One Day Translational Symposium (Run by University of Liverpool)	No	Difficulties with set up, due to the nature of the IMP. To determine safety and to characterise the toxicity profile of ADXS11-001. Results may lead to a changes in clinical practice.
University of Liverpool	Shaw	DAHANCA 21: Hyperbaric Oxygen Treatment of Mandibular Osteoradionecrosis. A randomised clinical trial.		2016	Trial iniitation teleconference held to discuss the study with several participating centres in June 2013.	Yes	The objective of the study is to evaluate the effect of hyperbaric oxygen (HBO) on mandibular osteoradionecrosis as an adjunctive to surgical treatment in patients previously irradiated for head and neck cancer. If HBO is proven to be worthwhile in this indication, then this study will be cited globally. Alternatively if not worthwhile on health economics grounds then avoiding HBO in the future will be a natural recommendation of the subsequent NICE guidelines. If HBO is proven to be worthwhile in this indication, then this study will be cited globally. Alternatively if not worthwhile on health economics grounds then avoiding HBO in the future will be a natural recommendation of the subsequent NICE guidelines.
The Institute of Cancer Research	Nutting (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Hall, ICR-CTSU)	CRUK/08/004: COSTAR: A Multicentre Randomised Study Of Cochlear Sparing Intensity Modulated Radiotherapy Versus Conventional Radiotherapy In Patients With Parotid Tumours	110/108	2014		Yes	This trial is at the forefront of technical radiotherapy delivery. If a reduction in toxicity is seen with IMRT this will be further evidence, adding to that from PARSPORT, to support continued roll-out of Head and Neck IMRT into centres across the UK. COSTAR will add to the international randomised evidence base for IMRT and, on the baiss of PARPSORT, is anticpated to have considerable impact internationally.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Nutting (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Hall, ICR-CTSU)	CRUK/10/018: ART-DECO: A randomised accelerated radiotherapy study of dose escalated IMRT vs conventional dose IMRT in patients receiving treatment for Laryngeal and Hypopharyngeal cancer.	97/354	2017		Yes	ART DECO, with IMRT used in both arms of the trial, acts as a vehicle for the widespread integration of quality assured IMRT into head and neck radiotherapy practice across the UK. If a disease control benefit is seen for accelerated, dose-escalated radiotherapy this is likely to define future standard practice. The trial has an associated translational research study which provides an opportunity to create a biorepository of tissue and blood samples which may be used for future evaluation of head and neck cancer molecular signatures for correlation with treatment response, toxicity and survival. Results of this trial will apply internationally.
The Institute of Cancer Research	Nutting (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Hall, ICR-CTSU)	CRUK/03/005: PARSPORT: A multicentre randomised study of parotid sparing intensity modulated radiotherapy versus conventional radiotherapy in patients with head and neck cancer	94/84	2010	NUTTING, C. M., et al. 2011. Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial. Lancet Oncol, 12, 127-136. KOHLER, R., et al. 2013. Two-Year and Lifetime Cost-Effectiveness of Intensity Modulated Radiotherapy versus 3-D Conformal Radiotherapy for Head and Neck Cancer. Int J Radiat Oncol Phys in press BUETTNER, F., et al. 2012. Novel approaches to improve the therapeutic index of head and neck radiotherapy: An analysis of data from the PARSPORT randomised phase III trial. Radiother Oncol, 103, 82-7. GULLIFORD, S. L., et al. 2012. Dosimetric explanations of fatigue in head and neck radiotherapy: An analysis from the PARSPORT Phase III trial. Radiother Oncol, 104, 205-212. CLARK, C. H., et al. 2009. Pre-trial quality assurance processes for an intensity-modulated radiation therapy (IMRT) trial: PARSPORT, a UK multicentre Phase III trial comparing conventional radiotherapy and parotid-sparing IMRT for locally advanced head and neck cancer. Br J Radiol, 82, 585-594. GUERRERO URBANO, M. T., et al. 2007. Target volume definition for head and neck intensity modulated radiotherapy: pre-clinical evaluation of PARSPORT trial guidelines. Clin Oncol (R.Coll.Radiol.), 19, 604-613. DEAN, J., et al. 2013. Evaluating the feasibility of sparing CNS structures to reduce acute fatigue from IMRT for head and neck cancer. Radiother Oncol, 106, S166 #OC-432. Oral presentation at ESTRO 2013	Yes	Intensity modulated radiotherapy (IMRT) significantly reduces risk of subjective xerostomia by about 50% and improves quality of life for patients with pharyngeal cancers compared with conventional radiotherapy. PARSPORT has resulted in a major change in clinical practice and contributed to IMRT adoption as the treatment of choice in North America, Europe, China and Asia. The trial has also been a platform for a number of exploratory analyses of associations between dosimetry and toxicity (e.g. fatigue). This trial established the standard for radiotherapy QA in Head and Neck cancers and is the first trial in a series of radiotherapy technology trials in this disease site. The trial established a head and neck cancer team at ICRCTSU and subsequent ICRCTSU head and neck radiotherapy trials have built on the network of clinical investigators and physicists established in PARSPORT PARSPORT has resulted in a major change in clinical practice and contributed to IMRT adoption as the treatment of choice in North America, Europe, China and Asia.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Harrington (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Hall, ICR-CTSU)	A randomised phase II study to evaluate the efficacy and safety of chemotherapy vs androgen deprivation therapy in patients with recurrent and/or metastatic, androgen receptor expressing, salivary gland cancer (EORTC-1206-HNCG) - an International Rare Cancers Initiative Study	unknown/30			Yes	This trial will provide valuable information about how to treat patients with metastatic and/or recurrent salivary gland carcinomas (SGC) and will contribute to the development of targeted therapies against specific histological subtypes of SGC. The clinical impact described for the UK is also applicable internationally. This is an international study conducted under the auspices of the International Rare Cancers Initiative (IRCI).
MRC	Alderson	CRUK/02/010: OE05: A prospective randomised trial comparing standard chemotherapy followed by resection vs infusional chemotherapy followed by resection in pts with resectable oesophageal adenocarcinoma	897/842	2014		Yes	Extension approved at CTAAC in July 2010. No cost extension approved Feb 2013. OE05 is a randomised controlled trial comparing pre-operative treatment with epirubicin, cisplatin and capecitabine (ECX regimen) with standard neo-adjuvant cisplatin/infused 5-FU chemotherapy for patients with operable adenocarcinoma of the oesophagus. if positive, would expect ECX to become standard therapy in UK
University of Birmingham	Aveyard	CRUK/03/026: A pragmatic randomised controlled trial to test the efficacy of nortryptiline plus NRT versus NRT alone in helping smokers to stop	839/900		Aveyard P et al., BMJ 2008;336:1223-1227.	Yes	Two small studies had provided contradictory evidence on whether the combination treatment was more effective than NRT alone. If the most optimistic estimate was correct, then this would have been the most effective treatment combination for smokers trying to quit. This study was large enough to show that the effects of combination treatment were not larger than the effect of NRT alone. Nortriptyline and nicotine replacement therapy are both effective for smoking cessation but evidence is lacking that combination treatment is more effective than either alone.
QMUL	Hutchison	CRUK/07/010: SEND: the role of elective neck dissection in patients with early oral squamous cell carcinoma and no clinical evidence of lymph node metastases in the neck	206/652	2015	The logistics and difficulties running this trial will be submitted for presentation at the April meeting of the British Association of Head and Neck Oncology. April meeting of the British Association of Head and Neck Oncology.	Yes	This surgical trial has the potential to change practice as it is currently not known whether performing a selective elective neck dissection is of more benefit or not to patients presenting with T1/T2 N0 OSCC. This surgical trial has the potential to change practice as it is currently not known whether performing a selective elective neck dissection is of more benefit or not to patients presenting with T1/T2 N0 OSCC. This surgical trial has the potential to change practice as it is currently not known whether performing a selective elective neck dissection is of more benefit or not to patients presenting with T1/T2 N0 OSCC.
Bradford Hospital NHS Trust	McCaul	CRUK/10/011: LIHNCS: Lugol's Iodine in Head and Neck Cancer Surgery	419/410	2014		Possibly	N/A Justify the use of Lugol's iodine to identify more readily the existence of dysplasia or carcinoma insitu at surgical margins, thereby increasing the levels of optimal surgical excision with the impact of less local recurrences in patients with sqamous cell carcinomaof the oral cavity or oropharynx As the trial in ongoing, the impact is unknown. The results will add to the knowledge base for the treatment of this group of patients.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University College London	Tobias	CRUK/90/004: UKHAN1: A trial looking at radiotherapy and chemotherapy for head and neck cancer.	966/966		Tobias JS et al., Chemotherapy for locally advanced head and neck cancer: 10 year follow-up of the UKHAN1 trial. Lancet. Oncol. 2010 Jan; 11 (1): 66-74. Tobias JS, Monson K and Gupta N et al, Proc Am Soc Clin Oncol 20 (2001) abstr 888.	Yes	Concurrent non-platinum chemoradiotherapy reduces recurrences, new tumours, and deaths in patients who have not undergone previous surgery, even 10 years after starting treatment. Chemotherapy given after radiotherapy (with or without concurrent chemotherapy) is ineffective. Patients who have undergone previous surgery for head and neck cancer do not benefit from non-platinum chemotherapy. This trial had a major impact on how head and neck cancers are treated in the UK.
University College London	Boshoff	CRUKE/07/048: DORA: A Phase I and Randomised Phase II study of Docetaxel and RAD001 (Everolimus) in advanced/recurrent or metastatic squamous cell carcinoma of the head and neck	4/120	N/A (trial closed due to poor recruitment)			End of Trials Declaration & Clinical Study Report submitted to MHRA 2011; no publication for this trial
University College London	Mallick	CRUK/06/030: HiLo-Multicentre randomised trial of high dose vs low dose radioiodine, with/without recombinant human TSH for remnant ablation following surgery for differentiated thyroid cancer	438/468	2012	Mallick U et al., Ablation with Low-Dose Radioiodine and Thyrotropin Alfa in Thyroid Cancer; N Engl J Med 2012;366:1674-85 Mallick U et al., The HiLo Trial: a Multicentre Randomised Trial of High- versus Low-dose Radioiodine, with or without Recombinant Human Thyroid Stimulating Hormone for Remnant Ablation after Surgery for Differentiated Thyroid cancer. Clin Oncol 2008; 20(5): 325-6.	Yes	The HiLo trial is the first ever national study aimed at patients with thyroid cancer. The study asks two very important questions: 1) Whethwer a low dose of radioiodine is ad effective as a high dose and 2) whether using Thyrogen adversely affects ablation success. It has the potential to demonstrate the whether a lower treatment dose is equally effective, provides a lower risk of a second malignancy, less chance of permenent salivary gland damage, a shorted hospital stay and overall reduced treatment costs. - Analysis of data and comparison of ablation success rates showed that low dose radioiodine plus thyrotropin-alfa was as effective as high dose radioiodine, with lower rate of adverse events. More patients in the high-dose group than in the low-dose group were hospitalised for at least 3 days (36.3% vs. 13.0%, P<0.001). The proportions of patients with adverse events were 21% in the low-dose group versus 33%in the high-dose group (P = 0.007) and 23% in the Thyrotropin-alfa group versus 30% in the group und Low dose (1.1 GBq) is now widely used in routine clinical practice.
University College London	Birchall	CRUK/04/024: EaStER: Early Stage Glottic Cancer: Endoscopic excision or Radiotherapy; a phase III randomised trial - a feasibility study.	15/50	N/A (trial closed due to poor recruitment)			Feasibility study failed to recruit patients, therefore will not move to phase III trial; no publication for this trial
University College London	Mallick	CRUK/11/010: IoN (previously Thy-low): Randomised trial comparing total thyroidectomy plus TSH suppression with or without radioactive iodine ablation, in low-risk patients with well-differentiated thyroid cancer	153/570	2021	Iodine or Not (IoN) for Low-risk Differentiated Thyroid Cancer: The Next UK National Cancer Research Network Randomised Trial following HiLo. Clin onc, Clinical Oncology. 2012; 24(3) ;159–161 IoN– Is ablative radio-iodine Necessary for low risk differentiated thyroid cancer patients? 35th ETA	Yes	
University College London	Forster	ORCA: A phase I/II study of olaparib in addition to cisplatin-based concurrent chemoradiotherapy for patients with high risk locally advanced squamous cell carcinoma of the head and neck (HNSCC)	0/0				Abandoned following regulatory approval due to withdrawal of support from AZ

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Centre for Drug Development							
University of Birmingham	Steven	CRUKD/13/001: A Cancer Research UK Phase Ib trial to determine the immunogenicity and tolerability of extended schedule vaccination with MVA-EBNA1/LMP2 in patients with Epstein Barr Virus (EBV) positive malignancies.	0/18	2016			Follow up Phase IB study to CRUKD/05/034 first in man trial. This trial will investigate XXXXXXX The Phase II trial of the same vaccine under a collaboration with Hong Kong investigators is ongoing.
University of Birmingham	Steven	CRUKD/05/034: A Cancer Research UK Phase I trial of recombinant MVA based vaccine encoding EBV target antigens (MVA.EBNA1-LMP2) for patients with EBV positive malignancies	16/16	2012	Hui EP, Taylor GS, Jet al. Cancer Res. 2013 Mar 15;73(6):1676-88. N. M. Steven, K. J. Harrington,et al. J Clin Oncol 29: 2011 (suppl; abstr e13028). E. P. Hui, G. S. Taylor, et al. J Clin Oncol 29: 2011 (suppl; abstr 2592). ASCO Meeting Abstracts 2008 26: 3052		First time in patients for this vaccine. If the vaccine is succcessful it could treat nasopharyngeal carcinoma which is a huge cancer burden in asian populations. Trial completed, data being analysed. Phase IB planned & Phase II trial in Hong Kong ongoing. Too early in development to assess clinical impact.
Institute of Cancer Research/Royal Marsden Hospital	O'Brien	CRUKD/99/017: A Phase I study of the rat monoclonal antibody ICR62 against the EGF receptor in squamous cell carcinoma of head and neck and lung	20/20	1995	Modjtahedi H, Hickish T, Nicolson M, Moore J, Styles J, Eccles S, Jackson E, Salter J, Sloane J, Spencer L, Priest K, Smith I, Dean C, Gore M. Phase I trial and tumour localisation of the anti-EGFR monoclonal antibody ICR62 in head and neck or lung cancer. Br J Cancer. 1996 Jan;73(2):228-35.		Early precursor of EGFR targeted therapies. Trial completed. Development discontinued after Phase I due to lack of antibody supply. EGFR targeted therapies are now an important class of cancer therapy.
Kings College London	Sarker	CRUKD/13/003 VIBRANT A Phase I clinical trial with VEGFR antagonist vandetanib combined with 131I-mIBG radiotherapy in patients with neuroendocrine tumours, advanced phaeochromocytoma and paraganglioma	0/18	2016			First time in patients for this combination in this group of very rare tumours. The outcome of this trial could inform future national treatment strategies for this patient population, and lead to a randomised Phase II study / registration strategy for this patient population. The outcome of this trial could inform future national treatment strategies for this patient population, and lead to a randomised Phase II study / registration strategy for this patient population.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Lung							
University of Birmingham	Ferry	BTOG2: A British Thoracic Oncology Group phase III trial of gemcitabine + cisplatin at 50mg/m2 vs gemcitabine + cisplatin at 80mg/m2 vs gemcitabine + carboplatin AUC5 in NSCLC	1363/1350	2012	BILLINGHAM, L. J., GAUNT, P., JARRETT, H. W., DUNLOP, D., THOMPSON, J., O'BYRNE, K. J., KUMAR, M., SKAILES, G., NICOLSON, M., SHAH, R., LEONARD, P., CHETIYAWARDANA, A., WELLS, P., LEWANSKI, C., WOLL, P., CROSSE, B., HILL, M. & FERRY, D. 2011. S86 Quality of life in advanced non-small cell lung cancer, effects of cisplatin dose and carboplatin in combination with gemcitabine: results from BTOG2, a British Thoracic Oncology Group phase III trial in 1363 patients. Thorax, 66, A41. FERRY, D., BILLINGHAM, L. J., JARRETT, H. W., DUNLOP, D., THOMPSON, J., KUMAR, M., SKAILES, G., NICOLSON, M., SHAH, R., LEONARD, P., CHETIYAWARDANA, A., WELLS, P., LEWANSKI, C., WOLL, P., CROSSE, B., HILL, M., PIRRIE, S. & O'BYRNE, K. J. 2011. S85 British Thoracic Oncology Group Trial, BTOG2: Randomised phase III clinical trial of gemcitabine combined with cisplatin 50 mg/m2 (GC50) vs cisplatin 80 mg/m2 (GC80) vs carboplatin AUC 6 (GCb6) in advanced NSCLC. Thorax, 66, A41. DUNLOP, D., FERRY, D., JARRETT, H. W., BILLINGHAM, L. J., THOMPSON, J., KUMAR, M., SKAILES, G., NICOLSON, M., SHAH, R., LEONARD, P., CHETIYAWARDANA, A., WELLS, P., LEWANSKI, C., WOLL, P., CROSSE, B. & O'BYRNE, K. J. 2011. S87 Delivered dose intensity of gemcitabine 1250 mg/m2 with cisplatin at 80 mg/m2 (GC80) and 50 mg/m2 (GC50) and carboplatin AUC 6 (GCb6) in a phase III trial of advanced non-small cell lung cancer (NSCLC): correlations with clinical outcomes. Thorax, 66, A41-A42. JARRETT, H., HILL, M., BILLINGHAM, L. J., O'BYRNE, K. J. & FERRY, D. 2011. S88 Day case cisplatin delivery for advanced NSCLC patients: faster, cheaper, more desirable. Thorax, 66, A42.	Yes	In advanced NSCLC the dose of cisplatin is important with GC50 giving the poorest outcome in terms of overall survival and response rate. GCb6 is not inferior to GC80 thus, in combination with gemcitabine, and in relation to survival time, carboplatin is clinically equivalent to that of cisplatin but other factors, such as quality of life, may influence treatment choice As with UK impact: In advanced NSCLC the dose of cisplatin is important with GC50 giving the poorest outcome in terms of overall survival and response rate. GCb6 is not inferior to GC80 thus, in combination with gemcitabine, and in relation to survival time, carboplatin is clinically equivalent to that of cisplatin but other factors, such as quality of life, may influence treatment choice
The University of Sheffield	Woll	STOMP: Small cell lung cancer trial of Olaparib (AZD2281) as maintenance programme: a randomised, double blind, multicentre phase II trial	0/128	2013			Lung cancer is the commonest cause of cancer death and about 15% of cases are small cell lung cancer. Most patients respond well to first line chemo/radiotherapy but rapidly relapse and die, with a median survival rate of 10 months from diagnosis. New active treatments are urgently required. This trial could lead to new treatments and better survival outcome

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
NHS Greater Glasgow and Clyde	Mohammed (Berry temp CI)	CART: Cardiac Toxicity in lung cancer patients after chemo-radiotherapy: Initial Pilot Study	6/20	2014			The primary objective of this study is to provide pilot data in patients being treated for non small cell lung cancer (NSCLC) of the frequency, nature and extent of acute myocardial radiation damage as determined by MRI. As per UK
The Institute of Cancer Research	Treasure (University College London) (Bliss, ICR-CTSU/Peto, London School of Hygiene and Tropical Medicine)	CRUK/04/003: Mesothelioma and Radical Surgery Trial (MARS) (including pilot)	50/50	2008	TREASURE, T., et al. 2011. Extra-pleural pneumonectomy versus no extra-pleural pneumonectomy for patients with malignant pleural mesothelioma: clinical outcomes of the Mesothelioma and Radical Surgery (MARS) randomised feasibility study. Lancet Oncol, 12, 763-772. TREASURE, T., et al. 2009. The Mesothelioma and Radical Surgery Randomized Controlled Trial: The MARS Feasibility Study. J Thoracic Oncology, 4, 1254-1258. TREASURE, T. 2010. Surgery for mesothelioma: MARS landing and future missions. Eur J Cardiothorac Surg, 37, 509-510. TREASURE, T., et al. 2004. Radical surgery for mesothelioma. BMJ, 328, 237-238. PECKITT, C., et al. 2004. The MARS (Mesothelioma and Radical Surgery) Trial, comparing extra-lpeural pneumonectomy (EPP) against no EPP surgery within a trimodality context. Clin Oncol (R Coll Radiol), 16, S37 #P4.04. DENHOLM, E., et al. 2002. The MARS (Mesothelioma and Radical Surgery) Trial. Clin Oncol (R Coll Radiol), 14, S47 #C2.5. BLISS, J.M. 2012. MARs: What have we learnt? British Thoracic Oncology Group (BTOG) Conference (Clinical Trials Session, Invited).	No	The MARS pilot trial concluded that although data were limited, radical surgery in the form of EPP within trimodality therapy offers no benefit and possibly harms mesothelioma patients compared with no EPP. A larger study with longer followup would be needed to provide reliable evidence of mortality patterns and longterm survival. In addition, MARS showed that patients are willing to accept randomisation between EPP, a complex surgical intervention, and no EPP. MARS is the only randomised trial worldwide investigating the role of radical EPP in the context of trimodality therapy in mesothelioma patients and produced informative and clinically useful results both in terms of its feasibility aspects and its clinical outcomes. The trial was instrumental in encouraging the focus towards less radical surgical approaches in an attempt to improve the quality as well as duration of treatment outcome.
University of Manchester	Faivre-Finn	CRUK/07/005: CONVERT: A 2-arm randomised controlled trial of concurrent chemo-radiotherapy comparing twice-daily and high dose once-daily radiotherapy in patients with limited disease small cell lung cancer	316/unknown target				Ongoing The trial will establish a standard chemo-raditoherapy regimen in good perfomance status, limited stage small cell lung cancer and therefore, will impact on the rountine clinical practice.
Christie Hospital Foundation Trust	Faivre-Finn	CRUKE/10/034: REST: A randomised trial on chest irradiation in extensive disease small cell lung cancer				Yes	
University of Manchester	Faivre-Finn	CRUK/11/052: LungART – A Phase III study comparing post-operative conformal radiotherapy to no post-operative radiotherapy in patients with completely resected non-small cell lung cancer and mediastinal N2 Involvement.	2/125	2019			Ongoing

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Christie Hospital, Manchester	Lorrigan	CRUKE/08/039: VOICE - A two stage randomised phase I/II open-labelled study to determine the efficacy of VOrInostat given with Cisplatinum + Etoposide in previously untreated extensive stage SCLC patients					Ongoing
MRC	Parmar	CRUK/03/001: MS01: Randomised controlled trial of active symptom control with or without chemotherapy in the treatment of patients with malignant pleural mesothelioma	409/420	2008	Muers at al, Lancet 2008, 371, 1685-94. Muers at al, Lancet 2008, 371, 1685-94. First results presented at ASCO 2007 and subsequently presented at the World Lung Conference (Seoul), ECCO (Barcelona), ERS (Stockholm), the NCRI (Birmingham) and the BTS (London)		PA performed and published Very few large randomised trials have been performed in mesothelioma. MS01 accrued 409 patients and is the 2nd largest trial reported. The addition of chemotherapy to active symptom control offers no significant benefits in terms of overall survival or quality of life. However, exploratory analyses suggested the Vinorelbine merits further investigation. The trial team are currently looking into QoL aspects and may present some data on this in 2009, with the possibility of a publication. Given minimal survival benefit from chemotherapy, and no benefit with respect to quality of life, the trial showed that active symptom control is a valid treatment option.
MRC	Hatton	CRUK/05/009: INCH: A randomised phase II/III trial of induction chemotherapy followed by CHART vs CHART alone in patients with inoperable NSCLC	46/500	2010	Induction Chemotherapy and Continuous Hyperfractionated Accelerated Radiotherapy (CHART) for Patients with locally Advanced Inoperable Non-small-cell Lung Cancer: The MRC INCH Randomized Trial. Hatton M et al. In J Rad Onc Biol Phys 2011 Induction Chemotherapy and Continuous Hyperfractionated Accelerated Radiotherapy (CHART) for Patients with locally Advanced Inoperable Non-small-cell Lung Cancer: The MRC INCH Randomized Trial. Hatton M et al. In J Rad Onc Biol Phys 2011; 81(3): 712-718. Results first presented at ECCO/ESMO in Sept 2009 and re-presented in the clinical trial showcase at the NCRI 2009 Conference. Mature results presented at ASCO 2010. A further presentation (in poster format) was made at ASCO GI 2011.	No	This trial has shown that chemotherapy followed by CHART is feasible with 2 year survival rates encouraging. However, it is underpowered having closed early due to poor accrual and therefore generates only a hypothesis for future corroboration.
MRC	Mulvenna	CRUK/07/001: QUARTZ - A phase III multicentre randomised controlled trial to assess whether optimal supportive care alone (including dexamethasone) is as effective as optimal supportive care (including dexamethasone)plus whole brain radiotherapy in the treatment of patients with inoperable brain metastases from non-small cell lung cancer	443/534	2015	Thorax 2008; 63, 1–2. : Oncology Times, September 2008, vol 5 no 9. : Clinical Oncology, 22; 365 – 373. : Letters/Clinical Oncology 22; 615 – 619 : Clinical Oncology, Volume 23, Issue 5, June 2011, Pages 375-376: Clinical Oncology, Volume 24, Issue 4, May 2012, Pages 229–231: Clin Onc 25 (3), e23-30 2013. Oral presentation at 3 Counties Cancer Network Lung Cancer Site Specific Group Annual Clinical Review day (October 18 2012). Oral presentation of baseline carer data at BTOG January 2013. Poster at BTOG conference January 2013; Lung cancer 79 (1) pS56 (165).	Yes	Open to accrual Very pragmatic, patient orientated trial. Experimental arm is No Whole Brain Radiotherapy (ie less treatment). Primary endpoint is Quality of Life Adjusted life Years (combining quality and duration of survival). Results from the trial may potentially re-define the use of Whole Brain Radiotherapy in this group of patients and impact on clinical practice worldwide.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Mount Vernon Hospital	Saunders	CRUK/88/006: CHART - The clinical trial of continuous hyperfractionated accelerated radiation therapy	563/563	1997	Radiother Oncol. 1997 Aug;44(2):123-36. A randomised multicentre trial of CHART versus conventional radiotherapy in head and neck cancer Br J Cancer. 2011 Sep 27;105(7):884-9. doi: 10.1038/bjc.2011.334. Epub 2011 Aug 30.	Yes	The analysis of the mature data showed that CHART was superior to conventional radiotherapy in achieving local tumour control and survival in locally advanced non-small cell lung cancer. This demonstrated the importance of cellular repopulation as a cause of failiure in radiotherapy of NSCLC. Local control leads to a reduction in the risk of metastases and an improvement in long-term survival. Groundbreaking trial, leading to a change in practice for the treatment of non-small cell lung cancer patients. A predecessor to INCH and CHART-ED.
Royal Free	Gilbert	CRUK/06/041: Effectiveness of computer-tailored smoking cessation advice in primary care: a randomised trial (ESCAPE)	2624/7250		Gilbert H et al., Trials, 2008 9:23.		Potential for rolling out the intervention at low cost in general practice and other outlets if found to be effective
University of Aberdeen	Campbell	CRUK/07/057: Reducing time to presentation with symptoms of lung cancer: phase II complex intervention study	229/210				This trial is currenlty ongoing, so no impact yet. If we show that it is possible to reduce the time between symptom onset and presentation with symptoms of lung cancer, then further work will be needed to translate our intervention into one that can be widely and effectively implemented in clinical practice.
QMUL	Szlosarek	CRUK/07/026: ADAM: A randomised stratified phase II multicentre clinical trial of single-agent ADI-PEG 20 (pegylated arginine deiminase) in patients with malignant pleural mesothelioma					Ongoing
University of Southampton	Ottensmeier	CRUKE/10/019: ICE: A Phase II trial of the addition of ipilimumab to carboplatin and etoposide chemotherapy for the first line treatment of extensive stage small cell lung cancer plus sample collection.	19/40	2014		Yes	Immune responses against SCLC appear to confer a better outlook to patients with this condition. In this phase II study we will examine, whether the addition of an immunostimulatory antibody against CTLA-4, ipilimumab, to chemotherapy could improve outcome and how immune responses against tumour associated antigens correlate with benefit
Velindre NHS Trust	Lester	CRUK/10/005: I-START: ISoToxic Accelerated Radiotherapy for Non-small cell lung cancer.	57/122	2014	Poster at CRUK event June 2013	No	This is a phase I/II trial. The result will be used to determine the experimental arm of a future phase II/III which, if positive, would lead to a change in clinical practice. Will contribute significantly to international knowledge base.
Velindre NHS Trust	Macbeth (Griffiths for the sample collection)	CRUK/06/007: FRAGMATIC: A randomised phase III clinical trial investigating the effect of FRAGMin® Added to standard Therapy In patients with lung Cancer. T-FRAG – Collection and storage of tumour and blood samples from patients with lung cancer in the FRAGMATIC clinical trial for future translational research	2202/2200	2014	Griffiths et al. FRAGMATIC: A randomised phase III trial investigating the effect of fragmatic added to standard therapy in patients with lung cancer. BMC Cancer 9,355,2009. Protocol paper. Poster at Welsh Government Meeting, 2013	Yes	Likely to lead to a change in clinical practice. Will contribute significantly to international knowledge base.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Velindre NHS Trust	Fennell	CRUK/11/055: PIN: A Randomised phase II trial of Olaparib maintenance versus placebo monotherapy in patients with non-small cell lung cancer	0/114	2014		Yes	This is a randomised phase II trial. The result will be used to determine the experimental arm of a future phase III which, if positive, would lead to a change in clinical practice. Will contribute significantly to international knowledge base.
Bangor University	Neal	EL CID: A pilot clinical trial looking at the effect on lung cancer diagnosis of giving chest X-ray to smokers	386/386	2014	NAEDI Research Conference April 2013 A pilot clinical trial looking at the effect on lung cancer diagnosis of giving a CXR to smokers aged over 60 with chest symptoms – the ELCID trial Richard Neal*, Kirsty Roberts, Chris Hurt, Trevor Rogers, Willie Hamilton, Rhiannon Tudor Edwards, Angela Tod, David Parker, Emma Thomas Jones, Annmarie Nelson, Hayley Prout, Kerenza Hood, Gareth Griffiths	No	This is a randomised phase II trial. The result will be used to determine the experimental arm of a future phase III which, if positive, would lead to a change in clinical practice. Will contribute significantly to international knowledge base.
Velindre NHS Trust	Lester	SKOPOS - A Phase II trial to assess the safety, immunological activity of TroVax® plus Pemetrexed/Cisplatin in patients with malignant pleural mesothelioma	11/26	2014		No	This is a phase II trial and a larger confirmatory trial is needed before any potential impact on changing practice. Will contribute significantly to international knowledge base.
Royal Free & University College Medical School	Siow Ming Lee	CRUK/99/001: Thalidomide in small cell lung cancer.	24/24	2001	Siow Ming Lee, Lindsay James, Tomas Buchler, Mike Snee, Paul Ellis, Allan Hackshaw. 'Phase II trial of thalidomide with chemotherapy and as maintenance therapy for patients with poor prognosis small-cell lung cancer. Lung Cancer 2007: 2868: 1-5 Lee S-M et al., Phase II trial of carboplatin and etoposide with thalidomide in patients with poor prognosis small-cell lung cancer. Lung Cancer 2008; 59(3):364-8. Lee S-M et al., 'Phase II trial of thalidomide with chemotherapy and as maintenance therapy for patients with poor prognosis small-cell lung cancer. Lung Cancer 2007: 2868: 1-5	no	Concurrent thalidomide with chemotherapy followed by maintenance thalidomide appeared to be be well tolerated. Response rates indicated this regimen should be examined in a phase III trial Trial showed that thalidomide appeared to be effective in increasing survival. Led to CRUK/02/004 being run.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Royal Free & University College Medical School	Siow Ming Lee	CRUK/02/004: A phase III randomised, double blind, placebo controlled trial of carboplatin/etoposide with or without thalidomide in small cell lung cancer (Study 12)	724/720	2008	Lee, SM; Woll, PJ; Rudd, R; et al. Anti-angiogenic Therapy Using Thalidomide Combined With Chemotherapy in Small Cell Lung Cancer: A Randomized, Double-Blind, Placebo-Controlled Trial. J.N.C.I, 101 (15): 1049-1057 Aug 5 2009 Lee, SM; Woll, PJ; Rudd, R; et al. Anti-angiogenic Therapy Using Thalidomide Combined With Chemotherapy in Small Cell Lung Cancer: A Randomized, Double-Blind, Placebo-Controlled Trial. J.N.C.I, 101 (15): 1049-1057 Aug 5 2009 Lee S-M, Woll P, Hatton M et al. A phase III randomised, double blind, placebo controlled trial of etoposide/carboplatin with or without thalidomide in advanced small cell lung cancer (SCLC). IASLC in publication 2007. British Journal of Cancer (2012) 106, 1153 – 1159. "Analysis of circulating angiogenic biomarkers from patients in two phase III trials in lung cancer of chemotherapy alone or chemotherapy and thalidomide" RJ Young, AW Tin, NJ Brown, M Jitlal, SM Lee and PJ Woll.	No	This large randomized trial of patients with SCLC, demonstrated that thalidomide in combination with chemotherapy did not improve survival but was associated with an increased risk of a thrombotic event. Trial showed that thalidomide is ineffective in this setting. This has implications for other ongoing trials on thalidomide and lung cancer.
University College London	Rudd	Study 10: A phase III study of gemcitabine/carboplatin versus cisplatin/etoposide in SCLC	241/241	2004	Lee SM, et al. Comparison of gemcitabine and carboplatin versus cisplatin and etoposide for patients with poor-prognosis small cell lung cancer. Thorax online 11 Sep 2008 and Thorax 2009;64;75-80; Lee SM, et al. Comparison of gemcitabine and carboplatin versus cisplatin and etoposide for patients with poor-prognosis small cell lung cancer. Thorax online 11 Sep 2008 and Thorax 2009;64;75-80; Presented at World Conference on Lung Cancer Tokyo 2000; at the British Thoracic Society meeting in Stockholm 2000 and Management of Lung Cancer Meeting, Lausanne 2000.	No	Gemcitabine with carboplatin is as effective as Cisplatin and etoposide in terms of overall toxicity and progression-free survival and has a toxicity profile more acceptable to patients Gemcitabine with carboplatin is as effective as Cisplatin and etoposide in terms of overall toxicity and progression-free survival and has a toxicity profile more acceptable to patients
University College London	Ledermann (Spiro)	CRUK/88/001: A randomised study of timing of thoracic irradiation in small cell lung cancer (Study 8)	325/325	2005	SG Spiro et al., Early Compared With Late Radiotherapy in Combined Modality Treatment for Limited Disease Small-Cell Lung Cancer: A London Lung Cancer Group Multicenter Randomized Clinical Trial and Meta-Analysis. JCO: 2006; 24 (24):3823-3830.; SG Spiro et al., Early Compared With Late Radiotherapy in Combined Modality Treatment for Limited Disease Small-Cell Lung Cancer: A London Lung Cancer Group Multicenter Randomized Clinical Trial and Meta-Analysis. JCO: 2006; 24 (24):3823-3830.; Hackshaw AK, Spiro SG. The timing of radiotherapy when given with chemotherapy in patients with small-cell lung cancer. Am J Hematology/Oncology 2007;6(2): 74-78. Presented at the World Conference on Lung	No	Demonstrated that the benefit of early radiotherapy appears dependant on patients receiving all planned chemotherapy cycles. Has added to the body of knowledge on the timing of thoracic radiotherapy. The meta-analysis showed that early radiotherapy is effective but only when patients complete their chemotherapy. Demonstrated that the benefit of early radiotherapy appears dependant on patients receiving all planned chemotherapy cycles. Has added to the body of knowledge on the timing of thoracic radiotherapy. The meta-analysis showed that early radiotherapy is effective but only when patients complete their chemotherapy.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
					Cancer 2003, Vancouver.		
University College London and Birmingham University	Cullen	CRUK/88/002: Mitomycin, Ifosfamide and Cisplatin in non-small cell lung cancer: a randomised trial of chemotherapy plus radiotherapy versus radiotherapy alone	797/unknown target	1999	1999 Cullen MH et al., 'Mitomycin, Ifosfamide and Cisplatin in unresectable non-small cell lung cancer: effects on survival and quality of life' JCO 1999; 17(10);3188-3194.; Cullen MH et al., Classic Papers & Current Comments: Highlights of Lung Ca Research 6, 1, 21-28, 2001	no	MIC chemotherapy prolongs survival in unresectable NSCLC without compromising QOL. One of the first trials looking at chemotherapy in NSCLC in the UK. Following this trial (and the MIC2 trial in the advanced NSCLC setting, run in Birmingham) MIC became one of the standard chemotherapy regimen used for advanced NSCLC in the UK.
University College London	Dr David Landau	CRUK/09/010: IDEAL CRT: A phase I/II trial of concurrent chemoradiation with dose-escalated radiotherapy in patients with stage II or stage III Non-Small Cell Lung Cancer	109/135	2014		Yes	If sucesssful this trial could be used to develop a potential experimental arm for a future phase III trial.
University College London	Lee	CRUKE/08/021: ET Trial: A multicentre, randomised, phase III, trial of platinum-based chemotherapy versus non-platinum chemotherapy, after ERCC1 stratification, in patients with advanced/metastatic non-small cell lung cancer.	648/1272	2015	ESMO 2014	Yes	ERCC1 assay proved to be equivocal - ERCC1 should not be relied on as a prognostic marker at this point in time ERCC1 should not be used as a prognostic marker - this may have implications for private healthcare ERCC1 should not be used as a prognostic marker - this may have implications for private healthcare
University College London	Lee	CRUK/05/034: TACTIC: A randomised phase II study of whole brain radiotherapy (WBRT) and Tarceva (OSI-774, erlotinib in patients with advanced non-small cell lung cancer (NSCLC)	78/80	2011	Siow Ming Lee, Conrad R. Lewanski, Nicholas Counsell, Christian Ottensmeier, Andrew Bates, Nirali Patel, Christina Wadsworth, Yenting Ngai, Allan Hackshaw, Corinne Faivre-Finn. Randomized Trial of Erlotinib Plus Whole-Brain Radiotherapy for NSCLC Patients With Multiple Brain Metastases. JNCI J Natl Cancer Inst (2014) 106(7): dju151	no	TACTIC showed no advantage in nPFS or OS for concurrent erlotinib and WBRT followed by maintenance erlotinib in patients with predominantly EGFR wild-type NSCLC and multiple brain metastases compared to placebo. Future studies should focus on the role of erlotinib with or without WBRT in patients with EGFR mutations If the addition of Tarceva to WBRT in NSCLC patient with multiple brain metastatses affects neurological progression free survival in patients who are not suitable for chemotherapy.
University College London	Seckl	CRUK/06/009: LungStar: A multicentre phase III randomised double blind placebo controlled trial of pravastatin added to first line standard chemotherapy in patients with small cell lung (SCLC)	846/1300	2015	Hackshaw A et al., Setting up non-commercial clinical trials takes too long in the UK: findings from a prospective study Soc Med. 2008Jun;101(6): 299-304.	No	Adding pravastatin 40mg OD to standard SCLC therapy is safe with no obvious increase in toxicity. The addition of pravastatin to standard therapy is ineffective
University College London	Spiro	CRUK/06/022: LUNG-SEARCH: A randomised controlled trial of surveillance for the early detection of lung cancer in an at risk group	1568/1300			Yes	To assess if more frequent screening will allow earlier detection of lung cancer when less advanced.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University College London	Lee	CRUK/03/007: TOPICAL: A randomised, placebo-controlled trial of Tarceva (OSI-774, erlotinib) in patients with advanced NSCLC unsuitable for chemotherapy.	670/664	2012	Siow Ming Lee, Iftekhar Khan, Sunil Upadhyay, Conrad Lewanski, Stephen Falk, Geraldine Skailes, Ernie Marshall, Penella J Woll, Matthew Hatton, Rohit Lal, Richard Jones, Elizabeth Toy, David Chao, Gary Middleton, Sue Bulley, Yenting Ngai, Robin Rudd, Allan Hackshaw, Chris Boshoff. First-line erlotinib in patients with advanced non-small-cell lung cancer unsuitable for chemotherapy (TOPICAL): a double-blind, placebo-controlled, phase 3 trial. Lancet Oncology 13(11):1161-1170.	Yes	The largest randomised trial investigating treatment of poor-performance advanced non-small-cell lung cancer patients unsuitable for first line chemotherapy. Results were presented at ASCO 2010 showing that Erlotinib/Tarceva (EGFR inhibitor) improves overall survival and progression free disease in female patients carrying a wild type copy of the EGFR gene. If positive, Tarceva may be recommended for 1st line treatment for advanced NSCLC in patients not suitable for chemotherapy. The trial has been promoted at the British Thoracic Oncology Group meeting in Jan 2008. - Erlotinib significantly improved progression-free and overall survival of patients, but only if they developed a treatment-related rash by 1 month. These findings would help change practice by giving poor prognosis patients an effective therapy that can be taken orally.
University College London	Maguire	CRUK/04/006: SOCCAR: A randomised phase III trial of sequential chemotherapy followed by radical radiotherapy v concurrent chemo-radiotherapy followed by chemotherapy in patients with inoperable stage III NSCLC and good performance status. Amended to Phase II on 25/	130/130	2011	J. Maguire, I. Khan, R. McMenemin, N. O'Rourke, S. McNee, V. Kelly, C. Peedell, M. Snee. SOCCAR: A randomised phase II trial comparing sequential versus concurrent chemotherapy and radical hypofractionated radiotherapy in patients with inoperable stage III Non-Small Cell Lung Cancer and good performance status. In press	Yes	Results will show whether cocurrent chemotherapy confers a survival advantage compared with sequential chemotherapy in patient with stage III non-small cell lung cancer. This trial will provide toxicty data on both arms of the trial.
University College London	Fennell	CRUKE/09/025: MESO-2: A phase I/II study of first line ganetespib with pemetrxed, in patients with malignant pleural mesothelioma	14/Max 27 patients for cisplatin; and 18 for carboplatin	2017		no	
University College London	Popat	TIMELY: Trial of afatinib (BIBW 2992) In suspected or confirmed Mutant EGFR Lung Cancer patients unfit for chemotherapY	19/37	2016		No	It is unknown at this stage if the trial will lead to new guidelines or become a control arm for another trial.
University College London	Siow Ming Lee	S14: A phase II/III randomised, double blind, placebo controlled trial of gemcitabine/carboplatin with or without thalidomide in advanced non-small cell lung cancer	722/722	2009	Lee SM, Rudd R, Woll PJ, Ottensmeier C, Gilligan D, Price A, Spiro S, Gower N, Jitlal M, Hackshaw A (2009a) Randomized double-blind placebo-controlled trial of thalidomide in combination with gemcitabine and carboplatin in advanced non-small-cell lung cancer. J Clin Oncol 27: 5248– 5254 British Journal of Cancer (2012) 106, 1153 – 1159. "Analysis of circulating angiogenic biomarkers from patients in two phase III trials in lung cancer of chemotherapy alone or chemotherapy and thalidomide" RJ Young, AW Tin, NJ Brown, M Jitlal, SM Lee and PJ Woll	no	This large randomized trial of patients with SCLC, demonstrated that thalidomide in combination with chemotherapy did not improve survival but was associated with an increased risk of a thrombotic event. Translational work: Circulating angiogenic biomarkers did not identify patients who benefited from thalidomide treatment. Trial showed that thalidomide is ineffective in this setting. This has implications for other ongoing trials on thalidomide and lung cancer.
University College London	Siow Ming Lee	CRUKE/13/020: Study 15: A phase II, multicentre, randomised trial comparing combination gemcitabine/carboplatin and hydroxychloroquine with	unknown/140				

Key:	Trials that are currently in set-up	Trials that are currently open	Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
		gemcitabine/carboplatin therapy alone in extensive stage small cell lung cancer (SCLC)					
University College London	Swanton	CRUK/14/020: TRACERx: TRAcking non small cell lung Cancer Evolution through Therapy Rx	94/842	2022		Yes	Identifying potential drivers which could lead to development of new therapies Not known at present
Centre for Drug Development							
University of Oxford	Higgins	CRUKD/12/016: A CR-UK Phase I study of PI3K inhibitor BKM120 in patients with non-small cell lung cancer receiving thoracic radiotherapy	3/30	2016			First time for this agent combined with thoracic radiotherapy. First time for this agent combined with thoracic radiotherapy. Provisional discussions underway to combine this drug with curative treatment in patients with NSCLC Will be dependent upon subsequent trials in the curative setting
University of Oxford	Talbot	CRUKD/11/001: VANSEL1: Phase I dose escalation trial of the oral VEGF/EGFR inhibitor, Vandetanib (ZD6474) in combination with the oral MEK inhibitor Selumetinib (AZD6244) in solid tumours and in patients with NSCLC	25/61	2016			First time for this combination in this group of patients. Trial open. Aims to assess safety, efficacy, pharmacokinetics, pharmacodynamics and identify the MTD of the combination and recommend doses and a schedule for Phase II. Also to determine the relationship between response and mutation status. Vandetanib is currently licenced for use in the EU (and US) to treat medullary thyroid cancer and Selumetinib is not licenced. The clinical impact, should the combination reach the market, would be extending the clinical utility of these agents and providing a novel approach to treating NSCLC. Vandetanib is currently licenced for use in the EU (and US) to treat medullary thyroid cancer and Selumetinib is not licenced. The clinical impact, should the combination reach the market, would be extending the clinical utility of these agents and providing a novel approach to treating NSCLC.
University of Birmingham	Ferry	CRUKD/97/014: A CRC Phase II study of PK1 [N-(2-hydroxypropyl)methacrylamide copolymer doxorubicin]: in non small cell lung cancer	29/29	2005	Seymour LW, Ferry DR, Kerr DJ, Rea D, Whitlock M, Poyner R, Boivin C, Hesslewood S, Twelves C, Blackie R, Schatzlein A, Jodrell D, Bissett D, Calvert H, Lind M, Robbins A, Burtles S, Duncan R, Cassidy J. Phase II studies of polymer-doxorubicin (PK1, FCE28068) in the treatment of breast, lung and colorectal cancer. Int J Oncol. 2009 Jun;34(6):1629-36.		Follow on Phase II trial to CRUKD/94/007 and companion trial to CRUKD/97/011 & CRUKD/97/016. Important because these trials were the first large scale trials of a polymer targeted agent in humans. Unlikely this would have been done by industry alone and also came from lab work supported by CRUK. Trial completed. PK1 shown to have some activity in lung and breast cancer, not felt to be sufficient to take forward into phase III evaluation. Development discontinued after Phase II. Too early in development to assess clinical impact.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Lymphoma							
University of Liverpool	Pettitt	PACIFICO: Phase III multicentre trial comparing two different Rituximab-Chemotherapy induction regimens for Follicular Lymphoma in Older Patients.	210/680	2017	The trial has been publicised at the NCRI conference and the annual NCRI lymphoma trials meeting in November 2012.	Yes	Follicular lymphoma predominantly affects the elderly, yet the optimum treatment for older patients with the disease has not been defined. The present study aims to address this question by comparing the drug combination that is currently considered the gold-standard (R-CVP) with a newer combination (R-FC lite) that might be more effective without being significantly more toxic. If positive, it would lead to a change in clinical practice, including potential for license expansion and change to NICE recommendations. Number of patients likely to be affected will be around 1500 patients per year. If successful, it will establish R-FC lite as a useful treatment option for older patients with follicular lymphoma.
University of Oxford	Schuh	CRUKE/09/038: Multi-centre non-randomised Phase II feasibility study of Ofatumumab in combination with CHOP in induction/consolidation followed by Ofatumumab maintenance every 2 months for one year in patients with biopsy proven Richter's Syndrome	Unknown/35	2014		Yes	Trial will provde evidence for treatment of Richter's syndrome none planned There are no other current clinical trials for patients with Richter's Syndrome.
MRC	Stenning	CRUK/01/006: LY10: A clinico-pathological study of Burkitt and Burkitt-like Non-Hodgkin's Lymphoma	128/120	2008	Mead GM, et al. A prospective clinicopathologic study of dose-modified CODOX-M/IVAC in patients with sporadic Burkitt lymphoma defined using cytogenetic and immunophenotypic criteria (MRC/NCRI LY10 trial). Blood. 2008;112(6):2248-2260. Preliminary results presented as a poster by J Walewski at ASCO in May 2006		50% of patients thought to have BL on previous diagnostic criteria do not; lower dose methotrexate appears to reduce toxicity without reduction in effiacy compared with historical data. This is a rare disease but the new diagnostic criteria will result in improved targeting of the very intensive treatment needed to cure BL to those who really need it.
MRC	Johnson	CRUK/95/017: A randomised controlled trial of ABVD vs two multi-drug regimens for advances Hodgkin lymphoma - Updated results of UKLG LY09	807/800	2005	Johnson et al, J Clin Oncol 2005: 23(36): p9208-9218: secondary publication W. S. Owadally et al, Ann. Onc., Advance Access published on August 14, 2009; doi: doi:10.1093/annonc/mdp		*was funded via a block grant to the UK lymphoma group through the MRC CTU rather than trial-specific funding. No evidence of benefit to the multidrug regimens; ABVD remains standard treatment for advanced Hodgkin Lymphoma

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Newcastle University	Proctor	CRUKE/03/020: SHIELD: A phase II study VEPEMB in patients with Hodgkin's lymphoma aged > 60 years	188/300	2011	Proctor et al. Evaluation of treatment outcome in 175 patients with Hodgkin lymphoma (HL) aged 60 years or over: the SHIELD study. Blood 119: 6005-6015 June 2012. 1) Proctor et al. International study of Hodgkin‟s lymphoma in the elderly. Eu. J. Haem. 2004:73 50-51 2) Proctor and Wilkinson. Extreme Hodgkin‟s lymphoma: current problem areas. Annals of Oncology. 2006:17 iv 15-17 3) Proctor et al. Improving the treatment of Hodgkin lymphoma in older patients. Lymphoma Matters, 2006:68 6-7 4) Proctor and Wilkinson. A web based study concept designed to progress clinical research for "orphan" disease areas in haematological oncology in the elderly: The SHIELD programme. Crit. Reviews Oncology/Haematology 2007:61 (1) 79-83 5) Proctor et al. Hodgkin lymphoma in the elderly: a clinical review of treatment and outcome, past present and future. Critical Reviews in Oncology 2009:71 222-232		VEPEMB therapy provides satisfactory disease control in early- and advanced-stage disease, with acceptable toxicity and sustained remission in those who have a complete response. ABVD in its standard form has demonstrated substantial toxicity and only moderate efficacy in this age group and should not be automatically considered as standard therapy. The aim of this study was to include all pathologically eligible patients in participating centres, whether or not they undergo protocol chemotherapy, in order to provide a clearer overall clinical picture of this disease. Unknown
University of Southampton	Johnson (Illidge)	CRUK/07/038: SCHRIFT (Phase II study of abbreviated immuno-chemotherapy followed by 90Y Ibritumomab tiuxetan in relapsed follicular lymphoma)	54/60	2011	Publication planned in Blood - currently in draft. Hampson G et al., (2010) Validation of an ELISA for the determination of rituximab pharmacokinetics in clinical trials subjects. J Immunol Methods; 360(1-2):30-8. Epub 2010 Jun 11. PMID 20547164 Poster presentation at ASCO 2012: Illidge T et al., UK NCRI Lymphoma Group; Effect of short-duration chemoimmunotherapy plus radioimmunotherapy on response rates in relapsed follicular lymphoma: A U.K. NCRI Lymphoma Group Study, CR UK/07/038. : J Clin Oncol 30, 2012 (suppl; abstr 8056)		The first clinical outcomes from this study were presented at ASCO 2012. (Illidge et al., J Clin Oncol, 2012 30 (suppl; abstr 8056). They showed that the combination of short duration chemotherapy plus radioimmunotherapy is capable of producing a high overall response rate of 96% (CR/CRu 28%). PFS was 31.4 months (95% CI 15.8 - not reached), with no difference in PFS according to FLIPI score at entry. The responses were of comparable duration to those seen after a full course of R-CHOP, offering an alternative approach to treatment

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Southampton	Johnson	CRUKE/06/035: IELSG-26: A clinico-pathologic study of primary mediastinal B-cell lymphoma	4/unknown target	2015	Luca Ceriani, Pierluigi Zinzani, Silvia Govi, Caterina Stelitano, Umberto Vitolo, Ercole Brusamolino, Giuseppina Cabras, Luigi Rigacci, Monica Balzarotti, Flavia Salvi, Silvia Montoto, Armando Lopez-Guillermo, Emanuele Zucca, Luca Giovanella, Peter Johnson, Maurizio Martelli. PET/CT response analysis in primary mediastinal diffuse B-cell lymphoma (PMBL): preliminary results of the IESLG-26 study. International Conference on Malignant Lymphoma (Lugano) June 15-18 2011. Ann Oncol 2011: 22 s4. a147 Poster presentation at ASH 2012: ROLE OF POSITRON EMISSION TOMOGRAPHY (PET/CT) IN PRIMARY MEDIASTINAL LARGE B CELL LYMPHOMA (PMLBCL): PRELIMINARY RESULTS OF AN INTERNATIONAL PHASE II TRIAL (IELSG-26 STUDY) CONDUCTED ON BEHALF OF THE INTERNATIONAL EXTRANODAL LYMPHOMA STUDY GROUP (IELSG), THE FONDAZIONE ITALIANA LINFOMI (FIL) AND THE UK NCRI LYMPHOMA GROUP L Ceriani, E Zucca, PL Zinzani, AJM Ferreri, U Vitolo, C Stelitano, E Brusamolino, MG Cabras, L Rigacci, M Balzarotti, F Salvi, G Pinotti, E Porro, E Finolezzi, F Merli, C Rusconi, S Montoto, A Davies, P Paesano, A Lopez-Guillermo, F Cavalli, L Giovanella, P Johnson and M Martelli PROGNOSTIC VALUE OF 18FDG BASELINE FUNCTIONAL PET PARAMETERS IN PRIMARY MEDIASTINAL DIFFUSE LARGE BCELL LYMPHOMA L. Ceriani, E. Zucca, P. L. Zinzani, A. Ferreri, U. Vitolo, C. Stelitano, E. Brusamolino, G. Cabras, L. Rigacci, F. Salvi, L. Gargantini, M. Balzarotti, F. Merli, G. Pinotti, S. Montoto, A. Lopez-Guillermo, F. Cavalli, L. Giovanella, P.W. Johnson, M. Martelli	Yes	Data will be obtained about the detailed immunophenotypic and molecular characteristics of PMBL, in order to examine their prognostic significance, and secondly the PET response rate following initial chemo-immunotherapy with anthracycline-based regimens containing Rituximab. This, together with information about the results of different chemotherapy schedules and different uses consolidation radiotherapy, will allow the design of a subsequent randomised trial which will have broad international support. Preliminary results show TLG on baseline PET is a powerful predictor of PMLBCL outcome, and its utility to risk stratify patients may warrant further studies.
University of Southampton	Johnson	CRUKE/10/024: REMoDL-B: A Randomised Evaluation of Molecular guided therapy for Diffuse Large B-cell Lymphoma with Bortezomib	512/940	2020	AACR 2012: poster presentation: Jack A, et al., Prospective stratification using gene expression arrays in a randomised trial of R-CHOP +/- Bortezomib in diffuse large B-cell lymphoma (DLBL): The UK NCRI REMoDL-B study. ISRCTN 51837425. Proc AACR 2012: 1753	Yes	This study of treatment for diffuse large B-cell lymphoma aims to determine whether adding bortezomib to standard combination chemotherapy and rituximab can improve progression-free survival. Molecular studies have indicated the heterogeneous biology of this disease, and this knowledge will be applied prospectively to determine whether a sub-group of patients might especially benefit.
Royal Free Hospital NHS	Cwynarski	CRUK/10/023: IELSG-32: Randomised Phase II Trial on primary CT with Methotrexate & Cytarabine +/- Thiotepa & Rituximab, followed by brain irradiation vs. high-dose CT supported by ASCT for immunocompetent patients with	22/30	2016		Yes	In the first randomisation the impact of adding Rituximab to the regimen on efficacy and toxicity is addressed. Clear evidence of the merit of using Rituximab (improving response rates and survival) for patients with DLBCL outside the brain is available. However there are no randomised data regarding its impact on outcome in patients with PCNSL. This question is highly important because of the potential

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
		CNS lymphoma					impact on efficacy and potential cost of treatment
University of Southampton	Davies	CRUK/12/040: IELSG-37 A randomized, open-label, multicentre, two-arm phase III comparative study assessing the role of mediastinal radiotherapy after Rituximab containing chemotherapy regimens to patients with newly diagnosed Primary Mediastinal Large B-Cell Lymphoma (PMLBCL)	unknown/90	2018		Yes	The trial should be able to demonstrate a non-inferior outcome in patients not receiving IFRT after immunochemotherapy. Such study may eventually allow individualising of treatment for each patient by adapting it to the PET response limiting the indication for additional radiotherapy only to the patients who show an inadequate response to immunochemotherapy.
East & North Herts NHS Trust	Hoskin	CRUK/02/002: STANFORD V: A randomised Phase III study of the Stanford V regimen compared with ABVD for the treatment of advanced Hodgkin's disease, a British National Lymphoma Investigation	370/700	2009	Hoskin PJ, Lowry L, Horwich A, Jack A, Mead B, Hancock BW, Smith P, Qian W, Patrick P, Popoval B, Pettit A, Cunningham D, Pettengell R, Sweetenham J, Linch D & Johnson PWM. 2009: Randomized comparison of the Stanford V regimen and ABVD in the treatment of advanced Hodgkin's lymphoma: United Kingdom National Cancer Research Institute Lymphoma Group Study ISRCTN 64141244. Journal of Clinical Oncology 27:5390-5396 PRIMARY ANALYSIS: Randomised Comparison of the Stanford V Regimen and ABVD in the Treatment of Advanced Hodgkin Lymphoma: Results from a UK NCRI Lymphoma Group Study, ISRCTN 64141244. Hoskin P et al (in press JCO). Sweetenham J et al, Blood, 2000; 96(11 Pt 2); 249B-249B. Johnson P, Blood, 2004; 104(11 Pt 1); 93A-93A. Diez P, Radiother Oncol, 2004; 73(Supp 1); S423-S423. Johnson P, Ann Oncol, 2005; 16(Supp 5); 115-115. Presented major findings at ASH 08, preliminary findings at ASH 2004 and ESTRO 2004.	No	In a large, randomised trial, the efficacies of Stanford V and ABVD were comparable, when given in combination with appropriate radiotherapy. Trial still in follow up will contribute significantly to international knowledge.
British National Lymphoma Institute	Rule	CRUK/02/005: National Mantle Cell Lymphoma Trial	156/156		Eve HE et al., Toxicity of fludarabine and cyclophosphamide with or without rituximab as initial therapy for patients with previously untreated mantle cell lymphoma: results of a randomised phase II study. Leukemia & Lymphoma, February 2009; 50(2): 211–215. Rule S, BJH. 145 Supplement 1:87, April 2009 137 Rule S, BJH, Supplement 1:17-18, April 2007. Rule S, Ann Oncol, 2005; 16(Supp 5); 95-95. HE Eve and SAJ Rule. BJH, 137, (Suppl. 1), abstract 52. Rule S et al, BJH. 137 Supplement 1:19, April 2007. Presented at BSH 2007 and ASCO 2009.	Yes	Phase II - Efficacy and toxicity was equivalent between the 2 arms. Phase III trial still in progress this is the largest randomised controlled trial determining the role of rituximab in the treatment of Mantle Cell Lymphoma.
Royal Free & University College Medical	Linch	CRUK/02/008: MISTRAL trial in lymphoma		2006	Betticher D, Ann Oncol, 2005; 16(Supp 5); 100-101. Betticher DC, Ann Oncol, 2006; 17(10); 1546-1552.	No	Demonstrated inefficacy of high dose sequential chemotherapy in NHL, thereby avoiding over-treatment of high risk patients.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
School							
University College London and Birmingham University	Linch	CRUK/92/003: Long term follow up and analysis of British National Lymphoma Investigation trials database			Swerdlow AJ et al., (2007) Myocardial infarction mortality risk after treatment for Hodgkin disease: a collaborative British cohort study. J Natl Cancer Inst 99[3]: 206-214. Mudie NY et al., (2006) Risk of second malignancy after non-Hodgkin's lymphoma: a British Cohort Study. J Clin Oncol 24: 1568-1574. Presented major findings at the International Symposium of Hodgkin's Lymphoma 2007.		Two papers on late effects, particularly risks of second malignancy and coronary disease. These have markedly influenced trial design and shifted practice away from the use of extended field radiotherapy.
University College London	Linch	LY02: A randomised trial to evaluate early high dose therapy and autologous bone marrow transplantation as part of planned initial therapy for poor risk intermediate/high grade NHL	457/500		Final analysis of the UKLG LY02 trial comparing 6-8 cycles of CHOP with 3 cycles of CHOP followed by a BEAM autograft in patients <65 years with poor prognosis histologically aggressive NHL. Linch DC et al., Br J Haematol. 2010 Apr;149(2):237-43. Epub 2010 Mar 1.		After initial 3 cycles of CHOP 19% were in CR, 53% PR. At end of treatment 86% of patients in CHOP arm had responded, 58% CR. In high-dose therapy arm, overall response rate was 83% with 64% in CR (difference between arms not significant). PFS and OS at 5 years for continuing CHOP arm were 38% and 50% respectively, and for autograft arm were 44% and 50% (differences not significant). Of the patients who attained CR and subsequently relapsed, there were no long-term survivors in the autograft recipients compared to 46% of the continuing CHOP recipients (P = 0.0008). In conclusion, no survival benefit was demonstrated for an early autograft in first response.
University College London	Johnson	CRUKE/04/016: A pilot study of CHOP plus Campath for the primary treatment of ALK-ve peripheral T cell Lymphoma	8/30	2014		Yes	To determine the best dose of campath to give with CHOP chemotherapy in T cell lymphoma.
University College London	Lennard	CRUK/04/023: A phase II evaluation of high dose chemotherapy and autologous stem cell transplantation for Intestinal T-cell lymphomas	25/60	2015			Safety and efficacy of this procedure in this patient population
University College London	Rule	CRUK/08/020: Mantle Miniallo	25/25	Jul-05		Yes	To determine whether reduced intensity transplantation is a curative procedure in these patients.
University College London	Rule	CRUK/06/013: Mantle Cell: Phase III, multicentre, randomised study of fludarabine/cyclophosphamide combination with or without Rituximab in patients with untreated mantle cell lymphoma. (Information includes phase II)	370/370	2014	Eve HE et al., Toxicity of fludarabine and cyclophosphamide with or without rituximab as initial therapy for patients with previously untreated mantle cell lymphoma: results of a randomised phase II study. Leukemia & Lymphoma, February 2009; 50(2): 211–215. Rule S, Ann Oncol, 2005; 16(Supp 5); 95-95. HE Eve and SAJ Rule. BJH, 137, (S1), abs 52. BJH. 137 S1 1:19, April 2007. BJH. 137 S1:17-18, April 2007. BJH. 145 Supplement 1:87, April 2009. Presentated at ASCO 2009 and BSH 2009.	No	Currently no 'gold standard' therapy for Mantle Cell Lymphoma. The trial aims to produce higher response rates than those currently seen with conventional, aggressive lymphoma-style treatment (i.e. CHOP) and to establish whether the addition of an anti-CD20 monoclonal antibody given in combination with chemotheraoy will improve survival. Central analysis of all diagnostic tissue samples will attempt to better characterise this disease at a molecular level. Completed randomised phase II providing basis for national phase III study.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University College London	Cunningham	CRUKE/03/019: R-CHOP 14/21: A phase III randomised trial comparing rituximab with CHOP-21 and rituximab with CHOP-14 for patients with non-Hodgkin's lymphoma	1080/1080		Cunningham, D et al. A phase III trial comparing R-CHOP 14 and R-CHOP 21 for the treatment of patients with newly diagnosed diffuse large B-cell non-Hodgkin's lymphoma. JOURNAL OF CLINICAL ONCOLOGY, 27 (15): -8506 Suppl. S MAY 20 2009. Presented preliminary data at ASCO 09.	yes	Initial results from this trial were presented at ASCO 2009 indicating that R-CHOP14 can be delivered as effectively as R-CHOP21 with comparable levels of acute toxicity. Potential to change standard treatment of DLBCL patients from R-CHOP using 21 day cycles to R-CHOP using 14 day cycles.
University College London	Johnson	CRUK/08/010: PRIMARY CNS LYMPHOMA: Phase I trial of escalating high dose methotrexate supported by glucarpidase to treat patients with primary central nervous system lymphoma (PCNSL)	3/18			Yes	Will determine safe dose of methotrexate in Primary CNS lymphoma when given in combination with Glucarpidase.
University College London	Johnson	CRUK/07/033: RATHL: A randomised trial to assess Response Adapted Therapy using FDG-PET imaging in patients with advanced Hodgkin Lymphoma.	861/unknown target		Barrington SF et al., Concordance between four European centres of PET reporting criteria designed for use in multicentre trials in Hodgkin lymphoma. Eur J Nucl Med Mol Imaging, DOI 10.1007/s00259-010-1490-5, Published online 27May2010. Presented at the International Symposium of Hodgkin's Lymphoma 2013.	Yes	If this trial is successful it will provide valuable information about the applicability of early PET imaging for guiding therapy in Hodgkin Lymphoma. It will give information about the desirabilitty of omitting bleomycin from chemotherapy regimens after a negative PET scan and will allow conclusions to be drawn about the potential role of treatment intensification after a positive PET scan.
University College London	Illidge	CRUK/07/016: Gembex:A phase II study of Gemcitabine and Bexaratene in the treatment of T-Cell Lymphoma	36/35-84 (depending on interim analysis)	N/A - primary analysis performed and published	British Journal of Cancer (2013) 109, 2566–2573 |	Yes	Examined the role of gemcitabine and bexarotene combination in the treatment of cutanaeous T cell lymphoma. The overall response rate of the combination did not reach the specified target to proceed further and was lower than that previously reported for gemcitabine as a single agent
University College London	Peggs	CRUKE/09/005: PAIReD: Phase II Study of Reduced Intensity Allogeneic Transplantation For Chemorefractory Hodgkin Lymphoma	34/32	2017		yes	To document the toxicity, feasibility and survival following reduced intensity transplantation from HLA-compatible sibling or unrelated donors in patients with primary refractory or relapsed refractory Hodgkin Lymphoma
University College London	Peggs	CRUKE/09/004: ReACH: Phase II Study of Reduced Intensity Siblings Allogeneic Transplantation For Relapsed Chemosensitive PET & Hodgkin Lymphoma	3/49	N/A			
University College London	Mikhaeel	CRUK/07/027: Blinded evaluation of prognostic value of FDG-PET after 2 cycles of chemotherapy in diffuse large B-cell Non-Hodgkin's Lymphoma (PET substudy of R-CHOP 14/21)	99/200			Yes	This substudy is looking to determine whether PET after 2 cycles of R-chemo is a predictor of outcome.
University College London	Hoskin	CRUK/05/015: FORT: A Phase III multi-centre randomised controlled trial of low dose palliative radiotherapy for follicular lymphoma.	614/650 (trial closed earlier due to futility)	N/A - primary analysis performed and published	The Lancet Oncology, Volume 15, Issue 4, Pages 457 - 463, April 2014 The Lancet Oncology, Volume 15, Issue 4, Pages 372 - 373, April 2014 (accompanying editorial)	No	The trial aimed to assess whether low dose radiation provides effective local disease control. However time to local progression with 4 Gy was not non-inferior to 24 Gy (hazard ratio 3·42, 95% CI 2·09—5·55, p<0·0001). 24 Gy in 12 fractions is the more effective radiation schedule for indolent lymphoma and should be regarded as the standard of care. However, 4 Gy remains a useful alternative for

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
							palliative treatment. There was no difference in overall survival.
University College London	Rudin	CRUK/06/023: Phase II Trial of Fludarabine and Cyclophosphamide Chemotherapy followed by Thalidomide Maintenance Treatment for Angioimmunoblastic Lymphoma	15/37	2014 - primary anaysis performed and publication pending		yes	Will explore the efficacy of fludarabine and cyclophosphamide in this sub group of T cell lymphoma. Will also examine the role of maintenance thalidomide.
University College London	Fields	CRUK/07/007: A phase II multicentre clinical trial of Rituximab, CVP and Gemcitabine for the treatment of patients with newly diagnosed diffuse large B-cell lymphoma considered unsuitable for R-CHOP (R-GCVP)	62/60		Fields PA, Townsend W, Webb A, Counsell N, Pocock C, Smith P, Jack A, El-Mehidi N, Johnson PW, Radford J, Linch DC & Cunningham D. 2014: De novo treatment of diffuse large B-cell lymphoma with rituximab, cyclophosphamide, vincristine, gemcitabine and prednisolone in patients with cardiac comorbidity: a United Kingdom National Cancer Research Institute Trial. Journal of Clinical Oncology 32:282-278	Yes	The results of this study could change the treatment option for a group of patients unsuitable for current optimal treatment regimens because of pre-existing cardiac impairment or intolerance of an anthracycline containing regime. If proven to be beneficial, it could be suitable for further investigation in a large phase III trial.
University College London	Ardeshna	CRUK/08/012: THE 18-30 STUDY: Phase 2 study evaluating the toxicity and efficacy of a modified German Paediatric Hodgkin's lymphoma protocol (HD95) in young adults (aged 18-30 years) with Hodgkin's Lymphoma (18-30)	14/45			Yes	Will determine the safety and efficacy of this paediatric regimen in young adults with particular reference to neurotoxicity.
University College London	Linch	CRUK/06/006: CORAL: Randomised study of ICE + rituximab (R-ICE) v DHAP + rituximab (R-DHAP) in previously treated patients with CD20 +ve diffuse large B-cell Non-hodgkins lymphoma, eligible for high dose chemotherapy followed by maintenance Rituximab.			J Clin Oncol. 2010 Sep 20;28(27):4184-90. J Clin Oncol. 2011 Nov 1;29(31):4079-87. J Clin Oncol. 2012 Dec 20;30(36):4462-9. Interim analysis presented at ASH 07. Poster presentation at the International Conference on Malignant Lymphoma – Lugano 2008.	Yes	This trial will clarify the role of maintenance Rituximab in relapsed DLBCL
University College London	Linch	CRUKE/03/016: An Intergroup Randomised Trial of Rituximab versus a Watch and Wait strategy in patients with advanced stage, asymptomatic non-bulky follicular lymphoma (Grades 1, 2 and 3a)		2011	Ardeshna, KM, Qian W, Smith P, Braganca N, Lowry L, Patrick P, Warden J, Stevens L, Pocock CFE, Miall F, Cunningham D, Davies J, Jack A, Stephens R, Walewski J, Ferhanoglu B, Bradstock K & Linch D. 2014: "Rituximab versus a watch-and-wait approach in patients with advanced-stage, asymptomatic, non-bulky follicular lymphoma: an open-label randomised phase 3 trial" Lancet Oncology 15(4):424-435 Accepted as a Plenary Lecture at ASH 2010. Poster presentation at the International Conference on Malignant Lymphoma – Lugano 2008.	yes	To determine whether early treatment with rituximab delays the need for chemotherapy or radiotherapy. Is expected to contribute significantly to international knowledge base.
University College London	Pettengell	CRUKE/10/055: FLYER: A randomised study comparing 4 and 6 cycles of chemotherapy with CHOP (cyclophosphamide, doxorubicin,		N/A		N/A	N/A - study abandoned during set-up N/A N/A

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
		vincristine and prednisone) at 21 day intervals, both with 6 cycles of immunotherapy with the monoclonal anti-CD20 antibody rituximab (R-CHOP) in p					
University College London	McMillan	A Phase II Single Arm Study of the use of CODOX-M/IVAC with Rituximab (R-CODOX-M/IVAC) in the treatment of patients with Diffuse Large B-Cell Lymphoma (DLBCL) or Burkitt's Lymphoma (BL) of International Prognostic Index (IPI) High or High Intermediate Risk	151/150	2017	American Society of Hematology 2013- Abstract ID - 60045		
University College London	Auer	CRUK/11/030: R2W: Subcutaneous Bortezomib, Cyclophosphamide and Rituximab (BCR) versus Fludarabine, Cyclophosphamide and Rituximab (FCR) for initial therapy of Waldenstrom's macrocroglobulinaemia (WM): a randomised phase II trial	35/56	2017	Poster presented by the CI at the International Workshop on Waldenström's Macroglobulinemia, London, August 13-17, 2014	Yes	Not yet
University College London	Montoto	SelRICE: Phase I/II study of methylselenocysteine (MSC) in combination with immunochemotherapy (R-ICE) for relapsed/refractory Diffuse Large B-Cell Lymphoma					
GELA	Lister	CRUKE/05/026: PRIMA: A phase III, RCT in patients with advanced follicular lymphoma evaluating the benefit of maintenance Rituximab (MabThera®) after induction of response with chemotherapy plus Rituximab in comparison with no maintenance therapy.			Rituximab maintenance for 2 years in patients with high tumour burden follicular lymphoma responding to rituximab plus chemotherapy (PRIMA): a phase 3, randomised controlled trial. The Lancet, Volume 377, Issue 9759, Pages 42 - 51, 1 January 2011	Yes	EMA,Swissmedic and FDA have approved the use of MabThera (rituximab) as maintenance therapy for patients suffering from follicular lymphoma (FL).
University College London	McMillan	CRUKE/11/060: INCA: A multicentre randomised phase II clinical trial of Inotuzumab Ozogamicin plus Rituximab and CVP (IO-R-CVP) versus Gemcitabine plus Rituximab and CVP (Gem-R-CVP) for the first line treatment of patients with diffuse large B cell lymphoma who are not suitab	17/154				

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Southampton	Davies	CRUKD/12/001: Preclinical development & a Phase I trial of anti-CD19 DI-B4 monoclonal antibody in patients with advanced CD19 positive indolent B-cell malignancies	0/37	2018			First time in man for this novel antibody. Trial planned. Aims to assess safety, efficacy, toxicity, pharmacokinetics, and identify the MTD . Also to determine the immunogenicity of DI-B4. Too early in development to assess clinical impact. If drug is registered could change SOC to be offered in combination with current drug given as SOC. Coul d be given to patients relaped on SOC. If drug is registered could change SOC to be offered in combination with current drug given as SOC. Coul d be given to patients relaped on SOC.
Royal Free & University College Medical School	Begent	CRUKD/01/016: A Cancer Research UK Phase I/II trial of radioimmunotherapy with 131I-CHT25 in patients with refractory IL-2 receptor expressing lymphomas	15/15	2008	Dancey G, Violet J, Malaroda A, Green AJ, Sharma SK, Francis R, Othman S, Parker S, Buscombe J, Griffin N, Chan PS, Malhotra A, Woodward N, Ramsay A, Ross P, Lister TA, Amlot P, Begent R, McNamara C. A Phase I Clinical Trial of CHT-25 a 131I-Labeled Chimeric Anti-CD25 Antibody Showing Efficacy in Patients with Refractory Lymphoma. Clin Cancer Res. 2009 Dec 15;15(24):7701-7710.		Novel radioimmunotherapy for IL-2 receptor expressing cancer. Trial completed. Overall response rate was 39%. Too early in development to assess clinical impact.
University of Manchester/Christie Hospital	Hawkins	CRUKD/99/016: A Phase I/II Study of Idiotypic Vaccination for Follicle Centre Lymphoma (LIFTT)	25/25	2007	McCarthy H, Ottensmeier CH, Hamblin TJ, Stevenson FK. Anti-idiotype vaccines. Br J Haematol. 2003 Dec;123(5):770-81.		First time in this population of patients for this treatment. Trial completed. Too early in development to assess clinical impact.
University of Manchester/Christie Hospital	Crowther	CRUKD/97/013: A CRC Phase II trial of bryostatin 1 in patients with low grade non-Hodgkin's lymphoma	17/17	2000	Blackhall FH, Ranson M, Radford JA, Hancock BW, Soukop M, McGown AT, Robbins A, Halbert G, Jayson GC; Cancer Research Campaign Phase I/II Committee. A phase II trial of bryostatin 1 in patients with non-Hodgkin's lymphoma. Br J Cancer. 2001 Feb;84(4):465-9.		First trial in Non-Hodgkin's Lymphoma for this agent. Follow up Phase II trial to CRUKD/91/006, companion trial to CRUKD/99/011 & CRUK/99/012. Trial completed. Development discontinued after Phase II due to lack of efficacy. Too early in development to assess clinical impact.
University of Southampton	Johnson	CRUKD/95/021: Phase 1 study of BU12-Saporin immunotoxinin patients with refractory or relapsed CD19 positive B-cell lymphoma	8/25	1998			First time in patients for this agent. Trial completed. Development discontinued after Phase I due to lack of efficacy. Too early in development to assess clinical impact.
Charing Cross Hospital	Newlands	CRUKD/93/009: Phase II trial of temozolomide (Temodal) in low-grade non-Hodgkin's lymphoma	18/18	1994	Woll PJ, Crowther D, Johnson PW, Soukop M, Harper PG, Harris M, Brampton MH, Newlands ES.Phase II trial of temozolomide in low-grade non-Hodgkin's lymphoma. Br J Cancer. 1995 Jul;72(1):183-4.		Follow up Phase II study in NHL following activity seen in Phase I trial CRUKD/87/003. Drug developed by Malcolm Stevens' CR-UK funded research group at Aston Unversity. Trial completed. Drug registered for clinical use in brain cancer as Temodal. Too early in development to assess clinical impact. Drug now licensed worldwide to treat brain cancer.
University College London	Linton	CRUK/12/019: ReBeL study: a randomized phase I/II trial of lenalidomide and rituximab with or without bendamustine in patients 18 years or older with relapsed follicular lymphoma. A HOVON/GLSG study.	0/174	2016			This study will assess the most promising targeted drug combination to evaluate in phase lll (LR vs LRB). It will add value of PET-CT in assessing treatment response in FL, will help to identify protein and gene response biomarkers in FL and allow exploration of treatment induced alternations in the microenvironment Not known at present Not known at present

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Melanoma							
Clatterbridge Centre for Oncology NHS Trust	Marshall	SUAVE - A Multi-Centre, Randomised Phase II Study Of Sunitinib and Standard Chemotherapy in Good Performance Status Patients with Metastatic Uveal Melanoma	84/124	2013	1) POSTER ASCO 2013 Sunitinib versus dacarbazine as first line treatment in patients with metastatic uveal melanoma (SUAVE, CRUK/09/017): J Sacco, P Nathan, S Danson, P Lorigan, S Nicholson, C Ottensmeier, P Corrie, N Steven, J Larkin, A Goodman, TRJ Evans, S Kumar, SE Coupland, P Silcocks and E Marshall. Monday 3rd June 2013, 8am-12pm, Melanoma/skin cancer, poster discussion session, abstract number 9031, Room S405 2) Ocular Oncology Group meeting 2012.	No	Study was stopped due to inferiority
Clatterbridge Centre for Oncology	Marshall	ITEM: A Phase II Study of Imatinib in the Treatment of Patients with Metastatic Uveal Melanoma	25/25	2013		Yes	To evaluate the 3 month progression free survival rate of patients with unresectable good performance c-kit positive metastatic uveal melanoma treated with Imatinib. If activity in the phase II trial is shown to be postive, a further evaluation in a larger randomised phase III study versus gemcitabine/treosulfan chemotherapy is intended. The Final Analysis is underway and a second larger randomised phase II evaluating sunitinib (SUAVE) has commenced. If positive, it could have lead to a change in clinical practice, including potential for license expansion and change to NICE recommendations. The end of study report indicated that the treatment showed no overall benefit in this patient population.
University of Liverpool	Damato	NITRO trial: Neoadjuvant IntraviTreal Ranibizumab treatment in high risk Ocular melanoma patients: A two stage single centre Phase II single arm study.	3/25	TBC		No	Slow recruitment due to difficult patient group and a shrtage of centres performing the resection procedure.
University of Oxford	Middleton	CRUK/10/008: ANZMTG-WBRT: Whole brain radiotherapy following local treatment on intracranial metastases of melanoma - a randomised phase III trial.	6/20	2017	Whole brain radiotherapy after local treatment of brain metastases in melanoma patients--a randomised phase III trial. BMC Cancer. 2011 Apr 17;11:142. Fogarty G et al.,	Yes	To determine the effect of adding WBRT to local treatment on distant intracranial control (primary), quality of life (QoL), performance status, neurocognitive function (NCF) and overall survival. If results are positive it could lead to a wider adoption of WBRT after local treatment of brain metastases related to melanoma
University of Oxford	Middleton	CRUKE/10/026: DOC-MEK: A phase 2 trial of docetaxel with or without AZD6244 in wt BRAF melanoma	83/80	2013	SMR 2012, ASCO 2013	Yes	The addition of selumetinib to docetaxel has not shown a significant difference in PFS compared with docetaxel treatment alone in patients with wt BRAF advanced melanoma. The combination of docetaxel and selumetinib can be administered effectively to patients with metastatic melanoma, although the combination is less well tolerated than docetaxel alone. There is merit in the combination of targeted agents with chemotherapy. Our data does not support the use of NRAS mutations to select melanoma patients for selumetinib treatment.
University of	Middleton	CRUKE/11/017: RADVAN: Randomized	13/86	2014		Yes	Based on the safety profileof the safety cohort the

Key:		Trials that are currently in set-up			Trials that are currently open		Trials that have closed, suspended, or withdrawn during set up
Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Oxford		phase 2 trial of whole brain radiotherapy with or without vandetanib in metastatic melanoma with brain metastases					randomised phase of the trial proceded with 100mg vandetanib/placebo once daily with 30Gy of whole brain radiotherapy.
University of Oxford	Middleton	CRUKE/11/033: The PACMEL study - Randomised phase 2 study of paclitaxel with or without GSK1120212 in advanced wt BRAF melanoma	28/136	2015		Yes	Dose escalation phase of trial successfully established the maximum tolerated dose of one IMP in combination with another which has now been taken forward into the randomised trial. No comments/issues to report to date Trial will provide evidence-based treatment for this group of patients with poor prognosis and few treatment options at present Trial will provide evidence-based treatment for this group of patients with poor prognosis and few treatment options at present
The Institute of Cancer Research	Eisen (Addenbrooke's Hospital, Cambridge) (Bliss, ICR-CTSU and Peto, London School of Hygiene and Tropical Medicine)	CRUK/99/003: MSG/BAPS - Randomised trial of width of excision of thick cutaneous malignant melanoma	792/900	2002, 2012	THOMAS, J. M., et al. 2004. Excision margins in high-risk malignant melanoma. N Engl J Med, 350, 757-766. NEWTON-BISHOP, J. A., et al. 2004. A quality-of-life study in high-risk (thickness > = or 2 mm) cutaneous melanoma patients in a randomized trial of 1-cm versus 3-cm surgical excision margins. J Investig Dermatol Symp Proc, 9, 152-9. THOMAS, J. M., et al. 2002. Surgical margin excision width in high (minimum depth 2mm) cutaneous malignant melanoma: a randomized trial of 1cm versus 3cm excision margins in 900 patients. Proc Am Soc J Clin Oncol 21, 15S #1358.	Yes	A 1cm margin of excision for melanoma with a poor prognosis (as defined by a tumour thickness of at least 2 mm) is associated with a significantly greater risk of regional recurrence than is a 3cm margin, but with a similar overall survival rate. Established safe excision margin width in ≥2mm deep melanoma. Referenced in national comprehensive cancer network (NCCN) UK clinical practice guidelines in oncology for melanoma, v2, 2007.
The Royal Marsden NHS Foundation Trust	Eisen (Addenbrooke's Hospital, Cambridge) (Bliss, ICR-CTSU and Peto, London School of Hygiene and Tropical Medicine)	CRUK/02/019: SLNB - Sentinel lymph node biopsy study in patients with melanoma - patients with positive node randomised to complete lymphadenectomy vs no surgery	22/24	2006		No	Accrual was too slow to make this trial feasible. The rate of acceptance of randomisation (47%) was significantly lower than originally deemed acceptable (65%, p=0.01) but the proportion of patients in whom the sentinel node could be detected was very high 97%.
The Royal Marsden NHS Foundation Trust	Larkin (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Bliss, ICR-CTSU)	CRUK/09/028: NICAM: A phase II trial of nilotinib in the treatment of c-KIT mutated advanced acral and mucosal melanoma	23/24	2014	LARKIN, J. M. G., et al. 2011. A phase II trial of nilotinib in the treatment of patients with KIT mutated advanced acral and mucosal melanoma (NICAM). J Clin Oncol, 29, 39s #TPS229.	Yes	This feasibility study is the first trial in the UK for patients with acral and mucosal melanoma evaluating the incidence of cKIT mutations in this rare group of patients and likely response to treatment with nilotinib. Outcomes from this study will inform whether treatment with nilotinib extends the life of patients with this disease. The trial has the potential to initiate the roll out of routine cKIT mutation testing in this group of patients via initiatives such as the CR UK Stratified Medicine Programme if the study demonstrates a benefit for nilotinib The trial will contribute to the international knowledge base in his disease.
Cambridge University	Corrie	CRUK/06/014: AVAST-M: Randomised trial evaluating the VEGF	1343/1320	2017	Corrie, Marshall et al Lancet Oncology 2014 Corrie, Marshall, et al. Effect of BRAF mutation	Yes	There is no role for Avastin in the treatment of melanoma, but could be used in a sub-group of patients. To compare

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Hospitals		inhibitor, bevacinumab (Avastin), as adjuvant therapy following resection of AJCC stage IIB (T4aN0M0), IIC (T4bN0M0) and III (TxN1-3M0) cutaneous melanoma			status on adjuvant bevacizumab as treatment for melanoma patients at high risk of recurrence. US Society for Melanoma Research meeting November 2013, USA. 9. Corrie , Marshall et al. Adjuvant bevacizumab as treatment for melanoma patients at high risk of recurrence: pre-planned interim results of the AVAST-M randomised trial. NCRI November 2013, Liverpool, UK. 11. Corrie, Marshall et al . AVAST-M - adjuvant bevacizumab as treatment for melanoma patients at high risk of recurrence. ASCO June 2013, Chicago, USA.		overall survival of patients with resected melanoma at high risk of recurrence treated with bevacizumab compared with observation only. This trial will evaluate the use of Avastin in Melanoma. Add to the body of knowledge
Centre for Drug Development							
Institute of Cancer Research/Royal Marsden Hospital	Judson	CRUKD/05/036: A Cancer Research UK Phase II Trial to Assess the Activity of the HSP90 molecular chaperone inhibitor 17-AAG (17-allylamino, 17-demethoxygeldanamycin) in Patients with Metastatic (M1a, M1b & M1c) Malignant Melanoma	14/14	2010	Pacey S, Gore M, Chao D, Banerji U, Larkin J, Sarker S, Owen K, Asad Y, Raynaud F, Walton M, Judson I, Workman P, Eisen T. A Phase II trial of 17-allylamino, 17-demethoxygeldanamycin (17-AAG, tanespimycin) in patients with metastatic melanoma. Invest New Drugs. Invest New Drugs. 2012 Feb;30(1):341-9		Follow on trial to CRUKD/99/013. Phase II trial in melanoma following stable disease seen in Phase I melanoma patients. Trial completed. More information gained about the side effects and toxicity profile. Agent in Phase III development. As yet no impact, but awareness of activity of HSP90 inhibitors in melanoma may inform future trials.
Institute of Cancer Research/Royal Marsden Hospital	Gore	CRUKD/95/022: Gene therapy with autologous, interleukin 2-secreting tumor cells in patients with malignant melanoma	12/12	1998	Palmer K, Moore J, Everard M, Harris JD, Rodgers S, Rees RC, Murray AK, Mascari R, Kirkwood J, Riches PG, Fisher C, Thomas JM, Harries M, Johnston SR, Collins MK, Gore ME. Gene therapy with autologous, interleukin 2-secreting tumor cells in patients with malignant melanoma. Hum Gene Ther. 1999 May 20;10(8):1261-8.		First time in patients for this treatment. Trial completed. 3 patients had SD 7-15 mths. Patient vaccination with autologous, genetically engineered tumor cells is feasible and safe. Anti-tumor DTH and CTLs can be induced in some patients with such a vaccine. Too early in development to assess clinical impact.
University of Cambridge	Bleehen	CRUKD/92/006: Cancer Research Campaign phase II trial of temozolomide (Temodal) in metastatic melanoma	60/60	1994	Bleehen NM, Newlands ES, Lee SM, Thatcher N, Selby P, Calvert AH, Rustin GJ, Brampton M, Stevens MF. Cancer Research Campaign phase II trial of temozolomide in metastatic melanoma. J Clin Oncol. 1995 Apr;13(4):910-3.		Follow up Phase II study in melanoma following activity seen in melanoma patients in Phase I trial CRUKD/87/003. Drug developed by Malcolm Stevens' CR-UK funded research group at Aston Unversity. Trial completed. Drug registered for clinical use as Temodal. Too early in development to assess clinical impact. Drug now licensed worldwide to treat brain cancer.
Non-specific							
University of Birmingham	Hale	GC2: GC- 2 (GC 1989 01): Germ Cell Tumour Study II	78/78	2000	MANN JR et al. The United Kingdom Children's Cancer Study Group's Second Germ Cell Tumor Study: Carboplatin, Etoposide, and Bleomycin Are Effective Treatment for Children With Malignant Extracranial Germ Cell Tumors, With Acceptable Toxicity. 2000 JCO 18(20): 3809-3818	Yes	Conservative surgery, a watch-and-wait approach after complete excision, and carboplatin, etoposide and bleomycin (JEB) for those requiring chemotherapy produced high cure rates and few serious complications.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Birmingham	Young	WARP: A multicentre prospective randomised controlled trial of thrombosis prophylaxis with warfarin in cancer patients with central venous catheters	1589/1600	2005	YOUNG AM, BILLINGHAM LJ, BEGUM G, KERR DJ, HUGHES AI, REA DW, SHEPHERD S, STANLEY A, SWEENEY A, WILDE J, WHEATLEY K ON BEHALF OF THE WARP COLLABORATIVE GROUP, UK (2009) Warfarin thromboprophylaxis in cancer patients with central venous catheters (WARP): an open-label randomised trial. Lancet p.373:567–74 YOUNG AM et al. Lancet, 2009, 373:567-574; Rea DW et al. J Clin Oncol, 2005, 23(16 Suppl): 1096S-1096S.	Yes	The findings show that prophylactic warfarin compared with no warfarin is not associated with a reduction in symptomatic catheter-related or other thromboses in patients with cancer and therefore newer treatments should be considered. The results of the WARP trial have had immediate and widespread impact on clinical practice worldwide. The use of low dose warfarin as thromboprophylaxis has been virtually eliminated. Clinicians now make careful judgement concerning fully warfarinising patients at higher risk of thrombosis mindful of the WARP findings of modest efficacy allied to significant bleeding complications. The results of the WARP trial have had immediate and widespread impact on clinical practice worldwide. The use of low dose warfarin as thromboprophylaxis has been virtually eliminated. Clinicians now make careful judgement concerning fully warfarinising patients at higher risk of thrombosis mindful of the WARP findings of modest efficacy allied to significant bleeding complications.
University of Birmingham	Cullen	SIGNIFICANT: A randomised, prospective double-blind, placebo-controlled trial of prophylactic oral levofloxacin following chemotherapy for lymphoma and solid tumours	1565/1500	2005	CULLEN, M., STEVEN, N., BILLINGHAM, L., GAUNT, C., HASTINGS, M., SIMMONDS, P., STUART, N., REA, D., BOWER, M., FERNANDO, I., HUDDART, R., GOLLINS, S., STANLEY, A. & GRP, S. T. 2005. Antibacterial prophylaxis after chemotherapy for solid tumors and lymphomas. New England Journal of Medicine, 353, 988-998. CULLEN, M., STEVEN, N., BILLINGHAM, L., GAUNT, C., HASTINGS, M., SIMMONDS, P., STUART, N., REA, D., BOWER, M., FERNANDO, I., HUDDART, R., GOLLINS, S., STANLEY, A. & GRP, S. T. 2005. Antibacterial prophylaxis after chemotherapy for solid tumors and lymphomas. New England Journal of Medicine, 353, 988-998. BILLINGHAM, L., CULLEN, M., STEVEN, N., GAUNT, C. & HASTINGS, M. 2005. Efficacy of antibacterial prophylaxis following myelosuppressive chemotherapy: Results from a randomised, double-blind, placebo-controlled trial of levofloxacin including 220 small cell lung cancer patients. Lung Cancer, 49, S55-S55. CULLEN, M. H., BILLINGHAM, L. J., GAUNT, C. H. & STEVEN, N. M. 2007. Rational selection of patients for antibacterial prophylaxis after chemotherapy. J Clin Oncol, 25, 4821-8. CULLEN, M. H., BILLINGHAM, L. J., GAUNT, C. H. & STEVEN, N. M. 2007. Rational selection of patients for antibacterial prophylaxis after chemotherapy. J Clin Oncol, 25, 4821-8. LEIBOVICI, L., PAUL, M., CULLEN, M., BUCANEVE, G., GAFTER-GVILI, A., FRASER, A. & KERN, W. V. 2006. Antibiotic prophylaxis in		Demonstrated that use of prophylactic levofloxacin reduced the risk of infection and infection-related mortality in patients receiving moderately myelosuppressive chemotherapy for solid tumours and lymphoma. Furthermore, Cycle-1 infections appear to identify patients at high risk of later febrile episodes, enabling targeted prophylaxis and thus limiting the potential for antibiotic resistance in these patients. Referenced in 2012 NICE Guidelines - Neutropenic sepsis: prevention and management of neutropenic sepsis in cancer patients. Guidelines now recommend that adult patients (aged 18 years and older) with solid tumours in whom significant neutropenia (neutrophil count 0.5 x 109 per litre or lower) is an anticipated consequence of chemotherapy, are offered prophylaxis with a fluoroquinolone during the expected period of neutropenia only. Referenced in - Antimicrobial Prophylaxis and Outpatient Management of Fever and Neutropenia in Adults Treated for Malignancy: American Society of Clinical Oncology Clinical Practice Guideline

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
					neutropenic patients: new evidence, practical decisions. Cancer, 107, 1743-51.		
University of Birmingham	Steven	DC-1: A phase I study of immunotherapy for patients with metastatic melanoma using dendritic cells transfected with a plasmid encoding two melanoma antigens	10/10	2010	STEELE JC, RAO A, MARSDEN JR, ARMSTRONG CJ, BERHANE S, BILLINGHAM LJ, et al. (2011) Phase I/II trial of a dendritic cell vaccine transfected with DNA encoding melan A and gp100 for patients with metastatic melanoma. Gene Ther 18(6):p.584-93.		Vaccination with mature DC non-virally transfected with DNA encoding antigen had biological effect causing tumour regression and inducing diverse T lymphocyte responses
University of Birmingham	Steven	SIGNIFICANT II: Feasibility Study - Colonization by antibiotic-resistant bacteria in patients undergoing cytotoxic chemotherapy for solid cancers: pilot study for a randomized controlled trial of antibiotic prophylaxis	57/50	2014			This pilot study data has not yet been analysed but it should demonstrate whether concerns over development of antibiotic resistance are justified in fluoroquinoloone prophylaxis in this group of patients.
University of Birmingham	Nathan	UKMCC-1 (previously PAZAM!) - Pazopanib in Advanced Merkel Cell Carcinoma	2/25	2015		Yes	This is an important study as it establishes the UK as an international centre for clinical research in this rare tumour. Future randomised studies in the advanced and adjuvant settings will require international collaboration. UKMCC-01 will establish the UK at the centre of international collaborative studies.
University of Birmingham	Marshall	ORANGE: Trial : Oral antibiotics for neutropenic sepsis giving early hospital discharge	27/400				

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Glasgow	Espie	CRUK/03/025: Randomised controlled clinical effectiveness trial of Cognitive Behaviour Therapy (CBT) versus Treatment As Usual (TAU) for insomnia in cancer patients	150/204	2007	ESPIE, C. A., FLEMING, L., CASSIDY, J., SAMUEL, L., TAYLOR, L. M., WHITE, C. A., DOUGLAS, N. J., ENGLEMAN, H. M., KELLY, H. L. & PAUL, J. 2008. Randomized controlled clinical effectiveness trial of cognitive behavior therapy compared with treatment as usual for persistent insomnia in patients with cancer. Journal of Clinical Oncology, 26, 4651-4658. ESPIE, C. A., FLEMING, L. M., CASSIDY, J., SAMUEL, L. & PAUL, J. 2008b. Psychological effects of Cognitive Behaviour Therapy (CBT) for persistent insomnia associated with cancer: randomised controlled trial (RCT). Journal of Sleep Research, 17, 34-34. ESPIE, C. A., FLEMING, L. M., TAYLOR, L. A. & PAUL, J. 2008c. Cognitive and attentional changes following cognitive behaviour therapy (CBT) for persistent insomnia associated with cancer: A randomized controlled trial (RCT). Sleep, 31, 695. FLEMING, L., ESPIE, C., CASSIDY, J., SAMUEL, L., TAYLOR, L., WHITE, C. & PAUL, J. 2010. SLEEP DISTURBANCE AND ITS ASSOCIATION WITH SYMPTOMS OF FATIGUE, ANXIETY AND DEPRESSION IN CANCER PATIENTS. Sleep, 33, A205-A206. RANDELL, K., ESPIE, C., MORRISON, D., PAUL, J. & FLEMING, L. 2012a. Insomnia, mood and fatigue symptoms among newly diagnosed breast cancer patients. Journal of Sleep Research, 21, 166-167. RANDELL, K., ESPIE, C. A., MORRISON, D., PAUL, J. & FLEMING, L. 2012b. UNDERSTANDING THE DEVELOPMENT OF PERSISTENT INSOMNIA IN BREAST CANCER PATIENTS. Sleep, 35, A297-A297.		Cognitive Behaviour Therapy demonstrates sustained improvements in sleep with large effect sizes for subjectively estimated time taken to fall asleep and nocturnal wake time, comparable to the primary insomnia literature. Establishes sound basis for CBT approach in this group of patients, but not routinelyadopted into NHS currently. Unknown to what extent this has impacted on practice outside UK.
University of Glasgow and Greater Glasgow and Clyde Health Board	Fallon	CRUK/07/031: KPS: A randomised double-blind controlled trial of s-ketamine versus placebo in conjunction with best pain management in neuropathic pain in cancer patients	191/214	2014		Yes	This is the first RCT to examine the role of s-ketamine in the management of malignant neuropathic pain. The outcome of this study will enhance the understanding s-ketamine in this area and will directly affect patient care. Results will be disseminated through peer reviewed publications and are expected to influence management of malignant neuropathic pain at an international level. Results will be disseminated through peer reviewed publications and are expected to influence management of malignant neuropathic pain at an international level.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Glasgow	Wasan	CRUK/08/006: CUP-ONE: A multi-centre randomised phase II study comparing epirubicin, cisplatin and capecitabine with and without Erlotinib in carcinomas of unknown primary (CUP): incorporating the prospective validation of molecular classifiers in diagnosis and class	397/400	2015		Yes	Perhaps the most important feature of the study is the prospective assessment of the prognostic classifiers and the collection of the associated translational material. This study is now a single arm phase II study because or problems in securing a biological agent to use in randomised phase II A guide on the minimum diagnostic work up for the molecular classifier CUP, which should save future clinical resourses by dropping low-utility clinical investigations. Devel;opment of future randomisation studies with molecular classifications allowing for future rational targeted approaches. Generate hypotheses for future designs in phase III. Confirm realistic accural rates for future studies. Inform non-CUP diagnostic and treatment trials for metastatic disease of known primaries if molecular profiles show promicing correlates with treatment responses and/ot toxicities. As per UK
University of Oxford	Nicum	CRUK/10/049: 6MP BRCA: Phase II Clinical Trial Of 6-Mercaptopurine and low-dose Methotrexate in Patients with BRCA Defective Tumours	48/65	2015		Yes	6MP uses a Simon two-stage minimax design. In stage one, 30 patients were evaluated. If fewer than 3 out of the first 30 evaluable patients had shown a response after 8 weeks, the trial would have been stopped for futility. The Trial Management Group met in March 2013 to discuss the results from the first efficacy analysis, and concluded that the trial will continue to the next recruitment target of 65 patients, because more than 3 patients from stage one had shown a response to the trial intervention (the definition of response includes complete response, partial response and stable disease as measured by RECIST criteria v1.1) If the efficacy criteria are met as defined in the protocol, and a multicentre approach for this group of patients proves to be feasible, then we anticipate moving straight on to a Phase III randomised controlled trial comparing this combination of drugs versus placebo in this setting. The Ovarian and Breast CSGs are in agreement with this strategy.
University of Leeds	Bennett	CRUK/07/035: Transcutaneous electrical nerve stimulation (TENS) in the management of cancer bone pain	24/38	2008	Bennett MI, et al. Feasibility study of Transcutaneous Electrical Nerve Stimulation (TENS) for cancer bone pain. (2009) Journal of Pain; 11 (4): 351-359 Bennett MI et al., Feasibility study of Transcutaneous Electrical Nerve Stimulation (TENS) for cancer bone pain. (2009) Journal of Pain; 11 (4): 351-359	No	Further work is required on recruitment strategies and refining the control arm before evaluating TENS in cancer bone pain in a phase III trial n/a n/a

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Sheffield Teaching Hospitals NHS Foundation Trust	Ross	CRUK/10/012: TRYMS: Testosterone replacement in young male cancer survivors	62/268	2016		Yes	Aim to determine whether testosterone replacement in young male cancer survivors improves adverse metabolic parameters and quality of life. The trial is designed to investigate whether testosterone treatment will result in a reduction of truncal fat mass and an increase in participant self-reported physical functioning scores. We anticipate that this trial will provide clear guidance to patients and clinicians by providing an evidence base for practice. Will contribute significantly to international knowledge base.
University of Manchester	McCollum	CRUK/01/007: The role of procoagulants in cancer and chemotherapy induced venous thromboembolism			Br J Cancer. 2008 Oct 7;99(7):1000-1006.		The investigators found that, before chemotherapy, significantly elevated levels of D-dimer and fibrinogen in patients who subsequently develop VTE. Both markers are therefore predictive for VTE, allowing targeted thromboprophylaxis to the high risk group.
King's College London	Armes	CRUK/00/010: A randomised controlled trial to evaluate the effectiveness of a brief psycho-educational intervention in reducing the distress associated with cancer-related fatigue	55/124		Armes J et al., Cancer. 2007, 15;110(6):1385-95. Armes PJ et al. Cancer, 2007; 110(6); 1385-1395. Armes J et al., 2007, Cancer, Volume 110, Issue 6, pages 1385–1395.		There are few proven treatments for fatigue and this study showed that a brief intervention aimed at supporting behavioural changes in lifestyle can improve fatigue and physical functioning. It adds to the growing literature that behavioural interventions are an effective technique for managing cancer-related fatigue. Individual clinicians are adapting their practice to incorporate it although few clinical centres are willing to fund dedicated staff as further work is required to eliminate the possibility that effectiveness is due to the nurse effect. Also pragmatic trials are required to show its effectiveness in clinical practice
Edinburgh University	Fallon	CRUK/07/051: Edinburgh Pain Assessment Tool (EPAT) Study. Does the institutionalisation of pain assessment using the EPAT package reduce pain in cancer unit inpatients more than usual care; a cluster randomised trial		2010			This trial is currently ongoing, so no impact yet. It is a multi-centre cluster randomised controlled trial of the institutionalisation of cancer pain assessment as a 5th vital sign (EPAT©) versus current best standard care. It is a UK-wide study, involving 18 cancer centres, and each centre will recruit 100 eligible patients (EPAT© will be introduced in the 9 centres randomised to the intervention).
University College London	Hoskin	CRUK/06/034: SCORAD III: A randomised phase III trial of single fraction radiotherapy compared to multifraction radiotherapy in patients with metastatic spinal cord compression	565/580	2015		Yes	The phase lll follows on from a successful phase ll study that showed randomisation was feasible. Analysis of feasibility study to be done with phase III trial. No separate analysis planned SCORAD is currently the only successful large scale trial of radiotherapy in end stage metastatic spinal cord compression (MSCC). If non inferiority is proven between the arms, the trial internationally will be the only strong evidence that 1 fraction of 8Gy radiotherapy can be the standard radiotherapy treatment for MSCC. If multifractionation is shown to provide a better outcome, this trial will be a confirmation that multifractionation should continue to be the standard treatment for MSCC in the UK. SCORAD is currently the only successful large scale trial of radiotherapy in end stage metastatic spinal cord compression (MSCC). If non inferiority is proven between the arms, the trial internationally will be the only strong evidence that 1 fraction of 8Gy radiotherapy can be the standard

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
							radiotherapy treatment for MSCC.
University College London	Hoskin	CRUK/04/002: SC20: A phase III International Randomised Trial of Single vs Multiple Fractions for Re-Irradiation of Painful Bone Metastases	52/unknown target	2014	Chow E, van der Linden YM, Roos D, Hartsell WF, Hoskin P, Wu JSY, Brundage MD, Nabid A, Tissing-Tan CJA, Oei B, Babington S, Demas WF, Wilson CF, Meyer RM, Chen BE, Wong RKS Single versus multiple fractions of repeat radiation for painful bone metastases: a randomised, controlled, non-inferiority trial The Lancet Oncology ,Volume 15, Issue 2, February 2014, Pages 164–171 Clinical Oncology 2006, 18: 125-128.	Yes	In patients with painful bone metastases requiring repeat radiation therapy, treatment with 8 Gy in a single fraction seems to be non-inferior and less toxic than 20 Gy in multiple fractions; however, as findings were not robust in a per-protocol analysis, trade-offs between efficacy and toxicity might exist.
University College London	Glynne-Jones	DESCARTES: A multicentre phase I/II Dose Escalation Study of Campto, 5FU and Leucovorin, RadioTherapy and Excisional Surgery.			A phase I/II study of irinotecan when added to 5-Fluorouracil and leucovorin and pelvic radiation in locally advanced rectal cancer: A Colorectal Clinical Oncology Group Study. BJC Feb 26; 96(4): 551-8, 2007		MTD: 20mg/m2 (days 1-5 and 29-33). 18mg/m2 recommend testing this dose in phase III
University College London	Hoskin	CRUK/06/034: SCORAD: A phase II randomised trial of single fraction radiotherapy compared to multi-fraction radiotherapy in patients with metastatic spinal cord compression (feasibility)	83/90	2015		Yes	Successful completion of this feasibility study has led to the running of the full phase III SCORAD III trial. No separate publication for feasibility study planned.
Centre for Drug Development							
Institute of Cancer Research/Royal Marsden Hospital	Harrington	CRUKD/14/007 The PATRIOT study: A Phase I trial of the ATR inhibitor AZD6738 alone and in combination with palliative radiotherapy	0/126	2017			Testing a novel combination
Institute of Cancer Research/Royal Marsden Hospital	Yap	CRUKD/14/004 ComPAKT A Phase I multi-centre trial of the combination of AZD5363 (AKT inhibitor) and olaparib (PARP inhibitor) in patients with advanced solid tumours	0/58	2017			Testing a novel combination
University of Oxford	Middleton	CRUKD/07/061 Preclinical development and a Cancer Research UK Phase I study to determine the MTD of oral Src/ABL inhibitor AZD0424, and to identify tolerable and effective AZD0424 combination regimens for the treatment of advanced solid tumours	12/77	2017			First time for this agent in patients and first time in patients for combinations regimens with this agent.
Institute of Cancer Research/Royal Marsden Hospital	Banerji	CRUKD/12/001: Exploratory & preclinical development & a Phase I first in man trial of AT13148, a novel AGC kinase inhibitor given orally to patients with advanced solid tumours	10/40	2016	Yap T et al. Cancer Res 2012;72(8 Suppl):Abstract nr 928. Yap TA, et al. Clin Cancer Res. 2012 Jul 15;18(14):3912-23.		First time in patients for this AGC kinase inhibitor. Too early in development to assess clinical impact. Too early in development to assess clinical impact.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Mount Vernon Hospital	Hoskin	CRUKD/11/007: A Cancer Research UK Phase I trial of NG-Nitro-L-arginine (L NNA), a nitric oxide synthase inhibitor, given as a single iv infusion over 10 minutes in patients with advanced solid tumours	0/18-27	not applicable (trial stopped early)			Follow up/continuation study to the first trial in cancer patients that stopped early due to drug supply issues. This trial aimed completion of the safety and efficacy profile of LNNA. Trial stopped early due to lack of recruitment.
University of Leeds	Twelves	CRUKD/10/029: A Cancer Research UK Phase I trial of GSK1070916, an aurora B inhibitor, in patients with solid tumours	36/36	2013	ASCO meeting abstracts Jun 17, 2013:2525. A Phase I pharmacokinetic (PK) and pharmacodynamic (PD) study of the selective aurora kinase inhibitor GSK1070916A		First time in patients for this Auroroa Kinase B inhibitor. First CR-UK Clinical Development Partnerships (CDP) agent in the clinic. Trial ongoing. Aims to look at dosing, PK/PD, side effects and efficacy. Too early in development to assess clinical impact.
University of Manchester/Christie Hospital	Jayson	CRUKD/08/041: A Cancer Research UK Phase I trial of GSAO (4-(N-(S-glutathionylacetyl) amino) phenylarsenoxide) given as daily intravenous infusions on days 1-5 and 8-12 of a 21-day cycle, to patients with advanced solid tumours	35/35	2012	Cancer Chemotherapy and Pharmacology reference tbc Elliott MA, Ford SJ, Prasad E, Dick LJ, Farmer H, Hogg PJ, Halbert GW. Pharmaceutical development of the novel arsenical based cancer therapeutic GSAO for Phase I clinical trial. Int J Pharm. 2012 Apr 15;426(1-2):67-75. ASCO Meeting Abstracts 2010 28: TPS167		First time in patients for this agent. Agent developed from research at the University of New South Wales, Australia. Trial aimed to identify a suitable dose, look at side effects, PK/PD and efficacy. Trial closed to recruitment, data being analysed. Too early in development to assess clinical impact.
University of Southampton	Johnson	CRUKD/07/063: A Cancer Research UK Phase I trial of Chi Lob 7/4 (anti-CD40 monoclonal antibody) in advanced cancer	29/30	2016	Chowdhury F, Tutt AL, Chan C, Glennie M, Johnson PW. Development, validation and application of ELISAs for pharmacokinetic and HACA assessment of a chimeric anti-CD40 monoclonal antibody in human serum. J Immunol Methods. 2010 Dec 15;363(1):1-8. ASCO Meeting Abstracts 2010 28: 2507		First time in patients for this novel antibody. Developed from academic research at the University of Southampton. Trial ongoing. Too early in development to assess clinical impact.
University of Newcastle	Plummer	CRUKD/04/036: A Cancer Research UK Phase I trial of Phortress (a novel antitumour benzothiazole)	38/38	2013	Seckl M, Cresti N, et al. A Cancer Research UK Phase I Trial of Phortress (Novel Antitumour Benzothiazole) Given Intravenously in Consecutive 21 Day Cycles with Treatment on Day 1 of Each Cycle. NCRI Cancer Conference 4-7 November 2012: Abstract LB79. Seckl M, Cresti N, et al. NCRI Cancer Conference 4-7 November 2012: Abstract LB79.		First time in patients for this agent. Drug developed from CR-UK funded research at the University of Nottingham. Trial aimed to identify suitable dose, side effects, PK/PD and efficacy. Trial closed to recruitment, data being analysed. Too early in development to assess clinical impact.
Mount Vernon Hospital	Rustin	CRUKD/05/035: A Cancer Research UK Phase I trial of Oxi4503, a prodrug of Combretastatin A1, (a Vascular Disrupting Agent) given by 3 x weekly intravenous infusions to patients with advanced solid tumours	43/43	2011	Patterson DM, Zweifel M, et al. Phase I Clinical and Pharmacokinetic Evaluation of the Vascular Disrupting Agent OXi4503 in Patients with Advanced Solid Tumors. Clin Cancer Res. 2012 Mar 1;18(5):1415-25. Cummings J, Zweifel M, et al. Evaluation of cell death mechanisms induced by the vascular disrupting agent OXi4503 during a phase I clinical trial. Br J Cancer.2012 May; 106(11):1766-71. ASCO Meeting Abstracts 2010 28: 2594 ASCO Meeting Abstracts 2009 27: e14510 ASCO Meeting Abstracts 2008 26: 3551 ASCO Meeting Abstracts 2007 25: 14146		First time in patients for this vascular disrupting agent. Drug was developed from academic research at the University of Arizona. Trial completed. DCE-MRI and PET data clearly show OXi4503 is a potent vascular disrupting agent (VDA). 12/17 patients receiving > 11 mg/m2 had significant reduction in tumour perfusion based on DCE-MRI (15 patients) or PET (2 patients). Reduction in tumour perfusion was seen with PET at all dose levels even 1.92 mg/m2, this was more consistent at higher dose levels. One RECIST confirmed partial response at 14 mg/m2 in platinum resistant ovarian carcinoma, it was also the largest decrease in tumour perfusion on DCE-MRI scan. One patient with ovarian carcinoma at 8.5 mg/m2, classified as stable disease and control of ascites for >6 months. 12 patients at 11 mg/m2 or higher were evaluable for assessment of tumour response, 5 showed signs of clinical efficacy, with 1 confirmed PR and 4 prolonged SD. RP2D

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
							range of 11 to 14 mg/m2.
University of Glasgow	Cassidy	CRUKD/04/038: A Cancer Research UK Phase I trial of the DNA-hypermethylating agent decitabine (Dacogen) in combination with epirubicin in patients with advanced solid tumours	14/14	2006			Came from CRUK funded lab work (R Brown) in Glasgow showing that decitabine had potential to reverse drug resistance. Testing a different combination partner to CRUKD/02/023 and therefore potentially different resistance mechanisms. Trial completed. Combination proved to be too toxic and thus not brought forward into phase 2. Too early in development to assess clinical impact.
Institute of Cancer Research/Royal Marsden Hospital	Judson	CRUKD/06/052: A Cancer Research UK Phase I trial to evaluate the safety, tolerability and pharmacokinetics of 17-DMAG (17-dimethylaminoethyl-amino-17-demethoxygeldanamycin) given as a once weekly infusion in patients with advanced solid tumours	25/25	2010	Pacey S, Wilson RH, et al. A Phase I study of the Heat Shock Protein 90 inhibitor alvespimycin (17-DMAG) given intravenously to patients with advanced, solid tumors. Clin Cancer Res. March 15, 2011 17:1561-1570 ASCO Meeting Abstracts 2009 27: 3534 ASCO Meeting Abstracts 2007 25: 3568		First time in patients for this HSP90 inhibitor. Analogue of agent in CRUKD/99/013. Trial completed. Agent in Phase II development. Too early in development to assess clinical impact. Led to Phase II evaluation.
University of Oxford	Middleton	CRUKD/04/035: A Cancer Research UK Phase I trial combining the dinitrobenzamide prodrug CB1954 (tretazicar) and the NQ02 substrate EP-0152R (caricotamide) intravenously (IV) every 3 weeks	33/33	2009	Middleton MR, Knox R, et al. Quinone oxidoreductase-2–mediated prodrug cancer therapy. Sci Transl Med 14 July 2010: Vol. 2, Issue 40, p. 40ra50. S. C. Waterman, M. Middleton, et al. Investigation of the safety, tolerability and pharmacokinetics of Prolarix (TM), which comprises the prodrug tretazicar and a novel synthetic cosubstrate, caricotamide, in patients with late stage cancers. Annals of Oncology 17: 49-49 (2006) J Clin Oncol 2008; 26 (May 20 Supplmt; abstr 2505)		First time in patients for this combination of a prodrug with a substrate for NQ02. Trial completed. Agents in Phase II development. Too early in development to assess clinical impact. Led to Phase II evaluation.
University of Oxford	Harris	CRUKD/04/039: A Cancer Research UK Phase I trial of copper-binding agent ATN224 in patients with solid tumours	18/18	2007	Lowndes SA, Adams A, et al. Phase I study of copper-binding agent ATN-224 in patients with advanced solid tumors. Clin Cancer Res. 2008 Nov 15;14(22):7526-34. ASCO Meeting Abstracts 2006 24: 2065		First time in patients for this agent. Trial identified suitable Phase II dose and toxicity profile. Trial completed. 2 patients had SD. Development led to a Phase II trial CRUKD/08/043. Too early in development to assess clinical impact. Led to Phase II evaluation.
Royal Free & University College Medical School	Hochhauser	CRUKD/04/037: A Cancer Research UK Phase I trial of sequence-selective minor groove DNA binding agent SJG136 in patients with advanced solid tumours	17/17	2008	Hochhauser D, Meyer T, et al. Phase I study of sequence-selective minor groove DNA binding agent SJG-136 in patients with advanced solid tumors. Clin Cancer Res. 2009 Mar 15;15(6):2140-7. Wu J, Clingen PH, et al. γ-H2AX foci formation as a pharmacodynamic marker of DNA damage produced by DNA cross-linking agents: results from two Phase I clinical trials of SJG-136 (SG2000). Clin Cancer Res. 2013 Feb 1;19(3):721-30. Hartley JA. Expert Opin Investig Drugs. 2011 Jun;20(6):733-44. ASCO Meeting Abstracts 2008 26: 2566 Arnould S, et al. Molecular Cancer Therapeutics 2006;5: 1602-9.		First time in patients for this sequence selective DNA binding agent. Drug developed from CR-UK funded research at the University of Portsmouth & University of London. Trial completed. Agent in Phase II development. Too early in development to assess clinical impact. Led to Phase II evaluation.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Manchester/Christie Hospital	Ranson	CRUKD/03/040: A Cancer Research UK Phase I trial of AEG35156 /GEM640 (X1AP antisense) Administered as a 7-Day and 3-Day Continuous Intravenous Infusion in Patients With Advanced Refractory Cancer	41/41	2008	Dean E, Jodrell D, et al. Phase I Trial of AEG35156 Administered as a 7-Day and 3-Day Continuous Intravenous Infusion in Patients With Advanced Refractory Cancer. J Clin Oncol. 2009 Apr 1;27(10):1660-6. Cummings J, Ranson M, Lacasse E, Ganganagari JR, St-Jean M, Jayson G, Durkin J, Dive C. Method validation and preliminary qualification of pharmacodynamic biomarkers employed to evaluate the clinical efficacy of an antisense compound (AEG35156) targeted to the X-linked inhibitor of apoptosis protein XIAP. Br J Cancer. 2006 Jul 3;95(1):42-8. ASCO Meeting Abstracts 2006 24: 3059		First time in patients for this antisense agent. Trial completed. Aimed to identify a Phase 2 dose, side effects, PK/PD and efficacy. Well tolerated, Phase 2 dose identified. Agent in Phase 3 development. Too early in development to assess clinical impact. Led to Phase II evaluation.
University of Manchester/Christie Hospital	Middleton	CRUKD/03/039: A Cancer Research UK pharmacodynamic study of primary tumour 06-alkylguanine-DNA alkyltransferase depletion by oral PaTrin 2	39/39	2009	Watson AJ, Sabharwal A, et al. Tumor O(6)-methylguanine-DNA methyltransferase inactivation by oral lomeguatrib. Clin Cancer Res. 2010 Jan 15;16(2):743-9. ASCO Meeting Abstracts 2008 26: 3597		Follow on pharmacodynamic trial to CRUKD/99/014. Trial completed. Development discontinued after Phase II due to insufficient efficacy. Too early in development to assess clinical impact.
University of Manchester/Christie Hospital	Ranson	CRUKD/03/041: A Cancer Research UK Phase I trial of RH1, a novel DT diaphorase activated alkylating agent, in patients with advanced solid tumours	18/18	2010	Danson SJ, Johnson P, et al. Phase I pharmacokinetic and pharmacodynamic study of the bioreductive drug RH1. Ann Oncol. 2011 Jul;22(7):1653-60]. Danson S, Ranson M, et al. Validation of the comet-X assay as a pharmacodynamic assay for measuring DNA cross-linking produced by the novel anticancer agent RH1 during a phase I clinical trial. Cancer Chemother Pharmacol. 2007 Nov;60(6):851-61. Elliott MA, Ford SJ, et al. Development of a lyophilised RH1 formulation: a novel DT diaphorase activated alkylating agent. J Pharm Pharmacol. 2002 Apr;54(4):487-92. ASCO Meeting Abstracts 2007 25: 2514		First time in patients for this agent. Agent developed from CR-UK funded research at the Paterson Institute for Cancer Research, Manchester. Trial completed. Side efects elucidated, 7 patients had SD. Development discontinued at Phase I. Too early in development to assess clinical impact.
University of Newcastle	Calvert	CRUKD/03/042: A Cancer Research UK Phase I trial of PARP inhibitor AG014699 in combination with Five Days of Oral Temozolomide Given Every Four Weeks	33/33	2007	Plummer R, Jones C, et al. Phase I Study of the Poly(ADP-Ribose) Polymerase Inhibitor, AG014699, in Combination with Temozolomide in Patients with Advanced Solid Tumors. Clin Cancer Res. 2008 Dec 1;14(23):7917-23. Jones C, Plummer ER. PARP inhibitors and cancer therapy - early results and potential applications. Br J Radiol. 2008 Oct;81 Spec No 1:S2-5. R. Plummer, et al. J of Clin Onc. 2005. 23(16S): Part I of II, 2005: 3065		First in Class. First time in patients for this novel agent and this combination. Drug was developed by CR UK funded laboratories at the Northern Institute for Cancer Research, Newcastle. Trial completed. PARP inhibitory dose identified and combination tolerated well. One patient with melanoma had a complete response, 1 patient with GIST had a PR. Agent currently in Phase II development. Too early in development to assess clinical impact. Led to Phase II evaluation.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Glasgow	Cassidy	CRUKD/02/023: A Cancer Research UK Phase I trial of the DNA-hypermethylating agent decitabine (Dacogen) in combination with carboplatin in patients with solid tumours	35/35	2006	Appleton K, Mackay HJ, et al. Phase I and pharmacodynamic trial of the DNA methyltransferase inhibitor decitabine and carboplatin in solid tumors. J Clin Oncol. 2007 Oct 10;25(29):4603-9. Lee C, Appleton K, et al. A phase I trial of the DNA-hypomethylating agent 5-Aza-2 '-Deoxycytidine in combination with carboplatin both given 4 weekly by intravenous injection in patients with advanced solid tumours. J Clin Oncol 2004 22 14 Supp 128S. ASCO Meeting Abstracts 2004 22: 2005		This study was dose finding study for rest of series (other combinations and Phase II trial CRUKD/04/038; CRUKD/07/065). Came from CRUK funded lab work (R Brown) in Glasgow showing that decitabine had potential to reverse drug resistance phenotype in ovarian cancer. Industry not keen to pursue this development route since they were keen to show single agent activity. Combination trial completed. Study achieved its aim of determining the doses for phase 2. Led to a Phase II trial of the combination in ovarian cancer: CRUKD/07/065. Too early in development to assess clinical impact. Led to Phase II evaluation in CRUKD/07/065.
University of Aberdeen	Cassidy	CRUKD/01/019 A CRC Phase I trial of a selective oral cyclin-dependent kinase inhibitor CYC202 (seliciclib; R-Roscovitine), administered twice daily for 7 days every 21 days in patients with advanced malignancy	22/22	2006	Benson C, White J, et al. A phase I trial of the selective oral cyclin-dependent kinase inhibitor seliciclib (CYC202; R-Roscovitine), administered twice daily for 7 days every 21 days. Br J Cancer. 2007 Jan 15;96(1):29-37. White JD, Cassidy J, et al. J Clin Oncol 2004 22(14): Supp 205S		First time in patients for this cyclin dependent kinase inhibitor. Trial completed. Phase II dose identified. Agent in Phase II development. Too early in development to assess clinical impact. Led to Phase II evaluation.
Institute of Cancer Research/Royal Marsden Hospital	Judson	CRUKD/00/014: A Cancer Research UK Phase I trial of the nitroimidazole hypoxia marker SR4554 using 19F magnetic resonance spectroscopy in patients with solid tumours	34/34	2006	Lee CP, Payne GS, et al. A phase I study of the nitroimidazole hypoxia marker SR4554 using 19F magnetic resonance spectroscopy. Br J Cancer. 2009 Dec 1;101(11):1860-8. Seddon BM, Payne GS, et al. A phase I study of SR-4554 via intravenous administration for noninvasive investigation of tumor hypoxia by magnetic resonance spectroscopy in patients with malignancy. Clin Cancer Res. 2003 Nov 1;9(14):5101-12.		First time in patients for this hypoxia targeted imaging agent. Trial completed. A safe Phase II dose was identified that worked with MRS scans and suggested that using SR4554 and MRS to show hypoxia in cancer cells should be studied further. Development discontinued after Phase I due to inadequate efficacy for imaging. Too early in development to assess clinical impact.
Imperial College	Coombes	CRUKD/00/017: A Phase I trial of TNF-alpha AutoVaccIne in patients with metastatic cancer	34/34	2004	Waterston AM, Gumbrell L, et al. Phase I study of TNFalpha AutoVaccIne in patients with metastatic cancer. Cancer Immunol Immunother. 2005 Sep;54(9):848-57.		First time in patients for this vaccine. Trial completed. Development discontinued after Phase I due to lack of immune response. Too early in development to assess clinical impact.
University of Newcastle	Calvert	CRUKD/00/016: A CRC Phase I and pharmacokinetic study of paclitaxel poliglumex (XYOTAX; CT2103), investigating both 3-weekly and 2-weekly schedules	30/30	2004	Boddy AV, Plummer ER, et al. A phase I and pharmacokinetic study of paclitaxel poliglumex (XYOTAX), investigating both 3-weekly and 2-weekly schedules. Clin Cancer Res. 2005 Nov 1;11(21):7834-40.		First time in patients for this agent. Trial completed. Phase 2 dose identified. Led to Phase II trial in breast cancer: CRUKD/02/024. Agent in Phase III development. Too early in development to assess clinical impact. Led to Phase II evaluation in CRUKD/02/024.
Institute of Cancer Research/Royal Marsden Hospital	Judson	CRUKD/99/013: A Cancer Research UK Phase 1 pharmacokinetic and pharmacodynamic study of the HSP90 molecular chaperone inhibitor 17-AAG (17-allylamino-17-demethoxygeldanamycin) via intravenous administration in patients with advanced malignancies.	31/31	2005	Banerji U, O'Donnell A, et al. Phase I pharmacokinetic and pharmacodynamic study of 17-allylamino, 17-demethoxygeldanamycin in patients with advanced malignancies. J Clin Oncol. 2005 Jun 20;23(18):4152-61. Banerji UI, O'Donnell A, et al. A pharmacokinetic (PK) - pharmacodynamic (PD) driven phase I trial of the HSP90 molecular chaperone inhibitor 17-allylamino-17-demethoxygeldanamycin (17-AAG). Proc Am Assoc Cancer Res 2002 43 272		First in class agent. First trial in UK with this HSP90 inhibitor. Trial completed. Identified a safe Phase II dose and side efects. Led to Phase II trial in melanoma: CRUKD/05/036. Agent in Phase III development. Too early in development to assess clinical impact. Led to Phase II evaluation in CRUKD/05/036.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Manchester/Christie Hospital	Ranson	CRUKD/99/015: Phase I dose escalation and pharmacokinetic study of pluronic polymer-bound doxorubicin (SP1049C; Biotransdox) in patients with advanced cancer.	26/26	2003	Danson S, Ferry D, et al. Phase I dose escalation and pharmacokinetic study of pluronic polymer-bound doxorubicin (SP1049C) in patients with advanced cancer. Br J Cancer. 2004 Jun 1;90(11):2085-91.		First time in patients for this polymer-drug conjugate. Trial completed. Agent in Phase III development. Too early in development to assess clinical impact. Led to Phase II evaluation.
University of Manchester/Christie Hospital	Ranson	CRUKD/99/014: A Phase I safety, pharmacodynamic, and pharmacokinetic trial of Patrin2 (Lomeguatrib), a potent inhibitor of O6-alkylguanine-DNA-alkyltransferase, in combination with temozolomide in patients with advanced solid tumors	36/36	2005	Ranson M, Middleton MR, et al. Lomeguatrib, a potent inhibitor of O6-alkylguanine-DNA-alkyltransferase: phase I safety, pharmacodynamic, and pharmacokinetic trial and evaluation in combination with temozolomide in patients with advanced solid tumors. Clin Cancer Res. 2006 Mar 1;12(5):1577-84.		First time in patients for this agent. Agent developed from CR-UK funded research at the Paterson Institute for Cancer Research, Manchester jointly with Trinity College Dublin. Trial completed. Led to a pharmacodynamic trial: CRUKD/03/039. Development discontinued after Phase II due to insufficient efficacy. Too early in development to assess clinical impact. Led to Phase II evaluation.
Institute of Cancer Research/Royal Marsden Hospital	Judson	CRUKD/99/018: A Phase 1 Trial of SU006668 a novel multiple receptor Tyrosine Kinase inhibitor via intravenous administration in patients with advanced malignancies	6/30	2000			First time in patients for this Tyrosine Kinase inhibitor. Trial did not complete recruitment due to drug supply issues. Parenteral formulation was impractical and drug was not developed beyond Phase I. Too early in development to assess clinical impact.
University of Aberdeen	Cassidy	CRUKD/99/010: Phase I and pharmacokinetic study of MAG-CPT (PNU 166148): a polymeric derivative of camptothecin (CPT) given as one single intravenous administration every 4 weeks in patients with advanced solid tumors.	23/23	2003	Bissett D, Cassidy J, et al. Phase I and pharmacokinetic (PK) study of MAG-CPT (PNU 166148): a polymeric derivative of camptothecin (CPT). Br J Cancer. 2004 Jul 5;91(1):50-5		First time in patients for this polymer targeted version of camptothecin. Trial completed. Development discontinued after Phase I due to unacceptable toxicity. Too early in development to assess clinical impact.
Mount Vernon Hospital	Rustin	CRUKD/98/010: A CRC Phase I clinical trial of weekly combretastatin A4 phosphate a novel vascular disrupting agent	34/34	2002	Rustin GJ, Galbraith SM, et al. Phase I clinical trial of weekly combretastatin A4 phosphate: clinical and pharmacokinetic results. J Clin Oncol. 2003 Aug 1;21(15):2815-22. O'Connor JP, Jackson A, Parker GJ, Roberts C, Jayson GC. Dynamic contrast-enhanced MRI in clinical trials of antivascular therapies. Nat Rev Clin Oncol. 2012 Feb 14;9(3):167-77.		First in class and first time in patients for this vascular disrupting agent. Drug was developed from academic research at the University of Arizona. Trial completed. Phase II dose identified. Led to a follow up combination trial: CRUKD/03/037. Agent in Phase III development. Too early in development to assess clinical impact. Led to Phase II evaluation.
Institute of Cancer Research/Royal Marsden Hospital	Kaye	CRUKD/97/015: A Phase I clinical and pharmacological study of cis-diamminedichloro(2-methylpyridine) platinum II (AMD473).	43/43	2002	Beale P, Judson I, et al. A Phase I clinical and pharmacological study of cis-diamminedichloro(2-methylpyridine) platinum II (AMD473). Br J Cancer. 2003 Apr 7;88(7):1128-34.		First time in patients for this agent. Trial completed. Led to Phase II trial in bladder cancer: CRUKD/01/022. Agent in Phase III development. Too early in development to assess clinical impact. Led to Phase II evaluation.
University of Aberdeen	Cassidy	CRUKD/96/013: Phase I dose-escalation and pharmacokinetic study of a novel folate analogue AG2034	28/28	2000	Bissett D, McLeod HL, et al. Phase I dose-escalation and pharmacokinetic study of a novel folate analogue AG2034. Br J Cancer. 2001 Feb 2;84(3):308-12.		First time in patients for this agent. Trial completed. Development discontinued after Phase I - superceded by improved analogue. Too early in development to assess clinical impact.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Auckland	Thompson	CRUKD/96/018: A CRC Phase I clinical and pharmacokinetic study of 5,6-dimethylxanthenone-4-acetic acid (DMXAA; ASA404), a novel antivascular agent given once every 3 weeks in patients with advanced cancer		2002	Jameson MB, Thompson PI, et al. Clinical aspects of a phase I trial of 5,6-dimethylxanthenone-4-acetic acid (DMXAA), a novel antivascular agent. Br J Cancer. 2003 Jun 16;88(12):1844-50. Jameson MB, Baguley BC, et al. Pharmacokinetics of 5,6-dimethylxanthenone-4-acetic acid (AS1404), a novel vascular disrupting agent, in phase I clinical trial. Cancer Chemother Pharmacol. 2007 Apr;59(5):681-7.		First time in patients for this anti-vascular agent with this schedule of administration. Companion trial to CRUKD/95/019. Drug developed from academic research at the University of Auckland, New Zealand. Trial completed. Identified a safe Phase II dose and side effects. Agent in Phase III development for lung cancer. Too early in development to assess clinical impact. Led to Phase II evaluation.
University of Manchester/Christie Hospital	Ranson	CRUKD/96/015: A CRC Phase I and pharmacologic study of CT-2584 HMS, a modulator of phosphatidic acid, in adult patients with solid tumours	30/30	1999	Cheeseman SL, Brannan M, et al. Phase I and pharmacologic study of CT-2584 HMS, a modulator of phosphatidic acid, in adult patients with solid tumours. Br J Cancer. 2000 Dec;83(12):1599-606.		First time in patients for this agent. Trial completed. Development discontinued after Phase II due to problems with the formulation. Too early in development to assess clinical impact. Led to Phase II evaluation.
University of Edinburgh	Smyth	CRUKD/96/016: A Phase I study of Antagonist G, an analogue of the peptide Substance P	24/24	2000	Clive S, Webb DJ, et al. Forearm blood flow and local responses to peptide vasodilators: a novel pharmacodynamic measure in the phase I trial of antagonist G, a neuropeptide growth factor antagonist. Clin Cancer Res. 2001 Oct;7(10):3071-8.		First time in patients for this agent. Trial completed. Development discontinued after Phase I due to lack of potency and rapid clearance. Too early in development to assess clinical impact.
Mount Vernon Hospital	Rustin	CRUKD/95/019: A CRC Phase I clinical and pharmacokinetic study of 5,6-dimethylxanthenone-4-acetic acid (DMXAA; ASA404), a novel antivascular agent given as a once weekly infusion in patients with advanced cancer	46/46	2002	Rustin GJ, Bradley C, et al. 5,6-dimethylxanthenone-4-acetic acid (DMXAA), a novel antivascular agent: phase I clinical and pharmacokinetic study. Br J Cancer. 2003 Apr 22;88(8):1160-7. O'Connor JP, Jackson A, Parker GJ, Roberts C, Jayson GC. Dynamic contrast-enhanced MRI in clinical trials of antivascular therapies. Nat Rev Clin Oncol. 2012 Feb 14;9(3):167-77. Galbraith SM, Rustin GJ, et al. Effects of 5,6-dimethylxanthenone-4-acetic acid on human tumor microcirculation assessed by dynamic contrast-enhanced magnetic resonance imaging. J Clin Oncol. 2002 Sep 15;20(18):3826-40.		First time in patients for this anti-vascular agent. Companion trial to CRUKD/96/018. Drug developed from academic research at the University of Auckland, New Zealand. Trial completed. Agent in Phase III development for lung cancer. Too early in development to assess clinical impact. Led to Phase II evaluation.
University of Auckland	Evans	CRUKD/94/010: A CRC Phase I and pharmacokinetic study of DACA (XR5000; N-[2-(dimethylamino)ethyl]acridine-4-carboxamide): a novel inhibitor of topoisomerase I and II, administered as a three hour infusion given on Day 1 only, with treatment repeated every three weeks		1998	McCrystal MR, Evans BD, et al. Phase I study of the cytotoxic agent N-[2-(dimethylamino)ethyl]acridine-4-carboxamide. Cancer Chemother Pharmacol. 1999;44(1):39-44.		First time in patients for this topoisomerase inhibitor with this schedule of administration. Companion trial to CRUKD/94/004. Trial completed. Development discontinued after Phase II due to insufficient activity. Too early in development to assess clinical impact. Led to Phase II evaluation.
University of Edinburgh	Jodrell	CRUKD/94/009: A phase I study of the lipophilic thymidylate synthase inhibitor Thymitaq (nolatrexed dihydrochloride; AG337) given by 10-day oral administration	23/23	1998	Jodrell DI, Bowman A, et al. A phase I study of the lipophilic thymidylate synthase inhibitor Thymitaq (nolatrexed dihydrochloride) given by 10-day oral administration. Br J Cancer. 1999 Feb;79(5-6):915-20. I Rafi, A V Boddy, et al. JCO Mar 1, 1998:1131-41		First time in patients for this agent with this schedule of administration. Companion trial to CRUKD/94/006. Trial completed. Led to paediatric trial: CRUD/95/020. Development discontinued after Phase III due to insufficient activity. Too early in development to assess clinical impact. Led to Phase II evaluation.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Newcastle	Calvert	CRUKD/94/006: Phase I studies with the nonclassical antifolate nolatrexed dihydrochloride (AG337, THYMITAQ) administered orally for 5 days	48/48	1998	Hughes AN, Rafi I, et al. Phase I studies with the nonclassical antifolate nolatrexed dihydrochloride (AG337, THYMITAQ) administered orally for 5 days. Clin Cancer Res. 1999 Jan;5(1):111-8.		First time in patients for this antifolate. One of the earliest trials to use PET scanners to look at tumour vasculature. Companion trial to CRUKD/94/009. Trial completed. Well tolerated, easily absorbed oral administration. Led to paediatric trial: CRUD/95/020. Development discontinued after Phase 3 due to insufficient activity. PET scanning is now used widely in clinical practice. Trial led to Phase II evaluation
University of Cambridge	Bleehen	CRUKD/94/004: A CRC Phase I and pharmacokinetic study of DACA (XR5000; N-[2-(dimethylamino)ethyl]acridine-4-carboxamide): a novel inhibitor of topoisomerase I and II, administered as a three hour intravenous infusion on three successive days, repeated every three weeks	41/41	1998	Twelves CJ, Gardner C, et al. Phase I and pharmacokinetic study of DACA (XR5000): a novel inhibitor of topoisomerase I and II. CRC Phase I/II Committee. Br J Cancer. 1999 Aug;80(11):1786-91. Saleem A, Harte RJ, et al. Pharmacokinetic evaluation of N-[2-(dimethylamino)ethyl]acridine-4-carboxamide in patients by positron emission tomography. J Clin Oncol. 2001 Mar 1;19(5):1421-9.		First time in patients for this topoisomerase inhibitor with this schedule of administration. Companion trial to CRUKD/94/010. Trial completed. Development discontinued after Phase II due to lack of activity. Too early in development to assess clinical impact. Led to Phase II evaluation.
Institute of Cancer Research/Royal Marsden Hospital	Calvert	CRUKD/94/005: A CRC phase I study of Etoposide phosphate (Etopophos) infusion with therapeutic drug monitoring in combination with carboplatin	8/8	1995	Porter D, Boddy A, et al. Etoposide phosphate infusion with therapeutic drug monitoring in combination with carboplatin dosed by area under the curve: a cancer research campaign phase I/II committee study. Semin Oncol. 1996 Dec;23(6 Suppl 13):34-44.		First time in patients for this combination. Follow up trial to CRUKD/90/004. Trial completed. Drug registered for clinical use as Etopophos. Too early in development to assess clinical impact. Led to Phase II evaluation and subsequently registration studies.
University of Aberdeen	Cassidy	CRUKD/94/007: Phase I clinical and pharmacokinetic study of PK1 [N-(2-hydroxypropyl)methacrylamide copolymer doxorubicin]: first member of a new class of chemotherapeutic agents-drug-polymer conjugates	36/36	1998	Vasey PA, Kaye SB, et al. Phase I clinical and pharmacokinetic study of PK1 [N-(2-hydroxypropyl) methacrylamide copolymer doxorubicin]: first member of a new class of chemotherapeutic agents-drug-polymer conjugates. Cancer Research Campaign Phase I/II Committee. Clin Cancer Res. 1999 Jan;5(1):83-94. Thomson AH, Vasey PA, Murray LS, Cassidy J, Fraier D, Frigerio E, Twelves C. Population pharmacokinetics in phase I drug development: a phase I study of PK1 in patients with solid tumours. Br J Cancer. 1999 Sep;81(1):99-107.		First in class and first time in patients for this drug-polymer conjugate. First clinical evaluation of this delivery concept. Trial completed. PK1 shown to be tolerated well in man with doses of anthracycline higher than could be tolerated of native drug. Promising pharmacokinetic data in patients suggested drug depot was being formed with slow release – similar to that seen in animal model systems encouraged development into phase 2 trials. Led to Phase II trials in breast, colorectal and lung cancer: CRUKD/97/016; CRUKD/97/011; CRUKD/97/014. Too early in development to assess clinical impact. Led to Phase II evaluation.
University of Nottingham	Carmichael	CRUKD/93/008: A study of amsalog (CI-921) administered orally on a 5-day schedule, with bioavailability and pharmacokinetically guided dose escalation.	20/20	2000	Fyfe D, Price C, et al. A phase I trial of amsalog (CI-921) administered by intravenous infusion using a 5-day schedule. Cancer Chemother Pharmacol. 2001 Apr;47(4):333-7. Fyfe D, Raynaud F, et al. A study of amsalog (CI-921) administered orally on a 5-day schedule, with bioavailability and pharmacokinetically guided dose escalation. Cancer Chemother Pharmacol. 2002 Jan;49(1):1-6.		First time in patients for this topoisomerase II inhibitor. Trial completed. Development discontinued after Phase I due to poor oral bioavailability. Too early in development to assess clinical impact.
University of Glasgow	Kaye	CRUKD/93/010: A phase I and pharmacokinetic study of LY231514 (pemetrexed; Alimta), the multitargeted antifolate, administered as a daily i.v. infusion over 10 minutes for 5 days, repeated every 3 weeks in	38/38	1997	McDonald AC, Vasey PA, et al. A phase I and pharmacokinetic study of LY231514, the multitargeted antifolate. Clin Cancer Res. 1998 Mar;4(3):605-10.		First time in patients for this antifolate. Trial completed. Drug registered as Alimta for treating mesothelioma and non small cell lung cancer and in Phase III development for other types of cancer. First trial of drug now used to treat mesothelioma and non-squamous non-small cell lung cancer. Led onto Phase II evaluation

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
		patients with advanced or refractory cancer					
University of Manchester/Christie Hospital	Crowther	CRUKD/91/006: A CRC Phase I study of intravenous bryostatin 1 in patients with advanced cancer	96/96	1992	Prendiville J, Crowther D, et al. A phase I study of intravenous bryostatin 1 in patients with advanced cancer. Br J Cancer. 1993 Aug;68(2):418-24. Philip PA, Rea D, et al. Phase I study of bryostatin 1: assessment of interleukin 6 and tumor necrosis factor alpha induction in vivo. The Cancer Research Campaign Phase I Committee. J Natl Cancer Inst. 1993 Nov 17;85(22):1812-8.		First time in patients for this agent developed from academic research at the University of Arizona. Trial completed. Led to Phase II trials in lymphoma, kidney and ovarian cancer: CRUKD/97/013; CRUKD/99/011; CRUKD/99/012. Development discontinued after Phase II due to lack of efficacy. Too early in development to assess clinical impact. Led to Phase II evaluation.
University of Newcastle	Calvert	CRUKD/90/004: Phase I and pharmacokinetic study of a water-soluble etoposide prodrug, etoposide phosphate (BMY-40481) in patients with cancer	68/68	1994	Millward MJ, Newell DR, et al. Phase I and pharmacokinetic study of a water-soluble etoposide prodrug, etoposide phosphate (BMY-40481). Eur J Cancer. 1995 Dec;31A(13-14):2409-11.		Important early pharmacokinetic study with this prodrug now registered for use. Trial completed. Led to combination trial: CRUKD/94/005. Drug registered for clinical use as Etopophos. Too early in development to assess clinical impact. Led to Phase II evaluation.
Charing Cross Hospital	Newlands	CRUKD/89/003: Phase I trial of elactocin	33/33	1995	Newlands ES, Rustin GJ, Brampton MH. Phase I trial of elactocin. Br J Cancer. 1996 Aug;74(4):648-9.		First time in patients for this agent. Trial completed. Development discontinued after Phase I due to dose limiting toxicity. Too early in development to assess clinical impact.
Charing Cross Hospital	Newlands	CRUKD/87/003: Phase I trial of temozolomide (CCRG 81045: M&B 39831: NSC 362856; Temodal).	178/178	1992	Newlands ES, Blackledge GR, et al. Phase I trial of temozolomide (CCRG 81045: M&B 39831: NSC 362856). Br J Cancer. 1992 Feb;65(2):287-91.		First time in patients for this agent. Drug was developed by Malcolm Stevens' CR-UK funded research group at Aston Unversity. Trial completed. Phase II dose identified. Led to Phase II trials in glioma, melanoma and lymphoma: CRUKD/92/008; CRUKD.92/006; CRUKD/93/009. Drug registered for clinical use as Temodal. Led to Phase II evaluation. First trial of drug developed from CR-UK funded research now licensed worldwide to treat brain cancer. Drug now licensed worldwide to treat brain cancer.
Charing Cross Hospital	Coombes	Phase I and pharmacokinetic study of D-limonene in patients with advanced cancer.	42/42	1997	Vigushin DM, Poon GK, Boddy A, English J, Halbert GW, Pagonis C, Jarman M, Coombes RC. Cancer Chemother Pharmacol. 1998;42(2):111-7		
Paediatric							
University of Birmingham	Mitchell	WT3: WT-3 (WT 1991 01): Trial of preoperative chemotherapy in biopsy proven Wilms' tumour versus immediate nephrectomy	928/928	2006	MITCHELL C et al. (2006) Immediate nephrectomy versus preoperative chemotherapy in the management of non-metastatic Wilms' tumour: Results of a randomised trial (UKW3) by the UK Children's Cancer Study Group. Eur J Cancer 42: p.2554-2562. VUJANIĆ GM et al (2009) Central pathology review in multicentre trials and studies: lessons from the nephroblastoma trials. Cancer 115(9):p.1977-83	Yes	Six weeks of preoperative chemotherapy with vincristine and actinomycin D results in a significant shift towards a more advantageous stage distribution and hence reduction in therapy, while maintaining excellent event free and overall survival in children with non-metastatic Wilms' tumour. Around 20% of survivors were therefore spared the late-effects of doxorubicin or radiotherapy. All children with non-metastatic Wilms' tumour should receive chemotherapy prior to tumour resection.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Birmingham	Vora	Interfant 99: International collaborative treatment protocol for infants under one year with acute lymphoblastic leukemia	71/60	2007	PIETERS R, et al. (2007) A treatment protocol for infants younger than 1 year with acute lymphoblastic leukaemia (Interfant-99): an observational study and a multicentre randomised trial. Lancet 370(9583):p.240-50. MANN G, et al. (2010) Improved outcome with hematopoietic stem cell transplantation in a poor prognostic subgroup of infants with mixed-lineage-leukemia (MLL)-rearranged acute lymphoblastic leukemia: results from the Interfant-99 Study. Blood; 116(15):p. 2644-50. PIETERS R, et al. (2007) A treatment protocol for infants younger than 1 year with acute lymphoblastic leukaemia (Interfant-99): an observational study and a multicentre randomised trial. Lancet; 370(9583):p.240-50. VAN DER LINDEN,M.H., et al. (2009) Outcome of congenital acute lymphoblastic leukemia treated on the Interfant-99 protocol. Blood, 114:p.3764-3768. VAN,D.V., V, et al. (2009) Prognostic significance of minimal residual disease in infants with acute lymphoblastic leukemia treated within the Interfant-99 protocol. Leukemia, 23: p.1073-1079.	Yes	Patients treated with the hybrid protocol, especially those who responded poorly to prednisone, had higher EFS than most reported outcomes for treatment of infant ALL. Delayed intensification of chemotherapy did not benefit patients. Results have informed successor trial, Interfant 06 Results have informed successor trial, Interfant 06
University of Birmingham	Kohler	Unresectable NB: Treatment of children over the age of 1 year with unresectable localised neuroblastoma without MYCN amplification	42/42	2008		Yes	
University of Birmingham	Pfizer	PNET 4: A prospective randomised controlled trial of hyperfractionated versus conventionally fractionated radiotherapy in standard risk medulloblastoma	18/70	2011	LANNERING L, RUTKOWSKI S, DOZ F, PIZER B, GUSTAFSSON G, NAVAJAS A, MASSIMINO M, REDDINGIUS R, BENESCH M, CARRIE C, TAYLOR R, GANDOLA L, BJÖRK-ERIKSSON T, GIRALT J, OLDENBURGER F, PIETSCH T, FIGARELLA-BRANGER D, ROBSON K, FORNI M, WARMUTH-METZ M, VON HOFF K, FALDUM A, MOSSERI V, KORTMANN R. (2012) Standard risk medulloblastoma: hyperfractionated vs. conventional radiotherapy followed by chemotherapy. Results from the randomized multicentre study HIT-SIOP PNET 4. J Clin Oncol 30(26):p.3187-93.	Yes	This trial compared hyperfractionated radiotherapy (HFRT) and standard (conventional) fractionated radiotherapy (STRT), followed by a common chemotherapy regimen consisting of eight cycles of cisplatin, lomustine, and vincristine. Survival rates were not significantly different between the two treatment arms. Patients with a delay of more than 7 weeks to the start of radiotherapy had a worse prognosis. Severe hearing loss was not significantly different for the two treatment arms at follow-up. In conclusion, excellent survival rates were achieved in patients without a large postoperative residual tumour and without radiotherapy treatment delays. Survival for HFRT was not superior to STRT, which therefore remains standard of care in this disease. Poor recruitment in UK. Important biological + quality of life outcomes await publication In this large randomized European study which enrolled patients with standard risk medulloblastoma from many centres, excellent survival rates were achieved in patients without a large postoperative residual tumour and without RT treatment delays. Event free and overall survival for hyperfractionated RT was not superior to conventionally fractionated RT that therefore remains standard of care in this disease. In this large

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
							randomized European study which enrolled patients with standard risk medulloblastoma from many centres, excellent survival rates were achieved in patients without a large postoperative residual tumour and without RT treatment delays. Event free and overall survival for hyperfractionated RT was not superior to conventionally fractionated RT that therefore remains standard of care in this disease.
University of Birmingham	Grundy	Infant Brain: Management of children aged less than 3 years with a brain tumour (CNS 9204)	194/194	2007	GRUNDY RG et al. (2007) Primary postoperative chemotherapy without radiotherapy for intracranial ependymoma in children: the UKCCSG/SIOP prospective study. Lancet Oncol 8: p.696–705 GRUNDY RG et al. (2010) Primary postoperative chemotherapy without radiotherapy for treatment of brain tumours other than ependymoma in children under 3 years: results of the first UKCCSG/SIOP CNS 9204 trial. Eur J Cancer 46(1):p.120-33	Yes	This trial aimed to assess the role of a primary chemotherapy strategy in avoiding or delaying radiotherapy in children younger than 3 years with malignant brain tumours other than ependymoma. Over all diagnostic groups the cumulative progression rate was 80.9% at 5 years while the corresponding need-for-radiotherapy rate for progression was 54.6%, but both rates varied by tumour type. There was no clear relationship between chemotherapy dose intensity and outcome. The outcome for very young children with brain tumours is dictated by degree of surgical resection and histological tumour type and underlying biology as an indicator of treatment sensitivity. Overall, the median age at radiotherapy was 3 years and radiotherapy was avoided in 45% of patients. This protocol avoided or delayed radiotherapy in a substantial proportion of children younger than 3 years without compromising survival. These results suggest, therefore, that primary chemotherapy strategies have an important role in the treatment of very young children with intracranial ependymoma.
University of Birmingham	Walker	LowGrade Glioma: Low Grade Glioma (CNS 1997 02)	773/773	2010	STOKLAND T et al. (2010) A multivariate analysis of factors determining tumor progression in childhood low-grade glioma: a population-based cohort study (CCLG CNS9702). Neuro-Oncology 12(12): 1257-1268 O'CONNOR A, BUJKIEWICZ S, STOKLAND T, TAYLOR R et al. (2009) Visual Outcomes of Childhood Optic Pathway Glioma Treated According to a Standardised Multidisciplinary Strategy: A Children's Cancer and Leukaemia Group Study. Arch Dis Child 2009;94 (Suppl I):A58 (G138)		The purpose of this study was to identify risk factors for the progression of low-grade glioma in children from a large population-based cohort. The influence of age and anatomical site upon the risk of tumor progression suggests that these factors strongly influence tumor behavior for the majority of pilocytic tumors. Age <1 year and 1-5 years, fibrillary histology, completeness of resection, and chiasmatic location are candidates for stratification in future studies.
University of Birmingham	Pritchard Jones	SIOP WILMS: SIOP nephroblastoma (wilms tumour) clinical trial and study	775/775	2013	PRITCHARD-JONES K. et al. (2011) Doxorubicin can be safely omitted from the treatment of stage II/III, intermediate risk histology Wilms Tumour: results of the SIOP WT 2001 randomised trial. Pediatric Blood & Cancer 57(5): p/741 (O137). 44th Congress of the International Society of Paediatric Oncology (SIOP), London, UK, 5th-8th October, 2012	Yes	Randomised trial demonstrated that doxorubicin can be removed safely from the treatment of stage II/III, intermediate-risk Wilms Tumour patients. Change to standard treatment of Wilms Tumour, to remove doxorubicin. Change to standard treatment of Wilms Tumour, to remove doxorubicin.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Birmingham	Brock	SIOPEL 3: Hepatoblastoma and hepatocellular carcinoma SIOPEL 3 (LT 1998 01)	116/116	2011	PERILONGO G et al, Cisplatin alone versus Cisplatin/Doxorubicin for standard risk hepatoblastoma; final report of the randomized international trial, SIOPEL 3 SR-HB. N Engl J Med 2009; 361:p.1662-1670 ZSÍROS J, et al Successful treatment of childhood high-risk hepatoblastoma with dose-intensive multiagent chemotherapy and surgery: final results of the SIOPEL-3HR study. J Clin Oncol. 2010 (15): p.2584-90 PURCELL R et al Potential biomarkers for hepatoblastoma: Results from the SIOPEL-3 study Eur J Cancer 2012 (12) 1853-59, MAIBACH R. et al., Prognostic stratification for children with hepatoblastoma: The SIOPEL experience, Eur J Cancer (July 2012), 1543–49.	Yes	The primary objective of the SIOPEL 3 trial was to determine the efficacy of a newly designed preoperative chemotherapy regimen in an attempt to improve the cure rate of children with high-risk hepatoblastoma. Patients were treated with alternating cycles of cisplatin and carboplatin plus doxorubicin and delayed tumour resection. A great proportion of tumours were rendered resectable and in comparison with previously published results led to an improved survival. The NEJM paper has enabled the current SIOPEL 6 trial which is still recruiting and is using the data from SIOPEL 3 to assume that we can treat SR HB with cisplatin monotherapy and are doing a randomised trial with the addition of a chemoprotectant to reduce toxicity.
University of Birmingham	Bailey	BSG: A phase II multi-centre study of concomitant and prolonged adjuvant temozolomide with radiotherapy in diffuse pontine gliomas (CNS 2007 04)	43/43	2012	BAILEY, S., HOWMAN, A., PIZER, B., HARRIS, D., JONES, D., KEARNS, P., PICTON, S., SARAN, F., WHEATLEY, K., GIBSON, M., GLASER, A., CONNOLLY, D. & HARGRAVE D. (2013) Diffuse intrinsic pontine glioma treated with prolonged temozolomide and radiotherapy - results of the United Kingdom trial (CNS 2007 04) European Journal of Cancer (IN PRESS) Abstract presented at the International Symposium on Pediatric Neuro-Oncology (ISPNO) June 2012 in Toronto, Canada		Diffuse intrinsic pontine glioma (DIPG) has a dismal prognosis with no chemotherapy regimen so far resulting in any significant improvement over standard radiotherapy. In this trial, a prolonged regimen (21/28 day) of temozolomide was studied with the aim of overcoming MGMT mediated resistance. This trial demonstrated no survival benefit of the addition of dose dense temozolomide, to standard radiotherapy in children with classical DIPG. However, a subgroup of adolescent DIPG patients did have a prolonged survival, which needs further exploration Temozolomide can be given to the majority of children without significant toxicity. There was no suggestion that prolonged temozolomide offers a clinically worthwhile benefit over either standard 5/28 temozolomide regimes or radiotherapy alone. With the recent publication of a number of studies reporting the biology of these tumours further efforts in treating this devastating disease should be based on more biologically directed therapy
University of Birmingham	Makin	TVD: Topotecan-Vincristine-Doxorubicin in children with stage 4 neuroblastoma failing to respond to COJEC	9/unknown target	2012		Yes	TVD combination was active and tolerable in patients with metastatic neuroblastoma after treatment with rapid COJEC. This trial has established TVD as the UK first line therapy for resistant neuroblastoma. This trial has established TVD as the European first line therapy for resistant neuroblastoma

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Birmingham	Taylor	HART: Hyperfractionated Accelerated Radiotherapy (hart) with chemotherapy (cisplatin, ccnu, vincristine) for metastatic (m1-3) medulloblastoma (CNS 2001 06)	36/29	2012	In press TAYLOR R et al. (2012) Hyperfractionated accelerated radiotherapy (HART) with chemotherapy for m1-3 medulloblastoma (mb): a children's cancer and leukaemia group/ national cancer research network (ncrn) study. SIOP Abstract Medical and Pediatric Oncology; 59 (6) 1086. TAYLOR et al. (2012) UKMB-41. Hyperfractionated accelerated radiotherapy (HART) with chemotherapy for M 1-3 medulloblastoma (MB) - a Children's Cancer and Leukaemia Group (CCLG)/National Cancer Research Network (NCRN) study. Neuro-Oncology, Abstracts from the 15th International Symposium on Paediatric Neuro-Oncology (ISPNO). Toronto, Ontario, Canada	Yes	Exploratory analysis showed that with a median follow-up of 4 years EFS and OS were 69% and 81% at 2 years and 59% and 71% at 3 years. Of 10 relapses, 1 was outside the CNS, 1 posterior fossa alone and 8 leptomeningeal with 3 of these also associated with posterior fossa relapse. The HART regimen was well tolerated and may have a place in the multimodality management of patients with high risk MB/PNET. HART has become one of the radiotherapy regimens employed routinely in the UK for treating patients with metastatic Medulloblastoma and CNS PNET Contribute to evidence base
University of Birmingham	Stevens	SIOP MMT 95 (STS 1995 07): For Rhabdomyosarcoma and other malignant soft tissue tumours of childhood	531/ unknown target	2012	Oberlin O et al. (2012) Randomized Comparison of Intensified Six-Drug Versus Standard Three-Drug Chemotherapy for High-Risk Nonmetastatic Rhabdomyosarcoma and Other Chemotherapy-Sensitive Childhood Soft Tissue Sarcomas: Long-Term Results From the International Society of Pediatric Oncology MMT95 Study. JCO 30(20): p.2457-2465	Yes	The MMT95 trial compared ifosfamide, vincristine and dactinomycin (IVA) with a 6-drug combination (IVA plus carboplatin, epirubicin and etoposide) as first-line treatment for paediatric patients with high-risk non-metastatic rhabomyosarcoma (RMS) and other chemotherapy-sensitive childhood soft tissue sarcomas. The trial concluded that Intensification of chemotherapy for nonmetastatic RMS and other chemotherapy-sensitive STS provides no survival advantage or reduction in the intensity of local therapy and adds toxicity.
University of Birmingham	Ronghe	SIOPEL 4: Intensified pre-operative chemotherapy and radical surgery for High Risk Hepatoblastoma	15/ unknown target	2013	ZSÍROS J et al. (2013) Dose-dense cisplatin-based chemotherapy and surgery for children with high-risk hepatoblastoma (SIOPEL-4): a prospective, single-arm, feasibility study. Lancet Oncol 14(9):p.834-42 Results of SIOPEL 4 were presented at the 44th Annual SIOP Congress, London, 5th - 8th October 2012.	Yes	The trial has shown that weekly cisplatin with doxorubicin is a toxic but feasible treatment for HR-HB. Compared to previous results the SIOPEL-4 strategy has further improved the outcome of patients with HR-HB. However more detailed analysis and longer follow up should elucidate which patients receive the most benefit of this intensive approach The SIOPEL 4 strategy will become the standard therapy for High Risk HB patients (Metastatic and those with low AFP & SCUD)
University of Birmingham	Glaser	GC Survivors: Cross-sectional evaluation of outcome following extra-cranial germ cell tumours treated according to UKCCGGC 7901 (GC I) and GC 8901 (GC II) Protocols	105/105	2013			

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Birmingham	Brock	GD2: A Phase I/II dose schedule finding study of ch14.18/CHO continuous infusion combined with subcutaneous aldesleukin (IL-2) in patients with primary refractory or relapsed neuroblastoma	9/20	2015		Yes	Immunotherapy is of proven benefit in high-risk neuroblastoma and has been incorporated into upfront protocols. This study provides access to immunotherapy for relapsed/refractory patients who would not otherwise be eligible and allows exploration of the efficacy of antibody therapy in this relapse setting. This study is also examining an alternative prolonged infusion regimen which may be associated with lower toxicity/enhanced efficacy. The dose finding part of the study is complete and is now in the confirmatory phase If this approach proves feasible and provides preliminary evidence of efficacy, prolonged antibody infusion with IL-2 may provide a basis for both further experimental approaches for managing relapsed/refractory neuroblastoma as well as potentially being incorporated into upfront management of newly diagnosed patients If this approach proves feasible and provides preliminary evidence of efficacy, prolonged antibody infusion with IL-2 may provide a basis for both further experimental approaches for managing relapsed/refractory neuroblastoma as well as potentially being incorporated into upfront management of newly diagnosed patients
University of Birmingham	Nanduri	HLH 2004: Treatment protocol of the second international HLH study 2004 (LCH 2006 02)	11/20	2013			Will contribute significantly to international knowledge base.
University of Birmingham	Ancliff	Interfant 06: International collaborative treatment protocol for infants under one year with acute lymphoblastic or biphenotypic leukaemia	56/55	2014		Yes	
University of Birmingham	Windebank	LCH 3: Treatment protocol of the third international study for Langerhans Cell Histiocytosis	56/56	2013	GADNER H, MINKOV M, GROIS N, PÖTSCHGER U, THIEM E, ARICÒ M, ASTIGARRAGA I, BRAIER J, DONADIEU J, HENTER JI, JANKA-SCHAUB G, MCCLAIN KL, WEITZMAN S, WINDEBANK K, LADISCH S; HISTIOCYTE SOCIETY. (2013) Therapy prolongation improves outcome in multisystem Langerhans cell histiocytosis. Blood. 121(25):p.5006-14	Yes	The trial showed that prolonged treatment in multi-system LCH in patients without risk organ involvement (treatment duration of 12 vs 6 months) is superior in preventing reactivations. Established longer maintenance better at preventing reactivations in single system disease. New guidelines based on LCH III in place whilst awaiting opening of LCH IV. Established longer maintenance better at preventing reactivations in single system disease. New guidelines based on LCH III in place whilst awaiting opening of LCH IV.
University of Birmingham	Picton	Rel Ependymoma: Phase II study of intravenous etoposide in patients with relapsed ependymoma	25/25	2013			The main aim of this study was to improve the survival rate for children with relapsed ependymoma, by investigating the use of a rapid scheduled single agent chemotherapy drug, etoposide, in this population. The data is yet to be formally analysed.
University of Birmingham	Hale	Relapsed Wilms: Protocol for the treatment of relapsed and refractory Wilms tumour and clear cell sarcoma of the Kidney (CCSK) UKW-R (WT 2001 02)	78/75	2013		Yes	

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Birmingham	Grundy	SIOP Ependymoma: SIOP study of combined modality treatment in childhood ependymoma	63/ unknown target	2013	Abstract presented at 44th Congress of the International Society of Paediatric Oncology (SIOP) 2012, London, United Kingdom, 5th–8th October, 2012 GRUNDY R. et al. (2012) International Society of Paediatric Oncology. Outcome of Children Treated For Intracranial Ependymoma: The First SIOP Trial. Pediatric Blood & Cancer		VEC is effective therapy for residual ependymoma, though the overall outcome following incomplete resection remains poor. 30% of those enrolled were ineligible for analysis. The outcome for ependymoma is likely to be enhanced by simply improving the accuracy of diagnosis and harmonising the standard of care following initial surgery, as well as investigating enhanced adjuvant strategies as planned in the next SIOP study.
University of Birmingham	Elliott (previously Brock)	HRNBL: High risk neuroblastoma study 1 of SIOP- Europe (SIOPEN) (NB 2002 06)	448/381	2018	VIPREY, VF et al. (2009) Clinical Cancer Research. 15(21). p.6742 LADENSTEIN, R et al. (2010) J Clin Oncol. 28(21). p.3516-24 GAZE, MN et al. (2010) Radiother Oncol. 97(3). p.593-5 LADENSTEIN, R et al. (2011) J Clin Oncol. 29(15). p.2 VEAL, GJ et al. (2012) European Journal of Cancer. 48. p.3063-3072	Yes	Results of the first randomisation (R0) have shown that the use of G-CSF during induction treatment showed a significant reduction of the mean number of febrile episodes. Overall results were in favour of G-CSF, and treatment recommendations have been made. The second randomisation (R1) closed early due to a recommendation made by the data monitoring committee due to early high significance favouring busulphan and melphalan (BuMel) vs carboplatin, etoposide and melphalan (CEM). Another main aim of the trial is to test the hypothesis that immunotherapy with chimeric 14.18 anti-GD2 monoclonal antibody and subcutaneous aldesleukin, and following MAT and autologous SCR, in addition to differentiation therapy with isotretinoin, willl improve 3-year EFS in patients with High Risk Neuroblastoma. This study has already recommended the use of G-CSF with induction treatment, as well as BuMel MAT therapy. If the results of the R2 randomisation are positive, it could change standard practice for differentiation therapy for this group of patients. This study has already recommended the use of G-CSF with induction treatment, as well as BuMel MAT therapy. If the results of the R2 randomisation are positive, it could change standard practice for differentiation therapy for this group of patients.
University of Birmingham	Picton (Grant holder: Walker)	LGG2: Cooperative multicenter study for children and adolescents with Low Grade Glioma	121 (rand)/90 (rand)	2014		Yes	The aim of this study is to determine whether an intensified chemotherapy induction and a prolongation of chemotherapy treatment will improve progression free survival in low grade glioma of childhood compared with the standard treatment. The radiotherapy trial will determine whether modern techniques will improve survival for older children treated with radiotherapy This study will contribute significantly to international knowledge base and lead to new treatment guidelines. The experimental arm may become the control arm in future trials. This trial may lead to new guidelines in clinical practice. This study will contribute significantly to international knowledge base and lead to new treatment guidelines. The experimental arm may become the control arm in future trials. This trial may lead to new guidelines in clinical practice.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Birmingham	Gaze	LUDO: A phase IIa study of 177Lutetium dotateate in children with primary refractory or relapsed high risk neuroblastoma.	0/24	2017		Yes	In March 2013 the LuDO study opened at University College Hospital London. No patients have been recruited into the trial to date as a new Radiation Detector had to be custom built, fitted and tested at UCLH so that the LuDO study can commence recruitment. It is anticipated that work will be complete by the end of September 2013 If found to have acceptable toxicity and to be effective then 177Lu DOTATATE therapy will be evaluated further by the International Society of Paediatric Oncology Europe Neuroblastoma Group (SIOPEN) in refractory and relapsed patients in frontline studies. The benefits of 177Lu DOTATATE compared to 131I-mIBG radionuclide therapy or a combination of both will be determined. The dosimetry data from this trial will help inform other 177Lu DOTATATE studies in adults and other potential somatostatin positive paediatric tumours. The results of this trial will underpin development of further phase III work. Potential to have similar impact as in UK clinical practice
University of Birmingham	Pearson	BEACON-Neuroblastoma: A randomised phase IIb trial of BEvACizumab added to Temozolomide ± IrinOtecan for children with refractory/relapsed Neuroblastoma	2/30	2016		Yes	In July 2013, BEACON-Neuroblastoma opened to recruitment in the UK. During 2013 regulatory applications will be carried out in order to open the study in the remaining 6-7 EU countries. This trial is much expected since there has not been a phase II trial to offer to children with relapsed neuroblastoma for several years in many European countries. This study is part of the joint European strategy to identify the best backbone chemotherapy regimen and this strategy will be further expanded to test new agents and address the best consolidation treatment for patients that respond This trial will determine the best chemotherapy regimen in patients with recurrent or resistant neuroblastoma. This regimen will then be used as a 'backbone' treatment, which can be combined with new drugs and therapies in future trials. Once the trial is finalised, this regimen will be incorporated into routine practice across Europe. The study will also establish the role of bevacizumab, a monoclonal antibody against VEGF in children with relapsed neuroblastoma. Finally, the study involves the development of several biomarkers which will evaluate relevant biological hypotheses for children treated with antiangiogenics and children with relapsed neuroblastoma. This will include genomic analysis of the tumours, evaluation of predictive biomarkers such as circulating neuroblastoma mRNAs, functional imaging or pharmacokinetics of bevacizumab. The trial will also provide a European network of centres for studies of relapsed neuroblastoma and a foundation for BEACON 2 trial This trial will determine the best chemotherapy regimen in patients with recurrent or resistant neuroblastoma. This regimen will then be used as a 'backbone' treatment, which can be combined with new drugs and therapies in future trials. Once the trial is finalised, this regimen will be incorporated into routine practice across Europe. The study will also establish the role of bevacizumab, a monoclonal

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
							antibody against VEGF in children with relapsed neuroblastoma. Finally, the study involves the development of several biomarkers which will evaluate relevant biological hypotheses for children treated with antiangiogenics and children with relapsed neuroblastoma. This will include genomic analysis of the tumours, evaluation of predictive biomarkers such as circulating neuroblastoma mRNAs, functional imaging or pharmacokinetics of bevacizumab. The trial will also provide a European network of centres for studies of relapsed neuroblastoma and a foundation for BEACON 2 trial
University of Birmingham	Chisholm	VIT0910: International Randomised Phase II Trial of the Combination of Vincristine and Irinotecan with or without Temozolomide (VI or VIT) in Patients with Refractory or Relapsed Rhabdomyosarcoma	7/20	2015		Yes	Recruitment interrupted after 40 patients were recruited (20 in each arm) to asses the preliminary efficacy as per the Optimum 2 stage Simon design. It was found that there was sufficient activity to continue recruitment up to 80 patients.
University of Birmingham	Jenney	RMS2005: A protocol for non metastatic rhabdomyosarcoma	134/125	2016		Yes	For patients with RMS stratified as high risk - to evaluate the role of doxorubicin given in dose intensity early treatment and to evaluate the role of maintenance chemotherapy with vinorelbine and cyclophosphamide. The results of this trial will be used to inform clinical decision making in the treatment of children with rhabdomyosarcoma. The results of this trial will be used to inform clinical decision making in the treatment of children with rhabdomyosarcoma.
University of Birmingham	Ronghe	SIOPEL 6: A multi-centre open label randomised phase III trial of the efficacy of sodium thiosulphate in reducing ototoxicity in patients receiving cisplatin chemotherapy for standard risk hepatoblastoma	27/29	2017		Yes	If the results are positive and STS is shown to reduce cisplatin-associated hearing impairment without compromising the efficacy of the Cisplatin then this could result in STS being recommended as standard practice. The results have the potential to be extrapolated to other disease areas and patient populations, and for STS to be used as a chemoprotectant.
University of Birmingham	Wynn	Euro LB 02: Treatment Protocol for T-Cell and B-Precursor Cell Lymphoblastic Lymphoma of the European inter-group Co-operation on Childhood Non-Hodgkin-Lymphoma (EICNHL)	8/70	2019		Yes	

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Birmingham	Wallace	EuroNet PHL-C1: First international Inter-Group Study for classical Hodgkin's Lymphoma in Children and Adolescents	339/ unknown target	2020		Yes	The main aims were to tailor the amount of treatment to the individual needs of the patient, safely reduce treatment (avoid radiotherapy) where not needed, and intensify treatment where indicated. This trial also aimed to eliminate Procarbazine from the chemotherapy regimens and replace it with Dacarbazine. Procarbazine is known to cause infertilty or premature menopause in a significant number of male and female patients respectively. The trial was also expected to deliver significant improvements in the way patients were treated through a strategy for treatment adapted to response (STAR). One year prior to end of trial accrual, interim analysis of the randomisation showed clearly that Dacarbazine was as equally efficacious as Procarbazine, and therefore no patients treated subsequently were given Procarbazine.This was the first ever pan-European trial in paediatric Classical Hodgkin's Lymphoma and it has introduced a permanent change and improvement in the way this group of patients are managed not just in the UK but worldwide. The experimental COPDAC arm from EuroNet PHL-C1 in combination with OEPA is now considered the new gold standard for treatment of paediatric Classical Hodgkin's Lymphoma. The strategy for treatment adapted to response, which was a new and radically different approach introduced through EuroNet PHL-C1 is now accepted as best practice (worldwide) in paediatric Classical Hodgkin's Lymphoma. This was the first ever pan-European trial in paediatric Classical Hodgkin's Lymphoma and it has introduced a permanent change and improvement in the way this group of patients are managed not just in the UK but worldwide. The experimental COPDAC arm from EuroNet PHL-C1 in combination with OEPA is now considered the new gold standard for treatment of paediatric Classical Hodgkin's Lymphoma. The strategy for treatment adapted to response, which was a new and radically different approach introduced through EuroNet PHL-C1 is now accepted as best practice (worldwide) in paediatric Classical Hodgkin's Lymphoma.
University of Birmingham	Nicholson	SIOP CNS GCT II: Prospective trial for the diagnosis and treatment of children, adolescents and young adults with intracranial germ cell tumours	4/100	2020		Yes	Likely to lead to combined chemo-radiotherapy as the gold standard for treatment of localised germinoma (rather than radiotherapy alone), and recognition of the need for additional treatment for high risk NGGCT Similar to UK in terms of countries (most of Europe) participating in this trial. Further afield, should lead to closer collaboration with other continents in terms of accepted first line treatments, which should facilitate development of larger scale trials to answer clinical questions in these rare tumours

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Birmingham	Brennan	Euro Ewing 2012: International randomised controlled trial for the treatment of newly diagnosed Ewing's sarcoma family of tumours	0/300	2020		Yes	The trial contains four randomisations, R1, R2zol, R2loc, and R2pulm. Patients are randomised at two different time points: at entry to the trial (R1) and following local control therapy (either R2zol, R2loc, or R2pulm, depending on initial diagnosis and/or the response to induction chemotherapy.) Depending on the outcome of these randomised studies, the positive arm will become the standard of treatment for patients with Ewings sarcoma As an international study the same applies as above for Europe. Furthermore which ever arm is successful in the R1 induction randomisation it will become the international standard of care and serve as a backbone for future international studies including USA.
University of Birmingham	Hale	GC-3: Protocol for the treatment of Extracranial Germ cell Tumours in children and young adolescents (GC 2005 04)	134/ unknown target	2020		Yes	
University of Birmingham	Michalski	PNET5: An international prospective study on clinically standard-risk medulloblastoma in children with low-risk biological profile (PNET5-LR) or average-risk biological profile (PNET5-SR)	0/150	2020		Yes	
University of Birmingham	Burke	Inter B NHL: Intergroup trial for children or adolescents with B-cell NHL or B-AL: Evaluation of rituximab efficacy and safety in high risk patients	0/125	2022		Yes	Rituximab use in paediatric NHL is increasing internationally especially where national/international trials do not exist. In the UK there has not been a B-NHL trial for almost 10 years and many investigators feel that rituximab should be used as first-line therapy. There is however little evidence to support this and this study represents the best (and almost certainly last) opportunity to answer this question in an international setting.
University of Birmingham	Visser	LCH-IV: International collaborative treatment protocol for Langerhans Cell Histiocytosis	0/180	2023		Yes	During the study LCH patients (<18y) who are enrolled on the study (we expect the majority of UK patients will be enrolled) will be investigated, treated and followed up in a systematic way. The most recent LCH study concluded that increasing the duration of therapy from 6 months to 12 months for patients who has LCH affecting more than one system of the body (multisystem LCH), reduced the number of patients who experienced reactivation of the disease. In the current study, half of the patients with multisystem LCH will be randomised to receive 24 months of therapy and the other half will receive 12 months of therapy in order to establish if a further prolongation of therapy can reduce the number of patients experiencing reactivation of the disease. The possible value of adding an additional chemotherapy drug to the treatment will also be tested in the same way. Patients will be carefully monitored during treatment to identify those patients who do not adequately respond to treatment and these patients will be offered a 2nd line therapy. The efficacy of these 2nd line treatments will be studied as part of the same study. LCH may cause significant long term problems (late effects) for patients and all patients

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
							enrolled in the study will be followed up to detect these early. During the study LCH patients (<18y) who are enrolled on the study in participating countries will be investigated, treated and followed up in a systematic way. The most recent LCH study concluded that increasing the duration of therapy from 6 months to 12 months for patients who has LCH affecting more than one system of the body (multisystem LCH), reduced the number of patients who experienced reactivation of the disease. In the current study, half of the patients with multisystem LCH will be randomised to receive 24 months of therapy and the other half will receive 12 months of therapy in order to establish if a further prolongation of therapy can reduce the number of patients experiencing reactivation of the disease. The possible value of adding an additional chemotherapy drug to the treatment will also be tested in the same way. Patients will be carefully monitored during treatment to identify those patients who do not adequately respond to treatment and these patients will be offered a 2nd line therapy. The efficacy of these 2nd line treatments will be studied as part of the same study. LCH may cause significant long term problems (late effects) for patients and all patients enrolled in the study will be followed up to detect these early.
University of Birmingham	Shankar	EuroNet PHL-LP1: First international Inter-Group Study for nodular Lymphocyte Predominant Hodgkin's Lymphoma in Children and Adolescents	9/ unknown target	2025			This is a treatment intensity reduction trial which aims to clarify whether: surgical resection alone is sufficient for a select group of children with fully resected disease; and a non-intensive chemotherapy regimen (Cyclophosphamide, Vinblastine and Prednisolone) could replace standard chemotherapy without compromising efficacy in children with unresectable early stage nodular Lymphocye Predominant Hodgkin's Lymphoma. It is expected that the conclusions of this study will form the basis of evidence-based guidelines for the treatment and monitoring of LCH patients (<18 years) worldwide and contribute to improving the outcome for these patients. It is expected that the conclusions of this study will form the basis of evidence-based guidelines for the treatment and monitoring of LCH patients (<18 years) worldwide and contribute to improving the outcome for these patients.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Birmingham	Lewis	EE99: EUROpean Ewing tumour working initiative of national groups. Ewing tumour studies 1999	854/ unknown target		JUERGENS C et al. (2006) Safety Assessment of Intensive Induction with Vincristine, Ifosfamide, Doxorubicin, and Etoposide (VIDE) in the Treatment of Ewing Tumours in the EURO-E.W.I.N.G. Ewing 99 Clinical Trial. Pediatr Blood Cancer; 47: p.22–29. LE DELEY MC et al. (2010) Impact of EWS-ETS fusion type on disease progression in Ewing's sarcoma/peripheral primitive neuroectodermal tumor: prospective results from the cooperative Euro-E.W.I.N.G. 99 trial. J Clin Oncol., 28(12): p.1982-8. LADENSTEIN R et al., (2010) Primary disseminated multifocal Ewing sarcoma: results of the Euro-EWING 99 trial. J Clin Oncol., 28(20): p.3284-91.	Yes	R1 randomisation findings: Cyclophosphamide and ifosfamide have a similar efficacy in consolidation treatment of standard risk Ewing's tumour. Late effects studies are ongoing to compare renal and gonadal toxicity of both arms. Aim of randomisation R2loc: To compare VAI consolidation chemotherapy with high-dose therapy (Busulfan-Melphalan) and PBPC rescue, in Group 2 localised patients. Aim of R2pulm randomisation: To compare VAI consolidation chemotherapy and whole lung irradiation with high-dose therapy (Busulfan-Melphalan) and PBPC rescue, in patients with pulmonary or pleural metastases at diagnosis. The results of this trial will be used to inform clinical decision making in the treatment of children with Ewing's sarcoma. The results of this trial will be used to inform clinical decision making in the treatment of children with Ewing's sarcoma.
University of Birmingham	Williams	ALCL 99: International protocol for the treatment of Childhood Anaplastic Large Cell Lymphoma (ALCL 99)	87/ unknown target	2009	LE DELEY MC et al. (2010) Vinblastine in children and adolescents with high-risk anaplastic large-cell lymphoma: results of the randomized ALCL99-vinblastine trial. J Clin Oncol 28(25):p.3987-93 WROBELG et al. (2011) Safety assessment of intensive induction therapy in childhood anaplastic large cell lymphoma: report of the ALCL99 randomised trial. PBC Jul 1;56(7):p.1071-7		Adding vinblastine during induction and as maintenance for a total treatment duration of 1 year significantly delayed the occurrence of relapses but did not reduce the risk of failure.
University of Birmingham	Traunecker	CPT-SIOP-2009: Intercontinental Multidisciplinary Registry and Treatment Optimization Study for Patients with Choroid Plexus Tumors	0/60			Yes	
University of Birmingham	Picton	Vinalo: Phase I-II study of Vinblastine in Combination with Nilotinib in Children, Adolescents, and Young Adults with Refractory or Recurrent Low-Grade Glioma		2018		Yes	
University of Birmingham	Williams	ALCL-relapse: Treatment protocol for relapsed anaplastic large cell lymphoma of childhood and adolescence	2/12				The trial was closed prematurely due to slow recruitment. The results will not be analysed as there is insufficient data, however analysis will be attempted as an approach to treatment of relapsed disease.
University of Birmingham	Hewitt	HD-3: United Kingdom Children's Cancer Study Group (UKCCSG) protocol for the treatment of children and adolescents with Hodgkin's disease	390/ unknown target	2010	SHANKAR et al. (2012) Clinical outcome in children and adolescents with Hodgkin lymphoma after treatment with chemotherapy alone – Results of the United Kingdom HD-3 national cohort trial. EJC 48: p.108-113		The trial showed that while some Patients could be safely treated with chemotherapy not all could - despite the desire to avoid and reduce late-effects.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Birmingham	Professor David Walker	INTREPID Trial: A phase 1 feasibility, safety and tolerability study on continuous intrathecal/intraventricular infusion of etoposide, investigating escalation in dose and duration of infusion in children and adolescents with leptomeningeal metastases of solid tumours.	0/60			Yes	If infusional etoposide is associated with acceptable toxicity, this information will inform phase 2 and phase 3 trials by selecting dose and method of administration of this drug in order to evaluate its effectiveness. Future studies will investigate efficaciousness of this drug. Moreover it might play a role in diminishing the need for whole brain radiotherapy and thereby diminishing its long term toxicity. Furthermore this information will assist in assessing the suitability of etoposide as a candidate for incorporation into novel drug delivery systems designed to be implanted or injected into brain tumour cavities or CSF as part of CNS directed drug delivery strategies in the future.
Centre for Drug Development							
Institute of Cancer Research/Royal Marsden Hospital	Chua	CRUKD/12/002: A phase II proof-of-concept study to compare the novel technique [124I]mIBG PET/CT to [123I]mIBG scintigraphy in paediatric patients with metastatic neuroblastoma	0/25	2017		Yes	First time this agent will be compared with existing diagnostics in paediatric neuroblastoma patients. If the trial is successful 124I-mIBG will potentially replace multiple scans and anaesthetics at diagnosis with a single scan. If the trial is successful 124I-mIBG will potentially replace multiple scans and anaesthetics at diagnosis with a single scan. If the trial is successful 124I-mIBG will potentially replace multiple scans and anaesthetics at diagnosis with a single scan.
University of Newcastle	Vormoor	CRUKD/10/017: A CR-UK/CCLG Phase 1 paediatric trial of AT9283, a selective aurora kinase inhibitor, in relapsed and refractory leukaemia	7/15	2016	Podesta JE, Sugar R, et al. Adaptation of the plasma inhibitory activity assay to detect Aurora, ABL and FLT3 kinase inhibition by AT9283 in pediatric leukemia. Leuk Res. 2011 Sep;35(9):1273-5.		First time in children with leukaemia (ALL and AML) for this Aurora Kinase inhibitor. Trial ongoing. Aims to assess safety, efficacy, pharmacokinetics and identify a dose for Phase II evaluation in acute paediatric leukaemia. Agent in Phase II development in adults. Too early in development to assess clinical impact. This trial is the first to assess this therapeutic (AT9283) in a paediatric population with haematological malignancies. This patient population (haematological malignancies) is of interest due to the potential multi-kinase activity anticipated This trial is the first to assess this therapeutic (AT9283) in a paediatric population with haematological malignancies. This patient population (haematological malignancies) is of interest due to the potential multi-kinase activity anticipated
Institute of Cancer Research/Royal Marsden Hospital	Hargrave	CRUKD/09/044: A CR-UK/CCLG Phase I paediatric trial of AT9283, a selective aurora kinase inhibitor, in relapsed and refractory solid tumours	33/33	2013	Darren R Hargrave, Andrew DJ Pearson, et al. A phase I trial of AT9283 (a selective inhibitor of Aurora kinases) given for 72 hours every 21 days via intravenous infusion in children and adolescents with relapsed and refractory solid tumours. J Clin Oncol 30, 2012 (suppl; abstr 9542)		First time in children for this Aurora Kinase inhibitor. Data from this trial will be used to inform a second paediatric trial in leukaemia. Trial ongoing. Aims to assess safety, efficacy, pharmacokinetics and identify a dose for Phase II evaluation in paediatric solid tumours. Agent in Phase II development in adults. Too early in development to assess clinical impact. This is only the second paediatric study of an Aurora kinase inhibitor in children and the first paediatric study of a pan-Aurora kinase (A & B) inhibitor to our knowledge This is only the second paediatric study of an Aurora kinase inhibitor in children and the first paediatric study of a pan-Aurora kinase (A & B) to our knowledge

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University College London/Great Ormond Street	Anderson	CRUKD/07/066: Clinical trial of the ability of tumour lysate pulsed monocyte-derived dendritic cell vaccination to induce antitumour immune responses in paediatric patients with osteosarcoma	16/16	2011	Himoudi N, Wallace R, et al. Lack of T cell responses following autologous tumor lysate pulsed dendritic cell vaccination, in patients with relapsed osteosarcoma. Clin Transl Oncol. 2012 Apr;14(4):271-9.		First autologous dendritic cell vaccination in paediatric osteosarcoma patients. Trial completed. Aimed to gain an increased understanding of how Dendritic cell vaccination interacts with immune function in paediatric cancer patients. DC vaccination was safe and feasible in osteosarcoma. Only 2/12 patients showed an immune response, with no evidence of clinical benefit. Comparison with a control group suggests osteosarcoma maybe immuno-inhibitory for DC vaccine. The methodology research governance and GMP aspects were successful as a feasibility DC vaccination study in paediatrics. DCs were generated to a high standard and the study has lead to a DC vaccination trial in paediatric glioma due to start in 2012.
Royal Free & University College Medical School	Amlot	CRUKD/03/036: A Cancer Research UK Phase I trial of EBV gp350 vaccine in paediatric transplant patients	25/25	2008	Rees L, Tizard EJ, et al. A phase I trial of epstein-barr virus gp350 vaccine for children with chronic kidney disease awaiting transplantation. Transplantation. 2009 Oct 27;88(8):1025-9.		First time in patients for this vaccine against Epstein Barr virus.Trial completed. Too early in development to assess clinical impact.
University of Newcastle	Pearson	CRUKD/95/020: A phase I study of nolatrexed dihydrochloride (AG337, THYMITAQ) in children with advanced cancer	16/16	2000	Estlin EJ, Pinkerton CR, et al. A phase I study of nolatrexed dihydrochloride in children with advanced cancer. A United Kingdom Children's Cancer Study Group Investigation. Br J Cancer. 2001 Jan 5;84(1):11-8.		First time in children for this agent. Follow up trial to CRUKD/94/006 & CRUKD/94/009. Trial completed. Development discontinued after Phase III due to insufficient activity. Too early in development to assess clinical impact.
Institute of Cancer Research/Royal Marsden Hospital	Pritchard-Jones	CRUKD/98/009: A combined Phase I (toxicity)/Phase II (immunological response) study of an anti-idiotypic cancer vaccine, 105AD7, in osteosarcoma of children and young adults	31/31	2004	Pritchard-Jones K, Spendlove I, et al. Immune responses to the 105AD7 human anti-idiotypic vaccine after intensive chemotherapy, for osteosarcoma. Br J Cancer. 2005 Apr 25;92(8):1358-65.		First time in children for this vaccine. Follow up trial to CRUKD/92/007 and CRUKD/94/008. Trial completed. Agent in Phase II development. Too early in development to assess clinical impact.
Penile							
The Institute of Cancer Research	Bahl (University of Bristol) (Hall, ICR-CTSU)	CRUK/09/001: PENILE -TPF: A Phase II Trial of docetaxel, cisplatin and 5FU chemotherapy in locally advanced and metastatic carcinoma of the penis	29/29	2012	NICHOLSON, S., et al. A single-arm, phase II trial of docetaxel, cisplatin and 5-fluorouracil (TPF) chemotherapy in locally advanced and metastatic carcinoma of the penis (CRUK/09/001). Submitted to Br J Cancer 2013. BAHL, A., et al. 2012. Phase II trial of docetaxel, cisplatin, 5-fluorouracil (TPF) in locally advanced and metastatic squamous cell carcinoma (SCC) of the penis (CRUK/09/001). J Clin Oncol, 30, #326 BAHL, A. K., et al. 2010. A phase II trial of docetaxel, cisplatin, and 5-fluorouracil (TPF) in locally advanced and metastatic carcinoma of the penis (CRUK/09/001). J Clin Oncol, 28, 15S #TPS240.. BAHL, A., et al. 2012. Phase II trial of docetaxel, cisplatin, 5-fluorouracil (TPF) in locally advanced and metastatic squamous cell carcinoma (SCC) of the penis (CRUK/09/001). J Clin Oncol, 30, #326. (GU ASCO 2012)	No	Response rate for TPF was not high enough to warrant further investigation of routine use of this regimen in penis cancer. Recruitment quicker than anticipated TPF was the first national trial of the penile subgroup of the NCRI Bladder CSG bringing together a network of trialists for future trials in this rare disease site. Successful conduct means we are now in a position to conduct further studies within a reasonable timeframe. Successful conduct of TPF led to international support for InPACT with ICR-CTSU as the lead CTU.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Nicholson (University Hospitals Leicester) (Hall, ICR-CTSU)	CRUK/12/021: VinCaP: A phase II trial of vinflunine in locally-advanced and metastatic carcinoma of the penis	0/22	2016		Yes	This trial will provide valuable information on how to treat the more elderly, more infirm patients with penis cancer who are not suitable for complex combination chemotherapy. VinCaP is the only trial of vinflunine in penis cancer internationally thus results will have impact outside of the UK
The Institute of Cancer Research	Nicholson (University Hospitals Leicester) (Hall, ICR-CTSU)	IntraCaP - Intralesional OncoVEXGM-CSF in Carcinoma of the Penis	0/18			No	Although funded by CTAAC in September 2011 the pharmaceutical company withdrew support for drug supply and distribution and the study was not developed. Optimal management of surgically incurable locoregional lymphadenopathy is unknown (such patients usually receive chemotherapy and/or radiotherapy). Any intervention that extends conservative local management and/or renders surgically incurable disease resectable is desirable. This trial would have established an evidence base for larger trials of OncoVEXGMCSF in primary or locally recurrent penis cancer. The impact in the UK iwould still have been relevant outside of the UK had this study completed.
The Institute of Cancer Research	Nicholson (Imperial NHS Trust) (Hall, ICR-CTSU)	InPACT - International Penile Advanced Cancer Trial (International Rare Cancers Initiative study)	unknown/200			Yes	The study will support clinical decision making and define best practice based on current standard modalities (surgery, chemotherapy, radiotherapy). It will, then, provide a basis for all future trials in this disease. The clinical impact described for the UK is also applicable internationally. This is an international study conducted under the auspices of the International Rare Cancers Initiative (IRCI). It is pioneering in its use of Bayesian methodology.
Prostate							
University of Birmingham	James	Alpharadin: Alpharadin and docetaxel randomised phase II trial to assess the feasibility and safety of the combination of docetaxel plus Ra-223 (Alpharadin) in the first line chemotherapy treatment of men with bony metastatic castrate resistant prostate cancer	0/100	2015		Yes	As combining active agents is usually better than sequential use in oncology, it seems logical to evaluate the two drugs together with a target endpoint of an improvement in overall survival in this poor prognosis patient group. The first stage in the development of the combination is to establish the feasibility and safety of the pairing with reference to the current standard of care as well as preliminary evidence of efficacy to justify a larger trial. As the effects of casemix are large in this patient group, this can only be done with confidence in the randomized setting.
University of Birmingham	James	Cantata: A multicentre, phase II randomised controlled trial evaluating cabazitaxel versus docetaxel re-challenge for the treatment of metastatic Castrate Refractory Prostate Cancer, previously treated with docetaxel at inception of primary hormone therapy (formerly known as Cab-prostate; please note also the change to "...cabazitaxel versus docetaxel re-challenge..." in the full title)	2/138	2018		Yes	This trial is linked to the STAMPEDE trial and is addressing second line chemotherapy strategies as preparatory work ahead of the main STAMPEDE results expected in 2015.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Glasgow	Jones	CRUKE/10/043: SAPROCAN: Saracatinib and docetaxel in metastatic, castrate-refractory prostate cancer: a randomized, phase I/ II study by the UK-NCRI Prostate Clinical Studies Group	10/158	2015			Prostate cancer which has spread and become resistant to initial hormone therapy is a deadly disease. Docetaxel chemotherapy is the only therapy proven to prolong survival in this setting, although benefits are modest. In this trial we explore whether the addition of a new tablet, saracatinib, improves outcomes for these men. If the results of this study are positive we hope to progress to phase III and possibly establish this as standard treatment in this setting. As a proof of consept study if this study adds efficacy we would propose a randomised phase III trial. It is possible that the secondary and expolatory outcomes surrounding bone metabolism will suggest a benefical effect of saracatinib over and above effects on PFS. As per UK
University of Glasgow	Leung	CRUK/10/048: CROP (previously CPC): A randomised controlled trial of cryotherapy versus androgen deprivation therapy in men with localised radiation recurrent prostate cancer (RRPC) to evaluate efficacy and toxicityevaluate efficacy and toxicity	7/540	Closed early so no primary analysis planned		Yes	Opening sites and recruiting to this study proved much more challenging than anticipated. In the face of this the Trials Steering Committee recommended closure earlier this year. Unfortunately none. Unfortunately none.
Newcastle University	Jones	CRUKE/12/024: MAdCap: A randomised phase II trial of aberaterone acetate with or without RO5045337 in patients with mCRCP who have not previously received docetaxel.	0/158	2016		Yes	The principal aims of this study are to demonstrate that the addition of RO5503781 (Mdm2 inhibitor) to abiraterone is both safe and potentially effective. In addition, the study will explore pharmacokinetic interactions between the two drugs and future methods to identify patients who may benefit from this combination. If concept that adding RO5503781 to hormone deprivation is proven, then this will lead to what is likely to be a first class registration trial in prostat cancer. If translational studies associated with the stuyd demonstrate that p%£ based patient selection biomarker is feasible, then this may lead to further work to validate a biomarker As per UK
The Institute of Cancer Research	Dearnaley (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Hall, ICR-CTSU)	CRUK/02/020: INTERCONTINENTAL: Intermittent vs continuous androgen suppression for patients with PSA progression	186/ unknown target	2011	CROOK, J. M., et al. 2012. Intermittent Androgen Suppression for Rising PSA Level after Radiotherapy.N Engl J Med, 367, 895-903. DUNCAN, G. G., et al. 2011. QOL/Outcomes of an international phase 3 trial of intermittent v. continuous hormone therapy for relapsed prostate cancer. Radiother Oncol, 99, S210 #517. HALL, E., et al. 2002. A phase III randomized trial of post-radiotherapy intermittent androgen suppression (IAS) for prostate cancer patients with rising PSA-survey of interest. Clin Oncol (R Coll Radiol), 14, S48 #D1.1.	Yes	In men with PSA recurrence after radical radiotherapy, Intermittent Androgen Suppression (IAS) is not inferior to Continuous Androgen Deprivation (CAD) with respect to overall survival; adverse events were similar between treatment groups. The results of INTERCONTINENTAL will change practice internationally, having a major impact on QoL and health care delivery pathways. The results of INTERCONTINENTAL will change practice internationally, having a major impact on QoL and health care delivery pathways.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Parker (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Hall, ICR-CTSU)	CRUK/07/037: ProSTART: a pilot study for a phase III clinical trial in patients with favourable risk prostate cancer comparing active surveillance therapy against radical treatment	6 (trial closed early)/40			No	The UK pilot study target of recruiting 40 patients in 1 year was not met thus the trial was not feasible in the UK, hence the phase lll trial continued without UK involvement. The phase III trial subsequently closed internationally on 13th May 2011 due to low accrual rates averaging 4 patients per month (target was 35/month). NCICCTG suggested this was due to a shift in clinical equipoise towards surveillance amongst eligible patients, and a corresponding reluctance to undergo randomisation by most patients.
Imperial College London	Darzi (imperial College London) (Hall, ICR-CTSU)	CRUK/09/008: LOPERA - Randomised controlled trial of laparoscopic, open and robot assisted prostatectomy as treatment for organ-confined prostate cancer	30 (trial closed early) /110	2013	MAYER, E., et al., Randomised controlled trial (RCT) of Laparascopic, OPEn and robot-assisted prostatectomy as treatment for organ-confined prostate cancer. LopeRA feasibility study. National Cancer Research Institute (NCRI) National Cancer Conference; 2011.	No	Trial not feasible and closed June 2013. The trial has highlighted issues around patient and surgeon led (lack of) equipoise in the evaluation of new surgical technologies which will inform design of future complex surgical intervention studies.
The Institute of Cancer Research	Dearnaley (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Hall, ICR-CTSU)	CRUK/10/022: PIVOTAL: A randomised phase II trial of Prostate and pelvIc Versus prOstaTe ALone radiotherapy treatment volumes using high dose IMRT for locally advanced prostate cancer	124/110	2013/14	HARRIS, V., et al. 2011. A National phase III trial of pelvic lymph node (LN) IMRT in prostate cancer (PIVOTAL): a comparison of LN outlining method. Radiother Oncol, 99, S486 #1299.	Yes	PIVOTAL has harmonised the outlining and delivery of pelvic lymph node irradiation within the UK, with guidelines developed by the Trial Management Group to ensure consistency in treatment between trial centres. The PIVOTAL guidelines are more detailed than previously published pelvic lymph node guidance, with a focus on practical application, and will form the basis of a publication on behalf of the TMG. The resulting trial documents will also aid efficient phase III roll out of the trial to additional centres should the phase II safety endpoint be met. It is anticipated that the results of PIVOTAL will contribute significantly to the international knowledge base as there exist significant disagreements about the interpretation of past clinical trials of pelvic lymph node irradiation, with no clinical consensus in the UK, Europe and US.
The Institute of Cancer Research	de Bono (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Hall, ICR-CTSU)	CRUK/11/029: TOPARP - Trial of Olaparib in Patients with Advanced Castration Resistant Prostate Cancer	13/44	2014 - part A	A'HERN, R., et al. 2011. Phase II investigation of a PARP inhibitor (olaparib) in castration resistant prostate cancer (CRPC) which incorporates the possibility that treatment effect may be restricted to biomarker defined subgroups. Trials, 12, A88. A'HERN, R., et al. 2012. A two stage phase II design incorporating the possibility that the treatment effect may be restricted to a biomarker defined subgroup: investigation of a PARP inhibitor (olaparib) in castration resistant prostate cancer (CRPC). Clin Trials, 9, 552 #P116.	No	Innovative, adaptive study design. Using a novel agent to investigate the response to PARP inhibition of treatment resistant prostate cancer. The trial tests whether predictive signatures can be identified to stratify the population and select patients most likely to respond. The trial has the potential to provide significant benefit to patients with few treatment options at present. The trial design has attracted much interest from collaborators in the UK and overseas and is impacting trial designs outside the UK.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Dearnaley (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Hall, ICR-CTSU)	CRUK/11/053: PROMPTS: A Prospective Randomised phase III study of Observation versus screening MRI and Pre-emptive Treatment in castrate resistant prostate cancer patients with Spinal metastasis.	43/541	2016		Yes	There is strong clinical evidence that patients with neurologic back pain benefit from investigations to rule out SCC. There is some information from single centre patient series that MRI scanning can detect the earliest indication of spinal cord compression in asymptomatic patients with castrate resistant prostate and that preemptive treatment with radiotherapy can prevent the devastating sequelae of overt spinal cord compression. Further research needs to target this patient subgroup which is one of the key research recommendations of the NICE guideline CG75 committee. Spinal Cord Compression has a profound influence on functional, social, and emotional wellbeing with a resulting increased burden on the health care system. Effective early intervention would ease this burden for patients, their carers and the NHS. The results of PROMPTS will contribute to the international knowledge base.
The Institute of Cancer Research	Dearnaley (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Hall, ICR-CTSU)	CRUK/06/016: CHHiP: a randomised phase III multicentre trial of conventional or hypofractionated high dose intensity modulated radiotherapy for prostate cancer	3216/3163	2015	DEARNALEY, D., et al. 2012. Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer: preliminary safety results from the CHHiP randomised controlled trial. Lancet Oncol, 13, 43-54. BARNETT, G. C., et al. 2012. Independent validation of genes and polymorphisms reported to be associated with radiation toxicity: a prospective analysis study. Lancet Oncol, 13, 65-77. DEARNALEY, D., et al. 2013. Evaluating the efficacy of statins and ACE-inhibitors in reducing gastrointestinal toxicity in patients receiving radiotherapy for pelvic malignancies. Letter EJC, 49, 1783-6. DEARNALEY, D., et al. 2011. A dosimetry comparison of forward- and inverse- planned IMRT for prostate cancer in the CHHiP Trial. Radiother. Oncol, 99(Suppl 1):S585. NAISMITH, O., et al. 2011. A survey of the benefits of RT processes and techniques of participating in the CHHiP Trial. Radiother. Oncol. 99(Suppl 1):S585.	Yes	Preplanned safety analysis of the first 400 patients suggests that hypofractionated radiotherapy schedules are safe. Radiotherapy side effects associated with the trial appear to have approximately halved compared to the previous national study (MRC RT01) the most likely explanation relating to the improved quality of treatment. Development of IMRT quality assurance programme which included elements relating to target outlining, radiotherapy planning, delivery and dosimetry. A new radiotherapy planning method was designed specifically for the trial and dose volume constraints were mandated for the first time in a UK prostate radiotherapy study. Introduction of IMRT for prostate cancer in many UK centres having impact on RT delivery. Once mature, the CHHiP trial will contribute significantly to international knowledge base and will lead to new guidelines. The experimental arm may become control arm of future trials and CHHiP is the largest trial in this group of patients. The main CHHiP study led to the design of the CHHiP IGRT substudy and the design of reduced treatment margins for IGRT treatments. These reduced margins are now being used in the DELINEATE phase 2 trial. CHHiP patients make a major contribution to radiogenomic research in the RAPPER study and a BIDD grant for CHHiP TRANS has been activated to assess the role of molecular markers in TMA to predict radioresponsiveness of individual prostate cancers. A hypofractionated patient cohort has been included in the phase 1/2 RMH/ICR NCRN approved study of prostate and pelvic LN radiotherapy which forms the basis for the phase 3 feasibility study PIVOTAL. The dose constraints designed for the CHHiP trial have been adopted in these other trials and are now in widespread use in routine practice in the UK outside clinical trials. Once mature, the CHHiP trial will contribute significantly to international knowledge base and will lead to new guidelines. The experimental arm may become control arm of future trials and CHHiP is the largest

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
							trial in this group of patients.
The Institute of Cancer Research	de Bono (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Hall, ICR-CTSU)	RE-AKT: A randomised Phase II study of enzalutamide (MDV3100) in combination with AZD5363 in Patients with Metastatic Castration- Resistant Prostate Cancer	unknown/138			No	RE-AKT is the first study to combine a novel and potent androgen receptor targeting drug (enzalutamide) with an AKT inhibitor (AZD5363). RE-AKT will provide a critically important answer to the importance of AKT/TOR signalling in this disease. Preclinical and clinical studies indicate that AKT/TOR blockade alone will be ineffective in this disease due to feedback loops inducing increased AR signalling. However, concurrent AR blockade and AKT/TOR blockade has impressive antitumor additive activity in in vivo models. The trial has the potential to provide significant benefit to patients with few treatment options at present. It will also generate important biomarker data identifying molecular sub groups of patients likely to benefit from this therapeutic strategy The trial has attracted interest from collaborators in the UK and overseas.
The Institute of Cancer Research	Van As (Royal Marsden Hospital NHS Foundation Trust) (Hall, ICR-CTSU)	PACE: International Randomized Study of Laparoscopic Prostatectomy vs Robotic Radiosurgery and Conventionally Fractionated Radiotherapy vs Radiosurgery for Early Stage Organ-Confined Prostate Cancer	69/1716			Yes	Prostate SBRT with profound hypofractionation has the potential to achieve equivalent tumour control rates compared to surgery and conventional radiotherapy while reducing radiation to normal tissues (bladder, rectal and penile bulb) and minimizing radiation-induced side effects. Shorter treatment duration compared to conventional radiotherapy is anticipated to appeal to patients and would have implications for service delivery. The results would support use of profound hypofractionation delivered using other technology platforms. The clinical impact described for the UK is also applicable internationally.
Imperial College London	Abel	CRUK/06/001: PATCH: A randomised controlled trial of trans-cutaneous oestrogen patches versus LHRH analogues in locally advanced and metastatic prostate cancer	719/725	2015	Langley, R.E., Cafferty, F. H., Alhasso, A. A., et al. 2013. Cardiovascular outcomes in patients with locally advanced and metastatic prostate cancer treated with luteinising-hormone-releasing-hormone agonists or transdermal oestrogen: the randomised, phase 2 MRC PATCH trial (PR09). The Lancet Oncology, 14, 306-316; Langley, R. E., Godsland, I. F., Kynaston, H., et al. 2008. Early hormonal data from a multicentre phase II trial using transdermal oestrogen patches as first-line hormonal therapy in patients with locally advanced or metastatic prostate cancer. BJU International, 102, 442-445; Norman G., Dean, M. E., Langley, R. E., et al. 2008. Parenteral oestrogen in the treatment of prostate cancer: a systematic review. British Journal of Cancer, 98, 697-707.	No	Open to accrual. An interim analysis is planned in 2013 to facilitate decisions and planning for a possible phase III trial. The trial is comparing the safety and efficacy of transcutaneous oestrogen patches with standard hormone therapy (LHRH) in prostate cancer. The 1st stage demonstrated that there was no excess cardiovascular toxicity associated with patches and the patches appeared to suppress testosterone to a similar extent as LHRH. The 2nd (current) stage will assess whether the patches are non-inferior LHRH in terms of progression-free survival and will indicate whether the therapy waarants further investigation in a phase III trial. As a potential alternative to LHRH which is low-cost and may reduce some of the serious side effects associated with the standard treatment, if the efficacy of the patches is demonstrated in a phase III trial, it could change practice in the UK and internationally, with the potential to reduce overall mortality, as well as improving health outcomes and quality of life and reducing the cost of treatment for these patients. If the efficacy of the patches is demonstrated in a phase III trial, it could change practice internationally, with the potential to reduce overall mortality, as well as improving health outcomes and quality of life and reducing the cost of treatment for these patients.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Medical Research Council	James (CI & Local Lead)	CRUK/06/019: STAMPEDE: Systemic therapy in advancing or metastatic prostate cancer: Evaluation of drug efficacy a multi-arm multi-stage randomised controlled trial (MAMS RCT)	4584/>5000	2015 (Original comparison arms)	James ND et al., Celecoxib plus hormone therapy versus hormone therapy alone for hormone-sensitive prostate cancer: first results from the STAMPEDE multiarm, multistage, randomised controlled trial. The Lancet Oncology. 2012; 13(5): 549-58. Sydes MR, Parmar MKB, Mason MD, Clarke NW, Amos C, Anderson J ... James ND, et al. Flexible trial design in practice - stopping arms for lack-of-benefit and adding research arms mid-trial in STAMPEDE: a multi-arm multi-stage randomized controlled trial. Trials. 2012;13(1):168. Parker CC, Sydes MR, Mason MD, Clarke NW, Aebersold D, de Bono JS ... James ND, et al. Prostate Radiotherapy for Men with Metastatic Disease: A New Comparison in the STAMPEDE Trial. Clinical Oncology. 2013. June 2013 - Survival with newly diagnosed metastatic prostate cancer in the "docetaxel era": Data from >600 patients in the control arm of the STAMPEDE trial- ASCo GU symposium Feb 2012 - Flexible trial design in practice: Dropping and adding arms in STAMPEDE (MRC PR08, CRUK/06/019)-A multi-arm, multistage randomized controlled trial. – ASCO GU symposium, Feb 2012 - Celecoxib plus hormone therapy versus hormone therapy alone for hormone-sensitive prostate cancer: First results from STAMPEDE (MRC PR08, CRUK/06/019), a randomized controlled trial. – ASCO GU symposium, Sept 2011 - Celecoxib plus Hormone Therapy vs Hormone Therapy Alone for Hormone-Sensitive Prostate Cancer: First Results from STAMPEDE a Randomised Controlled Trial (MRC PR08, CRUK/06/019) – ECCO conference	Yes	Note: After the third intermediate analysis at the end of May 2012 the Trial Steering Committee decided to continue recruitment to the origibal trial arms [arms A, B, C and E]. The study aims to identify the optimum systemic therapy for patients with advancing or metastatic prostate cancer Yes, results are expected to be internationally relevant.
MRC	Parker	CRUK/07/008: RADICALS: Randomised phase III trial of adjuvant vs selective salvage treatment after radical prostatectomy for localised prostate cancer	1889/3000	2020	Catton E et al., Int J Radiat Oncol Biol Phys 2011; 1:80(1)1-3; Oarker, NW et al., BJMSU 2010; 3(5): 190-193; Parker C, MR Sydes. J Clin Oncol 2008; 26(10):e3; Parker C, MR Sydes. JAMA 2008; 300(18):2119-211a; Parker C et al. BJU International (2007) 99: 1376 – 1379; Parker C et al., Clinical Oncology (2007) 19: 167 – 171; Parker C et al., Proceedings of the National Cancer Research Institute Conference 2007; Catton C et al. Proceedings of the Canadian Association of Radiation Oncology Conference 2007; Parker C, Catton C, Sydes M et al. Proc ASCO Prostate Cancer Symposium 2007, Abs #407. 2007	Yes	A substantial amendment was approved in July 2011 to reduce sample sizes and primary outcome measure of one randomisation. Recruitment is ongoing and showing marked improvement in both randomisations. Efficient design to answer multiple questions. Consideration for RADICALS has become the standard of care for this patient group in many centres. Trial has completed 5 years of recruitment.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Bristol	Donovan, Hamdy, Neal	CRUK/04/025: Evaluating population-based screening for localised prostate cancer in the UK: an extension to ProtecT treatment trial	420000/120000		Collin, S.M, et al., Lancet Oncology. 2008; 9: 445-452		Trial is ongoing and is in second 3 year period. Primary outcome is 10-year prostate cancer mortality.
University of Surrey	Faithfull	CRUK/06/040: Behavioural urinary management for prostate symptoms: a phase II trial for testing a self-management intervention for urinary problems following prostate radiotherapy	15/30		Cockle-Hearne, J. Faithfull, S. 2010. Psychooncology. 19(9), 909 -922.		Self-management intervention is feasible to be incorporated into routine clinical practice. Further Phase III research in an RCT will be valuable in proving effectiveness over time.
Bristol	Martin/Hamdy/Neal/Rodriguez/Donovan	CRUK/04/025: Evaluating population-based screening for localised prostate cancer in the United Kingdom: the CAP (Comparison Arm for ProtecT) study	230000/230000		Collin,S.M et al., Lancet Oncology. 2008; 9: 445-452; Metcalfe, C. Journal of Medical Ethics 2008; 34: 37 - 40; Martin RM et al., Nature Clinical Practice Oncology 2005;2(11)538-539. Hussain S et al., BJU International 2008;101:547-555.; Donovan JL et al., International Journal of Epidemiology 2007 doi:10.1093/ije/dy1305; Martin RM et al., Journal of Urology 2006;176:443-449.	Yes	
University of Cardiff	Elwyn	CRUK/07/052: A randomised controlled trial of the effects of a web-based PSA decision explorer, Prosdex	115/600		Evans R et al. BMC Primary Care 2007; 8:58.		The web-based decision support technology, Prosdex, is shown to promote informed decision making in men considering whether or not to have the PSA test - the aim of the UK Prostate Cancer Risk Management Strategy.
University of Southampton	Johnson	CRUK/07/022: SABRE 1 (Surgery And Brachytherapy: a Randomised Evaluation): A randomised controlled trial of brachytherapy versus radical prostatectomy in locallised prostate cancer	30/400	2012	BJUI 2013; 112, 330-337 SABRE 1 (Surgery Against Brachytherapy – a Randomised Evaluation): feasibility randomised controlled trial (RCT) of brachytherapy vs radical prostatectomy in low–intermediate risk clinically localised prostate cancer Bryony K. Eccles, William Cross, Derek J. Rosario, Andrew Doble, Chris Parker, John Logue, Louisa Little, Louise Stanton and David Bottomley Randomised Controlled Trial of Brachytherapy Versus Radical Prostatectomy in Good Risk Prostate Cancer: A Feasibility Study (SABRE) NCRI Cancer Conference, Liverpool 2012, Poster presentation, Abstract Reference 128	No	Feasibility trial closed early due to poor recruitment. The trial demonstrated the difficulty in recruiting to surgical trial without surgical CI. Lessons learned have been published for the benefit of future trials in this setting
University of Southampton	Crabb	CRUKE/12/023: Orteronal maintenance therapy in patients with metastatic castration resistant prostate cancer and non-progressive disease after first-line docetaxel therapy: A multicentre randomised double-blind placebo-controlled phase III trial.	0/80	2017		Yes	This will be the first trial to investigate whether disease progression, symptoms and the need for further therapy in non-progressing patients with metastatic prostate cancer can be delayed by using a maintenance therapy at the point of completion of first line docetaxel chemotherapy. This will also be the first randomised phase III trial to report data for orteronel according to the predicted timelines. Trials examining other advanced malignant diseases have shown that initiating an effective treatment earlier in the disease course may be beneficial to prolong disease control and delay the need for more toxic interventions such as subsequent chemotherapy or the risk of deterioration in performance status and exposure to symptoms such as pain.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Southampton	Crabb	CRUK/12/042: A phase I/randomised phase II study in metastatic castration resistant Prostate Cancer of AZD5363 In combination with Docetaxel and prednisolone chemotherapy (ProCAID)	unknown/168	2017		Yes	The survival benefit from first-line DP is modest but this remains the standard of care for suitably fit patients who progress following current hormonal interventions. Resistance to DP is a common clinical problem. The primary question in ProCAID is whether the addition of the AKT inhibitor AZD5363 to DP improves progression free survival (PFS) based on evidence that AKT inhibition has both single agent activity and can circumvent DP resistance in this disease.
Royal Free & University College Medical School	Hoskin	CRUK/02/011: RIB: A multicentre randomised phase III trial of single dose radiotherapy compared to Ibandronate for localised metastatic bone pain.	470/470	2013	RIB: a multicentre randomised trial of ibandronate compared to single dose radiotherapy for localised metastatic bone pain in prostate cancer European Journal of Cancer, Volume 47, Supplement 2, September 2011, Page 6 Oral presentation at ECCO11 - Presidential Session II: Best and Late Breaking Abstracts, Stockhom, September 2011	Yes	A single infusion of ibandronate had similar outcomes as a single dose of radiotherapy in metastatic prostate bone pain. Ibandronate could be considered when radiotherapy is not available or has been given previously. For prostate cancer patients, Ibandronate could be considered when radiotherapy is not available or has been given previously. For prostate cancer patients, Ibandronate could be considered when radiotherapy is not available or has been given previously.
Centre for Drug Development							
University of Newcastle	Plummer	CRUKD/12/004: A phase I pharmacokinetic and pharmacodynamic study of AZD3965, a potent Monocarboxylate Transporter 1 inhibitor (MCT1) in advanced cancer including prostate cancer & NHL expressing MCT1	4/63	2018	Keystone Tumour metabolism Conference, Feb 24th 2013		First in class, first in man trial. Trial planned. Aims to assess safety, efficacy, pharmacokinetics and identify a dose for Phase II evaluation. Too early in development to assess clinical impact. a first in man/ first in class study targeting a novel potential therapeutic pathway this has the potential to have enormous impact both within UK and Internationally a first in man/ first in class study targeting a novel potential therapeutic pathway this has the potential to have enormous impact both within UK and Internationally
King's College London	O'Doherty	CRUKD/10/027: A Cancer Research UK Phase I trial comparing Fluorine-18 and Carbon-11 Choline Positron Emission Tomography (PET) in assessment of prostate cancer metastases	0/45	not applicable (trial stopped early)			First clinical comparison between these 2 radioactive tracers. 18F choline will be more convenient to use in clinic as it has a much longer half life. Aimed to compare PET-CT scans from both agents and see if 18F choline is as good as C11. If successful 18F choline could be used in prostate diagnosis and staging in a wider number of hospitals. Trial closed early due to lack of recruitment.
Queen Mary, University of London/Barts	Avril	CRUKD/09/043: A Cancer Research UK Phase I trial of technetium labelled Demobesin (99m-Tc-Demobesin-4) for imaging prostate cancer	9/45	2012			First time in patients for this imaging agent targeting the gastrin releasing peptide receptor. Aimed to look at side effects, PK/PD, how well it worked and compare with existing imaging methods, to improve imaging, diagnosis and staging for prostate cancer. Trial closed early due to lack of recruitment.
Institute of Cancer Research/Royal Marsden Hospital	Judson	CRUKD/98/007: A CRC Phase I trial and pharmacokinetic study of a new 17a-HYDROXYLASE / C17,20-LYASE inhibitor, abiraterone acetate (CB7630) in patients with prostate cancer, a multiple dose study in non-castrate males	6/6	1999	O'Donnell A, Judson I, et al. Hormonal impact of the 17alpha-hydroxylase/C(17,20)-lyase inhibitor abiraterone acetate (CB7630) in patients with prostate cancer. Br J Cancer. 2004 Jun 14;90(12):2317-25.		First time in this cohort of prostate cancer patients for Abiraterone. Companion trial to CRUKD/96/014 & CRUKD/98/008. The drug was developed at the Institute of Cancer Research by Mike Jarman part funded by Cancer Research UK. Trial completed. Led on to Phase II trials and subsequent registration. Drug licensed by the FDA in 2011 to treat prostate cancer and its use will transform second

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
							line treatment of prostate cancer. NICE approved its use in prostate cancer in 2012.
Institute of Cancer Research/Royal Marsden Hospital	Judson	CRUKD/98/008: A CRC Phase I trial and pharmacokinetic study of a new 17a-HYDROXYLASE / C17,20-LYASE inhibitor, abiraterone acetate (CB7630) in patients with prostate cancer, a single dose study in non-castrate males	4/4	1999	O'Donnell A, Judson I, et al. Hormonal impact of the 17alpha-hydroxylase/C(17,20)-lyase inhibitor abiraterone acetate (CB7630) in patients with prostate cancer. Br J Cancer. 2004 Jun 14;90(12):2317-25.		First time in this cohort of prostate cancer patients for abriaterone. Companion trial to CRUKD/96/014 & CRUKD/98/007. The drug was developed at the Institute of Cancer Research by Mike Jarman part funded by Cancer Research UK. Trial completed. Led on to Phase II trials and subsequent registration. Drug licensed by the FDA in 2011 to treat prostate cancer and its use will transform second line treatment of prostate cancer. NICE approved its use in prostate cancer in 2012.
Institute of Cancer Research/Royal Marsden Hospital	Judson	CRUKD/96/014: A CRC Phase I trial and pharmacokinetic study of a new 17a-HYDROXYLASE / C17,20-LYASE inhibitor, abiraterone acetate (CB7630) in patients with prostate cancer, a single dose study in medically or surgically castrate males	16/16	1999	O'Donnell A, Judson I, et al. Hormonal impact of the 17alpha-hydroxylase/C(17,20)-lyase inhibitor abiraterone acetate (CB7630) in patients with prostate cancer. Br J Cancer. 2004 Jun 14;90(12):2317-25.		First time in patients for this agent abiraterone targeting CYP17. Companion trial to CRUKD/98/007 & CRUKD/98/008. The drug was developed at the Institute of Cancer Research by Mike Jarman part funded by Cancer Research UK. Trial completed. Led on to Phase II trials and subsequent registration. Drug licensed by the FDA in 2011 to treat prostate cancer and its use will transform second line treatment of prostate cancer. NICE approved its use in prostate cancer in 2012.
Renal							
University of Birmingham	Porfiri	Pazo2: A study of pazopanib efficacy and safety in patients with advanced clear-cell renal cell carcinoma and ECOG Performance Status 2	7/75	2016		Yes	Given its good tolerability profile and the route of administration, pazopanib could represent a valuable therapeutic option for advanced clear cell renal cell carcinoma patients with performance status 2 as it wouldn't affect their quality of life as severely as other drugs of the same family and could provide a substantial clinical benefit. Potential to have similar impact as in UK clinical practice
University of Birmingham	Arlt	ADIUVO: Efficacy of adjuvant mitotane treatment in prolonging recurrence-free survival in patients with adrenocortical carcinoma at low-intermediate risk of recurrence	0/20	2016		Yes	The results of the ADIUVO trial will inform the guidance regarding the use of adjuvant treatment in patients with ACC who have undergone apparently complete surgical removal of their primary tumour. The results of the ADIUVO trial will inform the guidance regarding the use of adjuvant treatment in patients with ACC who have undergone apparently complete surgical removal of their primary tumour.
University of Glasgow and Greater Glasgow and Clyde Health Board	Aitchison	CRUK/98/004: HYDRA: Adjuvant Interleukin-2, Interferon-Alpha and 5-Fluorouracil for Patients with high risk of relapse after surgical treatment for Renal Cell Carcinoma	215/215	2010	Accepted for publication by European Journal of Cancer 23/08/13, in press M. Aitchison, C. A. Bray, H. Van Poppel et al. Final results from an EORTC (GU Group)/NCRI randomized phase III trial of adjuvant interleukin-2, interferon alpha, and 5-fluorouracil in patients with a high risk of relapse after nephrectomy for renal cell carcinoma (RCC). J Clin Oncol 29: 2011 (suppl; abstr 4505); Aitchison M, Bray H, Van Poppel H et al. Preliminary results from a randomized phase III trial of adjuvant interleukin-2, interferon alpha and 5-fluorouracil in patients with a high risk of relapse after nephrectomy for renal cell carcinoma (RCC) J Clin Oncol 26:		This study indicated that significant toxicity was associated with adjuvant Interleukin-2, Interferonalpha and 5-Fluorouracil and found no statistically significant improvement in terms of disease-free or overall survival. This form of adjuvant treatment is not worthwhile pursuing in this disease. This form of adjuvant treatment is not worthwhile pursuing in this disease.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
					2008 (May 20 suppl; abstr 5040).		
NHS Greater Glasgow and Clyde	Aitchison	CRUK/10/031: CARMENA: A randomised phase III trial to evaluate the benefit of nephrectomy in patients with metastatic at diagnosis kidney cancer treated with Antiangiogenics (Sunitinib)	5/576	2017		Yes	The study is designed to determine if nephrectomy can be omitted without impairing overall survival in patients with metastatic renal cell carcinoma (mRCC) being treated with sunitinib therapy. The omission of nerphrectomy would lead to a substantial reduction in patient morbidity. As per UK
University of Leicester	Jones	CRUKE/10/015: ASPEN: A randomised Phase II study of Afinitor (everolimus) Vs. sutent (sunitinib) in patients with Metastatic Non-Clear Cell Renal Cell Carcinoma	36/36	2013			Non-clear cell variants represent 15 – 20% of all kidney cancers (RCC). Currently, there is no consensus standard-of-care for patients with these variants. The objective of this study is to compare the anti-tumour activity of everolimus and sunitinib, in patients with advanced non-clear cell RCC to guide future patient management in this disease. Results frrom the trial will provide confidence in choosing optimal therapy from drugs already licenced in this indication. In addition, as newer agents evolve, the results will enable high quality design of randomised trials of these agents with an Informed choice of control therapy As per UK
The Royal Marsden NHS Foundation Trust	Larkin (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Bliss, ICR-CTSU)	CRUKE/11/061: A-PREDICT: A Phase II Study Of Axitinib in Patients with Metastatic Renal Cell Cancer Unsuitable for Nephrectomy	8/99	2015		No	APREDICT will provide patients with poor prognosis advanced kidney cancer the opportunity to access the potent and specific antiVEGFR TKI axitinib as a first line treatment. APREDICT will set the standard for integrated translational research. The aim is to identify predictive markers which would allow selection of patients most likely to benefit from this treatment. If axitinib is found to have high activity in this patient population with an otherwise poor prognosis it could lead to adoption of axitinib as a first line treatment strategy in the UK for these patients. A-PREDICT aims to identify predictive markers for axitinib response, which can be used internationally to identify patients for whom axitinib treatment would be appropriate. A-PREDICT will also contribute to the evidence base for first line use of axitinib, which is currently licensed in the US and EU as a second line therapy . If axitinib is found to have high activity in this patient population with an otherwise poor prognosis it could lead to adoption of axitinib as a first line treatment strategy for these patients.
MRC	Eisen	CRUK/06/004: SORCE - A phase III randomised controlled study comparing sorafenib with placebo in patients with resected primary renal cell cancer carcinoma at high or intermediate risk of relapse. TRANS-SORCE - The sample collection associated with this clinical trial.	1331/896	2016			Open to accrual A very important question in the adjuvant patient population but one that was unlikely to have been answered without a collaboration between academia and industry. Potential impact on standard practice in the UK if Sorafenib is shown to improve disease free survival in patients with resected renal cell carcinoma.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Newcastle University	Soomro	CRUK/11/036: CONSERVE - A feasibility study for a multicentre randomised controlled trial to COmpare Surgery (partial Nephrectomy) with needle ablation techniques (Radiofrequency ablation / cryotherapy) for the treatment of people with small renal masses (4 cm)	1/68	2014			Ongoing
Queen Mary, University London	Powles	CRUKE/09/031: COSAK study: A randomized phase II study, evaluating cediranib v.s cediranib and AZD0530 in patients with relapsed metastatic clear cell renal cancer					
Cardiff University	Griffiths	CRUK/10/050: EORTC 30073:Randomised Phase III trial comparing immediate versus deferred nephrectomy in patients with synchronous metastatic renal cell carcinoma	6/25	2016		Yes	Will potentially change clinical practice. Will contribute significantly to international knowledge base.
Centre for Drug Development							
University of Oxford	Harris	CRUKD/99/011: A CRC Phase II trial of bryostatin-1 in hypernephroma	16/16	2002	Madhusudan S, Protheroe A, et al. A multicentre phase II trial of bryostatin-1 in patients with advanced renal cancer. Br J Cancer. 2003 Oct 20;89(8):1418-22.		First trial in kidney cancer for this agent. Follow up trial to CRUKD/91/006, companion trial to CRUKD/99/012 & CRUK/99/013. Trial completed. Development discontinued after Phase II due to lack of efficacy. Too early in development to assess clinical impact.
Sarcoma							
University of Sheffield	Robinson	VORTEX: Randomised trial of dose and volume of post-operative radiotherapy given to adult patients with extremity soft tissue sarcoma	215/210	2015			
University of Sheffield	Woll	Axi-STS: A clinicopathological phase II study of axitinib in patients with advanced angiosarcoma and other soft tissue sarcomas	111/152	2013			
The University of Sheffield	Woll	SCART: Phase I/II study of oral MEK inhibitor Selumetinib (AZD6244 Hyd-Sulphate) in Combination with Highly Active Anti-Retroviral Therapy (HAART) in AIDS-associated Kaposi's sarcoma (KS)	9/37	2015			

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Judson (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Bliss, ICR-CTSU)	CRUK/10/021: CASPS: A phase II study of Cediranib (AZD2171) in Patients with Alveolar Soft Part Sarcoma	12/24	2015	JUDSON, I., et al. 2012. Trial in progress: A phase II international trial of cediranib in the treatment of patients with aveolar soft part sarcoma (CASPS) CRUK ref: C2130/A12118. British Sarcoma Group Conference, #34. [poster] JUDSON, I., et al. 2013. Trial in progress: A phase II international trial of cediranib in the treatment of patients with aveolar soft part sarcoma (CASPS) CRUK ref: C2130/A12118. British Sarcoma Group Conference February 2013.	No	In 2011, AstraZeneca made the decision to cease development of cediranib. Discussions are also ongoing to investigate alternative sources. Participation beyond the UK, Spain and Australia has not been possible due to resource and financial issues for international collaborative groups. An extension to the recruitment period is being considered There is currently no standard treatment for this group of patients. Two studies of cediranib in ASPS sponsored by the NCI are open to recruitment in the US and preliminary results have shown unprecedented activity of cediranib in this patient group. However, CASPS is likely to be the only trial to run in this patient group outside of the US and is the only trial to compare cediranib activity to a placebo control. The optional tissue samples collected will provide representative samples from three informative timepoints in the course of the disease, i.e. primary diagnosis, first and second disease relapse. CASPS is the first international IMP study to be sponsored by the ICR/RMH and is the first NCRN/AZ initiative trial to open internationally. The study has paved the way in establishing models of international participation in IMP trials coordinated by ICR-CTSU and sponsored by the ICR/RMH. CASPS provides the only access to cediranib for ASPS patients outside the US and patient enquiries for participation in the study have been received from as far afield as Israel, China and Brazil. If a new drug application were to be sought by the NCI, as the only placebo-controlled randomised trial of cediranib, CASPS would provide vital supplementary data in this respect.
UCL	Whelan	CRUK/05/013: EURAMOS 1: A randomised trial to optimise treatment strategies for resectable osteosarcoma based on histological response to pre-operative chemotherapy	298/ unknown target	2013	1. Marina N, Bielack S, Whelan J, Smeland S, Krailo M, Sydes M et al. International Collaboration is Feasible in Trials for Rare Conditions: The EURAMOS Experience. Cancer Treat Res 152:339-353, 2010. 2. Whelan J, Patterson D, Perisoglou M, Bielack S, Marina N, Smeland S, Bernstein M. The role of interferons in the treatment of osteosarcoma. Pediatr Blood Cancer. 2010 Mar;54(3):350-4. ASCO 2013; oral presentation. Bielack et al. Journal of Clinical Oncology, 2013 ASCO Annual Meeting Proceedings (Post-Meeting Edition). Vol 31, No 18_suppl (June 20 Supplement), 2013: LBA10504	Yes	First results from the good response randomisation have been presented this year and the publication is in preparation. Follow-up continues for the poor response randomisation, secondary outcome measures for the good response randomisation and survival of the full registered patient cohort. Depending on the results of the randomisations, the trial has the potential to change practice in the UK. It will also demonstrate that treatment with MAP chemotherapy (the international standard treatment) is feasible in the UK. EURAMOS is a global trial and has the potential to change international practice. It is the first global trial in osteosarcoma and has shown that large, international trials are feasible in this rare disease. It has already stimulated further collaboration and plans for future trials.
University College London	Michelagnoli	CRUKE/09/013: OTIS - A Phase II Study to determine the efficacy and safety of conventional dose Oral Treosulfan In patients with advanced pre-treated Ewing's Sarcoma	21/25	2013	Oral Treosulfan in Ewing's Sarcoma: A Phase II Study to determine the efficacy and safety of conventional dose oral Treosulfan in patients with advanced pre-treated Ewing's Sarcoma. In press	Yes	No efficacy for this dose and schedule of treosulfan was demonstrated in this prospective phase II study. Little toxicity was apparent and one explanation for lack of efficacy may be relative underdosing None

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University College London	Seddon	CRUK/10/004: GeDDiS: Gemcitabine and docetaxel versus doxorubicin in sarcoma - A prospective randomised controlled phase III trial of gemcitabine and docetaxel compared with doxorubicin as first line treatment in previously untreated advanced unresectable or metastatic soft tissue sarcomas.	249/230	2015		Yes	May provide definitive decisions on standard treatment for soft tissue sarcoma in the UK (this is the first phase III trial in STS to be conducted) Unknown at present
MRC	Cunningham	CRUK/06/025: ST03: A Randomised Phase II/III trial of Peri-operative Chemotherapy with or without Bevacizumab in Operable Oesophagogastric Adenocarcinoma and (in selected centres) A Feasibility Study Evaluating Lapatinib in HER-2 Positive Oesophagogastric Adenocarcinomas	1031 ST03 main study (bevacizumab comparison) and 8 ST03 feasibility study (lapatinib comparison)/110 0 Main Study (bevacizumab comparison) 40 Feasibility Study (lapatinib comparison)	2016	AFC Okines et al. Safety results from ST03: A randomised phase II/III trial evaluating the addition of bevacizumab to peri-operative epirubicin, cisplatin and capecitabine in localised gastric or oesophagogastric junction adenocarcinoma. Ann Onc 24: 702-709, 2013. ASCO 2013 and 2012 (posters); Preliminary toxicity data presentated at ASCO 2010 (poster discussion) and again in 2011 (poster); Annual 2012 Upper GI NCRI meeting; ST03 Investigator meeting for Feasibility Study centres (following 2012 NCRI meeting);	Yes	A Feasibility Study Evaluating Lapatinib in HER-2 Positive Oesophagogastric Adenocarcinomas is now open to accrual. Application for an extension to the Project Grant was considered and supported by CTAAC, level of funding is in discussion with CTAAC. Currently recruiting. Primary objectives of main trial: Stage I assessed the safety and feasibility of combining bevacizumab with sECX chemotherapy. In Stage II the primary outcome will be overall survival. Primary objective of feasibility study: Determination of recommended dose levels for capecitabine and lapatinib; Sample testing turnaround time; HER-2 positivity rate. The results will be presented at international meetings and published in peer-reviewed journals. If positive they will change clinical practice and be incorporated into national guidelines. It will also support and help introduce HER-2 testing for oesophagogastric cancer in the UK. It aims to improve survival for patients that have very poor outcomes.
Testicular							
NHS Greater Glasgow and Clyde	White	RESTART: Rehabilitation Evaluation in Survivors of Testicular Cancer After Radical Treatment: Pilot Study	35/32	2013	ASCO General Poster Session May 31 – June 4 2013 Chicago, (Session: Patient and Survivor Care) Permanent Abstract ID: 9590 Abstract Title: RESTART: Rehabilitation Evaluation in Survivors of Testicular Cancer after Radical Treatment—Pilot study effect on HADS-anxiety subscore. Annual Cancer Accredited CTU Meeting, 8th July 2013, London: General Poster at CaCTUS CTU Stand: Abstract Title: RESTART: Rehabilitation Evaluation in Survivors of Testicular Cancer after Radical Treatment—Pilot study effect on HADS-anxiety subscore. NCRI Cancer Conference 3-6 November 2013, Liverpool: Abstract title: RESTART: Rehabilitation Evaluation in Survivors of Testicular Cancer After Radical Treatment: Pilot study effect on adjustment and psycho-social functioning, Poster Session: Reference: 131	Yes	The role of rehabilitation for cancer patients has been mainly investigated in breast cancer patients. Testis cancer patients represent a group of patients with a very high cure rate often undergoing significantly toxic treatments, thus return to normality is important. Thisis a feasibility study of a rehabilitation programme for patients who are less than eight weeks from completion of curative treatment for testicular cancer, prior to a randomised controlled trial of standard care versus standard care and rehabilitation programme. The aims are to provide an initial indication of the efficacy, feasibility and acceptance of a rehabilitation programme. As per UK

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
The Institute of Cancer Research	Cullen (Queen Elizabeth Hospital, Birmingham) (Hall, ICR-CTSU)	CRUK/09/011: 111 Testis: A single arm multi-centre study evaluating a single cycle of BEP as adjuvant chemotherapy in high risk, stage 1 non-seminomatous germ cell tumours of the testis (NSGCTT).	183/236	2016	KALAITZAKI, E., et al. 2012. Monitoring rare events in a single arm non-inferiority trial (111;CRUK/09/011). Clin Trials, 9, 539 #P88. Society for Clinical trials 2012 - KALAITZAKI, E., et al. 2012. Monitoring rare events in a single arm non-inferiority trial (111;CRUK/09/011). Clin Trials, 9, 539 #P88.	Yes	The relatively well characterised disease with a high cure rate has allowed implementation of a single group phase III design, and the requirement to monitor rare events in real time has led to the development of a novel model of sequential event rate monitoring presented at the SCT conference. This trial is the only interventional therapeutic trial in this disease site currently running in the UK. If a single cycle of BEP(500) had a similar high rate of relapsefree survival (cure) to that seen with two cycles of BEP(360) in this patient group, the overall burden of chemotherapy would be reduced, with associated healthcare resource usage savings and would be likely to lead to an international change in clinical practice. There are a small number of high risk patients who choose or are recommended to have surveillance. For those patients a positive result for this study might mean that more of them elect to have a single cycle of chemotherapy rather than none at all, and fewer would be offered surveillance. A German trial which attempted to randomise patients with high risk NSGCTT between one and two cycles of BEP(500) was not feasible. It is therefore anticipated that the outcome of 111, which is expected to complete accrual within the next year, will contribute significantly to the available data and is likely to lead to a change in practice internationally.
The Institute of Cancer Research	Huddart, UK CI, (Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research) (Hall, ICR-CTSU)	EA-001: Randomised phase III trial of initial salvage chemotherapy for patients with germ cell tumours	unknown/80		FELDMAN D, et al. 2011. Is High Dose Therapy Superior to Conventional Dose Therapy as Initial Treatment for Relapsed Germ Cell Tumors? The TIGER Trial. J of Cancer 2:374-377	Yes	Study is awaiting US and EU Sponsor (European Group for Blood and Marrow Transplantation) approval before UK regulatory submissions are made. Due to a lack of a definitive randomised trial, it remains unclear whether sequential HDCT or CDCT represents the optimal initial salvage approach for patients with relapsed or refractory GCT. The international investigators believe this represents the most pressing question remaining for defining treatment standards and optimising outcomes and the results of this study will influence practice globally. This is an international study led by the US. The proposed study will establish a network of international centres / collaborative groups through which future trials in this rare disease can be conducted.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
MRC	Huddart	CRUK/05/014: TE23: Randomised phase II comparing intensive induction chemotherapy (CBOP BEP) with standard BEP chemotherapy in poor prognosis male germ cell tumours	89/88	2011	Primary results presented at the ASCO Annual Meeting 2011 abstract number #4508 and ESMO 2011 and NCRI 2011. Publication in draft form.	No	Final publication prepared but not yet accepted for publication Favourable response rates (primary outcome) were 74% with CBOP/BEP and 61% with BEP (90% CIs [61%, 85%] and [48%, 73%]). 1-year PFS was 65% and 43% respectively (hazard ratio [HR] 0.6, 95% CI [0.33, 1.07]) and OS was 74% and 72% (HR 0.78, 95% CI [0.39, 1.57]). CBOP/BEP toxicity, largely haematological, was high (96% had CTC grade ≥3, 63% with BEP) 3/14 CBOP/BEP and 2/18 BEP deaths were attributed to toxicity, one (BLM toxicity on CBOP/BEP) after an overdose during treatment. Conclusions: The trial met its primary outcome with a 90% CI for CBOP/BEP excluding RRs < 60% but CBOP/BEP was more toxic. PFS is promising though with no clear impact on survival. Results should be confirmed in an international phase III trial If results of this phase II trial were to be confirmed in a phase III trial, it would have the potential to change practice internationally.
MRC	Joffe	CRUK/07/020: TRISST: A randomised phase III trial of imaging and schedule in Seminoma Testis (MRCTE24)	523/660	2017	Cafferty FH et al. UK Management Practices in Stage I Seminoma and the Medical Research Council Trial of Imaging and Schedule in Seminoma Testis Managed with SurveillanceClinical Oncology 24 (2012) 25-29. Gabe R et al. Design issues and solutions in a surveillance study for stage I seminoma (TRISST/MRC TE24, ISRCTN65987321). Poster at RSS conference, Edinburgh, September 2009. Gabe R et al. Use of imaging-based surveillance for post-operative management of stage I seminoma & the TRISST trial. Poster at NCRI conference October 2009, abstract A131	Yes	Recruitment still ongoing (not due to end until 2014). Potential to safely & effectively change future practice by reducing imaging frequency for Stage I seminoma testis patients, reducing their radiation exposure. Comparison of CT and MRI may alter usage of these imaging modalities relative to each other, with implications for service provision. Results will provide evidence for guidelines regarding the optimal technology (MRI or CT) and optimal number of scans (3 over 3 years or 7 over 5 years) in surveillance of patients treated for stage 1 seminoma. Approximately 500-600 patients diagnosed with stage 1 seminoma in the UK every year, all of whom woulf benefit from a reduction in radiation exposure should results support a recuced imaging frequency. This trial may influence practice internationally.
QMUL	Shamash	CRUK/05/011: Infusional BLEO - TE3. A randomised phase III Toxicity study of day 2,8,15 short (30 min) v's day 1,2,3 long (72 hours) infusion Bleomycin for patients with IGCCCG good prognosis TE3.l	171/210				Potential to change practice if long (infusional) Bleomycin is shown to have lower pulmonary toxicity than current standard short (conventional) Bleomycin for patients with IGCCCG good prognosis germ cell tumours (TE3). If lower toxicity is confimed, the trial will be extended to address the question of whether the long/infusional approach is also more efficacious. This trial isn't powered to assess efficacy however - many more patients would be needed to show equivalence or superiority.
University of Southampton	Wheater	CRUK/09/042: Gem-TIP: A multicentre phase II trial of salvage chemotherapy with Gem-TIP for relapsed germ cell cancer.	16/14	2014	ASCO 2009: Wheater M. J., Huddart R., White J., Rustin G., Abab J., Mead G. M. Salvage chemotherapy with gemcitabine, paclitaxel, ifosphamide, and cisplatin (Gem-TIP) for relapsed germ cell tumours (GCT). J Clin Oncol 27, 2009 (suppl; abstr e16031)	Yes	Protocols for the first line treatment of metastatic germ cell tumours are now well established and strictly adhered to nationally. In addition there seems to be a reduction in the proportion of patients presenting with poor risk disease in most centres. As such the rates of early relapse of metastatic germ cell cancers after first line BEP chemotherapy appears to be in decline. The outcomes for these patients however remains guarded with cure anticipated in only 50% and as such the development of more effective regimens for the treatment of relapsed germ cell cancers remains an important question.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Upper GI							
University of Birmingham	Steven	Homing of DCs: A clinical study of the homing of mature autologous dendritic cells in vivo in patients with hepatocellular carcinoma or liver metastases.	8/12	2009	PALMER DH, MIDGLEY RS, MIRZA N, TORR EE, AHMED F, STEELE JC, STEVEN NM, KERR DJ, YOUNG LS, & ADAMS DH (2009). A phase II study of adoptive immunotherapy using dendritic cells pulsed with tumour lysate in patients with Hepatocellular carcinoma. Hepatology 49(1): p.124-32		Autologous DC vaccination in patients with HCC is safe and well tolerated with evidence of antitumor efficacy assessed radiologically and serologically, with generation of antigen-specific immune responses in some cases.
University College London	Meyer	TACE 2: A randomised placebo-controlled, double blinded, phase III trial of sorafenib in combination with transarterial chemoembolisation (TACE) in hepatocellular cancer	173/412	2015	MEYER T, FOX R, BIRD D, WATKINSON A, HACKING N, STOCKEN D, JOHNSON PJ, PALMER DH. (2012) TACE 2: a randomized placebo-controlled, double blinded, phase III trial evaluating sorafenib in combination with transarterial chemoembolisation(TACE) in patients with unresectable hepatocellular carcinoma (HCC). J Clin Oncol 30, (suppl; abstr TPS4150).	Yes	This trial will influence the future management strategy for hepatocellular carcinoma worldwide. This trial will influence the future management strategy for hepatocellular carcinoma worldwide.
University of Birmingham	Bridgewater	Adjuvant chemotherapy with gemcitabine and cisplatin compared to observation after curative intent resection of cholangiocarcinoma (ACTICCA-1 trial)		2018		Yes	The trial will build on the current research knowledge gained from the ABC02 and BILCAP trials to further define the optimum treatment for the management of surgically resectable BTC. The trial complements both the ABC02 and BILCAP trials in utilising the knowledge gained from both to date to further ask questions and define treatment for the disease setting. The BILCAP trial has demonstrated that complex and rare disease sites can be explored in a clinical trial and will help define the national and international standard of care for patients with resected biliary tract cancer patients The trial will build on the current research knowledge gained from the ABC02 and BILCAP trials to further define the optimum treatment for the management of surgically resectable BTC. The trial complements both the ABC02 and BILCAP trials in utilising the knowledge gained from both to date to further ask questions and define treatment for the disease setting. The BILCAP trial has demonstrated that complex and rare disease sites can be explored in a clinical trial and will help define the national and international standard of care for patients with resected biliary tract cancer patients
University of Southampton	Primrose	BILCAP: Biliary tract cancer treatment with capecitabine. Trans-BILCAP is the associated sample collection for the trial.	358/360	2015	BRIDGEWATER, J. STUBBS, C. FOX, R, STOCKEN D, PRIMROSE, P. (2011) BILCAP: A randomized clinical trial evaluating adjuvant chemotherapy with capecitabine compared to expectant treatment alone following curative surgery for biliary tract cancer. J Clin Oncol 29: suppl; abstr 4125	Yes	The completed study will define the UK standard of care for resected biliary tract cancer and will have a dramatic worldwide impact The completed study will define the international standard of care for resected biliary tract cancer and will have a dramatic worldwide impact
University of Edinburgh	Garden	HEP1: Phase III trial evaluating the benefit of chemoembolisation in unresectable, advanced hepatocellular carcinoma	3/280				Study was closed early due to poor recruitment.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Liverpool	Neoptolemos(CI) Stocken (Local Lead)	European Study Group for Pancreatic Cancer (ESPAC) Trial 3 (v2). Adjuvant Chemotherapies in Resectable Pancreatic Cancer	707/700	2009	Ductal cohort: Neoptolemos, J. P., D. D. Stocken, C. Bassi, P. Ghaneh, D. Cunningham, D. Goldstein, R. Padbury, et al. (2010) "Adjuvant Chemotherapy with Fluorouracil Plus Folinic Acid Vs Gemcitabine Following Pancreatic Cancer Resection: A Randomized Controlled Trial.". JAMA 304, no. 10: 1073-81. Periampullary cohort: Neoptolemos, J. P., M. J. Moore, T. F. Cox, J. W. Valle, D. H. Palmer, A. C. McDonald, R. Carter, et al.(2012) "Effect of Adjuvant Chemotherapy with Fluorouracil Plus Folinic Acid or Gemcitabine Vs Observation on Survival in Patients with Resected Periampullary Adenocarcinoma: The Espac-3 Periampullary Cancer Randomized Trial.". JAMA 308, no. 2: 147-56. 1) CURRENTLTY IN THE PRESS Juan W Valle, Daniel Palmer, Richard Jackson, Trevor Cox, John P. Neoptolemos, Paula Ghaneh, Charlotte L. Rawcliffe, Claudio Bassi, David Cunningham, Derek O'Reilly, David Goldstein, Bridget A Robinson, Christos Karapetis, Andrew Scarfe, Francois Lacaine, Juhani Sand, Jakob R. Izbicki , Julia Mayerle, Christos Dervenis, Attila Oláh, Giovanni Butturini, Pehr A. Lind, Mark R Middleton, Alan. Anthoney, Kate. Sumpter, Ross. Carter, Markus W. Büchler, for the European Study Group for Pancreatic Cancer. (2013) "Optimal duration and timing of adjuvant chemotherapy after definitive surgery for ductal adenocarcinoma of the pancreas: ongoing lessons from the ESPAC-3 study". Journal of Clinical Oncology - IN PRESS. 2) Neoptolemos JP, Stocken DD, Tudur Smith C, Bassi C, Ghaneh P, Owen E, Moore M, Padbury R, Doi R, Smith D, Büchler MW. (2009) "Adjuvant 5-fluorouracil and folinic acid vs observation for pancreatic cancer: composite data from the ESPAC-1 and -3(v1) trials". Br J Cancer;100(2):246-50. . Optimal duration and timing of adjuvant chemotherapy after definitive surgery for ductal adenocarcinoma of the pancreas: ongoing lessons from the ESPAC-3 study" (Abstract No. 13100) has been accepted for oral presentation at the American Pancreatic Association Annual Meeting. Session Name: Cancer 2 Date of Presentation: Friday, November 1 Session Time: 8:30 – 10:00 am	No	This is the largest adjuvant therapy trial ever conducted in pancreatic ductal adenocarcinoma. The ESPAC-3 trial found a median survival of 23.0 months for patients treated with 5-fluorouracil and folinic acid and 23.6 months for patients treated with gemcitabine and a median PFS of 14.1 months and 14.3 months respectively. In the Periampullary cohort patients with resected periampullary adenocarcinoma, adjuvant chemotherapy, compared with observation, was not associated with a significant survival benefit in the primary analysis; however, multivariable analysis adjusting for prognostic variables demonstrated a statistically significant survival benefit associated with adjuvant chemotherapy. Results may lead to a changes in clinical practice, including potential changes to NICE recommendations. Many centres throughout the UK are now using Gemcitabine as standard care however the publication of the main paper may lead to more formal adoption of the regime. Possibly similar to the UK.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Liverpool/ Birmingham	Neoptolemos (CI) Stocken (Local Lead)	Clinical Trial in Pancreatic Cancer - ESPAC3 and ESPAC1 (including ESPAC-QoL - the development of outcome measure specific to quality of life of patients with pansreatic cancer.	289/280	2003	Neoptolemos JP, Stocken DD, Friess H, Bassi C, Dunn JA, Hickey H, Beger H, Fernandez-Cruz L, Dervenis C, Lacaine F, Falconi M, Pederzoli P, Pap A, Spooner D, Kerr DJ, Büchler MW; European Study Group for Pancreatic Cancer. (2004). A randomized trial of chemoradiotherapy and chemotherapy after resection of pancreatic cancer. N Engl J Med. 2004 Mar 18;350(12):1200-10. Erratum in: N Engl J Med. 2004 Aug 12;351(7):726. 1) Carter R, Stocken DD, Ghaneh P, Bramhall SR, Olah A, Kelemen D, Bassi C, Friess H, Dervenis C, Spry N, Büchler MW, Neoptolemos JP; European Study Group for Pancreatic Cancer (ESPAC).(2009) Longitudinal quality of life data can provide insights on the impact of adjuvant treatment for pancreatic cancer-Subset analysis of the ESPAC-1 data. Int J Cancer. Jun 15;124(12):2960-5. 2) Neoptolemos JP, Stocken DD, Tudur Smith C, Bassi C, Ghaneh P, Owen E, Moore M, Padbury R, Doi R, Smith D, Büchler MW. (2009) Adjuvant 5-fluorouracil and folinic acid vs observation for pancreatic cancer: composite data from the ESPAC-1 and -3(v1) trials. Br J Cancer. Jan 27;100(2):246-50. Epub 2009 Jan 6. 3) Bassi C, Stocken DD, Olah A, Friess H, Buckels J, Hickey H, Dervenis C, Dunn JA, Deakin M, Carter R, Ghaneh P, Neoptolemos JP, Buchler MW; European Study Group for Pancreatic Cancer (ESPAC). (2005) Influence of surgical resection and post-operative complications on survival following adjuvant treatment for pancreatic cancer in the ESPAC-1 randomized controlled trial. Dig Surg. 2005;22(5):353-63. Epub 2005 Nov 16. 4) Neoptolemos JP, Stocken DD, Dunn JA, Almond J, Beger HG, Pederzoli P, Bassi C, Dervenis C, Fernandez-Cruz L, Lacaine F, Buckels J, Deakin M, Adab FA, Sutton R, Imrie C, Ihse I, Tihanyi T, Olah A, Pedrazzoli S, Spooner D, Kerr DJ, Friess H, Büchler MW; European Study Group for Pancreatic Cancer. (2001) Influence of resection margins on survival for patients with pancreatic cancer treated by adjuvant chemoradiation and/or chemotherapy in the ESPAC-1 randomized controlled trial. Ann Surg. Dec;234(6):758-68. 5) Neoptolemos JP, Dunn JA, Stocken DD,	Yes	Adjuvant chemotherapy has a significant survival benefit in patients with resected pancreatic cancer, whereas adjuvant chemoradiotherapy has a deleterious effect on survival. Change in clinical practice. Possibly similar to the UK.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
					Almond J, Link K, Beger H, Bassi C, Falconi M, Pederzoli P, Dervenis C, Fernandez-Cruz L, Lacaine F, Pap A, Spooner D, Kerr DJ, Friess H, Büchler MW; European Study Group for Pancreatic Cancer.(2001) Adjuvant chemoradiotherapy and chemotherapy in resectable pancreatic cancer: a randomised controlled trial. Lancet. Nov 10;358(9293):1576-85.		
Royal Marsden/ University of Liverpool	Cunningham (CI) Stocken (Local Lead)	GEMCAP: A phase III multicentre randomised trial comparing gemcitabine alone or in combination with capecitabine for the treatment of patients with advanced pancreatic cancer	533/508	2008	Cunningham, D; Chau, I; Stocken, DD; et al. Phase III Randomized Comparison of Gemcitabine Versus Gemcitabine Plus Capecitabine in Patients With Advanced Pancreatic Cancer. (2009) JCO, 27 (33): 5513-5518. . 1) Cunningham D, et al. (2005) EJC Suppl;3(4):12-12. 2) Neoptolemos JP, et al (2005). Pancreas;31(4):459-459.	Yes	Trial and the meta-analysis, GEM-CAP should be considered as one of the standard first-line options in locally advanced and metastatic pancreatic cancer
University of Liverpool	Neoptolemos	ESPAC4: EUROPEAN STUDY GROUP FOR PANCREATIC CANCER (ESPAC) - Trial 4. Combination versus single agent adjuvant chemotherapy in resectable pancreatic cancer.	453/977	2016	A presentation on trial progress, but not results, was given at the EPC in Zurich; the EPC is an annual conference.	Yes	Compares a combination of gemcitabine and capecitabine, shown to be more effective than gemcitabine alone in the advanced setting, with gemcitabine alone in the adjuvant setting, looking at survival difference. Study is open across the UK and continues to be opened in new centres; trial opened in Sweden within 6 months of the UK and is open in Germany too. France recruited 24 patients who remain in follow-up but they will not recruit any more due to funding for capecitabine. India and Italy are in set-up. If positive, it would lead to a change in clinical practice, including potential for license expansion and change to NICE recommendations. If positive, it would lead to a change in clinical practice.
University of Liverpool	Middleton	TeloVac: A phase III multicentre randomised clinical trial comparing gemcitabine alone and in combination with telomerase vaccine for the treatment of Pancreatic cancer	1062/1110	2013	A draft manuscript for joint publication will be prepared and submitted in collaboration between CR-UK Liverpool Cancer Trials Unit and the investigators. 1) Oral Presentation at ASCo 2013 A phase III randomised trial of chemo-immunotherapy comprising gemcitabine and capecitabine (GemCap) with or without telomerase peptide vaccine GV1001 in patients with locally advanced or metastatic pancreatic cancer (TELOVAC) Gary William Middleton, Juan W. Valle, Paul Silcocks, Jonathan Wadsley, David Propper, Fareeda Y. Coxon, Paul J. Ross, Srinivasan Madhusudan, Tom Roques, David Cunningham, Pippa Corrie, William Greenhalf, Victoria Shaw, Gemma Nanson, Trevor F Cox, John P. Neoptolemos Mon, Jun 3 9:45 AM - 12:45 PM Hall D1 (Location) Abstract #LBA4004 2) NCRI upper GI conference (May 2008)	No	Trial closed due to inferiority Largest ever therapeutic anti-cancer vaccine trial

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Liverpool	Middleton	VIP: A prospective phase II controlled multicentre randomised clinical trial comparing combined gemcitabine and vandetanib therapy with gemcitabine therapy in advanced pancreatic cancer	125/140	2014		Yes	Primary aim: to assess whether survival times for patients receiving gemcitabine plus vandetanib are longer than for those patients receiving gemcitabine alone as first line treatment for advanced pancreatic cancer. Secondary aims : To compare between the two treatment groups: progression-free survival time (PFS), objective response rate; disease control rate; toxicity and safety. Exploratory aims: To discover possible biomarkers to predict additional benefit of vandetanib over gemcitabine alone for subsequent validation in larger scale studies. The results of this study, if positive, will critically inform future developments with vandetanib in this indication. At present the plan would be to run into a phase III programme. This trial is the pivotal global study for this drug in pancreatic cancer. Unknown
Greater Glasgow and Clyde Health Board	Wilson	CRUK/12/041: A global study to evaluate the potential benefit of adjuvant chemotherapy for small bowel adenocarcinoma (the Ballad study) (International Rare Cancers Initiative study - IRCI 002)	0/860	2021		Yes	Part of the IRCI group of trials and the first trial in SBA No standard practice internationally for this patient group. Hopefully the trial will result in agreed standard of treatment for these patients. As per UK
University of Oxford	Ferry	CRUK/07/017 COG: Randomised phase III trial of gefitinib 500mg once daily vs placebo in oesophageal cancer progressing after chemotherapy	450/450	2013	COG Launch: 22/09/2008, COG Investigator Meeting 17Sep2012, COG key data presented at ESMO in Vienna 29Sep2012, COG key data due to be presented at NCRI Clinical trials showcase on 06Nov2012 at NCRI Meeting in Liverpool. Abstract has been submitted to ASCO GI Meeting to present Qulaity of Life data.	Yes	The first phase III trial to address the need for second-line treatments in oesophageal cancer. Median progression-free survival was 35 days for patients who received placebo, and 49 days for those administered gefitinib. Treatment with the drug also improved dysphagia and odynophagia, two important indicators of quality of life in this patient group. In addition to the quality-of-life improvements and modest improvements in progression-free survival, some patients saw durable benefits from the treatment. Trial has completed recruitment and is currently in the close out stages. As there has been no trial of its kind before, and QofL is improved in a set of patients, treatment in this patient group could be changed. Sub-study TRANSCOG is planning to analyse over 300 COG patients' biopsies in an effort to identify a molecularly defined subgroup where the benefit is enriched.
University of Oxford	Jankowski	CRUK/05/006: ASPECT: Aspirin esomeprazole chemoprevention trial	2513/2500	2017	Jankowski JA, Moayyedi P. Aspirin as chemoprevention for Barrett's esophagus: a large RCT underway in the UK. Journal of National Cancer Institute 2004; 96:885-7 Am Soc of Clinical Oncology, San Francisco Am Inst Cancer Res, St Gallen, Switzerland United European Gastroenterology Week, Liverpool Int Soc Dis Eso, Venice, Italy European GI Meeting, Florence, Italy		Recruitment closed. Patients in follow up. If results are positive it will confirm the value of aspirin chemoprevention when given with acid suppressing therapy.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Leeds	Seymour	CRUK/08/033: 321GO. Three, two or one-drug chemotherapy for advanced gastroesophageal cancer: a randomised multicentre feasibility study in frail and/or elderly patients	55/45	2011	P. S. Hall, S. Lord, M. Collinson, H. Marshall, M. Jones, C. Olivier, H et al. Three, two or one drug chemotherapy for frail or elderly patients with advanced gastroesophageal cancer (321GO): A feasibility study. J Clin Oncol 30, 2012 (suppl 4; abstr 97) Currently in preparation European Cancer Congress 2013, "The feasibility of using comprehensive geriatric assessment in frail or elderly patients with advanced gastric or oesophageal cancer" and "Overall treatment utility: A novel outcome measure reflecting the balance of benefits and harms from cancer therapy"	No	A phase III trial randomising frail or elderly patients with advanced GO cancer to alternative chemotherapy regimens is feasible. EOX was associated with greater toxicity compared with OX; X offered no improvement in tolerability over OX. Informing design of other trials N/A
University of Leeds	Seymour	GO2 - Alternative chemotherapy for frailer or elderly patients with advanced gastric or oesophageal cancer	0/500	2017		Yes	All the global approvals are in place. It is anticipated that the trial will open to recruitment at the end of September 2013, subject to receipt of appropriate local approvals and documentation. This trial will provide the first randomised clinical trial evidence guiding the use of modern chemotherapy in the treatment of patients with advanced GO cancer who are unfit for intensive regimens. It will identify elements of a Comprehensive Health Assessment that can guide chemotherapy treatment decisions in routine practice. It will further develop the Overall Treatment Utility endpoint for research in palliative cancer therapy. The trial is being watched by SIOG (International Society of Geriatric Oncology).
University of Manchester	Price	CRUK/07/036: PACER: A phase II study of image-guided 3-Dimensional conformal radiotherapy with concurrent cetuximab in patients with locally advanced pancreatic cancer	10/40		Poster presentation at the Christie NHS Foundation Trust Gastro-Intestinal Disease Orientated Group annual meeting in December 2007. An oral presentation entitled: "Phase II study of cetuximab and radiotherapy in patients with locally advanced pancretic cancer" will be given at the Agate Rembielak at the UK radiation Oncology Conference in Cardiff, April 2009.		The investigators envisage that the subsequent phase III trial will compare combined cetuximab/RT with the current CRT standard in the UK. If the results are encouraging, this will lead to further studies where addition of cytotoxic agent/s could be added to the current investigational arm. The translational research aspects will provide feasibility and mechanistic/predictive information that will help guide the integration of such studies in a phase III setting in the future.
University of Cambridge	Fitzgerald	CRUK/10/041: BEST2: Evaluation of a Non-Endoscopic Immunocytological Device (Cytopill) for Barrett's Oesophagus Screening via a Case-Control Study				Yes	
QMUL	Williams	CRUK/93/001: Evaluation and improvement of photodynamic therapy for gastrointestinal cancer			Adjuvant intraoperative photodynamic therapy for colorectal carcinoma: a clinical study. Allardice JT, Abulafi AM, Grahn MF, Williams NS. Surg Oncol. 1994 Feb;3(1):1-10.		
Barts & QMUL	Wald	CRUK/96/012: Helicobacter pylori screening trial : A ranomised stomach cancer prevention trial	56000/56000	2019 is the likely earliest date		Yes	In follow up If the trial shows that most of the excess risk is reversible, this would mean that most cases of stomach cancer in the world could be prevented. The trial will also quantify the reduction in mortality from peptic ulcers that is attained by eradicating H The findings will be worldwide, not just relevant to the UK.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Southampton	Primrose	CRUK/12/048: ORANGE II PLUS trial	unknown/60	2016		Yes	With advances in treatments and surgical technique resulting in increasing numbers of patients amenable to surgical resection there is a need for a trial to determine the optimal surgical approach including an analysis of the economic implications to the NHS.
Cardiff University	Mukherjee	CRUK/07/040: SCALOP: A multi-centre randomised phase II trial of induction chemotherapy followed by gemcitabine or capecitabine based chemoradiotherapy for locally advanced non-metastatic pancreatic cancer	74/76	2013	S. Mukherjee et al. 2013. Gemcitabine-based or capectibaine-based chemoradiotherapy for locally advanced pancreatic concer (SCALOP): A multicentre, randomised phase 2 trial. Lancet onoclogy A Cancer Research UK multicenter randomized phase II study of induction chemotherapy followed by gemcitabine- or capecitabine-based chemoradiotherapy for locally advanced nonmetastatic pancreatic cancer. Mukherjee S et al., J Clin Oncol, Volume 28, 15s (2010). Presentation of results at ASCO and the upper GI NCRI meeting.	No	Main findings; Chemoradiotherapy is an effective and feasible way to trerat patients of this disease group. Capecitabine-based regimen might be preferable to a gemcitabine-based regimen. The results of this trial were used to determine the experimental arm of the SCALOP II trial. This study showed that chemoradiohterapy can be used to treat patients with pancreastic cancer.
Velindre NHS Trust	Crosby (Griffiths - sample collection)	CRUK/07/003: SCOPE 1: A randomised phase II/III multi-centre clinical trial of definitive chemoradiation, with or without cetuximab, in carcinoma of the oesophagus. T-SCOPE is the associated sample collection for this trial.	258/420	2013	T. Crosby et al. 2013. Chemoradiotherapy with or without cetuximab in patients with oesophageal cancer (SCOPE1): A multicentre, phase 2/3 randomised trial. Lancet oncology Gwynne S et al., Towards automated assessment of target volume delineation in radiotherapy trials: the SCOPE 1 pre trial test case (Accepted in Red Journal) ; SCOPE1: a randomised phase II/III multicentre clinical trial of definitive chemoradiation, with or without cetuximab, in carcinoma of the oesophagus. Hurt CN et al., BMC Cancer, Volume 11 (2011) pp.466-466 Presentation of results at ASCO and the upper GI NCRI meeting.	No	Main findings; Cetuximab did not improve patient response rate in comparison to the control arm. Patient response rate was significantly improved in comparison to all previously published data. This maybe down to the radiotherapy quality assurance aspect of the trial and the additional training provided to PIs regarding radiotherapy outlining. The study concluded that the use of cetuximab in this group of patients should not be promoted. Collection and storage of samples will enable future translational research into how the radiotherapy may have improved patient outcomes. The study concluded that the use of cetuximab in this group of patients should not be promoted.
Velindre NHS Trust	Crosby	C44694/A14614:NeoSCOPE - A randomised Phase II study of two pre-operative chemoradiotherapy regimes (oxaliplatin and capecitabine followed by radiotherapy with either oxaliplatin and capecitabine or paclitaxel and carboplatin) for resectable oesophageal cancer	0/85	2015	NeoSCOPE trial launch and radiotherapy workshop, Bristol, 25/02/2013. NeoSCOPE 4D radiotherpay workshop 15/07/2013	No	This is a randomised phase II trial. The result will be used to determine the experimental arm of a future phase III which, if positive, would lead to a change in clinical practice. Will contribute significantly to international knowledge base.
Cambridge University Hospitals	Ford	CRUK/07/013: COUGAR-02: a phase III randomised controlled trial of docetaxel versus active symptom control as second line treatment in advanced gastric cancer	168/164	2013	Ford, Marshall et al Lancet Oncology 2014 15:78-86 Cook, Marshall et al . COUGAR-02: A randomized phase III study of docetaxel versus active symptom control in patients with relapsed esophago-gastric adenocarcinoma. ASCO June 2013, Chicago, USA. 14. Ford, Marshall et al. COUGAR-02: A randomized phase III study of docetaxel versus active symptom control in patients with advanced esophagogastric adenocarcinoma. ASCO	Yes	Our findings suggest that Docetaxel can be recommended as an appropriate secondline treatment for patients with oesophagogastric adenocarcinoma Either a positive or negative result will change practice nationally and internationally and will set an evidence based benchmark for future trials. As well as the main findings, this study will add to the knowledge base for the treatment of this group of patients.

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
					Gastrointestinal Cancers Symposium January 2013, San Francisco, USA.		
University Hospitals Coventry & Warwickshire NHS Trust	Mehanna	CRUK/11/043: DeESCALaTE - HPV Determination of Epidermal growth factor receptor-inhbitor (cetuximab) versus Standard Chemotherapy (cisplatin) early And Late Toxicity Events in Human Papilloma Virus-positive oropharyngeal squamous carcinoma	82/304	2017	Tessa Fulton-Lieuw: De-ESCALaTE HPV: Yorkshire Head & Neck Research and Education Event. 27th September 2013	Possibly	N/A HPV+OPSCC patients are younger and have a better prognosis than those with HPV negative disease, hence will live much longer with the functional and psychological sequelae of treatment. This trial will define acute and late toxicities in chemotherapy compared with cetuximab to justify the use of less aggressive and less toxic treatments in this group of patients, As the trial in ongoing, the impact is unknown. The results will add to the knowledge base for the treatment of this group of patients.
University College London	Pereira	CRUK/08/011: Photostent-02 Porfimer sodium photodynamic therapy plus stenting versus stenting alone in patients with advanced or metastatic cholangliocarcinomas or other biliary tract tumours: a multicentre randomised phase II/III study.	92/240	2014	Oral presentation at ESMO 2010: Ann Oncol (2010) 21 (suppl 8): viii250-viii263; Abstr 8020.	No	ESMO 2010 (Milan) Results indicate that pts with BTC who received PDT + stenting had a poorer OS than those who had stenting alone. This may be partly explained by fewer PDT + stenting pts receiving subsequent palliative chemotherapy. None
Royal Free & University College Medical School	Bridgewater	CRUK/04/012: ABC02: Gemcitabine alone or in combination with cisplatin, in patients with advanced or metastatic cholangiocarcinomas and other biliary tract tumours	324/314	2009	Cisplatin and Gemcitabine Compared with Gemcitabine for Biliary Tract Cancer N Engl J Med. 2010 Apr 8;362(14):1273-81. Wasan H, et al. Ann Oncol. 2009;20(Supp 7):9-9. Bridgewater J, et al. EJC Suppl. 2009;7(2):361-361. Juan Valle, et al. Cisplatin plus Gemcitabine versus Gemcitabine for Biliary Tract Cancer; NEJM 362;14, 08 Apr 2010 Oral presentation at ASCO 2009: Valle JW, et al. J Clin Oncol. 2009;27(15 Supp):4503. Poster presentation at GI ASCO: GI ASCO 2010, abstr 199 - Cisplatin and gemcitabine for advanced biliary tract cancer: A meta-analysis of two randomized trials. J Clin Oncol 31, 2013 (suppl; abstr 4120) - Guidelines for the diagnosis and management of intrahepatic cholangiocarcinoma. J Hepatol. 2014 Mar 27. pii: S0168-8278(14)00067-1. doi: 10.1016/j.jhep.2014.01.021. [Epub ahead of print] - Cisplatin and gemcitabine for advanced biliary tract cancer: a meta-analysis of two randomised trials. Ann Oncol. 2014 Feb;25(2):391-8.	Yes	Gemcitabine and cisplatin give longer overall survival compared to cisplatin alone with similar levels of toxicity - Cisplatin and gemcitabine significantly improves overall survival by 3.6m, reduces risk of death by 36% (HR 0.64, p<0.001), and significantly improves progression-free survival and tumour control - The trial showed a significant survival advantage for the CisGem arm and this regimen has become the standard of care for this patient group. Investigational arm (CisGem) now standard of care for advanced biliary tract cancer. - ABC02 trial used to develop international guidelines

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University College London	Valle	CRUK/09/029: ABC-03: A randomised phase II/III study of cediranib (AZD2171) or placebo in combination with cisplatin/gemcitabine chemotherapy for patients with advanced biliary tract cancers.	85/136	2014	ABC-03: A randomised phase II trial of cediranib (AZD2171) or placebo in combination with gemcitabine/cisplatin (GemCis) chemotherapy for patients (pts) with advanced biliary tract cancers (ABC). J Clin Oncol 28:15s, 2010 (suppl; abstr TPS218) Poster presentation at ASCO 2010; J Clin Oncol 28:15s, 2010 (suppl; abstr TPS218) Oral presentation at ASCO 2014 Poster Presentation at NCRI conference 2014		Final Publication still being written Not known Not known at present
University College London	Bridgewater	CRUKE/10/036: ABC-04: A phase Ib study of Cisplatin, Gemcitabine and AZD6244 in patients with advance Biliary Tract Cancer	13/12	2013	In press ABC-04:A phase Ib study of cisplatin, gemcitabine and selumetinib in patients with advanced biliary tract cancers. ASCO 2014 (Chicago). In press Poster presentation at ASCO 2014 Poster presentation at NCRI Conference 2014	No	Not known Not known at present
University College London	Burroughs	TACE: Phase II/III randomised controlled trial of transarterial chemoembolisation vs embolisation alone in non-resectable hepatocellular carcinoma.			A randomised phase II/III trial of three weekly cisplatin based sequential transarterial chemoembolisation versus embolisation alone for hepatocellular Carcinoma. J Clin Oncol 28:15s, 2010 (suppl; abstr 4025)		Transarterial chemoembolisation according this novel schedule is feasible and associated with a higher response rate than TAE alone. The survival benefit of TACE over TAE remains unproven.
University College London	Hawkins	ABC-07: Addition of stereotactic radiotherapy to systemic chemotherapy in locally advanced biliary tract cancers	0/0			Yes	
Centre for Drug Development							
Queen Mary, University of London/Barts	Hagemann	CRUKD/12/011: A Phase I dose escalation trial of HDAC inhibitor CHR2845 for cancer associated inflammation in hepatocellular carcinoma	4/69	2015			First time for this agent in this group of patients. First in this population, first in class If trial positive it will have significant impact given the distribution / incidence of HCC in middle east / asia / world wide
University of Leicester	Thomas	CRUKD/12/007: DEBIOC a Phase I dose-escalating study of EGFR inhibitor AZD8931 in combination with oxaliplatin and capecitabine chemotherapy in patients with oesophago-gastric adenocarcinoma	7/72	2017			First time for this combination in this group of patients. The outcome of this study will inform future national randomized studies and could lead to change in clinical practice. The outcome of this study will inform future national randomized studies and could lead to change in clinical practice.
Christie NHS Foundation Trust	Jackson	CRUKD/11/012: ROCOCO: A phase I dose escalation trial of Radiotherapy and Olaparib (a PARP1 inhibitor), in combination for carcinoma of the oesophagus	0/36	2017			First trial of a novel combination with chemoradiotherapy in this group of patients. Trial planned for 2012. Aims to look at safety, efficacy, MTD in combination with RT and identify a dose for further evaluation. Too early in development to assess clinical impact. If successful in oesophageal the data may be relevant for other thoracic tumours treated with radiotherapy e.g. Lung

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
University of Glasgow	Evans	CRUKD/11/003: FACING A Phase I/IIa trial of AZD4547, an FGFR inhibitor, in combination with cisplatin and capecitabine (CX) in patients with locally advanced gastro-oesophageal cancer	19/140	2016			First trial of a novel combination in this group of patients. The aim is to develop a regimen combining an FGFR inhibitor with a chemotherapy backbone applicable to different tumour types. In particular, 30–40% of gastric cancer patients have polysomy or amplification of FGFR2 with limited therapy options and a poor overall survival, this combination could significantly improve overall survival in these patients. If successful Phase I results may lead to Phase II trials in other tumour types where CX is a treatment option. Phase IIa data may lead to a randomised Phase III in advanced gastro-oesophageal cancer providing a potential new therapy option for patients with poor survival. Successful Phase III trials could lead to this treatment being registered and more widely available for patients. If successful Phase I results may lead to Phase II trials in other tumour types where CX is a treatment option. Phase IIa data may lead to a randomised Phase III in advanced gastro-oesophageal cancer providing a potential new therapy option for patients with poor survival. Successful Phase III trials could lead to this treatment being registered and more widely available for patients.
University of Cambridge	Jodrell	CRUKD/10/028: A Cancer Research UK Phase I trial of MK0752, an oral notch inhibitor, alone or in combination with gemcitabine in locally advanced or metastatic pancreatic cancer	29/60	2016	Whitehead J, Thygesen H, Jaki T, Davies S, Halford S, et al. A novel Phase I/IIa design for early phase oncology studies and its application in the evaluation of MK-0752 in pancreatic cancer. Stat Med. 2012 Aug 15;31(18):1931-43.		First time in patients for this Notch inhibitor. If the trial is successful it will improve current treatment for pancreatic cancer. Trial aims to identify a suitable dose for the combination, look at side effects, PK/PD and efficacy. Potential Phase II study in combination with gemcitabine and abraxane (combination studies ongoing with gem/abraxane); folfirinox increasingly used as first-line treatment in advanced pancreatic cancer, but toxicity limits its utility therefore still a need for additional agents/combinations not known
Royal Free & University College Medical School	Begent	CRUKD/03/037: A Cancer Research UK Phase I trial of radioimmunotherapy with 131I-A5B7 in combination with Combretastatin A4 Phosphate for advanced gastrointestinal carcinoma	12/12	2008	Meyer T, Gaya AM, et al. A phase I trial of radioimmunotherapy with 131I-A5B7 anti-CEA antibody in combination with combretastatin-A4-phosphate in advanced gastrointestinal carcinomas. Clin Cancer Res. 2009 Jul 1;15(13):4484-9. ASCO Meeting Abstracts 2008 26: 14517		First time in patients for this novel combination of radioimmunotherapy and vascular disruption. Follow up trial to CRUKD/98/010. CR UK was involved in the development of both agents. Trial completed. Combretastatin A4P in Phase III development. Too early in development to assess clinical impact.
University of Leicester	Steward	CRUKD/01/017: A Cancer Research UK Phase I trial of AQ4N (banoxantrone), a novel hypoxic cell cytotoxin, prior to fractionated radiotherapy in patients with oesophageal carcinoma	22/22	2006	Steward W, Middleton M, et al. The use of pharmacokinetic and pharmacodynamic endpoints to determine the dose of AQ4N, a novel hypoxic cell cytotoxin, given with fractionated radiotherapy in a phase I study. Ann Oncol. 2007 Jun;18(6):1098-103.		First time in patients for this novel bioreductive agent. Trial completed. Safe Phase II dose in combination with radiotherapy identified. Development discontinued during Phase II development for financial reasons. Too early in development to assess clinical impact. Led to Phase II evaluation.
University of Edinburgh	Jodrell	CRUKD/00/019: A Phase II Trial of BBR 3464 as first line treatment in patients with gastric or gastro-oesophageal adenocarcinoma.	9/9	2003	Jodrell DI, Evans TR, et al. Phase II studies of BBR3464, a novel tri-nuclear platinum complex, in patients with gastric or gastro-oesophageal adenocarcinoma. Eur J Cancer. 2004 Aug;40(12):1872-7.		First evaluation of the efficacy of a non cross resistant platinum complex in first line gastric cancer. Companion trial to: CRUKD/00/015 and CRUKD/00/020. Trial completed. Development discontinued after Phase II due to lack of activity. Too early in development to assess clinical impact.
University of	Jodrell	CRUKD/00/020: A Phase II Trial of	26/26	2003	Jodrell DI, Evans TR, et al. Phase II studies of		First evaluation of the efficacy of a non cross resistant

Key: Trials that are currently in set-up | Trials that are currently open | Trials that have closed, suspended, or withdrawn during set up

Host Institution	Chief Investigator	Title	Patients recruited against target (e.g. 109/120)	Year of (planned) primary analysis	Publications and Presentations	Has led/will lead to New Guidelines	Main Findings and Impact
Edinburgh		BBR 3464 in patients with gastric or gastro-oesophageal adenocarcinoma who have failed first line chemotherapy			BBR3464, a novel tri-nuclear platinum complex, in patients with gastric or gastro-oesophageal adenocarcinoma. Eur J Cancer. 2004 Aug;40(12):1872-7.		platinum complex in 2nd line gastric cancer. Companion trial to: CRUKD/00/015 and CRUKD/00/019. Trial completed. Development discontinued after Phase II due to lack of activity. Too early in development to assess clinical impact.
University of Birmingham	Kerr	CRUKD/96/017: Phase I evaluation of PK2, polymer-bound doxorubicin	31/31	2001	Seymour LW, Ferry DR, et al. Hepatic drug targeting: phase I evaluation of polymer-bound doxorubicin. J Clin Oncol. 2002 Mar 15;20(6):1668-76.		First time in patients for this drug-polymer conjugate. Trial completed. Safe Phase II dose identified and potential activity in liver cancer seen. Development discontinued after Phase I due to lack of drug supply. Too early in development to assess clinical impact.

ECMC Supported studies
as of end March 2014

The Experimental Cancer Medicine Centre (ECMC) Network is a unique UK initiative jointly funded by Cancer Research UK and the Health Departments of England, Wales, Scotland and Northern Ireland. Consisting of eighteen centres of excellence across the UK. The funding is targeted at providing infrastructure to support Experimental Medicine and includes Research Nurses, Operational Staff, Pharmacists and Quality Assurance staff. Through a flexible model, centres can choose to fund those positions which will best balance their portfolio of expertise.

Note:
Some studies are not included for confidentiality reasons and the data is not in the public domain

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
Any Advanced Cancers (incl. all solid tumours)				
131I-L19SIP Radioimmunotherapy (RIT) in Combination With External Beam Radiation in Patients With Multiple Brain Metastases From Solid Tumors	Dr Paul Mulholland	UCL	UCL	0
A Bioequivalence Study of DOXIL/CAELYX Manufactured at a New Site in Subjects With Advanced or Refractory Solid Malignancies	Dr. Rebecca Kristeleit	UCL	UCL	2
A Cancer Research UK Phase I first in man study of the novel AGC kinase inhibitor AT13148 given orally in patients with advanced solid tumours	Dr Udai Banerjii	ICR	ICR	12
A Cancer Research UK Phase I Trial of 4-(N-(S-Glutathionylacetyl) Amino) Phenylarsenoxide (GSAO) Given as Daily Intravenous Infusions on Days 1-5 and 8-12 of a 21-Day Cycle, to Patients With Advanced Solid Tumors	Professor G Jayson	Manchester	Manchester, Oxford	0
A Cancer Research UK Phase I trial of Phortress (novel antitumour benzothiazole) given intravenously in consecutive 28 day cycles with treatments on days 1 and 8 of each cycle	Prof AH Calvert	Newcastle	Newcastle	0
A Cancer Research UK Phase I trial to evaluate safety, tolerability, pharmacokinetics and pharmacodynamics of Aurora B inhibitor GSK1070916A in patients with advanced solid tumours	Dr Chris Twelves	Leeds	Barts, Leeds	0
A Clinical Study to evaluate the Safety, Tolerability, and the effects of VX-970 in combination with Chemotherapy on the body in Subjects with Advanced Solid Tumors	Prof Ruth Plummer	Newcastle	Glasgow, Manchester, Newcastle, Oxford	17
A Clinical Trial to Determine the Most Suitable Dose of OPB-111001 in Patients With Advanced Cancer	Prof Johann De Bono	ICR	ICR	2
A Dose Finding and Safety Study of Oral LEQ506 in Patients With Advanced Solid Tumors	Prof Mark Middleton	Oxford	Oxford	0
A Dose-Escalating Study of RO4987655 in Patients With Advanced Solid Tumors	Prof M Middleton	Oxford	Oxford	0
A Drug Interaction Study of Tasisulam in Patients With Advanced Cancer or Lymphoma	Dr Christopher Twelves	Leeds	Leicester, Sheffield, UCL	0
A FIRST-IN-HUMAN PHASE 1 DOSE ESCALATION TRIAL OF THE HUMANIZED ANTI-CD47 MONOCLONAL ANTIBODY HU5F9-G4 IN PATIENTS WITH ADVANCED SOLID MALIGNANCIES	Dr Denis Talbot	Oxford	Oxford	
A Multicenter, Open-label, Phase 1b Study of MLN0128 (an Oral mTORC1/2 Inhibitor) in Combination With MLN1117 (an Oral PI3Kα Inhibitor) in Adult Patients With Advanced Nonhematologic Malignancies	Prof Johann De Bono	ICR	ICR	
A Non-randomised, Open-label, Sequential, Three-part, Phase I Study to Assess the Effect of Itraconazole (a CYP3A4 Inhibitor) on the Pharmacokinetics of Olaparib Following Oral Dosing of a Tablet Formulation, and to Provide Data on the Effect of Olaparib on QT Interval Following Oral Dosing of a Tablet Formulation to Patients With Advanced Solid Tumours	Dr Ruth Plummer	Newcastle	ICR, Newcastle, UCL	11
A PARALLEL ARMS PHASE 1 SAFETY, PHARMACOKINETIC AND PHARMACODYNAMIC STUDY OF THE INTRAVENOUS POLY(ADP-RIBOSE)POLYMERASE (PARP) INHIBITOR PF-01367338 (AG-014699) IN COMBINATION WITH SEVERAL CHEMOTHERAPEUTIC REGIMENS IN ADULT PATIENTS WITH ADVANCED SOLID TUMOR	Prof Ruth Plummer	Newcastle	Belfast, Glasgow, ICR, KCL, Newcastle, Oxford	6
A Phase 1 Dose Escalation Study of Continuous Oral OSI-906 Dosing in patients with Advanced Solid Tumours	Prof T R J Evans	Glasgow	Glasgow	0
A Phase 1 Dose-escalation Study of OSI-906 and Erlotinib (TarcevaÂ®)	Dr V Macaulay	Oxford	Oxford	0

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
A Phase 1 Open-Label, Dose-Finding Study to Evaluate the Safety and Pharmacokinetics of ONX 0801, a Novel a-Folate Receptor-Mediated Thymidylate Synthase Inhibitor, in Patients With Advanced Solid Tumours	Dr Udai Manerji	ICR	UCL	0
A phase 1 randomised, 2 period cross over study to determine the comparative bioavailability of two different formulations of AZD2281 in cancer patients with advanced solid tumors (AZD2281)	Dr Stanely Kaye	ICR	ICR, Manchester, Newcastle, Oxford, UCL	0
A Phase 1 Safety, Pharmacokinetic And Pharmacodynamic Study Of The Anti-A5B1 Integrin Monoclonal Antibody PF-04605412 Administered Intravenously To Adult Patients With Advanced Or Metastatic Solid Tumors	Dr Johann De-Bono	ICR	ICR	0
A Phase 1 Study of Dexanabinol in Patients With Advanced Solid Tumours	Prof. Ruth Plummer	Newcastle	Leeds, Newcastle	8
A Phase 1, Open-Label, Multiple Ascending Dose Study of DS-3078a, an Oral TORC1/2 Kinase Inhibitor, in Subjects With Advanced Solid Tumors or Lymphomas	Dr Udai Banerji	ICR	ICR	11
A Phase 1/2A Dose Escalation Study of 2-hydroxyoleic acid (2-OHOA; Minerval®) in Adult Patients with Advanced Solid Tumours including Malignant Glioma	Prof Johann De Bono	ICR	ICR, Newcastle	8
A Phase 1b/2, Multicenter, Randomized, Open-label, Dose-escalation and Confirmation Study of Eribulin in Combination with Capecitabine	Prof T R J Evans	Glasgow	Glasgow, Leeds, Newcastle	0
A phase 2, open-label test-retest study to assess the reproducibility of quantitative measurements of 18F uptake by solid tumours using PET imaging following intravenous administration of AH111585 (18F) Injection	Charles Coombes	ICR	Oxford	0
A Phase I clinical research study evaluating the safety, tolerability and biological effects of the chimeric anti-CD40 monoclonal antibody Chi Lob 7/4 given intravenously, weekly for four weeks in the treatment of patients with advanced malignancies refractory to conventional anti-cancer treatment	Dr Anne Thomas	Southampton	Birmingham, Southampton	0
A Phase I Dose-finding Study of E7050 Administered Orally to Patients With Advanced Solid Tumors.	Professor I Judson	ICR	Manchester	0
A Phase I multicentre trial of the combination of olaparib (PARP inhibitor) and AZD5363 (AKT inhibitor) in patients with advanced solid tumours	Prof. Johann de Bono	ICR	ICR	1
A Phase I Study of Oral MK-2206 in Combination With Oral AZD6244 in Patients With Locally Advanced or Metastatic Solid Tumors	Dr Johann De-Bono	ICR	ICR	0
A Phase I trial of ONX-0801 (a novel α-folate receptor-mediated thymidylate synthase inhibitor) exploring once weekly and alternate week dosing regimens in patients with solid tumours	Dr Udai Banerji	ICR	ICR	9
A Phase I Trial of OXi4503 (a Vascular Disrupting Agent) given by 3 x weekly intravenous infusions to patients with advanced solid tumours	Prof Gordon Rustin	UCL	Manchester, Oxford	0
A Phase I trial of RO5126766 (a dual RAF/MEK inhibitor) exploring intermittent, oral dosing regimens in patients with solid tumours or multiple myeloma	Dr Udai Banerji	ICR	ICR	19
A Phase I, Dose Escalation Study of INK1117 in Subjects with Advanced Solid Malignancies Followed by Expansion in Subjects with Measurable Disease	Prof. Johann De-Bono	ICR	ICR	6
A Phase I, Open Label, Multicentre Study to Assess the Safety, Tolerability, Pharmacokinetics and Preliminary Efficacy of the mTor Kinase Inhibitor AZD2014 Administered Orally to Patients With Advanced Solid Malignancies	Dr U Banergee	ICR	ICR, Manchester	47
A Phase I, Open-Label, Multicentre Study to Assess the Safety, Tolerability, Pharmacokinetics and Preliminary Anti-tumour Activity of Ascending Doses of AZD5363 in Patients with Advanced Solid Malignancies	Dr Udai Banerji	ICR	ICR, Manchester	15
A Phase I, Pharmacokinetic and Biological Evaluation of a Small Molecule Inhibitor of Poly ADP-Ribose Polymerase-1 (PARP-1), KU-0059436, in Patients With Advanced Tumours.	Prof Johann De-Bono	ICR	ICR	0
A Phase I/II Dose Finding and Efficacy Study of the Tumour Targeting Human 131I-F16SIP Monoclonal Antibody in Patients With Cancer	Tim Meyer	UCL	UCL	0
A Phase I/II Study of BEZ235 in Patients With Advanced Solid Malignancies Enriched by Patients With Advanced Breast Cancer	Prof M Ranson	Manchester	Manchester	0
A Phase I/II trial of Anti-CEA DNA vaccine (ACVA) with a CEA/pDom fusion gene given by intramuscular injection in patients with carcinomas expressing CEA	Prof Christian Ottensmeier	Southampton	Edinburgh, Southampton	14
A Phase I/IIa trial of AZD4547 in combination with Cisplatin and Capecitabine (CX)	Prof T R J Evans	Glasgow	Barts, Belfast, Glasgow, Leicester, Manchester, Oxford	15

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
A Phase I/IIa, First Time in Human, open-label dose-escalation study of GSK2636771 in subjects with advanced solid tumors with PTEN deficiency	Prof Johann De-Bono	ICR	ICR	0
A Phase I/IIa, First Time in Human, Study of GSK2636771 in Subjects With Advanced Solid Tumors With Phosphatase and Tensin Homolog (PTEN) Deficiency	Dr Johann De-Bono	ICR	ICR	4
A Phase Ib Study of MEK162 Plus BYL719 in Adult Patients With Selected Advanced Solid Tumors	Dr Johann De-Bono	ICR	ICR	10
A Safety and Dose-finding Study of JNJ-26481585 for Patients With Advanced Solid Malignancies and Lymphoma.	Dr Johann de Bono	ICR	Manchester, UCL	0
A single centre study of the effects of different treatments on the trafficking of adoptively transferred lymphocytes to tumours in cancer patients	Alan Melcher	Leeds	Leeds	1
A Study Evaluating Intermittent and Continuous OSI-906 and Weekly Paclitaxel in Patients With Recurrent Epithelial Ovarian Cancer (and Other Solid Tumors)	Professor Stanley Kaye	ICR	Manchester, Oxford, UCL	0
A Study of BYL719 in Adult Patients With Advanced Solid Malignancies, Whose Tumors Have an Alteration of the PIK3CA Gene	Prof Mark Middleton	Oxford	Oxford	4
A Study of Capecitabine Rapid Disintegrating Tablets (RDT) Versus Commercial Xeloda in Patients With Solid Tumours	CJ Twelves	Leeds	Leeds, Newcastle, UCL	5
A Study of MEK162 and AMG 479 in Patients With Selected Solid Tumors	Dr Udai Banerji	ICR	ICR	8
A Study of Oral Rucaparib in Patients With a Solid Tumor (Phase I) or With gBRCA Mutation Ovarian Cancer (Phase II)	Dr Rebecca Kristeleit	UCL	UCL	7
A Study Of PF-05212384 In Combination With Other Anti-Tumor Agents	Prof Johann De Bono	ICR	ICR, Oxford, UCL	0
A Study of RO6895882 in Patients With Advanced and/or Metastatic Solid Tumors	Prof Mark Middleton	Oxford	Oxford	
A Study to Test Safety and Efficacy of IMGN901 in Combination With Carboplatin/Etoposide in Patients With Advanced Solid Tumors and Extensive Stage Small Cell Lung Cancer	Dr Paul Lorigan	Manchester	Brighton, Manchester, UCL	4
A two-part study to evaluate the effect of repeat oral dosing of GSK2118436 on cardiac repolarization in subjects with V600 BRAF mutation-positive tumours: an open-label, dose-escalation safety lead-in study followed by a single-sequence, placebo-controlled, single-blind study	Dr T Arkenau		Oxford	
An Open Label, Dose-escalation Study to Evaluate Safety, Pharmacokinetics and Tumor Growth Control Rate of RO5083945, a Glycoengineered Antibody Against EGFR, in Patients With Metastatic and/or Locally Advanced Malignant EGFR+ Solid Tumors.	Alexander Passioukove - Roche, see notes	KCL	KCL	143
An Open-label Pharmacokinetic and Safety Study of Cabazitaxel in Patients With Solid Tumors With Moderately and Severely Impaired and With Normal Renal Function	Dr Richard Baird	Cambridge	Cambridge, Newcastle	0
An Open-Label Study of BAL101553 in Adult Patients With Solid Tumors	Dr Rebecca Kristeleit	UCL	ICR, Newcastle, UCL	6
An Open-label, Dose Escalation, Pharmacodynamic, Pharmacokinetic, and Effect of Food Phase 1 Study of E7820, Administered as a Once Daily and Twice Daily Oral Dose to Determine the Maximum Tolerated Dose in Subjects with Un-resectable Solid Tumors	Dr Jeff Evans	Glasgow	Glasgow, Manchester, Newcastle, UCL	0
An Open-label, Multicenter, Multiple Dose, Phase 1 Study to Establish the Maximum Tolerated Dose of E7389 Liposomal Formulation in Patients With Solid Tumors	Malcolm Ransom	Manchester	Glasgow, ICR, Manchester, UCL	17
An Open-label, Non-randomised, Multicentre, Comparative, Phase I Study to Determine the Pharmacokinetics, Safety and Tolerability of Olaparib Following a Single Oral 300 mg Dose to Patients With Advanced Solid Tumours and Normal Hepatic Function or Mild or Moderate Hepatic Impairment	Dr Elizabeth Ruth Plummer	Newcastle	ICR, UCL	0
An Open-Label, Phase I, Dose-Escalation Study Evaluating The Safety And Tolerability Of Gdc-0980 Administered Once Weekly In Patients With Refractory Solid Tumors Or Non-Hodgkin's Lymphoma	Professor G Jayson	Manchester	Manchester	0
An Open-label, Phase I, Dose-Escalation Study Evaluating the Safety, Tolerability, and Maximally Tolerated Dose of GDC-0980 Administered Once Daily in Patients With Refractory Solid Tumors and Non-Hodgkin's Lymphoma	Dr Johann De-Bono	ICR	ICR	1
An Open-Label, Phase I, Dose-Escalation Study Evaluating Two Dosing Schedules of PI3-Kinase Inhibitor (GDC-0941) in Patients With Locally Advanced or Metastatic Solid Tumors for Which Standard Therapy Either Does Not Exist or Has Proven Ineffective or Intolerable	Dr Johann De-Bono	ICR	ICR	0
Assessment Of The Ability For Circulating Markers Of Cell Death, DNA Methylation Status And Proteomic/Metabonomic Fingerprints To Predict Clinical Response To Conventional Chemotherapeutic Agents	Professor M Ranson	Manchester	Manchester	0

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
AUY922 + Lapatinib	Dr Udai Banerji	ICR	ICR	
AZD8186 First Time In Patient Ascending Dose Study	Dr Udai Banerji	ICR	ICR	3
CREATE: Cross-tumoral Phase 2 With Crizotinib	Dr Sandra Strauss	UCL	Leeds, Manchester	4
DDU BRAF	Dr Udai Banerji	ICR	ICR	
Dose Escalation Study of LTX-315 in Patients With Transdermally Accessible Tumours	Dr James Spicer	KCL	KCL	1
Dose Finding Study of RAD001 (Everolimus, AfinitorÂ®) in Combination With BEZ235 in Patients With Advanced Solid Tumors	Prof Ruth Plummer	Newcastle	Newcastle	1
Efficacy of Gelclair in reducing the pain of oral mucositis in children and young people with cancer	Dr Faith Gibson	UCL	UCL	0
Global Phase1 Study to Assess the Safety and Tolerability of AZD1208 in Advanced Solid Tumors and Malignant Lymphoma	Ranson, Professor M	Manchester	ICR, Manchester	19
HuMaxÂ®-TF-ADC Safety Study in Patients With Solid Tumors	Prof Johann De Bono	ICR	ICR	3
MAD in Cancer Patients: Safety of BMS-582664 in Patients With Advanced or Metastatic Solid Tumors	Professor G Jayson	Manchester	Manchester	0
Mechanisms and consequences of tyrosine kinase activation in chronic myeloproliferative disorders and related conditions	Prof Tim Maughan	Southampton	Southampton	5
MSB0010718C in Solid Tumors	Rebecca Roylance	Barts/Brighton	Barts	
Non-Invasive Assessment of the Temporal Relationship between Microvascular Heterogeneity and Tumour Growth - Phase I: Evaluation of oxygen enhanced magnetic resonance imaging of the abdomen and pelvis as a potential biomarker in human tissue and solid tum	Professor G Jayson	Manchester	Manchester	0
Non-invasive assessment of the temporal relationship between microvascular heterogeneity and tumour growth: Phase II: Evaluation of heterogeneity in solid tumours with magnetic resonance imaging (Part 2 of study 05_RADIO_46)	Professor G Jayson	Manchester	Manchester	0
NUC-1031 in Patients With Advanced Solid Tumours	Dr Sarah Blagden	Imperial	Imperial	32
Pharmacokinetics and pharmacogenetics of anticancer drugs in infants and young children	Dr Gareth Veal	Newcastle	UCL	0
Pharmacokinetics of actinomycin D in children with cancer	Dr Gareth Veal	Newcastle	UCL	0
Phase 1 Trial of CXD101 in Patients With Advanced Cancer	Prof M Middleton	Oxford	Oxford	2
Phase I Clinical Trial of CXR 1002 in Patients with Advanced Cancer	Prof T R J Evans	Glasgow	Glasgow	0
Phase I Dose Escalation Study of VS-5584 in Subjects With Advanced Non-Hematologic Malignancies or Lymphoma	Dr Udai Banerji	IICR	ICR	1
Phase I Multicenter, Open-label, Clinical and Pharmacokinetic Study of Lurbinectidine (PM01183) in Combination with Cisplatin in Patients with Advanced Solid Tumors	Dr. Martin Forster	UCL	UCL	
Phase I Multicenter, Open-label, Clinical and Pharmacokinetic Study of PM01183 in Combination With Doxorubicin in Non-heavily Pretreated Patients With Selected Advanced Solid Tumors	Dr Martin Forster	UCL	UCL	0
Phase I Multicenter, Open-label, Clinical and Pharmacokinetic Study of PM01183 in Combination With Gemcitabine in Non-heavily Pretreated Patients With Selected Advanced Solid Tumors	Dr Martin Forster	UCL	UCL	3
Phase I Study LJM716 Combined With Trastuzumab in Patients With HER2 Overexpressing Metastatic Breast or Gastric Cancer	Kong, Dr Anthony	Oxford	Oxford	3
Phase I study of MOv18, a first in class chimaeric IgE antibody against folate receptor-a, in patients with advanced solid tumours	Dr James Spicer		UCL	
Phase I study of oral PQR309 in Patients with Advanced Solid Tumours	Dr. Rebecca Kristeleit	UCL	UCL	1
Phase I Study of WX-037 Alone and in Combination With WX-554 in Solid Tumours	Dr Udai Banerji	ICR	ICR, KCL	10
Phase I/II Dose-escalation Study to Investigate Safety and Pharmacokinetics/ Pharmacodynamics of WX-554 in Patients With Solid Tumours	Dr Ruth Plummer	Newcastle	Belfast, Glasgow, Leeds, Manchester, Newcastle	16
Phase IB Study of MK-3475 in Subjects With Select Advanced Solid Tumors	Dr. Rhoda Molife	ICR	ICR	
Phase Ib, Dose Escalation Study of Oral LDE225 in Combination With BKM120 in Patients With Advanced Solid Tumors	Dr Udai Banerji	ICR	Glasgow, ICR	12

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
Phase II single arm studies of Gemcitabine in combination with Oxaliplatin in refractory and relapsed pediatric solid tumors.	Dr Julia Chisholm	UCL	UCL	0
Phase II Study of Brivanib (BMS-582664) to Treat Multiple Tumor Types	Stan Kaye	ICR	Glasgow	0
Safety Profile, MTD, and PK Profile Studies of ABT-263 When Administered in Combination With Standard and Weekly Regimens of Docetaxel in Subjects With Cancer	Dr Rhoda Molife	ICR	ICR	0
Study is Designed to Assess the Safety and Tolerability of AZD4547 at Increasing Doses in Patients With Advanced Tumours	Malcolm Ransom	Manchester	Edinburgh, Glasgow, Imperial, Manchester, Newcastle	1
Study of a Focal Adhesion Kinase Inhibitor in Subjects With Solid Tumors	Dr Sarah Blagden	Imperial	Glasgow, Imperial, Manchester, Newcastle, UCL	0
Study of AR-12 (2-Amino-N-[4-[5-(2 Phenanthrenyl)-3-(Trifluoromethyl)-1H-pyrazol-1-yl] Phenyl]-Acetamide) in Adult Patients With Advanced or Recurrent Solid Tumors or Lymphoma	Dr Johann De-Bono	ICR	ICR	0
Study of BMN 673, a PARP Inhibitor, in Patients With Advanced or Recurrent Solid Tumors	Prof. Johann De-Bono	ICR	ICR	10
Study of CEP-9722 as Single-Agent Therapy and as Combination Therapy With Temozolomide in Patients With Advanced Solid Tumors	Prof. Ruth Plummer	Newcastle	Newcastle	0
Study of CH5132799 Administered Orally in Patients With Advanced Solid Tumors	Dr Udai Banerji	ICR	ICR, KCL, Leeds	0
Study of Oral OSI-027 in Patients With Advanced Solid Tumors or Lymphoma	Prof. Stan Kaye	ICR	ICR	0
Study of PF-05212384 (Also Known as PKI-587)Administered Intravenously To Subjects With Solid Tumors	James Spicer	KCL	KCL	0
Study of Safety and Pharmacokinetics of MK-8242 in Participants With Advanced Solid Tumors (P07650)	Dr Udai Banerji	ICR	ICR	2
Study of the Effect of Rifampicin on the Pharmacokinetics (PK) of Multiple Doses of Cediranib in Patients With Solid Tumours	James Spicer	KCL	UCL	0
Study to Assess Safety & Tolerability of AZD2281 in Combination With Bevacizumab in Patients With Advanced Solid Tumours	Dr M Ranson	Manchester	Manchester, Oxford	0
Study to Assess Safety, Pharmacokinetics, and Efficacy of Oral CC-223 for Patients With Advanced Solid Tumors, Non-Hodgkin Lymphoma or Multiple Myeloma	Dr Tim Meyer	UCL	UCL	3
Study to Assess the Blood Levels and Safety of Olaparib in Patients With Advanced Solid Tumours and Normal or Impaired Kidney Function	Dr Rhoda Molife	Newcastle	ICR, Newcastle	0
Systemic Treatment of Resistant Metastatic Disease	H Phanda	Guilford	Leeds	1
TAX-TORC: A Phase I multi-centre trial of the combination of AZD2014 (dual TORC1 and TORC2 inhibitor) and weekly paclitaxel in patients with solid tumours	Dr Udai Banerji	ICR	Cambridge, ICR	15
Trial Exploring Afatinib (BIBW 2992) + Paclitaxel (Part A), Afatinib + Paclitaxel + Bevacizumab (Part B), Afatinib + Carboplatin (Part C) and Afatinib+ Paclitaxel +Carboplatin(Part D) in Patients With Advanced Solid Tumours	Dr Johann de Bono	ICR	KCL	9
Trial to Determine MTD of BI 836845 Administered Intravenously Once Every Three Weeks in Patients With Advanced Solid Tumours and Later a Weekly Dosing Schedule in Selected Tumour Types	Prof. Johann De-Bono	ICR	ICR, Leeds	16
Validation of Quantitative Biomarkers Derived from Magnetic Resonance Imaging in Patients with Cancer prior to their use in Studies - QuIBs	Jackson, Professor Alan	Manchester	Manchester	0
Biliary Tract				
Novel markers for the detection of dysplasia and malignancy and disease-specific immune responses in inflammatory and malignant hepatopancreatobiliary disorders	Dr Steve Pereira	UCL	UCL	
Bladder				
A Phase II multi-center, non-randomized, open-label study of TKI258 in patients with either FGFR3 mutated or FGFR3 wild type advanced urothelial carcinoma	Prof John Chester	Leeds	Southampton	0
A Phase II, Open Label, Multicenter Randomised Controlled Trial Comparing Hyperthermia Plus Mitomycin To Mitomycin Alone, In Patients with Intermediate Risk Non-Muscle Invasive Bladder Cancer.	Mr Paul Cathcart	Barts/Brighton	Barts	

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
Eribulin Mesylate Administered in Combination With Gemcitabine Plus Cisplatin Versus Gemcitabine Plus Cisplatin Alone as First-Line Therapy for Locally Advanced or Metastatic Bladder Cancer	Dr Stephen Nicholson	Leicester	Leicester, Manchester, Southampton	2
FGFR Inhibition for Epithelial Solid Tumours: a Phase Ib trial of AZD4547 in combination with gemcitabine and cisplatin	Prof John Chester	Cardiff	Cardiff, Glasgow, Leeds, Southampton	24
Phase II randomised placebo controlled NEOadjuvant chemotherapy study of Nintedanib with Gemcitabine and Cisplatin in locally advanced muscle invasive BLADder cancEr	Dr Syed Hussain		Birmingham	
Blood				
A Phase 1b/II, open-label, multi-center, dose-finding study to assess safety and efficacy of the oral combination of LDE225 and ruxolitinib (INC424) in patients with myelofibrosis.	Prof Claire Harrison	KCL	KCL	0
A phase Ib/IIb, open-label, multi-center, study of oral Panobinostat (LBH589) administered with 5-Azacitidine (Vidaza®) in adult patients with myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia (CMML) or acute myeloid leukemia (AML)	Dr Jamie Cavenagh	Barts/Brighton	Barts	0
A RandoMised study of best Available therapy versus JAK Inhibition in patients with high risk Polycythaemia Vera or Essential Thrombocythaemia who are resistant or intolerant to HydroxyCarbamide	Dr Claire Harrison	KCL	Barts, Belfast, Leicester, Manchester, Southampton	9
A Two-part Study to Assess the Safety and Preliminary Efficacy of Givinostat in Patients With Polycythemia Vera	Professor Mary Frances McMullin	Belfast	Belfast	
Phase II, Open Label, Single Arm Study of SAR302503 In Myelofibrosis Patients Previously Treated With Ruxolitinib	Prof Claire Harrison	KCL	KCL	2
Bone				
A Mechanistic Study Of Mifamurtide (MTPPE) In Patients With Metastatic And/Or Recurrent Osteosarcoma	Dr Andrew Bassim Hassan	Oxford	Oxford	
A phase I/II study of a combination of the PARP inhibitor, niraparib and temozolomide in patients with previously treated, incurable Ewing's Sarcoma			UCL	
A Randomized Phase II, Open-Label study of the Efficacy and Safety of Orally Administered SAR302503 in patients with polycythemia vera (PV) or essential thrombocythemia (ET) who are resistant or intolerant to hydroxyurea	Dr Claire Harrison	KCL	Belfast, Glasgow, KCL	0
A single centre, double-blind, randomised, crossover, phase II study to investigate the efficacy and safety of glucarpidase for routine use after high dose methotrexate in patients with bone sarcoma	Dr Jeremy Whelan	UCL	UCL	30
Phase II trial of Linsitinib (anti-IGFR/IR) in patients with relapsed and/or refractory Ewing Sarcoma	Dr Andrew Bassim Hassan	Oxford	Oxford	0
Brain and Nervous System				
A Cancer Research Uk pharmacokinetic study of BPA in patients with high grade glioma to optimise uptake parameters for clinical trials of BNCT	Professor Garth Cruickshank	Birmingham	Birmingham	0
A Cancer Research UK Phase I trial of IMA950 (a novel multi-peptide vaccine) plus GM-CSF in patients with newly diagnosed glioblastoma	Prof Roy Rampling	Glasgow	Edinburgh, Glasgow, Leeds, Manchester, Southampton, UCL	4
A Cancer Research UK Phase I trial of olaparib (AZD2281), an oral PARP Inhibitor, in combination with extended lowdose oral temozolomide in patients with relapsed glioblastoma	Prof Anthony Chalmers	Glasgow	Cambridge, Edinburgh, ICR, Manchester	13
A clinical study to evaluate the biological effects of preoperative intravenous administration of wild-type reovirus (REOLYSIN®) in patients prior to surgical resection of recurrent high grade primary or metastatic brain tumours	A Melcher	Leeds	Leeds	4
A Phase I Dose Finding and Safety Study of Oral LDE225 in Children and a Phase II Portion to Assess Preliminary Efficacy in Recurrent or Refractory MB	Awaiting information		UCL	
A phase II open-label, randomized, multi-centre comparative study of bevacizumab-based therapy in paediatric patients with newly diagnosed supratentorial high-grade glioma	Dr Darren Hargrave	UCL	UCL	3

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
A Phase IIa trial of 177 Lutetium Dotatate in Children with Primary Refractory or Relapsed High-Risk Neuroblastoma	Dr Mark Gaze	UCL	Birmingham, UCL	0
A Randomized, Phase 2 Study of Single-agent Erlotinib versus Oral Etoposide in Patients with Recurrent or Refractory Pediatric Ependymoma	Dr Stergios Zacharoulis	ICR	UCL	
A study of Concomitant and Prolonged Adjuvant Temozolomide with Radiotherapy in Diffuse Pontine Gliomas	Dr Simon Bailey	Newcastle	UCL	0
A Two Part Study to Assess the Tolerability, Safety and Pharmacodynamics of Sativex in Combination With Dose-intense Temozolomide in Patients With Recurrent Glioblastoma	Dr Susan Short	Leeds	KCL, Leeds, Manchester, UCL	2
An International, Randomized, Open-label Phase I/II Study of Vismodegib in Combination With Temozolomide Versus Temozolomide Alone in Adult Patients With Recurrent or Refractory Medulloblastomas Presenting an Activation of the Sonic Hedgehog (SHH) Pathway	Dr Paul Mulholland	UCL	UCL	
Dendritic cell vaccine immunotherapy in paediatric high grade glioma	Dr J Anderson	UCL	UCL	2
Hyperfractionated accelerated Radiotherapy (HART) with chemotherapy (Cisplatin, CCNU, Vincristine) for non-pineal Supratentorial Primitive Neuroectodermal tumours CNS 2004 01	Dr Frank Saran	ICR	UCL	0
NBT - National Brain Tumour Study	Dr Richard Houlston	ICR	UCL	0
Open Label Trial to Explore Safety of Combining Afatinib (BIBW 2992) and Radiotherapy With or Without Temozolomide in Newly Diagnosed Glioblastoma Multiform	Dr. Michael Brada	ICR	Cambridge, Edinburgh, Manchester	2
Open-label, combined dose-finding and efficacy-finding study of RO5323441 in combination with bevacizumab for patients with recurrent glioblastoma	Dr C Mcbain	Manchester	Manchester	0
Open-label, Phase 2 Study of Single-agent Erlotinib for Patients with Pediatric Ependymoma Previously Treated with Oral Etoposide in Protocol OSI-774-205	Dr Stergios Zacharoulis	ICR	UCL	
Phase I trial of escalating high dose methotrexate supported by glucarpidase to treat patients with primary central nervous system lymphoma (PCNSL)	Dr Rod Johnson		UCL	0
Phase II Study of High-Dose Methotrexate in Children with Residual Ependymoma	Dr Martin English	Birmingham	UCL	0
Radiation therapy and concurrent plus adjuvant Temsirolimus (CCI779) versus chemoirradiation with temozolomide in newly diagnosed glioblastoma without methylation of the MGMT gene promoter - a randomized multicenter, open label, Phase II study	Prof Susan Short	UCL	Edinburgh	0
Research into brain tumour biology and the brain's attempt to contain tumours		Manchester	Manchester	
Breast				
A Cancer Research UK Phase I/II Open Label Study to Evaluate the Activity of Abiraterone Acetate in Oestrogen (ER) or Androgen Receptor (AR) Positive Advanced or Metastatic Breast Carcinoma	Prof Johann De Bono	ICR	Birmingham, Edinburgh, Glasgow, ICR, KCL, UCL	7
A double-blind, randomized, placebo-controlled, Phase I/II Study evaluating the safety, immunogenicity and clinical activity of neoadjuvant treatment with WT1- A10 + AS15 Antigen-Specific Cancer Immunotherapeutic in combination with standard therapy in patients with WT1-positive Stage II or III breast cancer	Mr Mike Dixon	Edinburgh/Dundee	Belfast	
A multicenter randomized phase II study to compare the combination trastuzumab and capecitabine, with or without pertuzumab, in patients with HER2-positive metastatic breast cancer that have progressed after one line of trastuzumab-based therapy in the metastatic setting (PHEREXA)	Dr Peter Canney	Glasgow	Glasgow, Manchester	1
A Multicenter, Open-Label, Phase 2 Study to Evaluate the Safety and Efficacy of NKTR-102 (PEG-Irinotecan) When Given on a Q14 Day or a Q21 Day Schedule in Patients with Metastatic Breast Cancer Whose Disease has Failed Prior Taxane-Based Treatment	Prof Alan Hilary Calvert	Newcastle	Glasgow, Sheffield	0
A phase 1b/2 randomised placebo controlled trial of fulvestrant +/AZD5363 in postmenopausal women with advanced breast cancer previously treated with a third generation aromatase inhibitor.	Sacha Howell	Manchester	Cardiff, Manchester	
A Phase 1b/2 Randomized Study of MEDI-573 in Combination with an Aromatase Inhibitor (AI) Versus AI Alone in Women with Metastatic Breast Cancer (MBC)	Dr Adrian Murray Brunt	Birmingham	Glasgow, Southampton	1

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
A phase 2 single arm study to examine the effects of metformin on cancer metabolism in patients with early stage breast cancer receiving neoadjuvant chemotherapy	Prof Adrian Harris	Oxford	Dundee, Oxford	15
A Phase 2, Multicenter Study of the Effect of the Addition of SNDX-275 to Continued Aromatase Inhibitor (AI) Therapy in Postmenopausal Women With ER+ Breast Cancer Whose Disease is Progressing	Dr A Wardley	Manchester	Manchester, Newcastle, UCL	0
A Phase 2, Single-Arm, Open-Label, Multicenter Study of the Clinical Activity and Safety of Enzalutamide in Patients With Advanced, Androgen Receptor-Positive, Triple-Negative Breast Cancer	Prof Peter Schmid	Barts/Brighton	Brighton, Manchester	
A Phase I trial of the combination of AUY922 (HSP90 inhibitor) and lapatinib in patients with HER2 amplified, metastatic breast cancer	Dr Udai Banerji	ICR	ICR	1
A Phase I/II Multi-centre Study of AZD8931 in Combination with Weekly Paclitaxel to Assess the Safety, Tolerability, Pharmacokinetics and Efficacy in Patients with Advanced Solid Tumours and in a selected population with Low HER2-expressing Locally Recurrent and/or Metastatic Breast Cancer (THYME)	Dr Charles Swanton	UCL	Glasgow	0
A Phase Ib/II Study of BEZ235 and Trastuzumab in Patients With HER2-positive Breast Cancer Who Failed Prior to Trastuzumab	Dr A Wardley	Manchester	Manchester	0
A Phase Ib/II Study of LEE011 in Combination With Fulvestrant and BYL719 or BKM120 in the Treatment of Postmenopausal Women With Hormone Receptor Positive, HER2 Negative Locally Recurrent or Advanced Metastatic Breast Cancer	Dr Samreen Ahmed	Leicester	Leicester	
A phase Ib/II, open label, multi-centre study evaluating the safety and efficacy of BKM120 in combination with trastuzumab in patients with relapsing HER2 overexpressing breast cancer who have previously failed trastuzumab	Dr Steve Chan		Brighton, Oxford	2
A Phase Ib/IIa Trial of Panobinostat in Combination With Trastuzumab in Adult Female Patients With HER2 Positive Metastatic Breast Cancer Whose Disease Has Progressed During or Following Therapy With Trastuzumab		Birmingham	Manchester	
A phase II randomised, placebo controlled study of paclitaxel in combination with Akt inhibitor AZD5363 in triple negative advanced or metastatic breast cancer	Prof Peter Schmid	Barts/Brighton	Barts	
A phase II study of estradiol therapy in post-menopausal women with ER/PR positive advanced breast cancer after progression on third generation aromatase inhibitors	Dr Andrew Wardley	Manchester	Manchester	0
A Phase II study to assess the safety and efficacy of the steroid sulfatase inhibitor Irosustat when added to an aromatase inhibitor in ER positive locally advanced or metastatic breast cancer patients.	Dr Carlo Palmieri	Imperial	Edinburgh, Glasgow, Imperial, Manchester	17
A phase II study to evaluate the efficacy and safety of pertuzumab in combination with trastuzumab for the neo-adjuvant Treatment of Patients with early-stage HER 2 Positive Breast Cancer	Dr A Wardley	Manchester	Manchester	0
A phase II trial examining the feasability of treatment with weekly Nab-Paclitaxel in women aged 70 or over with advanced breast cancer	Dr Alastair Ring	Barts/Brighton	Barts	
A Phase II, multi-center, open-label, neoadjuvant, randomized study of weekly paclitaxel with or without LCL161 in patients with triple negative breast cancer	Prof Peter Schmid	Barts/Brighton	Brighton	0
A phase II, open-label, non-comparative, international, multicentre study to assess the efficacy and safety of KU 0059436 given orally twice daily in patients with metastatic BRCA1 or BRCA2-associated breast cancer	Dr Andrew Tutt	KCL	Manchester	0
A Phase II, Randomised, Double-Blind, Placebo-Controlled, Multi-Centre Study Of AZD8931 In Combination With Anastrozole in Postmenopausal Women With Hormone Receptor-Positive, Endocrine Therapy-Naive, Locally-Advanced or Metastatic Breast Cancer (MINT)	Prof Stephen Johnston	ICR	Leicester	0
A PHASE II, RANDOMIZED STUDY OF PACLITAXEL WITH GDC-0941 VERSUS PACLITAXEL WITH PLACEBO IN PATIENTS WITH LOCALLY RECURRENT OR METASTATIC BREAST CANCER	Prof Peter Schmid	Barts/Brighton	Barts, Brighton, Leicester	11
A Randomised Double-blind Phase IIa Study (with Combination Safety Run-in) to Assess the Safety and Efficacy of AZD4547 in Combination with Fulvestrant vs. Fulvestrant Alone in ER+ Breast Cancer Patients with FGFR1 Polysomy or Gene Amplification Who Have Progressed Following Treatment with Prior Endocrine Therapy (Adjuvant or First-line Metastatic)	Dr Nick Turner	ICR	Imperial, Manchester, Oxford	7
A randomised phase II screening trial with functional imaging and patient reported toxicity sub-studies comparing LApatiNib plus capecitabine versus continued Trastuzumab plus capecitabine after local therapy in patients with ERb B2 positive metastatic breast cancer developing braiN metastasis /es	Prof David Dodwell	Leeds	Glasgow, Leeds, Manchester, Sheffield, Southampton	4
A Randomised Phase II study of Oral Vinorelbine or I.V. Vinorelbine in patients with metastatic breast cancer previously treated with anthracyclines	Dr Andreas Makris		Manchester	0

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
A Randomized Phase II Study of Fulvestrant in Combination with the dual mTOR Inhibitor AZD2014 or Everolimus or Fulvestrant alone in Estrogen ReceptorPositive Advanced or Metastatic Breast Cancer	Prof Peter Schmid	Barts/Brighton	Barts, Brighton, Birmingham, UCL	0
A Randomized, 4-Arm, Placebo-Controlled Phase 2 Trial of AMG 386 in Combination With Bevacizumab and Paclitaxel or AMG 386 Plus Paclitaxel as First-Line Therapy in Subjects With Her2-Negative, Metastatic or Locally Recurrent Breast Cancer	Dr C Armstrong		Manchester, UCL	0
A randomized, multicenter, open-label Phase II trial investigating pertuzumab and trastuzumab plus an aromatase inhibitor in first-line patients with hormone receptor- and HER2-positive metastatic breast cancer	Prof Peter Schmid	Barts/Brighton	Brighton, Sheffield	4
A Randomized, Multicenter, Phase ii Study of the Efficacy and Safety of Trastuzumab-MCC-DM1 vs. Trastuzumab (Herceptin®) and Docetaxel (Taxotere®) in Patients With Metastatic HER2-positive Breast Cancer Who Have Not Received Prior Chemotherapy for Metastatic Disease			Manchester	
A Study of the Experimental Drug BKM120 With Paclitaxel in Patients With HER2 Negative, Locally Advanced or Metastatic Breast Cancer, With or Without PI3K Activation	Dr Iain Macpherson		Glasgow	2
A Study to Assess the Ability of a Novel Endocrine Treatment for Breast Cancer, Irosustat, to Slow Down Cancer Growth	Dr Carlo Palmieri	Imperial	Imperial	6
A study to identify biomarkers which offer a lead interval between predicted relapse and overt disease in post-operative, post-treatment breast cancer patients	Prof R Charles Coombes	Imperial	Imperial	2
A study to measure in vivo changes in oestrogen receptor DNA binding events in breast cancer treated with endocrine therapy for primary or recurrent breast cancer (VERB Study).	Dr Carlo Palmieri	Imperial	Imperial	0
Afatinib (BIBW2992) in HER2-overexpressing Inflammatory Breast Cancer	Charles Swanson	UCL	UCL	0
An exploratory phase II, single arm, multicenter study to evaluate the efficacy and safety of the combination of pertuzumab and Herceptin® (trastuzumab) in patients with HER2-positive metastatic breast cancer.	Dr A Wardley	Manchester	Manchester	0
AN OPEN LABEL MULTICENTER PHASE 2 WINDOW OF OPPORTUNITY STUDY EVALUATING GANETESPIB (STA-9090) MONOTHERAPY IN WOMEN WITH PREVIOUSLY UNTREATED METASTATIC HER2 POSITIVE OR TRIPLE NEGATIVE BREAST CANCER	Prof David Cameron	Edinburgh/Dundee	Edinburgh, Glasgow, Oxford	2
An Open-label Phase IIa, Non-randomized Study of Alpharadin® in Breast Cancer Patients With Bone Dominant Disease no Longer Considered Suitable for Endocrine Therapy	Prof R Coleman	Sheffield	Sheffield	0
Breast Cancer Stem Cells, Therapeutic Resistance And New Approaches To Therapy	Dr S Howell	Manchester	Manchester	0
Combination of AUY922 With Trastuzumab in HER2+ Advanced Breast Cancer Patients Previously Treated With Trastuzumab	Dr Karla Martins		Birmingham, Leicester, Manchester, Oxford	0
In vivo Evaluation of Terahertz Pulse Imaging of Breast Cancer and Sentinel Lymph Nodes.	Prof Anand David Purushotham	KCL	KCL	0
Investigating the Biological Effects of the Addition of Zoledronic Acid to Pre-operative Chemotherapy in Breast Cancer	Prof R Coleman	Sheffield	Sheffield	0
Molecular Markers of Breast Tumours	Peter Schmid	Barts/Brighton	Brighton	35
Non -invasive detection of Sentinel Lymph Nodes in Breast Cancer	Mr Michael Douek	KCL	KCL	0
Optimal Personalised Treatment of early breast cancer using Multiparameter Analysis	Dr Rob Stein	UCL	Barts, Edinburgh, Manchester	10
PDT using ALA activated by red or green light to eradicate dysplasia in Barrett's Columnar Lined Oesophagus		UCL	UCL	
PHASE 1/2, OPEN-LABEL, RANDOMIZED STUDY OF THE SAFETY, EFFICACY, AND PHARMACOKINETICS OF LETROZOLE PLUS PD 0332991 (ORAL CDK 4/6 INHIBITOR) AND LETROZOLE SINGLE AGENT FOR THE FIRST-LINE TREATMENT OF ER POSITIVE, HER2 NEGATIVE ADVANCED BREAST CANCER IN POSTMENOPAUSAL WOMEN	Prof David Cameron	Kent Oncology Centre	UCL	0
Phase I study: evaluation of MRI during neoadjuvant chemotherapy in breast cancer-treatment	Dr Andreas Makris	UCL	UCL	0
Post-operative Radiotherapy In Minimum-risk Elderly Phase II	Dr Ian Kunkler	Edinburgh/Dundee	Southampton	0
Randomised phase II window study of short term preoperative treatment with the PI3K inhibitor GDC0941 plus Anastrozole versus Anastrozole alone in patients with ERpositive primary breast cancer	Prof Peter Schmid	Barts/Brighton	Barts, Brighton, Dundee, KCL, Sheffield	23

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
Randomized, Open-Label Study of Abiraterone Acetate (JNJ 212082) Alone or in Combination with Exemestane in Postmenopausal Women with ER+ Metastatic Breast Cancer Progressing during or after Letrozole or Anastrozole Therapy	Dr Andreas Makris	UCL	Sheffield	1
Short term biological effects of Zoledronate and Letrozole on invasive breast cancer (pre-operative study)	Prof Nigel Bundred	Manchester	Edinburgh, Sheffield	0
Study Evaluating the Safety and Efficacy of Onartuzumab (Metmab) And/Or Bevacizumab in Combination With Paclitaxel in Patients With Metastatic, Triple Negative Breast Cancer	Dr Peter Schmid	Barts/Brighton	Brighton, Manchester	2
Study of GDC-0941 or GDC-0980 With Fulvestrant Versus Fulvestrant in Advanced or Metastatic Breast Cancer in Patients Resistant to Aromatase Inhibitor Therapy	Alison Jones	UCL	Brighton	10
The short term effects of an AKT inhibitor (AZD5363) on biomarkers of the AKT pathway and antitumour activity in a breast cancer paired biopsy study (STAKT Trial)	Dr John Robertson	Edinburgh/Dundee	Birmingham, Dundee, Leeds, Leicester	0
Use of NT-PRO BNP as a biomarker for cardiac failure in Breast Cancer patients on long-term Trastuzumab	Richard Simcock	Barts/Brighton	Brighton	5
Cervix				
A Phase II Study of Docetaxel and Gemcitabine as Second Line Chemotherapy in Cervical Cancer	Dr Paul Symonds	Leicester	Barts, Manchester	0
Colorectal				
A Clinical Study Of ColoAd1 Administered by Sub-Acute Fractionated Intravenous Injection: Dose Escalation in Metastatic Epithelial Solid Tumours and Randomised Controlled Trial in Metastatic Colorectal Cancer	Dr Rebecca Kristeleit	UCL	UCL	0
A dose finding study evaluating the safety and tolerability of Capecitabine and Aflibercept in patients with unresectable metastatic colorectal cancer deemed unsuitable for doublet/ triplet chemotherapy	Dr Paul Ross	KCL	KCL, Manchester, UCL	1
A Multicenter, Open-Label, Randomized, Phase 2 Study to Evaluate the Efficacy and Safety of NKTR-102 Versus Irinotecan in Patients With Second-Line, Irinotecan-Naive, KRAS-Mutant, Metastatic Colorectal Cancer (mCRC)			Manchester	
A multicentre randomised phase II clinical trial comparing oxaliplatin (Eloxatin), capecitabine (Xeloda) and pre-operative radiotherapy with or without cetuximab followed by total mesorectal excision for the treatment of patients with magnetic resonance imaging (MRI) defined high risk rectal cancer	Prof David Cunningham	ICR	Southampton	0
A multicentre randomized phase II study to assess the safety and resectability in patients with primarily unresectable liver metastases secondary to colorectal cancer receiving 1st line treatment either with mFOLFOX-6 plus bevacizumab or FOLFOXIRI plus bevacizumab	Professor Graeme Poston	Liverpool	Manchester, UCL	0
A Multinational, Randomized, Double-blind Study, Comparing the Efficacy of Aflibercept Once Every 2 Weeks Versus Placebo in Patients With Metastatic Colorectal Cancer (MCRC) Treated With Irinotecan / 5-FU Combination (FOLFIRI) After Failure of an Oxaliplatin Based Regimen	Dr Juan Walle	Manchester	KCL	0
A PHASE 1 STUDY OF SU011248 IN COMBINATION WITH FOLFIRI (IRINOTECAN, 5-FLUOROURACIL AND LEUCOVORIN) IN PATIENTS WITH METASTATIC COLORECTAL CANCER	Professor David Cunningham	ICR	Manchester, Southampton	0
A PHASE 2 OPEN-LABEL RANDOMISED, TRIAL OF CS-1008 IN COMBINATION WITH IRINOTECAN VS IRINOTECAN ALONE IN SUBJECTS WITH METASTATIC COLORECTAL CARCINOMA WHO FAILED FIRST LINE OXALIPLATIN BASED CHEMOTHERAPY	Dr R Midgley	Oxford	Oxford	0
A Phase 2 Study of EZN-2208 (PEG-SN38) Administered With or Without Cetuximab in Patients with Metastatic Colorectal Carcinoma (mCRC)	Prof David Cunningham	ICR	Edinburgh, Glasgow, Manchester	0
A Phase 2, Open Label, Multicenter, Randomized Trial Comparing Tivozanib in Combination with mFOLFOX6 with Bevacizumab in Combination with mFOLFOX6 in Stage IV Metastatic Colorectal Cancer (mCRC) Subjects	Dr Hugo Ford	Cambridge	Glasgow, Manchester, UCL	10
A Phase 2b, Double-Blind, Randomized Study Evaluating the Efficacy and Safety of Sorafenib Compared with Placebo When Administered in Combination with Chemotherapy (Modified FOLFOX6) for the Treatment of Metastatic Colorectal Cancer in Subjects Who Have Not Been Previously Treated for Stage IV disease	Mr Jim Cassidy	Glasgow	Manchester	0
A phase I / II study evaluating the use of concurrent irinotecan, oxaliplatin and UFT in the first line treatment of patients with metastatic colorectal cancer	Dr M Saunders	Manchester	Manchester	0

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
A phase I/IIa study combining curcumin (Curcumin C3 Complex, Sabinsa) with standard care FOLFOX chemotherapy in patients with inoperable colorectal cancer	Prof William Steward	Leicester	Leicester	13
A PHASE II DOUBLE BLIND, RANDOMISED CONTROLLED TRIAL OF VEGF INHIBITOR AXITINIB MONOTHERAPY WITH EARLY DYNAMIC CONRAST ENHANCED ULTRASOUND MONITORING IN CHEMOREFRACTORY THIRD LINE METASTATIC COLORECTAL CANCER	Dr Harpreet Wasan	Imperial	Imperial	16
A Phase II Study Evaluating the Use of Concurrent Cetuximab, Irinotecan, Oxaliplatin and UFT in the First Line Treatment of Patients With Metastatic Colorectal Cancer	Dr M Saunders	Manchester	Belfast, Manchester	0
A PHASE II, MULTICENTER, OPEN-LABEL, RANDOMIZED STUDY EVALUATING THE EFFICACY AND SAFETY OF FOLFIRI + MEHD7945A VERSUS FOLFIRI + CETUXIMAB IN SECOND LINE IN PATIENTS WITH KRAS WILD-TYPE METASTATIC COLORECTAL CANCER	Dr John Bridgewater		Oxford, UCL	4
A Phase IIA Open Label, Adaptive, Randomized Clinical Trial of Dalotuzumab (MK-0646) Treatment in Combination with Irinotecan versus Cetuximab and Irinotecan for Patients with Metastatic Rectal Cancers (mRC) Expressing High IGF-1/Low IGF-2 Levels	Dr David Watkins	ICR	UCL	0
A Phase1b/11 study of MEK1/2 inhibitor PD-032255901 with cMET inhibitor PF -02341066 in KRASMT and KRASWT Colorectal Cancer patients	Dr. Richard Wilson and Professor Mark Middleton	Oxford	Cardiff	
A pilot study to assess the effect of regulatory T cell depletion on 5T4- containing MVA (TroVax) vaccination in patients with inoperable metastatic colorectal cancer	Dr Andrew Godkin	Cardiff	Cardiff	14
A Randomised Double Blind Placebo-Controlled Clinical Trial Of a Single Oral Cholecalciferol Treatment Against Surrogate End Point Biomarkers (SEBs) In Colon Cancer (CRC) Patients	Professor Charles Campbell/Dr Richard Wilson	Belfast	Belfast	9
A Randomized, Phase 1b/2 Trial of AMG 102 or AMG 479 in Combination With Panitumumab Versus Panitumumab Alone in Subject With Wild-Type KRAS Metastatic Colorectal Cancer	Dr John Bridgewater	ICR	UCL	0
A Study of RO5083945 in Combination With FOLFIRI Versus FOLFIRI Plus Cetuximab or FOLFIRI Alone as Second Line Treatment in Patients With Metastatic Colorectal Cancer	Professor James Cassidy	Glasgow	Belfast, Glasgow, KCL, UCL	0
A two-arm phase II randomised trial of intermittent chemotherapy plus continuous cetuximab and of intermittent chemotherapy plus intermittent cetuximab in first line treatment of patients with K-ras-normal (wild-type) metastatic colorectal cancer	Dr Harpreet Wasan	Imperial	Sheffield	0
An open label, multicenter Phase 1-2 study to investigate the effectiveness, safety and immunogenicity of a monotherapy with intradermal IMA910 plus GM-CSF following pre-treatment with low-dose cyclophosphamide in advanced colorectal carcinoma patients who have successfully completed a 12 week first-line treatment with oxaliplatin-based chemotherapy	Dr Charles Wilson	Cardiff	Cambridge, Oxford	0
An open label, partially randomised Phase II trial to investigate the efficacy and safety of BIBW 2992 in patients with metastatic colorectal cancer who never received prior anti-EGFR treatment	Dr Tamas Hickish	bournemouth	Barts, Glasgow, Manchester, Sheffield, Southampton	0
An Open-Label, Pharmacokinetic Study of the Safety and Tolerability of Pazopanib in Combination With FOLFOX 6 orCapeOx in Subjects With Colorectal Cancer	Prof M Middleton	Oxford	Oxford	0
An open-label, randomized, controlled, multi-center, Phase I/II trial investigating 2 EMD 525797 doses in combination with cetuximab + irinotecan versus cetuximab + irinotecan alone, as second-line treatment for subjects with k-ras wild type (WT) metastatic colorectal cancer (mCRC)	Mr Jim Cassidy	Glasgow	Barts, Glasgow, Manchester	4
An uncontrolled, open-label, phase II study in subjects with metastatic adenocarcinoma of the colon or rectum who are receiving first line chemotherapy with mFOLFOX6 (oxaliplatin/ folinic acid/5-fluorouracil [5-FU]) in combination with regorafenib	Mr Jim Cassidy	Glasgow	Glasgow, Manchester	0
AZD8931, an inhibitor of EGFR, ERBB2 and ERBB3 signalling, in combination with FOLFIRI: A Phase I/II study to determine the importance of schedule and activity in colorectal cancer	Prof Daniel Hochhauser	UCL	Barts, Manchester, UCL	
DREAM: Dual REctal Angiogenesis or MEK inhibition radioTHERAPY trial	Dr Mark Saunders	Manchester	Manchester	3
EXCITE: Erbitux, Xeloda, Campto, Irradiation Then Excision for locally advanced rectal cancer (North West Clinical Oncology Group-04 on behalf of the NCRI rectal cancer subgroup)	Dr Simon Gollins	Cardiff	Manchester	0
modulation of Radiotherapy according to HYpoxia: exploiting changes in the Tumour Microenvironment to improve outcome in rectal cancer	Maughan, Prof Tim	Oxford	Oxford	4

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
Multi-Center, Randomized, Placebo-Controlled Phase II Study of Regorafenib in Combination With FOLFIRI Versus Placebo With FOLFIRI as Second-Line Therapy in Patients With Metastatic Colorectal Cancer	Cunningham, Professor David	ICR	Manchester	
Phase I/II study of Irinotecan, Capecitabine and Radiotherapy as preoperative treatment for locally advanced rectal cancer	Dr Simon Gollins		Manchester	0
Phase II clinical trial of capecitabine and oxaliplatin plus bevacizumab as neoadjuvant treatment for patients with previously untreated unresectable liver-only metastases from colorectal cancer	Prof David Cunningham	ICR	Manchester	0
Phase II Study with Symadex (C-1311) in Patients with Metastatic Colorectal Cancer after Oxaliplatin and/or Irinotecan Failure	Unknown	Leicester	Southampton	0
Randomised Phase II study of cetuximab alone or in combination with irinotecan in patients with metastatic CRC with either KRAS WT or G13D mutation.	Dr Harpreet Wasan	Imperial	Imperial	2
Randomized phase II trial evaluating the efficacy of FOLFOX alone, FOLFOX plus bevacizumab and FOLFOX plus panitumumab as perioperative treatment in patients with resectable liver metastases from wild type KRAS colorectal cancer	Dr Rob Glynne-Jones	Mount Vernon Cancer Centre	Manchester	
SONATINA: A Phase II Multi-Centre Randomised Controlled Study of Nelfinavir Addition to Radiotherapy Treatment in Neo-Adjuvant Therapy for Rectal Cancer - Nelfinavir Addition to Radiotherapy Treatment for Rectal Cancer	Dr R Sharma	Oxford	Oxford	2
Study of Aflibercept And Modified FOLFOX6 As First-Line Treatment In Patients With Metastatic Colorectal Cancer	Dr Anne Thomas	Leicester	Leicester, Manchester	0
Study of CS-7017 in Colorectal Cancer Patients Who Have Achieved Disease Control Following First-Line Chemotherapy	Dr. Mark Harrison	UCL	Barts, Glasgow, Manchester	0
Study of LX1606 in Subjects With Symptomatic Carcinoid Syndrome	Martyn Caplin	UCL	Manchester	0
Treatment of patients with KRAS wild type advanced colorectal cancer with 5-Fluorouracil (5-FU) or 5-FU plus an Epidermal Growth Factor Receptor inhibitor (Cetuximab) based on a Comprehensive Geriatric Assessment.	Dr Richard Adams	Cardiff	Manchester	
Endocrine				
A Phase I trial of vandetanib combined with 131I-mIBG radiotherapy in patients with neuroendocrine tumours, advanced phaeochromocytoma and paraganglioma	Dr. Jeremy Steele	Barts/Brighton	UCL	
A randomised phase II study comparing capecitabine plus streptozocin with or without cisplatin in the treatment of unresectable or metastatic gastroenteropancreatic neuroendocrine tumours.	Dr Pippa Corrie, Dr Tim Meyer	Cambridge	Edinburgh, Glasgow, Manchester, Oxford, UCL	0
A randomized, open-label phase II multicenter study evaluating the efficacy of oral Everolimus alone or in combination with Pasireotide LAR i.m. in advanced progressive pancreatic neuroendocrine tumors (PNET)	Dr Juan Valle	Manchester	Cambridge, Glasgow, Manchester	0
Multicenter 3-arm trial to evaluate the efficacy and safety of Pasireotide LAR or Everolimus alone or in combination in patients with well differentiated neuroendocrine carcinoma of the lung and thymus	Dr Tim Meyer	UCL	Manchester	4
Endometrial				
A phase II, open-label, single-arm, non-randomized, multi-center study to evaluate the efficacy of oral TKI258 as second-line therapy in patients with either FGFR2 mutated or wild-type advanced and/or metastatic endometrial cancer	Dr Rebecca Kristeleit	UCL	Glasgow, Leeds, UCL	0
A randomized phase 2 non-comparative study of the efficacy of PF-04691502 and PF-05212384 in patients with recurrent endometrial cancer	Prof Martin Gore	ICR	UCL	0
A Single Arm Phase II Trial of BMN 673 for Inoperable, Advanced Endometrial Cancer With Retrospective PTEN, MSI and MRE11 Analysis			UCL	
Gastrointestinal				
A Dose-finding Phase Ib Multicenter Study of Imatinib in Combination With the Oral Phosphatidyl-inositol 3-kinase (PI3K) Inhibitor BYL719 in Patients With Gastrointestinal Stromal Tumor (GIST) Who Failed Prior Therapy With Imatinib and Sunitinib	Stark, Dr Dan	Leeds	Leeds, Manchester	
A Phase I dose-escalating and safety study of AZD8931 in combination with Oxaliplatin and Capecitabine chemotherapy in patients with Oesophago-gastric adenocarcinoma	Dr Anne Thomas	Leicester	Belfast, Leicester, Oxford	7
Germ cell				

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
GAMEC-SHORT (S) & GAMEC-ANTHRACYCLINE (A) RISK-ADAPTED PROTOCOL FOR RELAPSED GERM CELL TUMOURS (GCT)	Dr J Shamash	Barts/Brighton	Barts	0
Haematological other				
A Phase 2, Exploratory, Placebo-Controlled, Multicenter, Double-Blind Evaluation of the Safety, Pharmacokinetics, Pharmacodynamics, and Clinical Effects of Two Dose Regimens of Aes-103 Given for 28 Days to Subjects With Stable Sickle Cell Disease	Dr Tim Mant	Quintiles	KCL	8
A Phase I Open-label, Dose Escalation Study to Investigate the Safety, Pharmacokinetics, Pharmacodynamics, Immunogenicity and Clinical Activity of the Antibody Drug Conjugate GSK2857916 in Subjects with Relapsed/Refractory Multiple Myeloma and Other Advanced Hematologic Malignancies Expressing BCMA	Pr. Kwee Yong	UCL	UCL	
A Phase I Safety, PK and PD Study of KW-2478 in Patients With Multiple Myeloma, Chronic Lymphocytic Leukaemia or B-cell Non-Hodgkin's Lymphoma	Dr Jamie Cavenagh	Barts/Brighton	Barts, Manchester, Southampton, UCL	4
A phase I/II study to evaluate the safety and tolerabiility of the NFKappa B inhibitor LC1 I nthe tratment of high risk haematological malignancies	Prof Alan Burnett - co-investigator is Steve Knapper	Cardiff	Cardiff	0
A prospective phase II study to investigate the efficacy and safety of pre-emptive Cytomegalovirus Adoptive Cellular Therapy in patients receiving allogeneic haematopoietic stem cell transplant from an unrelated donor	Dr Karl Peggs	UCL	Manchester	0
A UK Open-label, Multicentre, Exploratory Phase II Study of INC424 for Patients With Primary Myelofibrosis (PMF) or Post Polycythaemia Myelofibrosis (PPV MF) or Post Essential Thrombocythaemia Myelofibrosis (PET-MF)	Prof Robert Coleman	KCL	KCL	0
Proteomic analysis of the B-cell surface membrane	Professor Martin J.S. Dyer	Leicester	Leicester	26
Study of BMN 673, a PARP Inhibitor, in Patients With Advanced Hematological Malignancies	Prof Ghulam Mufti	KCL	Manchester, Newcastle, UCL	0
Head and Neck				
64CU-AtSM PET imaging in patients with squamous cell carcinoma of the head and neck: correlation with Pimonidazole staining and hypoxia	Professor Michele Saunders	UCL	UCL	0
A Cancer Research UK Phase Ib trial to determine the safety, immunogenicity and tolerability of extended schedule vaccination with MVAEBNA1/LMP2 in patients with Epstein Barr Virus (EBV) positive nasopharyngeal carcinoma.	Dr Neil Steven	Birmingham	Birmingham, Cardiff, Manchester, UCL	2
A Pharmacokinetic Study of Single Doses of Sativex in Treatment-induced Mucositis	Dr james Ritter	Quintiles	KCL	3
A Phase 2 study of Sorafenib (BAY 43-9006) in patients with advanced salivary Adenoid Cystic Carcinoma	Dr N J Slevin	Manchester	Manchester	0
A Phase II, Open-label, 1:1 Randomized, Controlled Trial Exploring the Efficacy of EMD 1201081 in Combination with Cetuximab in Second-Line Cetuximab-Naïve Subjects with Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck (R/M SCCHN)	Dr Christopher Nutting	ICR	Manchester, Sheffield, Southampton	0
A PHASE II, OPEN-LABEL, RANDOMIZED STUDY OF MEHD7945A VERSUS CETUXIMAB IN PATIENTS WITH RECURRENT/METASTATIC SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK WHO HAVE PROGRESSED DURING OR FOLLOWING PLATINUM-BASED CHEMOTHERAPY	Dr Christopher Nutting	ICR	Glasgow	0
A Randomized, Double-Blind, Placebo-Controlled, Multicentre, Phase II Study of Oral Lapatinib in combination with Concurrent Radiotherapy and Cisplatin versus Radiotherapy and Cisplatin alone, in Subjects with Stage III and IVA,B Squamous Cell Carcinoma of the Head and Neck (SCCHN)		ICR	Sheffield	
An Open-Label, Multicenter, Randomized, Phase Ib/II Study of E7050 in Combination with Cetuximab versus Cetuximab Alone in the Treatment of Platinum-Resistant Squamous Cell Carcinoma of the Head and Neck	Dr Andrew Sykes	Manchester	Glasgow, Manchester, UCL	9
Phase Ib pilot study evaluating serial [(18)]FDG PET-CT and [(18)]FLT PET-CT images acquired during conventionally fractionated radiotherapy with and without concurrent chemotherapy for squamous cell carcinomas of the head and neck	Professor Michele Saunders	UCL	UCL	0
Phase Ib trial of Atu027 in Combination With Cisplatin, 5FU and Cetuximab in Patients With Head and Neck Cancer	Prof Hisham Mehanna	Birmingham	Birmingham	
Phase II multicenter randomized, double blind, placebo controlled study assessing the efficacy of BKM120 plus paclitaxel vs. paclitaxel plus placebo in patients with recurrent or metastatic head and neck squamous cell carcinoma.	Dr Martin Forster	UCL	KCL, Manchester	1

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
Phase II, Multicenter, Open-label, Single Arm Trial to Evaluate the Safety and Efficacy of Oral E7080 in Medullary and Iodine-131 Refractory, Unresectable Differentiated Thyroid Cancers, Stratified by Histology.	Dr Nicholas Reed	Glasgow	Glasgow	0
Safety Study of Amphinex Based Photochemical Internalisation (PCI) of Bleomycin in Patients With Cutaneous Cancer	Dr Colin Hopper	UCL	UCL	0
Kidney				
A Phase II Study Investigating Upfront Pazopanib in Metastatic Clear Cell Renal Cancer	Dr Thomas Powles	Barts/Brighton	Barts, Glasgow, Oxford, Southampton, UCL	0
A Phase II Trial Of PF-04856884 (CVX-060), A Selective Angiopoietin-2 (Ang-2) Inhibitor In Combination With Axitinib In Patients With Previously Treated Metastatic Renal Cell Carcinoma	Dr. Martin Gore	ICR	Birmingham, Manchester	
A Phase II Uncontrolled Study of BAY73-4506 in Previously Untreated Patients With Metastatic or Unresectable RCC	Dr Paul Nathan	UCL	KCL	0
A PHASE II, OPEN LABEL, RANDOMIZED STUDY OF GDC-0980 VERSUS EVEROLIMUS IN PATIENTS WITH METASTATIC RENAL CELL CARCINOMA WHO HAVE PROGRESSED ON OR FOLLOWING VEGF-TARGETED THERAPY	Dr Thomas Powles	Barts/Brighton	Barts, Leeds, Manchester	0
A Phase II, Randomised, Double-blind, Parallel Group Study to Assess the Efficacy of Cediranib 45mg Versus Placebo Following 12 Weeks of Treatment in Patients With Metastatic or Recurrent Renal Cell Carcinoma Who Have Had no Previous Anti-VEGF Therapy.	Emilio Parfin	Birmingham	Manchester, Oxford	0
A randomised phase II study evaluating cediranib vs cediranib and saracatanib in patients with relapsed metastatic clear cell renal cancer	Dr Thomas Powles	Barts/Brighton	Barts, Edinburgh, KCL, Manchester, Sheffield, Southampton, UCL	9
A Single Arm, Multicenter Phase II Trial of RAD001 as Monotherapy in the Treatment of Advanced Papillary Renal Cell Cancer		UCL	Manchester	
A study comparing the treatment benefits of MPDL32018 used alone and used together with Avastin to Sunitinb. Benefit is being studied in patients who have advanced kidney cancer or kidney cancer which has spread to other parts of the body and has not been treated before.	Dr Thomas Powles	Barts/Brighton	Barts, Manchester	
A SU011248 Expanded Access Protocol for Metastatic RCC Patients Who Are Ineligible for Participation in Other SU011248 Protocols But May Derive Benefit From Treatment With SU011248	Dr GM Mead	Southampton	Southampton	0
AN OPEN LABEL RANDOMISED PHASE II STUDY COMPARING AZD2014 VERSUS EVEROLIMUS IN PATIENTS WITH ADVANCED METASTATIC RENAL CANCER AND PROGRESSION ON VEGF TARGETED THERAPY	Dr Thomas Powles	Barts/Brighton	Barts, Brighton, Southampton, UCL	19
An Open-Label, Multicenter Phase 1b/2 Study of E7080 Alone, and in Combination with Everolimus in Subjects with Unresectable Advanced or Metastatic Renal Cell Carcinoma Following One Prior VEGF-Targeted Treatment	Dr James Larkin	ICR	Glasgow, Leeds, Leicester, Manchester, Southampton	5
Compare Safety and Efficacy of BIBF 1120 Versus Sunitinib.	Professor Timothy Eisen	Cambridge	Glasgow	0
Dose Escalation Study Investigating Everolimus and Dovitinib in Metastatic Clear Cell Renal Cancer	Prof. T. Powles	Barts/Brighton	Barts	0
Investigation of pathways regulating cell survival and early antiangiogenic response to single agent Everolimus or Rapamycin in renal cancer	Prof Valentine Macaulay	Oxford	Oxford	0
Neoadjuvant Sunitinib Therapy in Patients With Metastatic Clear Cell Type Renal Cell Carcinoma Patients: a Prospective Study	Prof. Tim Eisen	Cambridge	Cambridge	3
Safety and Efficacy of Bevacizumab Plus RAD001 Versus Interferon Alfa-2a and Bevacizumab in Adult Patients With Kidney Cancer	Dr James Larkin	ICR	Southampton	0
Upfront Sunitinib (SU011248)® Therapy Followed By Surgery In Patients With Metastatic Renal Cancer: A Pilot Phase II Study	Prof. T. Powles	Barts/Brighton	Barts	0
Leukaemia				
A Pivotal Phase 2 Trial of Ponatinib (AP24534) in Patients with Refractory Chronic Myeloid Leukemia and Ph+ Acute Lymphoblastic Leukemia	Prof Jane Apperley	Imperial	Imperial	0
An Open-Label, Phase 1/Phase 2 Study to Evaluate the Safety, Tolerability, and Antitumor Activity of the DNA Minor Groove Binding Agent SG2000 in the Treatment of Advanced CLL and AML	American Study		UCL	6
CMV TCR Gene Therapy: A Phase I Safety, Toxicity and Feasibility Study of Adoptive Immunotherapy with CMV TCR-transduced Donor-derived T cells for Recipients of Allogeneic Haematopoietic Stem Cell Transplantation.	Dr Emma Morris	UCL	UCL	2

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
Phase I/II clinical trial to assess the efficacy and safety of olaparib, a PARP-inhibitor, in relapsed and refractory Chronic Lymphocytic Leukaemia patients with an 11q deletion or ATM mutation and relapsed/refractory patients with T-Prolymphocytic Leukaemia and Mantle Cell Lymphoma.	Dr Guy Pratt	Birmingham	Leicester, Manchester	2
WT1 Immunity via DNA fusion Gene Vaccination in Haematological Malignancies by intramuscular injection followed by intramuscular electroporation	Prof Christian Ottensmeier	Southampton	Imperial, Southampton	5
WT1 TCR Gene Therapy for Leukaemia: A Phase I/II Safety and Toxicity Study (WT1 TCR-001)	Dr Emma Morris	UCL	Barts, UCL	0
A confirmatory multicenter, single-arm study to assess the efficacy, safety, and tolerability of the BiTE® antibody blinatumomab in adult patients with minimal residual disease (MRD) of B-precursor acute lymphoblastic leukemia.	Dr Adele Fielding	UCL	Birmingham	0
A First-in-Human Phase I dose escalation trial of the Humanized Anti-CD47 Monoclonal Antibody Hu5F9-G4 in Acute Myeloid Leukaemia (AML).	Prof Paresh Vyas	Oxford	Oxford	
A multi-center, open-label, Phase I study of single agent RO5045337 administered orally in patients with acute myelogenous leukemia (AML), acute lymphocytic leukemia (ALL), chronic myelogenous leukemia (CML) in blast phase, or refractory chronic lymphocytic leukemia/small cell lymphocytic lymphoma (CLL / SCLL).	Prof Bowen	Leeds	Oxford	0
A phase 1 study of the human pharmacokinetics of elacytarabine	Dr Steven Knapper	Cardiff	Barts, Brighton, Southampton	2
A Phase 2 Study of Dasatinib Added to Standard Chemotherapy in Pediatric Patients with Newly Diagnosed Philadelphia Chromosome Positive Acute Lymphoblastic Leukemia	Prof Vaskar Saha	Manchester	UCL	0
A phase I dose escalating study to evaluate the safety, pharmacokinetics, and pharmacodynamics of CHIR-258 in subjects with acute myeloid leukemia. (H77)	GARETH MORGAN	ICR	Glasgow	0
A Phase I Study of Lentivirus Transduced Acute Myeloid Leukaemic Cells (AML) expressing B7.1 (CD80) and IL-2 for the potential enhancement of Graft versus Leukaemia (GvL) effect in Poor Prognosis AML	Ghulam J Mufti	KCL	KCL	1
A Phase I trial of combined azactidine and lenalidomide salvage therapy in patients with acute myeloid leukaemia who relapse after allogeneic stem cell transplantation	Prof Charles F Craddock	Birmingham	Barts, Manchester	
A phase II multi-center, open label, randomized, efficacy and schedule-finding study of oral LDE225 in adult patients with relapsed/refractory acute leukemias.	Prof Nigel Russell		UCL	1
A phase II study of oral single agent Panobinostat in patients with refectory Acute Myelogenous Leukaemia (AML)	Prof David Cameron	Liverpool	KCL	7
A Phase II Trial of Clofarabine in Older Patients With Acute Myeloid Leukemia for Whom Intensive Chemotherapy is Not Considered Suitable	Professor Alan Bernett	Cardiff	Manchester	0
A Pilot Study of Clofarabine Pre-conditioning Prior to Full or Reduced Intensity Allogeneic Transplantation in the Treatment of High Risk Acute Myeloid Leukaemia and Myelodysplasia	Dr Deborah Richardson	Southampton	Southampton	4
A pilot study of prophylactic re-infusion of non-alloreactive donor lympocytes after T-cell depleted allogenic peripheral blood stem cell transplantation for the treatment of selected patients with acute myeloid leukaemia	Prof Stephen MacKinnon	UCL	UCL	0
A Study of RO5045337 in Combination With Cytarabine in Patients With Acute Myelogenous Leukemia	Drummond, Dr Mark	Glasgow	Glasgow, Manchester	2
A Study of RO5503781 as Single Agent or in Combination With Cytarabine in Patients With Acute Myelogenous Leukemia	Mark Drummond	Glasgow	Glasgow	4
A study to establish the pharmacokinetics (how the human body processes the drug) and safety of a new anti-cancer drug, ORY-1001 in cancer of blood and bone marrow after treatment or remission		Manchester	Manchester	
An open label, multicenter, phase II study to evaluate efficacy and safety of the BiTE antibody blinatumomab in adult patients with relapsed/refractory B-precursor acute lymphoblastic leukemia (ALL)	Dr Adele Fielding	UCL	Manchester, UCL	16
An open-label, two-period, fixed-sequence study to evaluate the effects of multiple doses of nilotinib on the pharmacokinetics of midazolam in CML patients who are resistant and/or intolerant against at least one prior therapy with a BCR-ABL tyrosine kinase inhibitor	Prof Tessa Holyoake	Glasgow	Glasgow	0
NK cell infusion for the treatment of relapsed acute myeloid leukaemia in patients unable to receive donor leukocyte infusions due to evidence of graft versus host disease	Prof Ghulam Mufti	KCL	KCL	2

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
Phase I study in recipients of allogenic stem cell transplantation of adoptive immunotherapy using donor-derived CMV specific T-cells that have been selected in vitro	Prof S Mackinnon	UCL	UCL	0
Phase I/II Study combining humanised anti-CD20 (veltuzumab), anti-CD22 (epratuzumab) and both monoclonal antibodies with chemotherapy in adults with recurrent or refractory B-precursor acute lymphoblastic leukaemia (ALL)	Dr Matthew Smith	Barts/Brighton	Barts, Birmingham, Glasgow, UCL	4
Phase II Randomised Trial of Azacitidine versus Azacitidine in combination with Vorinostat in patients with Acute Myeloid Leukaemia or High Risk Myelodysplastic Syndromes ineligible for Intensive Chemotherapy	Prof Charles F Craddock	Birmingham	Barts, Belfast, Birmingham, Glasgow, Oxford, Southampton	37
Phase II Study of the Tolerability and Efficacy of the Histone Deacetylase Inhibitor Sodium Valproate given in Conjunction with 5-azacytidine and ATRA (all trans retinoic acid) in Patients with Acute Myeloid Leukaemia. - Val/Aza	Prof Charles Craddock	Birmingham	Barts, Birmingham	0
PHASE II STUDY OF THE TOLERABILITY OF ADJUNCTIVE AZACITIDINE IN PATIENTS UNDERGOING REDUCED INTENSITY ALLOGENEIC STEM CELL TRANSPLANTATION FOR ACUTE MYELOID LEUKAEMIA	Prof Charles Craddock	Birmingham	Birmingham, Manchester, Sheffield	0
Radiolabelled anti-CD45 monoclonal antibody YAML568 with the conditioning regimen prior to haemopoietic stem cell transplantation: Phase I study in patients with refractory or residual disease	Dr K Orchard	Southampton	Southampton	0
ROMAZA: Phase I trial of combination therapy with romidepsin and azacitidine in patients with newly diagnosed, relapsed or refractory Acute Myeloid Leukaemia ineligible for conventional chemotherapy	Prof Charles F Craddock	Birmingham	Birmingham, Oxford	4
Safety Study of AKN-028 in Patients With Acute Myelogenous Leukemia	Matthew Smith	Barts/Brighton	Barts	0
To Establish the Feasibility of Combining Either the Tyrosine Kinase Inhibitor AC220 or the CXCR4 Inhibitor Plerixafor or the HSP90 Inhibitor, Ganetespib, with Chemotherapy in Older Patients with Acute Myeloid Leukaemia and High Risk Myelodysplastic Syndrome in Patients Over 60 Years	Prof Alan Burnett	Cardiff	Barts, Belfast, Cardiff, Oxford, UCL	0
WT1 peptide Vaccination for Leukaemia: A Phase I/II Pilot study	Dr Emma Morris	UCL	UCL	0
A Phase 2 Open-Label Study of the Efficacy of ABT 199 (GDC-0199) in Subjects with Relapsed or Refractory Chronic Lymphocytic Leukemia Harboring the 17p Deletion	Prof Peter Hillmen	Leeds	Barts, Leicester, Manchester, Oxford	4
A PHASE Ib MULTICENTER DOSE-FINDING AND SAFETY STUDY OF GDC-0199 AND OBINUTUZUMAB IN PATIENTS WITH RELAPSED OR REFRACTORY OR PREVIOUSLY UNTREATED CHRONIC LYMPHOCYTIC LEUKEMIA	Prof Peter Hillmen	Leeds	Barts, Leicester	0
A Phase II Multi-center, Open-label, Study of Nilotinib at a Dose of 300mg Twice Daily in Adult Patients With Newly Diagnosed Philadelphia Chromosome Positive (Ph+) Chronic Myelogenous Leukemia in Chronic Phase (CML-CP)	Professor Mary Frances McMullin	Belfast	Belfast	0
A pilot study to establish the safety and efficacy of a combination of dexamethasone and lenalidomide in patients with relapsed or refractory chronic lymphocytic leukaemia (CLL)	Dr Amit Nathwani		UCL	3
A Randomised phase II trial of Imatinib (IM) versus hydroxycholorquine (HCQ) and IM for patients with Chronic Myloid Leukaemia (CML) in Major Cytogenetic Response (MCyR) with residual disease detectable by quantitative polymerase chain reaction (Q-PCR).	Prof Tessa Holyoake	Glasgow	Glasgow, Imperial	12
A randomised, phase IIB trial in previously untreated patients with chronic lymphocytic leukaemia (CLL) to compare fludarabine, cyclophosphamide and rituximab (FCR) with FC, mitoxantrone and low dose rituximab (FCM-miniR)	Dr Peter Hillmen	Leeds	Barts, Manchester, Southampton	1
Combination FC plus Ofatumumab at Standard or Mega dose In CLL	Dr Peter Hillmen	Leeds	Leicester, Manchester, UCL	6
Dasatinib Combo With SMO Inhibitor (BMS-833923)	Dr Mhairi Copland	Glasgow	Glasgow	0
IciCLLe: Assessment of the Mechanism of Action of Ibrutinib (PCI-32765) in B-cell Receptor Pathway Inhibition in CLL.	Prof Peter Hillmen	Leeds	Manchester	
Phase i/ii Study of the Adjunctive Use of Nilotinib in Patients Undergoing Reduced Intensity Allogeneic Transplantation for Imatinib Resistant or Intolerant Chronic Myeloid Leukaemia	Professor Charles craddock	Birmingham	Birmingham	0
Single-arm phase II to evaluate the safety and efficacy of Campath in combination with high-dose methylprednisolone in CLL patients with deletion of the p53 tumour suppressor gene.	Prof Andrew Pettitt	Liverpool	Manchester	0
Study Evaluating SKI-606 (Bosutinib) In Philadelphia Chromosome Positive Leukemias	Prof Jane Apperley	Imperial	Imperial	0
Study of Lenalidomide to Evaluate Safety and Efficacy in Patients With Relapsed or Refractory Chronic Lymphocytic Leukemia	Prof. Peter Hillmen	Leeds	Barts, Manchester	0

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
Leukaemia and Lymphoma				
A Cancer Research UK Phase I trial of the Anti-CD19 DI-B4 monoclonal antibody given intravenously, weekly for four weeks in patients with advanced CD19 positive indolent B-cell malignancies.	Dr Andrew Davies	Southampton	Manchester, Oxford, Southampton	3
An Open-label, Single Arm, Multicenter Phase 2 Study of the Bruton's Tyrosine Kinase Inhibitor PCI-32765 (Ibrutinib) in Patients With Relapsed or Refractory Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma With 17p Deletion (RESONATE™-17)	Professor Peter Hillmen	Leeds	Leicester, Manchester	2
De-escalation Protocol. Phase II Study of Low Intensity Allogeneic Stem Cell Transplantation Using a Conditioning Regimen Containing Fludarabine and Melphalan. Effect of Campath-1H Dose Reduction on the Incidence of Graft-Versus-Host Disease and Infecti	Dr Stephen Mackinnon	UCL	UCL	0
KW 0761 or Investigator's Choice in Subjects With Previously Treated Adult T-cell Leukemia-Lymphoma (ATL)	Dr Paul Fields	KCL	KCL	3
Single arm NCRI feasibility study of CHOP in combination with Ofatumumab in induction and maintenance for patients with newly diagnosed Richter's Syndrome	Dr Anna Schuh	Oxford	Barts, Manchester	1
Transplantation of umbilical cord blood from unrelated donors in patients with haematological diseases using a reduced intensity conditioning regimen	Dr Rachael Hough	UCL	Barts, Sheffield, UCL	7
Liver				
A multicenter, global, randomized, double-blind study of axitinib versus placebo in patients with advanced hepatocellular carcinoma following failure of one prior antiangiogenic therapy	Dr Tim Meyer	Leeds	Imperial	0
A multicentre, open label, phase I/ randomized phase II study to evaluate safety, pharmacokinetics and efficacy of BIBF 1120 in comparison with oral sorafenib for advanced hepatocellular carcinoma patients	Dr Dan Palmer	Birmingham	Birmingham, Manchester, Southampton, UCL	2
A Phase 2 Study of SGI-110 in the Treatment of Advanced Hepatocellular Carcinoma (HCC) Subjects Who Failed Prior Treatment with Sorafenib			UCL	
A Phase I Trial of Stereotactic Radiosurgery following systemic chemotherapy for unresectable Hilar Cholangiocarcinoma	Dr Andrew Hartley	Birmingham	Birmingham	
A PHASE I/II DOSE ESCALATION TRIAL OF HDAC INHIBITOR TEFINOSTAT (CHR2845) FOR CANCER ASSOCIATED INFLAMMATION IN HEPATOCELLULAR CARCINOMA	Dr Thorsten Hagemann	Barts/Brighton	Barts, UCL	5
A Phase I/IIa study investigating the safety, tolerability and efficacy of intra-arterial injections of the selectively replication-competent herpes simplex virus Seprehvir in combination with TACE in patients with unresectable hepatocellular carcinoma	Prof Nagy Habib	Imperial	Imperial	
A randomised phase II clinical trial of conditioning cyclophosphamide and chemoembiolisation with or without vaccination with dendritic cells pulsed with HepG2 lysatein vivo in patients with hepatocellular carcinoma	Prof David Adams	Birmingham	Birmingham	
A Research Study to Treat Patients With Advanced Hepatocellular Carcinoma	Professor Philip Johnson	Birmingham	Birmingham	0
A Study of RO5137382 (GC33) in Patients With Advanced or Metastatic Hepatocellular Carcinoma	Dr Tim Meyer	UCL	UCL	0
An Open Label Multicenter Extension Study to Evaluate the Long-Term Safety, Tolerability, and Efficacy of SBC-102 in Adult Subjects With Liver Dysfunction Due to Lysosomal Acid Lipase Deficiency Who Previously Received Treatment in Study LAL-CL01	P Deegan	Cambridge	Leeds	0
An Open-Label, Multicenter, Randomized, Phase Ib/II Study of E7050 in Combination with Sorafenib versus Sorafenib Alone as First Line Therapy in Patients with Hepatocellular Carcinoma	Dr Richard Hubner	Manchester	Glasgow, Manchester, UCL	10
Assessment of Frailty in patients with advanced Hepatocellular Cancer			Newcastle	7
Evaluation of Sorafenib in Combination With Local Micro-therapy Guided by Gd-EOB-DTPA Enhanced MRI in Patients With Inoperable Hepatocellular Carcinoma	Prof Jens Ricke		Birmingham	
Irinotecan single-drug treatment for children with refractory or recurrent hepatoblastoma	Dr Penelope Brock	UCL	UCL	0
Nemorubicin hydrochloride (PNU-152243A) administered via intrahepatic artery in combination with cisplatin in adult patients with unresectable hepatocellular carcinoma: Phase II study preceded by dose-escalation.	Prof M Middleton	Oxford	Manchester, Oxford	0
Lung				

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
4D computerised tomography (4D-CT) imaging for treatment planning of lung tumours	Dr Matthew Hatton	Sheffield	Sheffield	0
A randomised, Double-blind, placebo-controlled study to evaluate the Long-term safety and efficacy of darbopoetin alfa administered at 500µg once every 3 weeks in anaemic subjects with advanced stage non-small cell lung cancer receiving multi-cycle		Cambridge	Manchester	
A Cancer Research UK Phase I dose escalation trial of oral VEGFR and EGFR inhibitor, Vandetanib in combination with the oral MEK inhibitor, Selumetinib (VanSel-1) in solid tumours (dose escalation) and NSCLC (expansion cohort)	Dr Denis Talbot	Oxford	Cambridge, Manchester, Oxford	22
A Clinical Study on the Safety and Efficacy of Debio 0932 in Combination With Standard of Care in Patients With Non-small Cell Lung Cancer	Prof. Ruth Plummer	Newcastle	Newcastle	3
A CR-UK phase I dose escalation study of BKM120 in patients with non-small cell lung cancer (NSCLC) receiving thoracic radiotherapy	Dr Rohit Lal	Oxford	Oxford	0
A Dose Ascending Study of Gemcitabine Elaidate (CO-101) in Combination With Cisplatin	Dr Rebecca Kristeleit	UCL	Glasgow, UCL	0
A dose-finding phase Ib study followed by a randomized, double-blind phase II study of carboplatin and paclitaxel with or without buparlisib in patients with previously untreated metastatic non-small cell lung cancer (NSCLC) of squamous histology		Birmingham	Leicester	
A Multicenter Phase Ib Trial to Measure [18F]- Fluorodeoxyglucose Uptake by Positron Emission Tomography in Stage IIIB and IV Non-Small Cell Lung Cancer Before and After Chemotherapy With Gemcitabine/Cisplatin	Dr F Blackhall	Manchester	Manchester, Oxford	0
A multicenter, open-label, randomized, PhII study to evaluate the efficacy of AUY922 or comparator Pemetrexed or Docetacel in patients with EGFRm+ NSCLC who have experience disease progression during EGFR Tki's therapy	Dr Samreen Ahmed		KCL	
A Phase 2 Study of MPDL3280A (an Engineered Anti-PDL1 Antibody) in Patients With PD-L1 Positive Locally Advanced or Metastatic Non-Small Cell Lung Cancer - \FIR\""	Peter Schmid	Barts/Brighton	Barts	3
A Phase I/II study to assess the safety and immunogenicity of recMAGE-A3+AS15 cancer immunotherapeutic given as adjuvant therapy, with or without standard adjuvant chemo(-radio)therapy, to patients with MAGE A3-positive Non-Small Cell Lung Cancer (stage IB, II or III) - MAGE3-AS15-NSC-001 (ADJ-Chemo)	Prof Thatcher	Manchester	KCL, Southampton	0
A Phase Ib/II study of docetaxel with or without buparlisib as second line therapy for patients with metastatic squamous non-small cell lung cancer (NSCLC)		KCL	KCL	
A Phase II study of the selective BRAF kinase inhibitor GSK2118436 in subjects with advanced non-small cell lung cancer and BRAF mutations	Dr Sanjay Popat	ICR	Manchester, Oxford	1
A PHASE II, MULTICENTER, SINGLE-ARM STUDY OF MPDL3280A IN PATIENTS WITH PD-L1-POSITIVE LOCALLY ADVANCED OR METASTATIC NON-SMALL CELL LUNG CANCER	Peter Schmid	Barts/Brighton	Barts	
A phase II, multicenter, single-arm study of oral LDK378 in adult patients with ALK-activated non-small cell lung cancer previously treated with chemotherapy and crizotinib	Dr Rohit Lal	KCL	KCL, Manchester	3
A phase II, multicenter, single-arm study of oral LDK378 in crizotinib naïve adult patients with ALK-activated non-small cell lung cancer	Dr Rohit Lal	KCL	KCL	2
A phase II, open-label, multicentre, randomised study to investigate the efficacy and safety of MPDL3280A (anti-PD-L1 antibody) compared with docetaxel in patients with non-small cell lung cancer after platinum failure	Dr Conrad Lewanski	Charing Cross	KCL	1
A Phase II, Randomized, Double-Blind, Placebo-Controlled Study of Oral E7080 in Addition to Best Supportive Care (BSC) versus BSC Alone in Patients with Locally Advanced or Metastatic Non-Squamous Non-Small Cell Lung Cancer Who Have Failed at Least Two Systemic Anticancer Regimens	Prof Christian Ottensmeier	Southampton	Manchester, Southampton	0
A Project of the European Thoracic Oncology Platform (master protocol): ETOP Lungscape 001 – ALK: A Retrospective Cohort Study of ALK gene rearrangement: prevalence and clinical outcomes in patients with non-small cell lung cancer in Europe	Blackhall, Dr F	Manchester	Manchester	0
A Randomized Phase 2 Study of LY2181308 in Combination with Docetaxel versus Docetaxel in Patients with Locally Advanced or Metastatic Non-Small Cell Lung Cancer (NSCLC) Who Were Previously Treated	Prof David Cameron	Oxford	KCL, Manchester, Oxford, Sheffield	0
A Randomized, Double-blind, Multi-center Phase 2 Trial of Denosumab in Combination With Chemotherapy as First-line Treatment of Metastatic Non-small Cell Lung Cancer Amgen Protocol Number 20120249(Denosumab)	Dr Conrad Lewanski	Charing Cross	KCL	
A Randomized, Open-label Phase 2 Study of EC145 Single-agent and the Combination of EC145 Plus Docetaxel Versus Docetaxel Alone in Participants With Folate-receptor Positive [FR(++)] Second Line NSCLC	Dr Martin Forster	UCH	KCL, UCL	7

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
A Single Arm, Phase 2 Study of Ganetespib in Subjects with Advanced Non- Small-Cell Lung Cancer with Anaplastic Lymphoma Kinase Gene Rearrangement (ALK-Positive NSCLC)	Dr Fiona Blackhall	Manchester	Manchester	0
A Study for Non-Smoker Patients With Nonsquamous Non-Small Cell Lung Cancer	Mr Mayukh Das		Manchester	0
A Study of Avastin (Bevacizumab) in Combination With Thoracic Radiation and Chemotherapy in Patients With Advanced Non-Squamous Non-Small Cell Lung Cancer.	Dr F Blackhall	Manchester	Manchester	0
A Study of Onartuzumab (MetMAb) in Combination With Bevacizumab (Avastin) Plus Platinum And Paclitaxel or With Pemetrexed Plus Platinum in Patients With Non-Squamous Non-Small Cell Lung Cancer	Joyce Thompson	Birmingham	Leeds	0
A Study of Onartuzumab (MetMAb) Versus Placebo in Combination With Paclitaxel Plus Platinum in Patients With Squamous Non-Small Cell Lung Cancer	Joyce Thompson	Birmingham	Leeds	0
A Study of RO5083945 in Combination With Chemotherapy Versus Chemotherapy Alone in Patients With Advanced or Recurrent Non-Small Cell Lung Cancer	Alexander Passioukove - Roche, see notes	KCL	KCL	136
A Study of the Effect of R1507 in Combination With Tarceva (Erlotinib) on Progression-Free Survival in Patients With Stage IIIb/IV Non-Small Cell Lung Cancer (NSCLC).	Dr Mark Middleton	Oxford	Newcastle	0
An Investigational Drug, PF-02341066, Is Being Studied In Patients With Advanced Non-Small Cell Lung Cancer With A Specific Gene Profile Involving The Anaplastic Lymphoma Kinase (ALK) Gene	Dr Fiona Blackhall	Manchester	Manchester, Oxford, Southampton	2
An open label two-stage study of orally administered BKM120 in patients with recurrent or metastatic non-small cell lung cancer with activated PI3K pathway	Dr Rohit Lal	KCL	KCL, Leicester, Manchester	3
An Open-label, Randomized Phase II Study to Evaluate the Efficacy of AUY922 vs Pemetrexed or Docetaxel in NSCLC Patients With EGFR Mutations	Dr Samreen Ahmed	Leicester	Leicester	1
Assess Safety & Efficacy of Selumetinib When Given in Combination With Standard First Line Treatment for Advanced Non-small Cell Lung Cancer	Dean, Dr E	Manchester	Manchester	16
BELIEF (Bevacizumab and ErLotinib In EGFR Mut+ NSCLC)	Popat, Dr Sanjay	ICR	Manchester	
Continuous Hyperfractionated Accelerated Radiotherapy - Escalated Dose Study	Dr Matthew Hatton	Sheffield	Sheffield	0
Dose Escalation by Boosting Radiation Dose Within the Primary Tumor on the Basis of a Pre-treatment FDG-PET-CT Scan in Stage IB, II and III NSCLC: a Randomized Phase II Trial	Faivre-Finn, Dr C	Manchester	Manchester	
Hyperpolarised Helium MRI for the pre-treatment assessment and radiotherapy treatment planning of lung cancer patients	Dr Matthew Hatton	Sheffield	Sheffield	0
JTBB: A Randomized, Controlled Phase 2 Study Evaluating LY2875358 plus Erlotinib versus Erlotinib as First-Line Treatment in Metastatic Non-Small Cell Lung Cancer Patients with Activating EGFR Mutations Who Have Disease Control after an 8-Week Lead-In Treatment with Erlotinib	Dr Conrad Lewanski	Imperial	Oxford	0
JTBC: A Randomized, Open-Label Phase 2 Study Evaluating LY2875358 Plus Erlotinib and LY2875358 Monotherapy in MET Diagnostic Positive NSCLC Patients with Acquired Resistance to Erlotinib	Dr D Talbot	Oxford	Oxford, Southampton	0
Longitudinal study of patients with pre-invasive lesions of the bronchus	Dr Sam Janes	UCL	UCL	9
LUME Lung 3: A Phase I/II study of continuous oral treatment with BIBF 1120 added to standard gemcitabine/cisplatin therapy in first line NSCLC patients with squamous cell histology.	Dr Siow Ming Lee	UCL	Manchester, UCL	3
MEERKAT Trial of AZ6244 in combination with thoracic radiotherapy in stage III and IV NSCLC The MeerKat trial	C Faivre-Finn	Manchester	Manchester	8
Multi-drug, genetic marker-directed, non-comparative, multi-centre, multi-arm Phase II trial in Non-Small Cell Lung Cancer	Professor Gary Middleton	Birmingham	Birmingham	
Phase 1 Study in Subjects With Tumors Requiring Arginine to Assess ADI-PEG 20 With Pemetrexed and Cisplatin (ADIPemCis) (TRAP Study)	Dr Peter Szlosarek	Barts/Brighton	Barts, KCL	
Phase 2 Study of Maintenance OSI-906 Plus Erlotinib (TarcevaÂ®), or Placebo Plus Erlotinib in Patients With Nonprogression Following 4 Cycles of Platinum-based Chemotherapy	Dr F Blackhall	Manchester	Leeds, Leicester, Manchester, Southampton, UCL	0

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
Prospective Study of 18F-RGD PET-CT in Assessment of Response to Antiangiogenic Treatment in Patients With Cancer and Comparison With Perfusion CT	Fergus Gleeson	Oxford	Oxford	5
Radical Lung Radiotherapy Plus Nelfinavir	Niki Panakis	Oxford	Oxford	0
Randomised Phase II Trial of PF-00299804 versus Erlotinib for the treatment of advanced NSCLC after failure of at least one prior chemotherapy regimen	Dr F Blackall	Manchester	Manchester, Oxford	0
Randomized, placebo controlled, Double-blind Phase 1b/2 Study of U3-1287 (AMG 888) in Combination with Erlotinib in EGFR Treatment Naïve Subjects with Advanced Non-Small Cell Lung Cancer (NSCLC) Who Have Progressed on at Least One Prior Chemotherapy	Dr Andreas Polychronis	UCL	UCL	0
Randomzied Phase 2 Trial of AG-013736 or Bevacizumab in Combination with Paclitaxel and Carboplatin as First Line Treatment For Patients with Advanced Non-small Cell Lung Cancer	Prof CH Ottensmeier	Southampton	Southampton	0
Safety Study of Sequential and Synchronous ChemoRadiation and Cetuximab (Erbitux) in Patients with Stage III Non Small Cell Lung Cancer. SCRATCH Pilot Study - SCRATCH Pilot Study		KCL	KCL	
Study Evaluating the Safety and Efficacy of Carboplatin/Paclitaxel and Carboplatin/Paclitaxel/Bevacizumab With and Without GDC-0941 in Patients With Previously Untreated Advanced or Recurrent Non-small Cell Lung Cancer	Fiona Blackhall	Manchester	Leicester	1
TRAcking Non-small Cell Lung Cancer Evolution Through Therapy (Rx)	Dr Charles Swanton	UCL	Leicester, Manchester, UCL	0
Trial of Dasatinib in Subjects With Advanced Cancers Harboring DDR2 Mutation or Inactivating B-RAF Mutation	Blackhall, Dr F	Manchester	Manchester	0
A Phase 1b/2 Double-Blind Randomized Trial of the Hedgehog/SMO Antagonist LY2940680 in Combination with Carboplatin and Etoposide Followed by LY2940680 versus Carboplatin and Etoposide Plus Placebo Followed by Placebo in Patients with Extensive-Stage Small Cell Lung Cancer	Dr Martin Forster	UCL	Birmingham, KCL, Manchester, Oxford	1
A Phase 1b/2 Trial of LY2940680 in Patients with Extensive-Stage Small Cell Lung Cancer			UCL	2
A Phase I, Open-Label, Dose Escalation Study of Daily Dosing With BB-10901	Dr Paul Lorigan	Manchester	Manchester, Sheffield	0
A Phase II, randomised, open-label study of Gemcitabine/Carboplatin first-line chemotherapy in combination with or without the antisense oligonucleotide Apatorsen (OGX427) in advanced squamous cell lung cancers	Prof Peter Schmid	Barts/Brighton	Barts	
Amgen Protocol 20060534 - A Phase 1b/2 Trial of AMG 479 or AMG 102 in Combination With Platinum-based Chemotherapy as First-Line Treatment for Extensive Stage Small Cell Lung Cancer		Manchester	Manchester	
Phase II Study of ADI-PEG 20 in Patients with Relapsed Sensitive or Refractory Small Cell Lung Cancer	Peter Szlosarek	Barts/Brighton	Barts	3
Photodynamic therapy with mTHPC for dysplasia and early carcinoma in the oesophagus	Dr Laurence Lovat & Professor Steven Bown	UCL	UCL	0
Study of Amrubicin With or Without Cisplatin Versus Etoposide-cisplatin for Extensive Stage Small Cell Lung Cancer	Dr Mary O'Brien	ICR	Manchester	0
Lymphoma				
A phase I study to investigate dose escalation of doxorubicin in cycles 1-3 of ABVD chemotherapy for Hodgkin lymphoma and to correlate this with molecular markers of tumour response and toxicity	Prof John Radford	Manchester	Barts, Manchester, Southampton	0
A phase II trial of radioimmunotherapy with intravenous 131Iodine-labelled chimeric (mouse/human) monoclonal antibody (CHT25) to the IL-2 receptor-expressing lymphoma	Prof Richard Begent	UCL	UCL	0
BREVITY: A phase II study of brentuximab vedotin using a response adapted design in patients with Hodgkin lymphoma unsuitable for chemotherapy due to age, frailty or co-morbidity	Prof John Radford	Manchester	Leicester, Manchester, Southampton	0
Phase 2 study evaluating the toxicity and efficacy of a modified German Paediatric Hodgkin's lymphoma protocol (HD95) in young adults (aged 18-30 years) with Hodgkin's Lymphoma	Dr Kirit Ardeshna	UCL	Manchester	0
Phase II Study of Oral Panobinostat in Adult Patients With Relapsed/Refractory Classical Hodgkin's Lymphoma	Dr John Radford	Manchester	Manchester, Southampton	0
Study of Brentuximab Vedotin (SGN-35) in Pediatric Patients With Relapsed or Refractory Systemic Anaplastic Large-Cell Lymphoma or Hodgkin Lymphoma	Dr Stephen Daw	UCL	UCL	3

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
The response of non-Hodgkin lymphoma and Hodgkin's diseases to low intensity bone marrow transplantation, assessed by FDG-PET scans (phase 1) (ARSAC)	Professor Steven MacKinnon	UCL	UCL	0
A clinicopathological study in Burkitt's and Burkitt-like non-Hodgkin's Lymphoma.	Dr Andrew Jack, Dr Ben Mead, Ms Sally Stenning	Southampton	Southampton	0
A Multicenter Study to Evaluate the Effect of Rituximab (IDEC 102) on Primary Humoral Response, Recall Response, and Maintenance of Acquired Immunity to Specific Antigens Simplified title for UK: A multicenter study to evaluate the effect of Rituximab on	Professor Barry Hancock	Sheffield	Manchester	0
A Multicenter, Phase 1-2 Study of MLN8237, an Oral Aurora A Kinase Inhibitor, in Patients With Relapsed or Refractory Aggressive B-Cell Lymphoma Treated With Rituximab and Vincristine	Dr Eve Gallop-Evans	Southampton	Southampton	
A parallel randomised phase II trial of CHOP chemotherapy with or without Bortezomiib in relapsed mantle cell lymphoma	Prof Simon Rule	Plymouth	Barts, Southampton	0
A Pharmacokinetic Study of Subcutaneous and Intravenous MabThera (Rituximab) in Patients With Follicular Lymphoma	J A Radford	Manchester	Manchester	0
A Phase 1 Study of Brentuximab Vedotin Given Sequentially and Combined With Multi-Agent Chemotherapy for CD30-Positive Mature T-Cell and NK-Cell Neoplasms	Prof Tim Illidge	Manchester	Manchester, Southampton	0
A Phase 2 Open Label Trial of Brentuximab Vedotin (SGN-35) for Systemic Anaplastic Large Cell Lymphoma	Professor T Illidge	Manchester	Manchester	0
A Phase 2 Study to Assess the Efficacy and Safety of CAL-101 in Patients with Indolent B-Cell Non-Hodgkin Lymphoma Refractory to Rituximab and Alkylating Agents	Dr Andrew Davies	Southampton	Barts, Manchester, Southampton	0
A Phase 2 Trial of AZD1152 in Relapsed/Refractory Diffuse Large B-cell Lymphoma	Chris Hatton	Oxford	Manchester, Oxford	3
A Phase 2, Multicenter, Single-Arm Study to Evaluate the Efficacy and Safety of Single-Agent Bruton's Tyrosine Kinase (BTK) Inhibitor, Ibrutinib, in Subjects with Mantle Cell Lymphoma Who Progress after Bortezomib Therapy	Prof Simon Rule	Plymouth	Barts, UCL	0
A Phase I Open-label, Dose Escalation Study to Investigate the Safety, Pharmacokinetics, Pharmacodynamics and Clinical Activity of GSK2816126 in Subjects With Relapsed/Refractory Diffuse Large B Cell and Transformed Follicular Lymphoma	Prof P Johnson	Southampton	Southampton	0
A phase I/II study of idiotypic vaccination for follicle centre lymphoma	Prof Robert Hawkins	Manchester	Manchester, Southampton	0
A Phase II Multi-Dose Study of SGN-30 (Anti-CD30 mAb) in Patients With Refractory or Recurrent Hodgkin's Disease or Anaplastic Large Cell Lymphoma	Prof PWM Johnson	Southampton	Manchester, Southampton	0
A pilot study of CHOP plus alemtuzumab for the primary treatment of ALK-ve peripheral T cell lymphoma		Leeds	Barts, Sheffield	
A Single-Arm, Open-Label Phase 2 Study of Nivolumab (BMS-936558) in Subjects with Relapsed or Refractory Follicular Lymphoma (FL)	Prof Peter Johnson	Southampton	Manchester, Southampton	0
A Single-Arm, Open-Label, Phase 2 Study of Nivolumab (BMS-936558) in Subjects with Relapsed or Refractory Diffuse Large B-Cell Lymphoma (DLBCL) After Failure of Autologous Stem Cell Transplant (ASCT) or After Failure of At Least One Prior Multi-Agent Chemotherapy Regimen in Subjects Who Are Not Candidates for ASCT (CHECKMATE)	Prof Peter Johnson	Southampton	Manchester, Southampton	0
A Study of PCI-32765 (Ibrutinib) in Patients With Refractory Follicular Lymphoma	Marcus, Dr Robert	KCL	Manchester, Southampton	5
A study of PCI-32765 in patients with relapsed or refractory mantle cell lymphoma	Dr Simon Rule	Plymouth	Barts, Manchester, Southampton	0
A Study of the Histone Deacetylase Inhibitor (HDACi) JNJ-26481585 in Patients With Previously Treated Stage Ib-IVa Cutaneous T-cell Lymphoma	Dr Sean Whittaker	KCL	KCL, Manchester	0
A Study of YM155 Plus Rituximab in Subjects With Non-Hodgkin's Lymphoma Who Have Received Prior Treatment	Dr Christian Hatton	Oxford	Manchester, Southampton	0
A Study to Determine the Efficacy of Lenalidomide Versus Investigator's Choice in Patients With Relapsed or Refractory Mantle Cell Lymphoma (MCL)	Dr Simon Rule	Plymouth	Manchester, Southampton	1
An Open-Label Therapeutic Exploratory Clinical Trial of HuMax-CD4, a Fully Human Monoclonal Anti-CD4 Antibody, in Patients With Refractory or Relapsed Non-Cutaneous CD4+ T-Cell Lymphoma	John Gribben	Southampton	Manchester	0
An Open-label, Multicenter, Phase 2 Study of Oral MLN9708 in Adult Patients With Relapsed and/or Refractory Follicular Lymphoma	Prof John Radford	Manchester	Manchester, Southampton, UCL	2
An Open-label, Multi-centre, Randomized, Phase Ib Study to Investigate the Safety and Efficacy of RO5072759 Given in Combination With CHOP, FC or Bendamustine Chemotherapy in Patients With CD20+ B-cell Follicular Non-Hodgkin's Lymphoma	Dr Robert Marcus	KCL	Manchester, Southampton	0

