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A controlled trial of Orlistat (Xenical) for patients with non-alcoholic steatohepatitis (NASH)

Submission date 19/09/2005	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 27/10/2005	**Overall study status** Completed	
Last Edited 11/10/2016	**Condition category** Digestive System	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof Christopher Day

Contact details
SCMS, Floor 4
William Leech Building
Medical School
Framlington Place
Newcastle upon Tyne
United Kingdom
NE2 4HH

Additional identifiers

Protocol serial number
04/Q0904/47

Study information

Scientific Title
A controlled trial of Orlistat (Xenical) for patients with non-alcoholic steatohepatitis (NASH)

Study objectives
The principal research objective is to determine if treatment with the drug Orlistat (product name Xenical), one tablet three times a day, along with a weight reducing diet and two multivitamin tablets a day, as compared to diet and multivitamins alone, is beneficial to the liver of overweight patients suffering from non-alcoholic steatohepatitis (NASH). The beneficial effect will be judged by performing a repeat liver biopsy to assess whether the degree of liver damage has improved since the biopsy on which the diagnosis of NASH was made.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Nonalcoholic steatohepatitis

Interventions
Orlistat (Xenical) one tablet (120 mg) three times a day for one year, along with a weight reducing diet and two multivitamin tablets a day versus diet and multivitamins alone.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Orlistat

Primary outcome(s)
Overall necroinflammatory grade or fibrosis stage on repeat liver biopsy. A change of one point in grade or stage will be considered significant.

Key secondary outcome(s))
1. Liver biochemistry (alanine transaminase, aspartate transaminase, gamma, glutamyl transferase)
2. Insulin sensitivity assessed by HOMA index (derived from fasting glucose and insulin measurements)
3. Body mass index (BMI)
4. Quality of life assessed by the chronic liver disease questionnaire (CLDQ)

Completion date
31/12/2006

Eligibility

Key inclusion criteria
1. Adult more than 18 but less than 75 years
Children will not be included in this study for three reasons:
1.1. The development of NASH in children may be due to different age-related metabolic processes than in adults
1.2. Children with NASH are always obese and their elevated aminotransferases normalise with weight loss or vitamin E treatment
1.3. The natural history of NASH in children is unknown and may not be sufficient to warrant the risk of using a new class of drug and performing a follow up liver biopsy. Orlistat is not approved for use in children
2. Body mass index (BMI) more than 28 kg/m^2. Orlistat is only licensed for patients with this degree of obesity
3. Liver biopsy obtained no more than six months before randomisation with a pathology report confirming that the histological diagnosis is consistent with NASH. A longer time period would increase the chances that the liver pathology had altered since the original biopsy
4. No more than 5% weight loss since liver biopsy. More weight loss would increase the chances that the liver pathology had altered since the original biopsy
5. Raised alanine transaminase (ALT) and/or aspartate transaminase (AST) and/or gamma-glutamyltransferase (GGT). This allows assessment of whether treatment improves liver blood tests
6. Ability to give informed consent
7. A satisfactory blood count, renal function and albumin. Ensures second biopsy likely to be safe (blood count, renal function) and that liver disease is not too far advanced (albumin)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Evidence of decompensated liver disease such as a history of or presence of ascites, bleeding varices, or spontaneous encephalopathy. These patients are considered too advanced to benefit from treatment
2. Any cause for chronic liver disease other than NASH
3. Alcohol consumption greater than sensible alcohol limits three units (~8-10 g) per day for

males and two units per day for females during the past five years
4. Markers of active hepatitis virus infection (hepatitis B surface antigen [HBsAg], hepatitis C virus antibody [HCV Ab])
5. Patients on medications known to be associated with NASH
6. Total parenteral nutrition (TPN) within the past six months
7. Prior obesity surgery including gastric or intestinal bypass procedures
8. Evidence of genetic haemochromatosis - patients with raised ferritin or transferrin and either homozygous for the C282Y HFE mutation or compound C282Y/H63D heterozygotes to be excluded. All these groups of patients are considered to have alternative causes for their liver disease or 'secondary' rather than true 'primary' NASH.
9. Type one diabetes or type two diabetes mellitus on any form of treatment (either insulin or oral hypoglycaemic)
10. Previous therapy for NASH including ursodeoxycholic acid, metformin, glitazones
11. Current treatment with fibrates. These treatments may be of benefit in NASH and would therefore confound any effects of Orlistat
12. History of prior organ transplantation. Immunosuppression and risk of recurrent disease (in liver transplant recipients) likely to confound any effects of Orlistat

Date of first enrolment
01/01/2005

Date of final enrolment
31/12/2006

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Medical School
Newcastle upon Tyne
United Kingdom
NE2 4HH

Sponsor information

Organisation
The Newcastle upon Tyne Hospitals NHS Trust (UK)

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Industry

Funder Name
Unrestricted educational grant from Roche Products Limited

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration