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A preliminary study to examine and evaluate the effect of obeticholic acid (INT-747) for the treatment of portal hypertension in patients with alcoholic liver disease

Submission date
05/05/2011

Recruitment status
No longer recruiting

Registration date
15/07/2011

Overall study status
Completed

Last Edited
28/05/2020

Condition category
Nutritional, Metabolic, Endocrine

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Dr Rajeshwar Mookerjee

Contact details
Department of Hepatology
Royal Free Hospital
Pond Street
Hampstead
London
United Kingdom
NW3 2QG
+44 (0)207 433 2874
r.mookerjee@ucl.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2010-023241-29

Protocol serial number

747-204

Study information

Scientific Title
A pilot study to evaluate the safety, tolerability and efficacy of obeticholic acid (INT-747) for the treatment of portal hypertension

Acronym
PESTO

Study objectives
1. Obeticholic acid (OCA) is safe and tolerated in patients with cirrhosis and portal hypertension
2. Obeticholic acid (OCA) will reduce the Hepatic Venous Pressure Gradient (HVPG) in patients with portal hypertension

Ethics approval required
Old ethics approval format

Ethics approval(s)
National Research Ethics Service (NRES) North London REC 3 Committee approval granted on:
10/12/2010 (Final Protocol)
01/03/2011 (Amendment 1)
05/04/2011 (Amendment 2)
02/12/2011 (Amendment 3)

Primary study design
Interventional

Study design
Pilot open-label single-centre study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Portal hypertension in patients with alcoholic cirrhosis of the liver

Interventions
1. Physical examination
2. Vital signs
3. 12-lead electrocardiogram (ECG)
4. Blood sampling and analysis peripheral and hepatic blood samples
5. Urine collection and analysis
6. Hepatic vein catheterisation to measure HVPG and other hepatic haemodynamic measures (efficacy cohort only)

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Obeticholic acid (OCA)

Primary outcome(s)
1. Safety and tolerability as measured and assessed throughout the study by monitoring adverse experiences, clinical laboratory values in blood and measures of blood pressure and heart rate, all at baseline, Day 4, Day 7 and at follow up after 2-4 weeks and ECG at baseline and Day 7
2. Portal hypertension measured at baseline and Day 7 by HPVG. Outcome measure of a reduction of ≥15% at Day 7 compared to baseline or a reduction to <12 mmHg

Key secondary outcome(s)
1. Hepatic haemodynamics including hepatic blood flow (measured from the concentration of indocynanine green in the hepatic venous blood vs peripheral venous blood using the Fick Principle) and intrahepatic resistance (fluoroscopic examination after catheterisation of the right hepatic vein following injection of contrast medium)
2. Liver function: measured by gamma glutamyl transpeptidase (GGT), alanine transaminase (ALT), alkaline phosphatase (ALP), albumin, prothrombin time and bilirubin (total and unconjugated)
3. Pharmacokinetics: measured by plasma drug and metabolite concentrations
4. Inflammation: measured by C-reactive protein

Completion date
31/12/2012

Eligibility

Key inclusion criteria
1. Male or female age 18-70 years
2. History of alcoholic cirrhosis with clinical or radiological and biochemical evidence of cirrhosis
3. Evidence of early decompensated cirrhosis (Child-Pugh score ≥7 to ≤12)
4. Patients recruited into the cohort evaluation of efficacy must have significant portal hypertension defined as an HVPG ≥ 12 mmHg
5. Patients with large or grade 3 oesophageal varices as identified by endoscopy within 6 months of screening should be in an endoscopic band ligation program at the time of study entry
6. Female patients must be postmenopausal, surgically sterile, or if premenopausal, must be prepared to use at least one effective (≤1% failure rate) method of contraception during the course of the study and for 14 days after the end of dosing. Male patients with female partners of child bearing potential must be prepared to use at least one effective method of contraception with all sexual partners unless they have had a prior vasectomy. Effective methods of contraception are considered to be:
6.1. Condom (male or female)
6.2. Diaphragm, with spermicide
6.3. Hormonal (e.g. contraceptive pill, patch, intramuscular implant or injection)
6.4. Intrauterine device (IUD)
6.5. Vasectomy (partner)
7. Must be willing and able to give written informed consent and agree to comply with the study protocol

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
70 Years

Sex
All

Total final enrolment
34

Key exclusion criteria
1. Patients with co-existing disease including:
1.1. Significant organ failure defined as:
1.2. Respiratory: PaO2 < 8kPa
1.3. Renal: serum creatinine >150 µmol/L
1.4. Cardiovascular: haemodynamic requirement for inotropic support
1.5. Central nervous system (CNS): hepatic encephalopathy West Haven Criteria score >2
1.6. Decompensated cirrhosis with requirement for organ support
1.7. Concomitant hepatobiliary disease (except hepatitis B or C viral disease), e.g., gallstones, primary sclerosing cholangitis, primary biliary cirrhosis
1.8. Known or suspected hepatic or extra hepatic malignancy, unless adequately treated or in complete remission for ≥ 3 years
1.9. Concomitant pancreatitis
2. Use of treatments for hepatitis B or C virus within 12 months of randomisation, or anticipated use during the study
3. Use of the following drugs within 6 months of randomisation: Immuno-modulatory treatment (including azothiaprine, methotrexate, anti-TNF therapies)
4. Use of concomitant vasoactive drugs within 3 months of randomisation:
4.1. Beta blockers
4.2. Nitrates
4.3. Vasopressin or analogues
5. Use of the following drugs within 3 months of randomisation:
5.1. Systemic corticosteroids
5.2. Pentoxifylline
5.3. Potentially hepatotoxic drugs (including methyl-dopa, sodium valproic acid, isoniazid, or nitrofurantoin)
5.4. Ursodeoxycholic acid (UDCA)
5.5. Known or suspected use of illicit drugs or drugs of abuse (allowed if medically prescribed or indicated)
6. Change in dose or regimen within 3 months of randomisation of:

6.1. Fibrates or statins
6.2. Angiotensin II receptor antagonist or angiotensin converting enzyme (ACE) inhibitor
7. Presence of human immunodeficiency virus (HIV)
8. If female: pregnant, lactating, or positive serum or urine pregnancy test
9. Body mass index (BMI) >40, or >35 with complications
10. Other concomitant disease or condition likely to significantly decrease life expectancy (e.g., moderate to severe congestive heart failure)
11. Any patient who has received any investigational drug or device within 4 months of dosing, or who is scheduled to receive another investigational drug or device during the course of this study

Date of first enrolment
01/07/2011

Date of final enrolment
31/12/2012

Locations

Countries of recruitment
United Kingdom

England

Belgium

Study participating centre
Department of Hepatology, Royal Free Hospital
Pond Street
Hampstead
London
United Kingdom
NW3 2QG

Study participating centre
University Hospital Leuven (Universitat Ziekenhuis Leuven (UZL))
Dept Hepatology and Pancreaticobiliary Disorders
Herestraat 49
Leuven
Belgium
B - 3000

Sponsor information

Organisation
Intercept Pharmaceuticals Inc

ROR
https://ror.org/01sx6jc36

Funder(s)

Funder type
Industry

Funder Name
Intercept Pharmaceuticals Inc

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			28/05/2020	No	No