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
An Open-label, Randomized, Phase 1 Study of R-CVP or R-GDP in Combination with Inotuzumab Ozogamicin in Subjects with CD22-Positive Non-Hodgkin's Lymphoma	Prof David Cameron	Edinburgh/Dundee	Southampton	0
An Open-Label, Single-Arm, Phase 2 Study Of Inotuzumab Ozogamicin Plus Rituximab In Subjects With Relapsed/Refractory CD22-Positive Diffuse Large B-Cell Lymphoma, Eligible For Autologous Stem Cell Transplantation	J A Radford	Manchester	Manchester	0
An Open-label, Single-arm. Multi-center Phase 2 Trial With Ofatumumab in Patients With Relapsed/Progressive Diffuse Large B-Cell Lymphoma (DLBCL) Ineligible for Transplant or Relapse/Progression After Autologous Transplant	Professor Martin Dyer	Leicester	Manchester, Southampton	0
Belief: A Multicenter, Open-Label Trial of Belinostat in Patients with Relapsed or Refractory Peripheral T-Cell Lymphoma (PTCL)	Dr Claire Dearden	ICR	Barts, Leicester, Manchester	0
Cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP) versus gemcitabine, cisplatin and methyl prednisolone (GEMP) in the first line treatment Of T-cell Lymphoma, a multicentre randomised phase II study	Prof David Cunningham	ICR	Glasgow, Southampton, UCL	1
Evaluation of engineered T Cells to target B-cell malignancies		Manchester	Manchester	
Feasibility study of R-CHOP plus Bevacizumab in patients with diffuse large B-cell lymphoma	Prof David Cunningham	ICR	Southampton	0
Forodesine in the Treatment of Cutaneous T-Cell Lymphoma	Dr Julia Scaribrick	KCL	KCL, Manchester	0
Global polyA cDNA amplification for lymphoma diagnosis and monitoring		Manchester	Manchester	
Phase I/II study to determine the maximum tolerated dose and activity of the combination of romidepsin and carfilzomib in relapsed or refractory peripheral T-cell lymphoma	Dr Graham Collins	Birmingham	Barts, Oxford, Southampton	
Phase II Single Agent Lenalidomide (Revlimid) in Relapsed / Refratory Mantle Cell Lymphoma. - Lenalidomide Study	Dr Simon Rule	Plymouth	Barts, Manchester, Southampton	1
Phase II Study of Fractionated 90Y Ibritumomab tiuxetan (ZevalinTM) as initial therapy of Follicular Lymphoma	Professor T Illidge	Manchester	Manchester, Southampton	0
Phase II study of low intensity allogeneic transplantation in Mantle Cell Lymphoma	Prof Simon Rule	Plymouth	Manchester, Sheffield	0
Phase II trial of PI3K inhibitor BAY 80-6946 in patients with indolent and aggressive Non-Hodgkin's lymphomas.	Dr Kim Linton	Manchester	Manchester, Southampton	0
Phase II Trial of Single Agent Ofatumumab in Relapsed / Refractoy Mantle Cell Lymphoma	Prof Simon Rule	Plymouth	Leicester	0
Rituximab, High Dose Ara-C and Dexamethasone Followed by BEAM in Mantle Cell Lymphoma Patients <66 Years	Dr Stephen Robinson	Imperial	Southampton	
Safety and Efficacy of AEB071 and EVEROLIMUS in Patients With CD79-mutant or ABC Subtype Diffuse Large B-Cell Lymphoma			Southampton	
SAR3419 as Single Agent in Relapsed-Refractory Diffuse Large B-Cell Lymphoma (DLBCL) Patients	Prof Martin Dyer	Leicester	Leicester, Manchester	6
Study Evaluating CMC-544 Administered In Combination With Rituximab In Subjects With Non-Hodgkin's Lymphoma (NHL)	Dr Simon Rule	Plymouth	Barts, Southampton	0
Study of AEB071 (a Protein Kinase C Inhibitor) in Patients With CD79-mutant Diffuse Large B-Cell Lymphoma	Professor J A Radford	Manchester	Manchester, Southampton	18
Study of KW-0761 (Mogamulizumab) in Subjects With Previously Treated Peripheral T-cell Lymphoma (PTCL)	Dr John Radford	Manchester	KCL, Manchester, Southampton	1
Study to Learn if 200mg Test Drug (Fostamatinib) Helps People With Large B-Cell Lymphoma,a Type of Blood Cancer	Dr Kirit Ardeshna	UCL	Southampton	0
Melanoma				
A Multicenter, Open Label, Randomized Phase II Trial of the MEK Inhibitor Pimasertib or Dacarbazine in Previously Untreated Subjects With N-Ras Mutated Locally Advanced or Metastatic Malignant Cutaneous Melanoma	Dr James Larkin	ICR	Cambridge, KCL, Newcastle, Southampton	4
A Multicenter, Randomized, Double-blind Study of Dacarbazine With or Without Genasense in Chemotherapy-naive Subjects With Advanced Melanoma and Low LDH (The AGENDA Trial)	Prof Martin Gore	ICR	KCL	0
A Pharmacodynamic Study Of The Effects of Neo-Adjuvant Sodium Valporate and Bortezemib In Patients With Melanoma or Colorectal Cancer	Prof M Middleton	Oxford	Oxford	4
A Phase 1/2, Multi-Center, Blinded, Randomized, Controlled Study Of The Safety And Efficacy Of The Human Monoclonal Antibody To Human Alpha V Integrins (CNTO 95), Alone And In Combination With Dacarbazine, In Subjects With Stage IV Melanoma.		ICR	Manchester, Sheffield, Southampton	

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
A Phase I/II Trial of SCIB1, a DNA Immunotherapy, in the Treatment of Patients With Malignant Melanoma	Dr Poulam Patel		Leeds, Manchester, Newcastle, Southampton	5
A phase Ib/II, multicenter, study of LEE011 in combination with LGX818 in adult patients with BRAF mutant melanoma	Dr James Larkin	ICR	Manchester	
A Phase II, double blind, randomised study to assess the efficacy of AZD6244 (Hyd-Sulfate) in combination with dacarbazine compared with dacarbazine and placebo to AZD6244 in first line patients with BRAF positive advanced cutaneous melanoma	Dr Mark Middleton	Oxford	Manchester, Newcastle, Oxford	0
A phase II, randomized study of high and low dose oral LDE225 to evaluate efficacy and safety in patients with locally advanced or metastatic basal cell carcinoma	Dr Jerry Marsden	Birmingham	Barts, Newcastle	3
A randomised double blind phase 2 trial of whole brain radiotherapy with or without vandetanib in metastatic melanoma with brain metastases	Prof Mark Middleton	Oxford	Barts, Manchester, Oxford, Sheffield	9
A Randomised Phase II Study in Metastatic Melanoma to Evaluate the Efficacy of Adoptive Cellular Therapy with Tumour Infiltrating Lymphocytes (TIL) and Assessment of High versus Low Dose Interleukin-2	Prof Robert Hawkins	Manchester	Manchester	0
A Randomized, Double-Blind, Placebo-Controlled, Phase 2 Study Evaluating the Efficacy of ABT-888 in Combination with Temozolomide Versus Temozolomide Alone in Subjects with Metastatic Melanoma	Dr Mark Middleton	Oxford	Glasgow, Manchester, Newcastle, Oxford	0
A Randomized, Open-Label, Multicenter Phase II Study of Ipilimumab Retreatment versus Chemotherapy for Subjects with Metastatic Melanoma who Progressed after Initially Achieving Disease Control with Ipilimumab Therapy	Prof Christian Ottensmeier		Southampton	0
A Rollover Study for Patients Who Received CP-675,206 in Other Protocols, to Allow the Patients Access to CP-675,206 Until This Agent Becomes Commercially Available or Development is Discontinued.	Prof. Ruth Plummer	Newcastle	Newcastle	0
A Study of RO5185426 in Patients With Metastatic Melanoma	Dr James Larkin	ICR	Manchester, Oxford	0
An Open-Label, 2-Cohort, Multicenter, Study of E7080 in Previously Treated Subjects With Unresectable Stage III or Stage IV Melanoma	Prof Jeff Evens	Glasgow	KCL	0
An Open-Label, Multicenter, Randomized, Phase Ib/II Study of E7080 in Combination with Dacarbazine versus Dacarbazine Alone as First Line Therapy in Patients with Stage IV Melanoma	Dr Mark Middleton	Oxford	Glasgow, Manchester, Oxford, Southampton	0
Clinical first-in-human dose escalation study evaluating the safety and tolerability of intranodal administration of an RNA-based cancer vaccine targeting the tumor-associated antigens NY-ESO-1 and tyrosinase in patients with advanced melanoma	Prof CH Ottensmeier	Southampton	Southampton	
Docetaxel +/- AZD6244 in Melanoma - A double blind randomised phase 2 trial of docetaxel with or without AZD6244 in wt BRAF advanced melanoma	Dr Mark Middleton	Oxford	Leeds, Manchester, Newcastle, Oxford, Sheffield, Southampton	0
Efficacy Study of Pharmacokinetic(PK)/Pharmacodynamic(PD) Relationship of Monotherapy MORAb-004 in Metastatic Melanoma	Dr Sarah Danson	Sheffield	Sheffield	0
Investigating resistance to gene-targeted melanoma therapies	Corrie, Dr Pippa	Cambridge	Oxford	8
Pharmacokinetic Study of Thalidomide in Subjects With Multiple Myeloma	Davies, Dr Faith	ICR	Manchester	1
Phase II pilot study of intravenous high dose interferon with or without maintenance treatment in melanoma at high risk of recurrence. MREC/02/01/77	Dr Mark Middleton	Oxford	Manchester, Oxford	0
Phase II Study of Bortezomib (VELCADE) With Cisplatin as First Line Treatment of Malignant Mesothelioma	Prof T R J Evans	ICR	Oxford, Sheffield, Southampton	0
Phase II Study to Evaluate the Safety, Tolerability and Efficacy of CT-011 Administered Intravenously to Patients With Metastatic Melanoma	Dr Mark Middleton	Oxford	Southampton	0
Phase II trial of 17-AAG (geldanamycin) in patients with metastatic melanoma	Dr Paul B. Chapman		UCL	0
Randomised Study to Compare the Efficacy of AZD6244 vs TMZ	Dr T R Jeffry Evans	Glasgow	Manchester, Oxford	0
Randomized double-blind phase II trial of NY-ESO-1 ISCOMATRIX and ISCOMATRIXadjuvant alone in patients with resected stage III or IV malignant melanoma	Professor Martin Gore (Chief Inv)	ICR	Southampton	0
Sentinel Node Biopsy using Magnetic Nanoparticles: A prospective multicentre feasibility non-randomised clinical trial to compare sentinel node biopsy using magnetic nanoparticles vs. standard technique	Mr Michael Douek	KCL	KCL	18
STEVIE: A Study of Vismodegib in Patients With Locally Advanced or Metastatic Basal Cell Carcinoma	Dr Kate Fife	Cambridge	KCL, Newcastle	6

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
Study of GSK2241658A Antigen-Specific Cancer Immunotherapeutic in Patients With Unresectable and Progressive Metastatic Cutaneous Melanoma	Dr Stephen Nicholson	Leicester	KCL, Leicester, Southampton	0
Study of MLN2480 in Patients With Relapsed or Refractory Solid Tumors Followed by a Dose Expansion in Patients With Metastatic Melanoma	Prof Mark Middleton	Oxford	Manchester, Newcastle, Oxford	11
Study to Assess the Tolerability of a Bispecific Targeted Biologic IMCgp100 in Malignant Melanoma	Prof Mark Middleton	Oxford	Birmingham, Cambridge, Glasgow, Leeds, Oxford	18
Mesothelioma				
A double blind, placebo-controlled, randomised phase II study of Pemetrexed and Cisplatin with and without Ruxolitinib in Malignant Pleural Mesothelioma	Profesor Gary Middleton	Birmingham	Birmingham	
A phase I/II study of first line Ganetespib with pemetrexed-cisplatin, in patients with malignant pleural mesothelioma	Dr Dean Fennell	UCL	Leicester, Oxford, Sheffield, UCL	7
A phase Ib trials of AZD2014 and AZD6244 in Non Small Cell Lung Cancer	Thomas Powles	Barts/Brighton	Birmingham	
COMMAND: A PHASE II RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTICENTER STUDY OF VS-6063 IN SUBJECTS WITH MALIGNANT PLEURAL MESOTHELIOMA	Dr Dean Fennell	Leicester	Barts, Cambridge, KCL, Leicester	18
Evaluating the effect of immune cells on the outcome of patients with mesothelioma	Prof Christian Ottensmeier	Southampton	Southampton	37
Intrapleural Administration of HSV1716 to Treat Patients With Malignant Pleural Mesothelioma.	Professor PJ Woll	Sheffield	Sheffield	4
Phase 2, Randomized, Double-blind Study Comparing Tremelimumab to Placebo in Second- or Third-line Treatment of Subjects with Unresectable Pleural or Peritoneal Malignant Mesothelioma	Prof Christian Ottensmeier	Southampton	Barts, KCL, Leeds, Leicester, Southampton	6
Multiple Sites				
A Cancer Research UK Phase I study to determine the maximum tolerated dose of the oral Src/ABL inhibitor AZD0424, and to identify tolerable and effective AZD0424 combination regimens for the treatment of advanced solid tumours	Prof Adrian Harris	Oxford	Belfast, Oxford	10
A Cancer Research UK Phase I Trial of AZD3965, a monocarboxylate transporter 1 inhibitor (MCT1) in patients with advanced cancer	Prof Ruth Plummer	Newcastle	ICR, Newcastle	8
A Cancer Research UK Phase II Proof of Principle Trial of the activity of the PARP-1 inhibitor, AG-014699, in known carriers of a BRCA1 or BRCA2 mutation with locally advanced or metastatic breast or advanced ovarian cancer	Prof Ruth Plummer	Newcastle	Birmingham, Glasgow, Leeds, Manchester, Newcastle, Southampton, UCL	6
A Four-Part, Open-Label Study to Evaluate the Effects of Repeat Dose GSK2118436 on the Single Dose Pharmacokinetics of Warfarin, the Effects of Repeat Dose Oral Ketoconazole and Oral Gemfibrozil on the Repeat Dose Pharmacokinetics of GSK2118436, and the Repeat Dose Pharmacokinetics of GSK2118436 in Subjects with BRAF Mutant Solid Tumors.	Mark Middleton	Oxford	Oxford	0
A MULTICENTRE, OPEN-LABEL, EARLY STOPPING DESIGN, PROOF OF CONCEPT STUDY WITH TASQUINIMOD IN TREATING PATIENTS WITH ADVANCED OR METASTATIC HEPATOCELLULAR, OVARIAN, RENAL CELL AND GASTRIC CARCINOMAS	Prof Ruth Plummer	Newcastle	Leicester, Manchester, Newcastle, Southampton	19
A Phase 1 Study of MPDL3280A (an Engineered Anti-PDL1 Antibody) in Patients With Locally Advanced or Metastatic Solid Tumors	Prof. T. Powles	Barts/Brighton	Barts	15
A phase 1/2 study of HKI-272 in combination with vinoreline in subjects with solid tumours and metastatic breast cancer.	Dr Anna Rigg	KCL	Manchester, Southampton	0
A Phase 1/2a Study Evaluating the Safety, Pharmacokinetics, and Efficacy of ABT-263 in Subjects with Small Cell Lung Cancer or Other Non-Hematological Malignancies	Unknown		UCL	0
A Phase 2 Study of Temozolomide (SCH 52365) in Subjects With Advanced Aerodigestive Tract Cancers Selected for Methylation of O6-Methyl-Guanine-DNA Methyltransferase (MGMT) Promoter	Prof M Middleton	Oxford	Oxford	0
A Randomized, Double Blind, Multi-Center, Phase 2 Study to Estimate the Efficacy and Evaluate the Safety and Tolerability of Cisplatin & Capecitabine (CX) in Combination with AMG 386 or Placebo in Subjects with Metastatic Gastric, Gastroesophageal Junction, or Distal Esophageal Adenocarcinoma	Dr Charles Brigden Amgen UK Medical Director		Belfast	0
A Rollover Study to Provide Continued Treatment With GSK2118436 to Subjects With BRAF Mutation-Positive Tumors	Mark Middleton	Oxford	Oxford	0

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
A Study of The Impact of Severe Hepatic Impairment on the Pharmacokinetics and Safety of Vemurafenib in BRAF V600 Mutation-Positive Cancer Patients	Dr Steve Nicholson	Imperial	Cardiff	0
An observational Pilot Study of Near infrared imaging of sentinel nodes in early stage vulval, cervical, endometrial, breast and skin(melanoma) cancers using indocyanine green and methylene blue as fluorophores to assess clinical feasibility.	Ahmed Ahmed	Oxford	Oxford	28
An Open-Label, Multicenter, Phase 1/2 Study of Poly(ADP-Ribose) Polymerase (PARP) Inhibitor E7449 as Single Agent in Subjects with Advanced Solid Tumors or with B-cell Malignancies and in Combination with Temozolomide (TMZ) or with Carboplatin and Paclitaxel in Subjects with Advanced Solid Tumors - PHASE I	Prof Ruth Plummer	Newcastle	KCL, Newcastle, Oxford	12
Assessment of Ovarian toxicity during chemotherapy	Prof Richard Anderson	Edinburgh/Dundee	Edinburgh	0
Changes in tyrosine phosphorylation in peripheral blood cells and tumour samples from renal cancer patients treated with sunitinib and from liver cancer treated with sorafenib	Dr Emilio Porfiri	Birmingham	Birmingham	0
Dose-escalation, Safety, Pharmacokinetics Study of AVE8062 Combined With Bevacizumab in Patients With Advanced Solid Tumors	Rhoda Molife	ICR	ICR	0
ENUMERATION AND CHARACTERIZATION OF CIRCULATING TUMOUR CELL (CTC) IN PATIENTS WITH ADVANCED/METASTATIC NEURO-ENDOCRINE TUMOURS AND GASTROINTESTINAL CANCERS	Dr Tim Meyer	UCL	UCL	
Enumeration and Molecular Characterization of Circulating Endothelial Cells (CECs) and Circulating Endothelial Progenitors (CEPs) in Patients with Advanced Epithelial Ovarian and Endometrial Cancer	Dr Gordon Jayson	Manchester	Manchester	3
Phase II pharmacokinetic study to assess the age-dependency in the clearance of doxorubicin in paediatric patients with solid tumours and leukaemia	Prof Alan Boddy	Newcastle	UCL	1
Phase II study in recipients of allogeneic stem cell transplantation of prophylactic adoptive immunotherapy using donor-derived CMV-specific T-cells that have been cultured in vitro (CMV-TC01) for patients who are CMV PRC positive	Professor Steven MacKinnon	UCL	UCL	0
Phase one study of Decitabine in patients receiving ECF (epirubicin, cisplatin and infusional 5-FU) for advanced gastric or oesophageal cancer	Mark Middleton	Oxford	Glasgow, Oxford	0
Proof-of-concept study of AZD 4547 in patients with FGFR1 or FGFR2 amplified tumours	Prof David Cunningham	ICR	Leicester, Manchester, Newcastle	1
Study of Additive Omega-3 Fish Oil to Palliative Chemotherapy to Treat Oesophagogastric Cancer	Mr David Bowrey	Leicester	Leicester	7
Study of PEP02, Irinotecan or Docetaxel in Gastric or Gastroesophageal Junction Adenocarcinoma	Professor David Cunningham	ICR	Southampton	0
Study of the Pharmacokinetics and Safety of Carfilzomib in Subjects With Advanced Malignancies and Hepatic Impairment	Dr Ruth Plummer	Newcastle	Belfast, Cardiff, Glasgow	2
The Cancer Research UK Stratified Medicine Programme: Pilot Study	Prof Peter Johnson		Leicester, Southampton	
Transplantation of umbilical cord blood from unrelated donors in patients with haematological diseases using a myeloablative conditioning regimen	Dr Rachael Hough	UCL	Barts, Birmingham, UCL	1
Validating predictive models and biomarkers of radiotherapy toxicity to reduce side-effects and improve quality-of-life in cancer survivors	Dr Catharine West	Manchester	Manchester	
Myeloma				
A double-blind, placebo-controlled, randomized phase 2 study of BHQ880, an anti Dickkopf1 (DKK1) monoclonal antibody (mAb), in patients with untreated multiple myeloma and renal insufficiency	Dr Kwee Yong	UCL	KCL, Oxford, Southampton, UCL	0
A phase 1/2a, dose escalation study of CHR3996 in combination with Tosedostat in subjects with relapsed, refractory multiple myeloma	Dr Faith Davies	ICR	Barts, UCL	1
A PHASE 2 MULTICENTER, OPEN-LABEL STUDY TO DETERMINE THE EFFICACY AND SAFETY OF POMALIDOMIDE (CC-4047) IN COMBINATION WITH LOW-DOSE DEXAMETHASONE IN SUBJECTS WITH RELAPSED OR REFRACTORY MULTIPLE MYELOMA AND MODERATE OR SEVERE RENAL IMPAIRMENT INCLUDING SUBJECTS UNDERGOING HEMODIALYSIS	Dr Matthew Streetly	KCL	KCL, Oxford	
A Phase 2, Randomized, Double-blind, Placebo-controlled, Multicenter Study of Siltuximab (Anti-IL-6 Monoclonal Antibody) in Subjects with High-risk Smoldering Multiple Myeloma	Dr Jamie Cavenagh	Barts/Brighton	Barts, Glasgow, KCL, Manchester, UCL	4

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
A Phase I dose escalating study to evaluate the safety, pharmacokinetics and pharmacodynamics of CHIR-258 in subjects with refractory or relapsed multiple myeloma. Protocol CHIR-258-004		ICR	Manchester	
A Phase I/IIa trial of VTD-panobinostat treatment and panobinostat maintenance in relapsed and relapsed/refractory multiple myeloma patients	Dr Jamie Cavenagh	Barts/Brighton	Barts, UCL	27
A phase II randomised trial of carfilzomib, cyclophosphamide and dexamethasone (CCD) vs cyclophosphamide, velcade and dexamethasone (CVD) for first relapse or primary refractory multiple myeloma.	Dr Kwee Yong	UCL	Barts, Brighton, Manchester, Southampton, UCL	20
A pilot study of donor idiotypic vaccination for the purpose of targeted post-transplant immunotherapy following allogeneic bone marrow transplantation for multiple myeloma	Prof CH Ottensmeier	Southampton	Southampton, UCL	0
A pilot study of idiotypic vaccination for multiple myeloma using a genetic approach	Prof CH Ottensmeier	Southampton	Southampton	0
An International, Multicenter, Open-Label Study of Vorinostat (MK0683) in Combination With Bortezomib in Patients With Relapsed or Refractory Multiple Myeloma		KCL	Manchester	
An open label, multi-centre, randomised, parallel group phase II selection trial to identify the optimal starting dose of bendamustine (60 vs 100 mg/m2) when given in combination with thalidomide and dexamethasone in patients with relapsed/refractory multiple myeloma	Mr Steve Schey	KCL	Barts, Manchester	0
An Open-Label, Dose Escalation, Multicenter Phase 1/2 Study of KW-2478 in Combination with Bortezomib in Subjects with Relapsed and/or Refractory Multiple Myeloma	Dr Jamie Cavenagh	Barts/Brighton	Barts, UCL	0
An Open-Label, Dose-Escalation, Phase 1/2 Study of the Oral Form of MLN9708, a Next-Generation Proteasome Inhibitor, Administered in Combination With a Standard Care Regimen of Melphalan and Prednisone in Patients With Newly Diagnosed Multiple Myeloma Requiring Systemic Treatment	Jamie Cavenagh	Barts/Brighton	Barts, Brighton, Oxford, UCL	1
An Open-label, International, Multicenter, Dose Escalating Phase I/II Trial Investigating the Safety of Daratumumab in Combination With Bortezomib and Dexamethasone in Patients With Relapsed or Refractory Multiple Myeloma	Jamie Cavenagh	Barts/Brighton	Barts	
Daratumumab in Combination With Lenalidomide and Dexamethasone in Relapsed and Relapsed-refractory Multiple Myeloma	Jamie Cavenagh	Barts/Brighton	Barts	0
PHASE II STUDY OF BORTEZOMIB CONSOLIDATION AFTER HIGH DOSE THERAPY AND AUTOLOGOUS STEM CELL TRANSPLANTATION FOR MULTIPLE MYELOMA	Dr Kwee Yong		UCL	7
Phase II study of Bortezomib, Adriamycin and Dexamethasone (PAD) therapy for previously untreated patients with multiple myeloma: Impact of minimal residual disease (MRD) in patients with deferred ASCT (PADIMAC)	Dr Kwee Yong	UCL	Barts, Imperial, UCL	20
Phase II study of high dose therapy in multiple myeloma followed by consolidation with cyclophosphamide and dexmethasone and thalidomide	Dr Kwee Yong	UCL	UCL	0
Phase II Study to Assess the Safety, Efficacy, and Tolerability of Combination Therapy with VelcadeÔ (Bortezomib), Adriamycin, and Dexamethasone (PAD) as Therapy for Patients with relapsed or refractory Multiple Myeloma	Prof. T C M Morris	Belfast	Barts, Belfast	0
TARGETED RADIOTHERAPY WITH CONDITIONING PRIOR TO HAEMATOPOIETIC STEM CELL TRANSPLANTATION - A randomised phase II clinical trial using targeted radiotherapy delivered by an Yttrium 90 radiolabelled anti-CD66 monclonal antibody with high dose melphalan compared to melphalan alone, prior to autologous stem cell transplantation for multiple myeloma	Dr Kim Orchard	Southampton	Manchester, Southampton, UCL	0
Oesophageal				
A Multicenter, Double-Blind, 3-Arm, Phase 1b/2 Study in Subjects With Unresectable Locally Advanced or Metastatic Gastric or Esophagogastric Junction Adenocarcinoma to Evaluate the Safety and Efficacy of First-line Treatment With Epirubicin, Cisplatin, and Capecitabine(ECX) Plus AMG 102	Dr Charles Brigden		Manchester, Southampton	0
A Multicenter, Phase 2, Single Arm, Two Cohort Study Evaluating the Efficacy, Safety, and Pharmacokinetics of AMG 337 in Subjects with MET Amplified Gastric/Gastroesophageal Junction/Esophageal Adenocarcinoma or Other MET Amplified Solid Tumors	Dr Anne Thomas	Leicester	KCL, Leicester, Manchester	
A phase Ib/II, open-label study of LJM716 in combination with BYL719 compared to taxane or irinotecan in patients with previously treated esophageal squamous cell carcinoma	Dr Was Mansoor	Manchester	Manchester	1
A Phase II Trial to Assess the Activity of NY-ES-O1 Targeted T Cells in Advanced Oesophagogastric Cancer	Dr Flona Thistlethwaite	Manchester	Manchester	

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
A Phase II, open label, single arm study to evaluate Ticilimumab in Advanced Gastric/Oesophageal Adenocarcinoma	Professor Robert Hawkins	Manchester	Manchester	0
A phase IIa, open-label, multi-centre study of TP300 as a single agent first line therapy in patients with advanced gastric or gastro-oesophageal junction adenocarcinoma	Prof T R J Evans	Glasgow	Glasgow, Manchester	0
A randomised control trial to study the efficacy of treatment with HALO Radiofrequency Ablation versus standard surveillance endoscopy on patients with Aneuploidy but no high grade dysplasia in Barrett's columnar lined oesopahgus	Dr Laurence Lovat & Professor Steven Bown	UCL	UCL	0
A RANDOMISED CONTROLLED TRIAL TO STUDY THE SIDE EFFECT PROFILE AND TO ESTABLISH MEASURES OF EFFICACY USING PHOTOFRIN OR 5 AMINOLAEVULINIC ACID PHOTODYNAMIC THERAPY IN THE ERADICATION OF DYSPLASIA IN BARRETT'S COLUMNAR LINED OESOPHAGUS	Dr Laurence Lovat & Professor Steven Bown	UCL	UCL	0
An analysis of Relative Telomere Length (RTL) during chemotherapy in patients with advanced gastro-oesophageal adenocarcinoma	Prof Jeff Evans	Glasgow	Edinburgh	1
Assessment of Frailty in elderly patients with advanced oesophagogastric cancers			Newcastle	2
Efficacy and Safety of AZD4547 Versus Paclitaxel in Advanced Gastric or Gastro-oesophageal Junction Cancer Patients	Dr W Mansoor	Manchester	Manchester	0
Phase Ib/II, multicentre, open-label, randomized, clinical study with dose optimization of two different schedules of Elisidepsin Trifluoroacetate (Irvalec) as a single agent in patients with unresectable, locally advanced or metastatic Esophageal, Esophagogastric Junction or Gastric Cancer after failure of one but not more than two prior lines of systemic therapy	Prof T R J Evans	Glasgow	Glasgow	0
Randomized, Open Label, Phase 2 Study of MM-111 and Paclitaxel With Trastuzumab in Patients With HER2 Positive Carcinomas of the Distal Esophagus, Gastroesophageal (GE) Junction and Stomach Who Have Failed Front Line Metastatic or Locally Advanced Therapy	Watkins, Dr David	ICR	Manchester	0
ROCOCO: Radiotherapy and Olaparib in COmbination for Carcinoma of the Oesophagus. A phase I study.	Dr Andrew Jackson	Newcastle	Southampton	3
The use of breath-gas analysis for molecular oriented detection of gastric and oesphagael cancer	Dr Laurence Lovat	UCL	UCL	0
Other				
A Blinded Placebo Controlled Single Ascending Dose Phase 1 for Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics After Subcutaneous Administration of VRS-317 in Adults With Growth Hormone Deficiency	Dr G Conroy	UCL	Manchester	0
A Dose Finding Study With Oral LDK378 in Patients With Tumors Characterized by Genetic Abnormalities in Anaplastic Lymphoma Kinase (ALK)	Jeff Evans	Glasgow	Leicester	1
A Double Blind Parallel Group Randomised Multiple Dose Study To Evaluate The Pharmacodynamic Response And Safety Of PHA-794428 In Adult Growth Hormone Deficient Patients	Professor JAH Wass	Oxford	Manchester	0
A Double-blind, Randomised, Placebo-controlled Study to Evaluate the Safety and Efficacy of A-60444 in Adults With RSV Infection Following Stem Cell Transplantation	Prof Steven Mackinnon	UCL	UCL	0
A multi-centre phase II study using Carboplatin AUC-10 for metastatic seminoma with IGCCCG good prognosis disease - therapy directed by initial metabolic response on PET-CT [CAR-PET]	Dr J Shamash	Barts/Brighton	Barts	8
A Novel Single Arm Phase II Study for Relapsed Germ Cell Tumours With Poor Prognosis	Jonathan Shamash	Barts/Brighton	Barts	6
A Phase 1/2 Combined Dose Ranging and Randomized, Open-label, Comparative Study of the Efficacy and Safety of Plerixafor in Addition to Standard Regimens for Mobilization of Haematopoietic Stem Cells Into Peripheral Blood, and Subsequent Collection by Apheresis, Versus Standard Mobilization Regimens Alone in Pediatric Patients, Aged 1 to <18 Years, With Solid Tumours Eligible for Autologous Transplants.	Dr Bruce Morland	Birmingham	UCL	0
A phase 2 study of the efficacy and safety of Deferasirox administered at early iron loading in patients with transfusion-dependent Myelodysplastic Syndromes	Dr Dominic Culligan		Southampton	0
A phase I clinical trial of the vaccination of healthy human volunteers against the minor histocompatibility antigen (mHAg) HA-1 using a DNA and MVA 'prime/boost' regimen	Prof Paul Moss	Birmingham	Birmingham	2
A phase I, open-label, dose-escalation study to investigate the safety, tolerability, pharmacodynamics and pharmacokinetics of EMD 525797 using DCE-MRI as a pharmacodynamic measure of response in colorectal and ovarian cancer patients with liver metastas	Professor G Jayson	Manchester	Manchester	6

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
A Phase I/II Study of CP-4055 in Patients With Refractory/Relapsed Hematologic Malignancies	Dr M Dennis	Manchester	Manchester	0
A Phase I/II study of DNA vaccination against CMX/FrC of tetanus toxin fusion gene in allograft donors and recipients (GTAC 069)	Dr Christian Ottersmeier	Southampton	UCL	0
A Phase Ib, open-label, dose-finding study of the JAK inhibitor INC424 tablets administered orally to patients with Primary Myelofibrosis (PMF), Post-Polycythemia Vera-Myelofibrosis (PPV-MF) or Post-Essential Thrombocythemia-Myelofibrosis (PET-MF) and baseline platelet counts = 50 x109/L and <100 x109/L	Dr Claire Harrison	KCL	Belfast, KCL	0
A Phase II Trial of Sequential treatment with Cytoreductive therapy and Reduced Intensity Conditioning Allogeneic Stem Cell Transplantation for Relapsed/ Refractory Acute Myeloid Leukemia, High Risk Myelodysplasia,or other High Risk Myeloid Malignancies	Dr J Cavenagh	Barts/Brighton	Barts	2
A Randomized, Double Blind, Placebo Controlled Study Evaluating the Efficacy and Safety of Romiplostim Treatment of Thrombocytopenia in Subjects With Low or Intermediate-1 Risk Myelodysplastic Syndrome (MDS)		Leeds	Manchester	
An Open-label, Multicenter Study to Evaluate the Safety of Long-term Treatment With Siltuximab in Subjects With Multicentric Castleman's Disease	Schey, Dr Steve	KCL	Manchester	0
Efficacy and Safety of Midostaurin in Patients With Aggressive Systemic Mastocytosis or Mast Cell Leukemia	John Reilly	Sheffield	Glasgow	0
Eltrombopag Treatment of Thrombocytopenia in Subjects With Advanced Myelodysplastic Syndrome (MDS) or Secondary Acute Myeloid Leukemia After MDS (sAML/MDS)	David Bowen	Leeds	Glasgow	0
Immune reconstitution studies in umbilical cord blood transplantation	Bronwen Shaw	UCL	Barts	0
PCR based pre-emptive therapy with valgancyclovir or gancyclovir for active CMV infection following reduced intensity allogenic stem cell transplant			UCL	
Phase I study in recipients of allogeneic stem cell transplantation using blood infusions collected from the original marrow donor, depleted of the CD8 T cell subset (CD8-TC-01)	Professor Steven MacKinnon	UCL	UCL	0
Phase I Study of ONO-4059 Given as Monotherapy in Patients With Relapsed/Refractory NHL and CLL	Prof Martin Dyer	Leicester	Leicester	14
Phase I/II dose-escalation study of oral administration of the Pan-Histone Deacetylase (HDAC) Inhibitor S 78454 in Hodgkin's Disease, non-Hodgkin Lymphoma and Chronic Lymphocytic Leukaemia	Professor Martin Dyer	Leicester	Leicester	0
Radiolabelled anti-CD66 Monoclonal Antibody (BW250/183) in the conditioning regimen prior to haemopoietic stem cell transplantation: Phase I study in patients with poor-risk disease	Dr K Orchard	Southampton	Southampton	4
Study of the immune response to haematological malignancies	Prof Paul Moss	Birmingham	Birmingham	0
The VSASL MRI Study v1.0			Oxford	
Thymic Epithelial Tumours – A Retrospective Analysis Clinical, pathological and molecular genetic study of thymic epithelial neoplasms	Summers, Dr Yvonne	Manchester	Manchester	
Ovary/Fallopian tube				
A Cancer Research UK Randomised, Multicentre, Phase II Trial of the DNA-hypomethylating Agent, 5-Aza¬2'-deoxycytidine (Decitabine) given intravenously in Combination with Carboplatin, versus Carboplatin alone given 4 weekly in Patients with Progressive, Advanced Ovarian cancer.	Prof Stanley Kaye	ICR	Barts, Edinburgh, Glasgow, Sheffield	0
A Clinical Study of ColoAd1 Administered Intraperitoneally: Dose Finding and Proof of Concept in Platinum-Resistant Epithelial Ovarian Cancer	Iain McNeish	Glasgow	Barts	
A Multicenter, Open-Label, Phase 2 Study to Evaluate the Safety and Efficacy of NKTR-102 (PEG-Irinotecan) When Given on a Q14 Day or a Q21 Day Schedule in Patients with Metastatic or Locally Advanced Platinum-Resistant Ovarian Cancer.	Prof Hilary Calvert	Newcastle	Glasgow, Newcastle	0
A Phase 2, Open-Label Study of Rucaparib in Patients with Platinum-Sensitive, Relapsed, High-Grade Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer	Prof Iain Mc Neish	Glasgow	Imperial, Leeds, Manchester	
A Phase Ib/II trial of CA4P (Combretastin A-4 Phosphate) in Combination with Carboplatin and Paclitaxel Chemotherapy in Patients with Advanced Cancer and Advanced Ovarian Carcinoma	Prof Gordon Rustin	UCL	Glasgow, Manchester, Oxford, UCL	0

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
A randomised phase II trial of deforolimus (AP23573;MK-8669) compared to progestin in female adult patients with advanced endometrial carcinoma following one line of chemotherapy	Dr Nicholas Reed	Glasgow	Glasgow, Manchester	0
A Randomised Placebo-Controlled Phase II Study of Continuous Maintenance Treatment with BIBF 1120 Following Chemotherapy in Patients with Relapsed Ovarian Cancer	Prof Jonathan Ledermann	UCL	Barts, Manchester	0
A Randomised, Phase II Study Evaluating MK-1775 in Combination with Paclitaxel and Carboplatin versus Paclitaxel and Carboplatin Alone in Adult Patients with Platinum Sensitive p53 Mutant Ovarian Cancer	Susan Bannerjee	ICR	Glasgow	0
A Randomized, Controlled, Open-Label, Phase 2 Trial of SGI-110 and Carboplatin in Subjects with Platinum-Resistant Recurrent Ovarian Cancer	Dr Sarah Blagden	Imperial	Cambridge, Imperial, Leeds	7
A Randomized, Double-blind, Placebo Controlled, Multi-center, Phase II Study of Adding AMG 479, a Fully Human Monoclonal Antibody Against Insulin-like Growth Factor Type 1 Receptor (IGF-1R) to First Line Chemotherapy in Patients With Optimally Debulked (< 1 cm) Epithelial Ovarian Cancer	GJS Rustin	UCL	Leeds, UCL	0
A Trial of ABT-888 in Combination With Temozolomide Versus Pegylated Liposomal Doxorubicin Alone in Ovarian Cancer	Shibani Nicum	Oxford	Oxford	0
AKTRES study: A Biologic Study of the early effects and determinants of AKT inhibition using GSK2110183 alongside chemotherapy in patients with Platinum RESistant Adenocarcinoma of the ovary	Dr Sarah Blagden	Imperial	Imperial	0
An Open Label Study To Investigate the Pharmacokinetics and Pharmacodynamics of Repeat Escalating Doses of the Oral AKT Inhibitor GSK2141795 by 18F FDG PET Analysis in Subjects With Ovarian Cancer	Professor Hani Gabra	Imperial	Imperial	0
An Open-Label Phase I/II Study of GSK2110183 in Combination with Carboplatin and Paclitaxel in Subjects with Platinum-Resistant Ovarian Cancer	Dr Sarah Blagden	Imperial	Imperial	12
Assessing Treatment Response of Peritoneal Metastases in Ovarian Cancer Using Diffusion Weighted Magnetic Resonance Imaging	Dr Nandita DeSouza	ICR	Imperial	1
BriTROC1: Sample collection study to investigate the role of Homologous Recombination Deficiency in platinum sensitivity in recurrent high grade serous ovarian cancer	Prof Iain McNeish	Barts/Brighton	Barts, Manchester	14
Defining angiogenesis in patient with ovarian cancer, using dynamic contrast enhanced magnetic resonance imaging	Prof G Jayson	Manchester	Manchester	0
Oxford Ovarian Cancer Predict Chemotherapy Response 01	Ahmed Ahmed	Oxford	Oxford	17
p53 Suppressor Activation in Recurrent High Grade Serous Ovarian Cancer, a Phase Ib/II Study of Systemic Carboplatin Combination Chemotherapy With or Without APR-246	Dr John Green	Liverpool	Cambridge, Imperial	0
Phase 1b exploratory study of [18F]AH111585-PET as a marker of angiogenic response to combination therapy with the pan-VEGF inhibitor, pazopanib, and weekly paclitaxel in platinum resistant ovarian cancer	Dr Rohini Sharma	Imperial	Imperial	7
Phase II randomised, double blind, multicentre study to assess the efficacy of AZD2281 in the treatment of patients with platinum sensitive serous ovarian cancer following treatment with two or more platinum containing regimens	Prof Jonathan Ledermann	UCL	Manchester	0
Phase II Study of NGR-hTNF in Combination With Doxorubicin in Platinum-resistant Ovarian Cancer	Nick Reed	Glasgow	Glasgow	4
Randomized Phase 2 Trial Investigating Liposomal Doxorubicin With or Without Anti-Platelet Derived Growth Factor Receptor-Alpha (PDGFRα) Monoclonal Antibody IMC-3G3 in Patients With Platinum-Refractory or Platinum-Resistant Advanced Ovarian Cancer	Prof Martin Gore	ICR	Glasgow, Manchester, UCL	0
Randomized, Multicenter, Prospective Two-Arm, Open-Label Phase II Study to Investigate the Efficacy and Safety of Two ZK219477 i.v. Infusions (3-Hour Infusion of 16mg/m2 Versus 0.5-Hour Infusion of 16 mg/m2) in Patients With Recurrent Ovarian Cancer Progressing During, or Within 6 Months of the End of Platinum-Based Chemotherapy	Prof Gordon J Rustin	UCL	Manchester, Newcastle	0
RANDOMIZED, OPEN-LABEL, PHASE 2 STUDY OF THE IDO INHIBITOR INCB024360 VERSUS TAMOXIFEN FOR SUBJECTS WITH BIOCHEMICAL-RECURRENT-ONLY EPITHELIAL OVARIAN CANCER, PRIMARY PERITONEAL CARCINOMA, OR FALLOPIAN TUBE CANCER FOLLOWING COMPLETE REMISSION WITH FIRST-LINE CHEMOTHERAPY	Dr Rebecca Kristeleit	UCL	Imperial, Leeds, Manchester, Oxford, UCL	5
Pancreas				
A Cancer Research UK Phase I Trial of an Oral Notch inhibitor (MK-0752) in Combination with Gemcitabine in Patients with Stage III and IV Pancreatic Cancer	Prof Duncan Jodrell	Cambridge	Barts, Cambridge, Leeds, Leicester	7

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
A multi-center, phase I/II study of BAY 86-9766 in combination with gemcitabine in patients with locally advanced inoperable or metastatic pancreatic cancer	Dr Paul Ross	KCL	KCL, UCL	4
A multicenter, two stage, phase II study, evaluating the efficacy of oral BEZ235 plus best supportive care (BSC) versus placebo plus BSC in the treatment of patients with advanced pancreatic neuroendocrine tumors (pNET) after failure of mTOR inhibitor therapy.	Dr Nicholas Reed	Glasgow	Glasgow	0
A Phase 1 Trial of Verteporfin Photodynamic Therapy in Unresectable Pancreatic Carcinoma (VERTPAC-01 study) - VERTPAC-01	Dr Steve Pereira	UCL	UCL	0
A Phase 2, Multicenter, Randomized, Double-Blind, Placebo Controlled, Trial of AMG 479 or Placebo in Combination with Gemcitabine as First-line Therapy for Locally Advanced Unresectable Adenocarcinoma of the Pancreas	Prof David Cunningham	ICR	KCL	0
A Phase I trial of pre-operative, margin intensive, stereotactic body radiation therapy for previously untreated borderline resectable pancreatic cancer	Dr Maria Hawkins	Oxford	Oxford	
A phase I, open-label, study of the safety and tolerability of KU-0059436 in combination with gemcitabine in the treatment of patients with advanced pancreatic cancer.	Prof M Middleton	Oxford	Oxford	0
A Phase I/II Trial of TG01 and Gemcitabine as Adjuvant Therapy for Treating Patients with Resected Adenocarcinoma of the Pancreas	Prof Dan Palmer	The Clatterbridge Cancer Centre NHS Foundation Trust	Manchester	0
A Phase II study in patients with locally advanced pancreatic carcinoma: ARC-II – Akt-inhibition by Nelfinavir plus chemoradiation with gemcitabine and cisplatin - ARC-II in locally advanced pancreatic carcinoma	Dr Thomas Brunner	Oxford	Oxford, Southampton	6
A Randomized Phase 2 Placebo-Controlled Study of LY2495655 in Patients with Advanced or Metastatic Pancreatic Cancer Receiving Chemotherapy	Prof Kenneth CH Fearon	Edinburgh/Dundee	Imperial, KCL, Southampton	12
A Study Comparing CO-1.01 With Gemcitabine as First Line Therapy in Patients With Metastatic Pancreatic Adenocarcinoma (LEAP)	Jeff Evans	Glasgow	Glasgow, Manchester	0
A Study of the Effect of Gemcitabine With Fish Oil in Patients With Advanced Pancreatic Cancer	Ashley Dennison	Leicester	Leicester	0
Feasibility evaluation of proliferation and nucleoside transport using FLT PET imaging in advanced pancreatic cancer patients.	Dr Azeem Saleem	Manchester	Manchester	0
Locally Advanced Pancreatic Cancer: Phase II study of Cetuximab and 3-D Conformal image guided Radiotherapy	Dr Andrew Jackson, Prof Patricia Price	Manchester	Manchester	0
Phase 2 Placebo-controlled Double-blind Trial of Dasatinib Added to Gemcitabine for Subjects with Locally-advanced Pancreatic Cancer	Prof Jeff Evans	Glasgow	Leeds	0
Phase II randomised study of chemo-anticoagulation (Gemcitabine_LMWH) vs chemotherapy alone (Gemcitabine) for locally advanced and metastatic pancreatic adenocarcinoma	Dr Anthony Maraveyas	Leeds	Barts	0
Phase II randomized trial of MEK inhibitor MSC1936369B or placebo combined with gemcitabine in metastatic pancreas cancer subjects	Dr John Bridgewater	UCL	UCL	1
Proof of mechanism study of an oral hedgehog inhibitor (GDC-0449) in patients with resectable pancreatic ductal adenocarcinoma in the pre-operative window period.	Dr David Tuveson	Cambridge	Cambridge	0
RAMSETE: A single arm, multicenter, single-stage phase II trial of RAD001 in Advanced and Metastatic Silent neuro-Endocrine Tumours in Europe	Dr Nicholas Reed	Glasgow	Glasgow, Manchester	0
Randomized Phase II Study of BEZ235 vs. everolimus in Advanced Pancreatic Neuroendocrine Tumors	Dr Juan Valle	Manchester	Glasgow, KCL, Sheffield	3
Scheduling nabpaclItaxEl with GEmcitabine (SIEGE): Randomised phase II trial to investigate two different schedules of nabpaclitaxel (Abraxane) combined with gemcitabine as first line treatment for metastatic pancreatic ductal adenocarcinoma	Dr Pippa Corrie	Cambridge	Birmingham, Cambridge, Leicester, Manchester	1
Study of PM01183 as Treatment in Patients with Pancreatic Cancer	D Cunningham	ICR	Glasgow, Leeds	0
The impact of combined modality positron emission tomography with computerised tomography scanning (PET/CT) in the diagnosis and management of pancreatic cancer.	Miss Paula Ghaneh	Liverpool	Barts	0
The PanORAMA project: Pancreatic Cancer Predisposition, ObesityRelated Deposition Assessment using Magnetic Resonance ImAging	Coe, Mr Peter	Manchester	Manchester	0
Penis				

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
Characterising metastatic penile cancer using molecular imaging - hybrid MRI-PET	Mr Manit Arya	Barts/Brighton	Barts	0
Prostate				
A double blind, randomised, dose finding, repeat dose, phase II, multi-centre study of alpharadin for the treatment of hormone refractory patients with prostate cancer and skeletal metastases	Dr Christopher Parker	ICR	Belfast	0
A Phase I, Open-Label, Multicentre Study to Assess the Safety, Tolerability, Pharmacokinetics and Preliminary Anti-tumour Activity of Ascending Doses of AZD3514 in Patients With Metastatic Castration-Resistant Prostate Cancer	Dr Tony Elliot	Manchester	Glasgow, ICR, Manchester, UCL	0
A Phase I/ randomised phase II trial of abiraterone acetate with or without R05503781 in patients with metastatic Castrate Resistant Prostate Cancer (mCRPC) who have not previously received docetaxel	Dr Rob Jones	Glasgow	Belfast	
A phase II single arm, multi-centre trial of triamcinolone with a GnRH analog for castration resistant prostate cancer	Dr Jonathan Shamash	Barts/Brighton	Barts, Brighton	7
A PHASE II STUDY EVALUATING INTRAVENOUS MELPHALAN WITH AUTOLOGOUS WHOLE BLOOD STEM CELL TRANSPLANTATION (PBSCT) OVER THREE CYCLES IN PATIENTS WITH CASTRATION-RESISTANT PROSTATE CANCER	Dr Jonathan Shamash	Barts/Brighton	Barts	8
A Proof of Concept Study of Maintenance Therapy With Tasquinimod in Patients With Metastatic Castrate-resistant Prostate Cancer Who Are Not Progressing After a First Line Docetaxel Based Chemotherapy	Dr Simon Chowdhury	KCL	KCL, UCL	6
A Randomised Phase II Study of Neoadjuvant TAK-700 and Leuprorelin Acetate versus Surgery Alone in Intermediate and High Risk Clinically Localized Prostate Cancer	Dr Thomas Powles	Barts/Brighton	Barts, Southampton	7
A Randomised, Double-Blind, Placebo-Controlled, Multicentre Phase II Study to Compare the Efficacy, Safety and Tolerability of Olaparib Versus Placebo When Given in Addition to Abiraterone Treatment in Patients With Metastatic Castrate-Resistant Prostate Cancer Who Have Received Prior Chemotherapy Containing Docetaxel	Prof Noel Clarke	Manchester	Cardiff, Manchester	0
A Randomized, Double-Blind, Phase II, Efficacy and Safety Study of MDV3100 (ASP9785) vs. Bicalutamide in Castrate Men with Metastatic Prostate Cancer	Dr Simon Chowdhury	KCL	Cambridge, Glasgow, KCL, Manchester, UCL	18
A Study of HSP90 Inhibitor AT13387 Alone or in Combination With Abiraterone Acetate	Prof Johann De Bono	ICR	Brighton, Cardiff, Manchester, Southampton	3
AdUP: A Phase I Clinical Trial of a replication defective type 5 adenovirus vector expressing nitroreductase and GMCSF (AdNRGM) given via trans-perineal, template-guided, intra-prostatic injection, followed by intravenous CB1954, in patients with locally relapsed hormone-refractory Prostate Cancer.	Mr Prashant Patel	Birmingham	Birmingham	2
Investigating Safety, Tolerability and Efficacy of AZD5363 in Prostate Cancer.	John Radford	Manchester	Cardiff, Southampton, UCL	3
MDV3100 + AZD5363 in CRPC	Dr Johann De-Bono	ICR	ICR	
Molecular profiling of Tumour pathways determining Cabazitaxel sensitivity and resistance	Mr Rakesh Heer	Newcastle	Newcastle	4
Phase I Study of ZD4054 (Zibotentan) and Docetaxel in Patients With Metastatic HRPC	Dr Heather Payne	ICR	UCL	0
Phase I/II Study of ASP9521 in Castrate-Resistant Prostate Cancer (CRPC) Patients	Prof Johann De Bono	ICR	Glasgow, ICR	0
Phase Ib of Abiraterone Acetate Plus BEZ235 or BKM120 in Castration-resistant Prostate Cancer (CRPC) Patients	Dr Udai Banerji	ICR	ICR	3
Robotic surgery after focal ablation therapy	Mr Mark Emberton/Mr Paul Cathcart	Barts/Brighton	Barts	
SAFETY AND PHARMACOKINETICS OF ODM-201 IN PATIENTS WITH CASTRATE RESISTANT PROSTATE CANCER: OPEN, NON-RANDOMISED, UNCONTROLLED, MULTICENTRE, MULTIPLE DOSE ESCALATION STUDY	Dr NCRN Coordinating Centre	Birmingham	Cardiff, Manchester	20
Safety and Tolerability of ODM-201 in Castrate Resistant Prostate Cancer; Extension Study to Study 3104001	James, Professor Nicholas	Birmingham	Manchester	0
Sipuleucel-T Manufacturing Demonstration Study	Prof. T. Powles	Barts/Brighton	Barts	1
Study of GDC-0068 Or GDC-0980 With Abiraterone Acetate Versus Abiraterone Acetate in Patients With Castration-Resistant Prostate Cancer Previously Treated With Docetaxel Chemotherapy	Prof Johann De Bono	ICR	Leeds, Southampton	2

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
Study Using WST11 in Patients With Localized Prostate Cancer	Mr Mark Emberton	UCL	UCL	0
The use of Peroxisome Proliferator Activator Receptor Agonists in the management of Androgen Independent Prostate Cancer - PPAR	Dr J Shamash	Barts/Brighton	Barts	5
The Use of Rectal Balloons in Radical Pelvic Radiotherapy - a Feasibility Study	Stratford, Ms J	Manchester	Manchester	2
Skin				
Identification of critical molecular and biological events in the genesis of non-melanoma skin cancers and their modification by environment, immune status and viral infection	Dr Charlotte Proby	Edinburgh/Dundee	Dundee	28
Soft Tissue				
A Dose-finding Study of a Combination of Imatinib and BKM120 in the Treatment of 3rd Line GIST Patients	Leahy, Dr M	Manchester	Manchester	1
A Phase 2, Double-Blind, Placebo-Controlled Study Evaluating the Safety and Efficacy of IPI-926 in Patients With Metastatic or Locally Advanced (Unresectable) Chondrosarcoma	Dr Jeremy Whelan	UCL	Glasgow, Newcastle, UCL	0
A Phase II Study of Pazopanib in the Treatment of Surgically Unresectable or Metastatic Chondrosarcoma	Dr. Vijay Agarwal	Birmingham	Birmingham	
A Study of R1507 in Patients With Recurrent or Refractory Sarcoma.	Dr Beatrice Seddon	UCL	Manchester, UCL	0
Clinical Study of the Ability of Tumour Lysate Pulsed Dendritic Cells to induce Anti Tumour Immune Responses in Paediatric Oncology Patients	Dr John Anderson & Dr Anthony Michalski	UCL	UCL	0
Multi-center, open-label, non-randomised phase II study to evaluate the activity and tolerability of GW786034 in patients with advanced and/or metastatic soft tissue sarcoma who have relapsed following standard therapies or for whom no standard therapy exists.	Dr Fiona Cowie	Glasgow	Manchester, Sheffield	0
Open-label, multicentre, randomised, 2 stage design study of Bevacuzimab in combination with standard chemotherapy in minor patients with metastatic rhabdomyosarcoma and non rhabdomyosarcoma soft tissue sarcomas	Dr Julia Chisholm	UCL	UCL	2
Phase I feasibility study to compare early response assessment and planning volumes with contrast-enhanced computed tomography (CT), MRI including diffusion weighted MRI (DWI) and dynamic-contrast enhanced (DCE) MRI in patients with limb sarcoma undergoing pre-operative radiotherapy	Manoharan, Dr P	Manchester	Manchester	0
Phase II pilot of moderate radiotherapy for inoperable aggressive fibromatosis	Dr Martin Robinson	Sheffield	Sheffield	0
Phase II Study of NGR-hTNF in Combination With Doxorubicin in Patients Affected by Soft Tissue Sarcomas.	Dr M Leahy	Manchester	Manchester	0
Pilot Study of Circulating Tumour Cells in Sarcomas	McCabe, Dr M	Manchester	Manchester	0
Randomized Phase II Study of Brostallicin (PNU-166196A) Versus Doxorubicin as First Line Chemotherapy in Patients With Advanced or Metastatic Soft Tissue Sarcoma	Professor Ian Judson	ICR	Manchester	0
Study Of CP-751,871 In Patients With Ewing's Sarcoma Family Of Tumors	Prof B Hassan	Oxford	Oxford, UCL	0
Solid Tumour of Childhood				
A Phase I Study of Monotherapy Dalotuzumab and Ridaforolimus-Dalotuzumab Combination Treatment in Pediatric Patients with Advanced Solid Tumors	Prof Andrew Pearson	ICR	UCL	0
A Phase I Study of Ridaforolimus in Paediatric Patients with Advanced Solid Tumours	Prof Andrew Pearson	ICR	UCL	0
A Phase I/II study of Sunitinib in young Patients with Advanced Gastrointestinal Stromal Tumor	Prof Andrew Pearson	ICR	Manchester	
Pharmacokinetics of actinomycin D and vincristine in infants and older children with Wilms' tumour.	Dr Gareth Veal	Newcastle	UCL	0
Two part, multi-centre, single arm, open label study to determine the safety, tolerability and pharmacokinetics of oral Dabrafenib in paediatric subjects aged 1 month to < 18 years with advanced BRAF V600-mutation positive solid tumours	Prof Andrew Pearson	ICR	UCL	2

Study title	Chief Investigator	Lead	Centres Reporting	Patients recruited (£yr)
Stomach				
A dose finding study of Bortezomib in addition to Epirubicin, Carboplatin and Capecitabine (ECarboX) in advanced Gastric and Gastro-Oesophageal Junction Adenocarcinoma	Dr Martin Eatock	Belfast	Belfast	0
E7050 in Combination With Cisplatin and Capecitabine Versus Cisplatin and Capecitabine Alone in Patients With Advanced or Metastatic Solid Tumors and Previously Untreated Gastric Cancer	Dr W Mansoor	Manchester	Manchester	0
Urethra				
A phase II, single arm, single agent, multicentre, adaptive 2-stage study to evaluate the efficacy, safety and pharmacokinetics of AZD4877 administered weekly in patients with recurrent advanced urothelial cancer	Dr Robert Jones	Glasgow	Manchester, Southampton	0
Uterine/endometrial				
A Phase II, Single-arm Study of Orally Administered BEZ235 as Second-line Therapy in Patients With Advanced or Metastatic Endometrial Carcinoma	Dr Rebecca Kristeleit	UCL	Manchester	0
The Study of Oral Steroid Sulphatase Inhibitor BN83495 Versus Megestrol Acetate (MA) in Women With Advanced or Recurrent Endometrial Cancer	Dr John Green	Liverpool	Glasgow, Manchester	0
Vulva				
GROningen INternational Study on Sentinel nodes in Vulvar cancer (GROINSS-V) II	Mr Peter Baldwin	Cambridge	Barts	0