Diagnostic Criteria

The Criteria for diagnosis of pancreatitis for this trial is:

Hereditary Pancreatitis

The diagnosis of Hereditary Pancreatitis in a family is made on the basis of one or more of the following being present:

1. Two first-degree relatives or three or more second-degree relatives, in two or more generations with recurrent acute pancreatitis and/or chronic pancreatitis, for which there were no precipitating factors
2. A defining gene mutation known to cause hereditary pancreatitis, including gene mutations in the PRSS1 gene, namely R122H, R122C, N291, N29T and A16V, and others already published or identified during the course of the study.

Chronic Pancreatitis

The diagnosis of chronic pancreatitis is accepted if one or more of the following are present:

1. Recurrent bouts of 'pancreatic pain' with documented rises in the serum amylase for at least one year with supporting imaging evidence of pancreatitis
2. Pancreatic Calcification
3. Histological diagnosis confirming pancreatitis
4. Unequivocal pancreatic ductal morphology demonstrated radiologically
5. Abnormal pancreatic function tests (pancreato-lauryl test, faecal elastase).

Idiopathic Chronic Pancreatitis

A diagnosis of idiopathic chronic pancreatitis is defined as chronic pancreatitis occurring in an individual for which there was no known cause after a detailed history, biochemical testing and radiology, including that of both the biliary and pancreatic ducts and in the absence of autosomal dominant pancreatic disease within that family.

The LCTU

The Liverpool Cancer Trials Unit works closely with **Cancer Research UK** in the clinical research of new and existing products for the treatment of cancer, easing suffering and improving the quality of life for cancer patients.

Further Information

Trial Coordinator
Miss Sarah Jones
e: europac2@liverpool.ac.uk
t: 0151 794 8937

UK Chief Investigator
Professor J.P. Neoptolemos
e: john.neoptolemos@liv.ac.uk

There are co-ordinating centres in France, Germany and the UK. The LCTU is the co-ordinating centre for UK.

For more information about pancreatitis or current trials running within the Liverpool Cancer Trials Unit, please email:

lctu@liverpool.ac.uk

Or visit the LCTU website:

www.lctu.org.uk

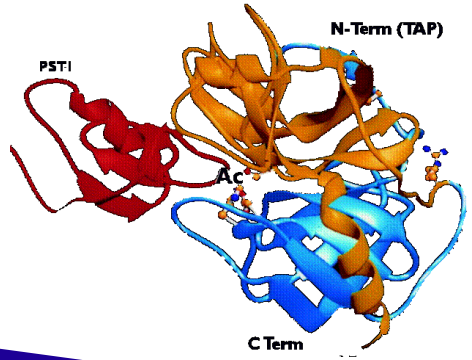
LCTU

CANCER RESEARCH UK

Liverpool Cancer Trials Unit

EUROPAC2

Double Blind Randomised Controlled trial to investigate the efficacy of ANTOX (vers)1.2 and MGCT (Magnesiocard®) for the treatment of Hereditary Pancreatitis and Idiopathic Chronic Pancreatitis



EUROPAC2 Trial

EUROPAC2 is a multi-centre, double blind, and placebo-controlled, randomised, parallel group study.

The objectives of this study are to determine the efficacy of **ANTOX™ (vers)1.2** and **MGCT (Magnesiocard®)** compared to placebo in the treatment of pain in patients with Hereditary Pancreatitis (HP) and Idiopathic Chronic Pancreatitis (ICP).

Statistical Considerations

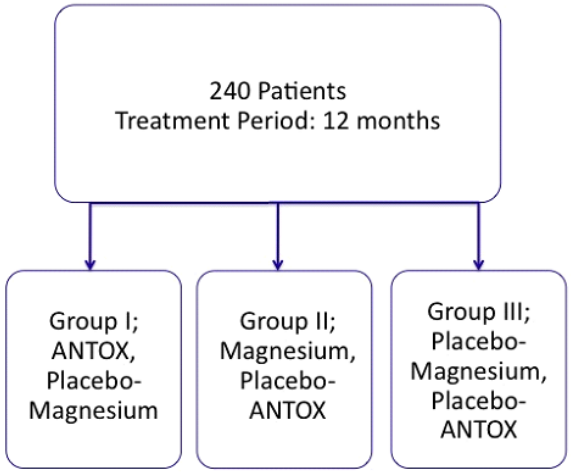
Primary Outcome:

- Pancreatic pain, defined as the number of days of typical 'pancreatic' pain during one year, calculated by the number of days recorded with any pancreatic pain.

Secondary Outcome:

- Intensity of pain recorded using a score (0-10) where 0 is no pain and 10 is worst pain imaginable
- Analgesic consumption assessed using 'morphine equivalents'
- The number of days spent in hospital due to painful exacerbations of pancreatitis or due to complications arising due to pancreatitis will be obtained from the patient. The clinician responsible for the care of the patient will independently verify this
- Quality of Life (QoL) including activities of daily living.

Treatment



Antox™ (vers)1.2 contains methionine, vitamin C, vitamin E, selenium and beta carotene

MGCT is a magnesium supplement.

Inclusion Criteria

- Patients with pancreatitis diagnosed for at least one year
- Patients who have provided written informed consent
- Patients who are willing to be followed up regularly for at least one year
- Patients who are able and willing to complete Quality of Life and Pain Assessment questionnaires
- Patients who are able and willing to provide urine and faecal samples within two weeks of each study visit
- Patients aged 5 to 65 years of age
- Patients with characteristic pancreatic pain that is either intermittent or continuous (2 or more episodes during the last 12 months)
- Patients with documented HP, clinically defined or proven by gene mutations in the PRSS1 gene, or patients with ICP and no mutations detected in the PRSS1 gene.

Exclusion Criteria

- Patients that do not consent to be involved in the trial, or patients under the age of 16 whose parents/guardians do not consent for them to be involved in the trial
- Patients or parents/guardians of underage patients with learning disabilities or other cognitive or sensory impairments that would prevent adequate understanding of the study requirements
- Patients who are currently receiving treatment with antioxidants or magnesium tablets or who have had such treatment within the last 3 months
- Patients who are currently receiving treatment with oral hypoglycaemics or steroids or who have had such treatment within the last 3 months
- Patients with renal failure (serum creatinine $\geq$200µmol/l)
- Patients with atrio-ventricular-block
- Patients with Serum triglyceride levels $\geq$1000mg/dl
- Patients who are dependent on daily opiate analgesia (morphine or equivalent for more than 12 months)
- Patients who have chronic hepatic failure or serious impairment of pulmonary, cardiac, neurological or cerebral function
- Patients who are participating in another drug trial
- Patients who are pregnant
- All men and women of reproductive potential unless using at least 2 types of contraception, one of which must be a condom
- Lactating mothers
- Patients with any disorder that would prevent adequate absorption of the active treatment
- Patients suffering from schizophrenia
- Patients who smoke more than 20 cigarettes a day.