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Double blind randomised controlled trial to investigate the efficacy of ANTOX (version 1.2) and MGCT (Magnesium) for the treatment of hereditary and idiopathic chronic pancreatitis

Submission date 05/01/2007	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 30/05/2007	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 17/04/2019	**Condition category** Digestive System	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Study website
http://www.pancreas.de

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2006-000087-83

IRAS number

ClinicalTrials.gov number
NCT00142233

Secondary identifying numbers
N/A

Study information

Scientific Title
Double blind randomised controlled trial to investigate the efficacy of ANTOX (version 1.2) and MGCT (Magnesium) for the treatment of hereditary and idiopathic chronic pancreatitis

Acronym
EUROPAC-2

Study objectives
In patients with chronic pancreatitis, pain can be reduced significantly by a treatment with ANTOX (version 1.2) or Magnesium (MGCT) compared to the control group.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval received from the following local ethics committees:
1. Germany:
1.1. Greifswald (date: 16th April 2004, ref: III-UV-92-03)
1.2. Heidelberg (date: 12th December 2005, ref: 325-2005)
1.3. Hamburg (date: 11th May 2005, ref: M-135/05)
1.4. Muenster (date: 11th May 2006, ref: AZ 2006-092-b-A)
1.5. Munich (date: 7th August 2006, ref: 193-06)
1.6. Leipzig (date: 17th July 2006, ref: 129-2006)
1.7. Kiel (date: 20th June 2006, ref: B 260/06)
1.8. Tuebingen (date: 14th March 2007, ref: 87-2007-G)
2. United Kingdom: Liverpool (date: 12th June 2006, since then they have put in an amendment [001] and have received approval for this on the 3rd April 2007, ref: 06/Q1502/4)
3. France: Clichy (date: 6th December 2010, ref. 2010-Nov.-12458)

Applications with the Ethics committee are under way at:
1. Austria: Vienna
2. Czech Republic: Brno

Study design
Randomised placebo-controlled three-armed trial

Primary study design
Interventional

Secondary study design

Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Patient information can be found on the website at http://www.pancreas.de/ (only in German)

Health condition(s) or problem(s) studied
Hereditary or idiopathic chronic pancreatitis

Interventions
Current interventions as of 16/02/2012
Group 1:
Two ANTOX (version 1.2) tablets, three times daily; antioxidant treatment (daily):
1. 300 µg organic selenium
2. 720 mg vitamin C
3. 228 mg vitamin E
4. 2880 mg methionine

Group 2:
Two Magnesium-L-Aspartate-hydrochloride (MGCT) (Magnesio-card 2.5 mmol) tablets three times a day, total dose 15 mmol (365 mg/per day)
Group 3:
The same number of tablets as in groups one and two but placebo instead of active drug.

Children aged 5 to 9 years will take half the number of tablets per day. Duration of intervention is 48 weeks for each group.

As this trial started prior to the changes in the Good Clinical Practice (GCP) guidelines and EU 2002 guidelines are applicable, the main part of the trial held in Germany did not need and therefore did not name a sponsor. The University of Liverpool trials unit takes over responsibilities as a sponsor for the UK, and these are the details held below in the sponsor section.

Previous interventions
Group 1:
Two ANTOX (version 1.2) tablets, three times daily; antioxidant treatment (daily):
1. 300 µg organic selenium
2. 54000 IU beta-carotene = 18 mg
3. 750 mg vitamin C
4. 540 IU of vitamin E = 240 mg
5. 2700 mg methionine

Group 2:
Two Magnesium-L-Aspartate-hydrochloride (MGCT) (Magnesio-card 2.5 mmol) tablets three times a day, total dose 15 mmol (365 mg/per day)

Group 3:
The same number of tablets as in groups one and two but placebo instead of active drug.

Children aged 5 to 9 years will take half the number of tablets per day. Duration of intervention is 48 weeks for each group.

As this trial started prior to the changes in the Good Clinical Practice (GCP) guidelines and EU 2002 guidelines are applicable, the main part of the trial held in Germany did not need and therefore did not name a sponsor. The University of Liverpool trials unit takes over responsibilities as a sponsor for the UK, and these are the details held below in the sponsor section.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
ANTOX (version 1.2), Magnesium (MGCT)

Primary outcome measure
Reduction in the number of days of pancreatic pain during 12 continuous months of treatment

Secondary outcome measures
Current secondary outcome measures as of 16/02/2012:
1. Intensity of pain recorded using a score (0-10) where 0 is no pain and 10 is worst pain imaginable
2. Analgesic consumption assessed using morphine equivalents
3. 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
4. Quality of life (QoL) including activities of daily living

Previous secondary outcomes
1. Intensity of pain recorded using a visual analogue score (0 to 10) where 0 is no pain and 10 is the worst pain imaginable; this will be recorded daily in a pain diary by the patient
2. Analgesic consumption assessed using pethidine equivalents; this will be recorded daily in the pain diary by self report (or in case of children by parents report)
3. 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; hospital stays will be reported as Serious Adverse Events (SAE) and therefore recorded within 24 hours at the leading trial centre
4. Quality of Life (QoL) including activities of daily living, recorded every 12 weeks by self report
5. Inflammatory response and pancreatic activity measured at pre-defined time points and during symptomatic attacks of pancreatitis assessed by the pancreatic inflammation markers, urinary Trypsinogen Activation Peptide (TAP) and urinary amylase and the exocrine sufficiency marker, faecal elastase; this will be recorded every 12 weeks during the study visit
6. Oxidant stress as measured by urinary thiobarbituric acid, at fixed time points and during symptomatic attacks of pancreatitis; this will be recorded every 12 weeks

7. Changes in the urinary levels of magnesium, selenium and vitamin C; this will be recorded every 12 weeks
8. Data acquisition including markers of inflammatory response during acute attack of chronic pancreatitis

Overall study start date
01/05/2005

Completion date
01/09/2020

Eligibility

Key inclusion criteria
Current inclusion criteria as of 16/02/2012:
1. Patients with pancreatitis diagnosed for at least one year
2. Patients who have provided written informed consent
3. Patients who are willing to be followed up regularly for at least one year
4. Patients who are able and willing to complete Quality of Life and Pain Assessment questionnaires
5. Patients who are able and willing to provide urine and faecal within two weeks of each study visit
6. Patients aged 5 to 65 years of age
7. Individuals with characteristic pancreatic pain that is either intermittent or continuous (two or more episodes during the last 12 months)
8. Patients with documented Hereditary Pancreatitis (HP), clinically defined or proven by gene mutations in the PRSS1 gene, or patients with Idiopathic Chronic Pancreatitis (ICP) and no mutations detected in the PRSS1 gene.

Current inclusion criteria as of 10/07/2007:
1. Patients with pancreatitis diagnosed for at least one year
2. Patients who are willing to be followed up regularly for at least one year
3. Patients aged 5 to 65 years of age
4. Individuals with characteristic pancreatic pain that is either intermittent or continuous (two or more episodes during the last 12 months)
5. Patients with documented Hereditary Pancreatitis (HP), clinically defined or proven by gene mutations in the PRSS1 gene, or patients with Idiopathic Chronic Pancreatitis (ICP) and no mutations detected in the PRSS1 gene.

Previous inclusion criteria:
1. Patients must have had pancreatitis diagnosed for at least one year
2. Patients must be willing to be followed up regularly for at least one year
3. Patients aged 5 to 40 years
4. Individuals must have characteristic pancreatic pain that is either intermittent or continuous (two or more episodes during the last 12 months)

Participant type(s)
Patient

Age group
Not Specified

Sex
Not Specified

Target number of participants
240

Total final enrolment
295

Key exclusion criteria
Current exclusion criteria as of 16/02/2012:
1. 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
2. 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
3. Patients who are currently receiving treatment with antioxidants or magnesium tablets or who have had such treatment within the last 3 months
4. Patients who are currently receiving treatment with oral hypoglycaemics or steroids or who have had such treatment within the last 3 months
5. Patients with renal failure (serum creatinine ≥ 200µmol/l)
6. Patients with atrio-ventricular-block
7. Serum triglyceride levels ≥ 1000mg/dl
8. Patients who are dependent on daily opiate analgesia (morphine or equivalent for more than 12 months)
9. Patients who have chronic hepatic failure, or serious impairment of pulmonary, cardiac, neurological or cerebral function
10. Patients who are participating in another drug trial
11. Patients who are pregnant
12. All men and women of reproductive potential unless using at least two types of contraceptive precautions, one of which must be a condom
13. Lactating mothers
14. Patients with any disorder that would prevent adequate absorption of the active treatment
15. Patients suffering from schizophrenia
16. Patients who smoke more than 20 cigarettes per day
17. Patient has had pancreatic surgery since their last attack of pancreatitis, or is planning to have elective pancreatic surgery within the trial duration

Current exclusion criteria as of 10/07/2007:
1. Patients that do not consent to be involved in the trial, or underage patients whose parents /guardians do not consent for them be involved in the trial
2. 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
3. Patients who are currently receiving treatment with antioxidants or magnesium tablets or who have had such treatment within the last three months
4. Patients who are currently receiving treatment with oral hypoglycaemics or steroids or who have had such treatment within the last three months
5. Patients with renal failure (serum creatinine greater than or equal to 200 µg/l)
6. Patients with atrio-ventricular-block

7. Serum triglyceride levels greater than or equal to 1000 mg/dl
8. Patients who are dependent on daily opiate analgesia (morphine or equivalent) for more than 12 months
9. Patients who have chronic hepatic failure, or serious impairment of pulmonary, cardiac, neurological or cerebral function
10. Patients who are participating in another drug trial
11. Patients who are pregnant
12. Women of childbearing age who are not using contraception
13. Lactating mothers
14. Patients with any disorder that would prevent adequate absorption of the active treatment
15. Patients suffering from schizophrenia
16. Patients who smoke more than 20 cigarettes per day

Previous exclusion criteria:
1. Patients that do not consent to be involved in the trial, or whose parents do not consent for their children to be involved
2. Patients or guardians of underage patients, with learning disabilities or other cognitive or sensory impairments that would prevent adequate understanding of the study requirements
3. Patients who have had treatment for less than three months, or are currently receiving treatment with antioxidants or magnesium tablets
4. Patients who have had recent (less than three months), or are currently receiving treatment with oral hypoglycaemics or steroid treatment
5. Patients with renal failure (serum creatinine greater than or equal to 200 µg/l)
6. Patients with atrio-ventricular-block
7. Serum triglyceride levels greater than or equal to 1000 mg/dl
8. Patients under the age of 5 years or over the age of 40 years
9. Patients who are dependent on daily opiate analgesia (morphine or equivalent) for more than 12 months
10. Patients who have chronic hepatic failure, or serious impairment of pulmonary, cardiac, neurological or cerebral function
11. Patients who are participating in another drug trial
12. Patients who are pregnant
13. Women of childbearing age who are not using contraception
14. Lactating mothers
15. Any disorder that would prevent adequate absorption of the active treatment

Date of first enrolment
01/05/2005

Date of final enrolment
01/04/2018

Locations

Countries of recruitment
France

Germany

United Kingdom

Study participating centre
Universitätsmedizin Greifswald
Greifswald
Germany
17475

Sponsor information

Organisation
The University of Liverpool Clinical Trials Unit (UK)

Sponsor details
Director of Research
Faculty of Medicine
University of Liverpool
Liverpool
England
United Kingdom
L69 3GA

Sponsor type
University/education

Website
http://www.lctu.org.uk

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Other

Funder Name
Investigator initiated trial in each study centre, without industrial sponsoring. Pharma Nord will be contributing towards the UK trial coordinator.

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration