

# 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

<b>Submission date</b> 05/05/2011	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
<b>Registration date</b> 15/07/2011	<b>Overall study status</b> Completed	<input type="checkbox"/> Protocol
<b>Last Edited</b> 28/05/2020	<b>Condition category</b> Nutritional, Metabolic, Endocrine	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

Not provided at time of registration

## Contact information

### Type(s)

Scientific

### Contact name

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## Additional identifiers

### EudraCT/CTIS number

2010-023241-29

### IRAS number

**ClinicalTrials.gov number**

**Secondary identifying numbers**

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)

### **Study design**

Pilot open-label single-centre study

### **Primary study design**

Interventional

### **Secondary study design**

Non randomised study

### **Study setting(s)**

Hospital

### **Study type(s)**

Treatment

### **Participant information sheet**

Not available in web format, please use the contact details to request a patient information sheet

### **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 measure**

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  $\geq 15\%$  at Day 7 compared to baseline or a reduction to  $< 12$  mmHg

### **Secondary outcome measures**

1. Hepatic haemodynamics including hepatic blood flow (measured from the concentration of indocyanine 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

### **Overall study start date**

01/07/2011

### **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  $\geq 7$  to  $\leq 12$ )

4. Patients recruited into the cohort evaluation of efficacy must have significant portal hypertension defined as an HVPG  $\geq 12$  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 ( $\leq 1\%$  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

**Age group**

Adult

**Lower age limit**

18 Years

**Upper age limit**

70 Years

**Sex**

Both

**Target number of participants**

Up to 39, depending on number of cohorts studied (3 cohorts up to 39, 2 cohorts up to 26)

**Total final enrolment**

34

**Key exclusion criteria**

1. Patients with co-existing disease including:
  - 1.1. Significant organ failure defined as:
    - 1.2. Respiratory: PaO<sub>2</sub> < 8kPa
    - 1.3. Renal: serum creatinine >150  $\mu$ mol/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  $\geq 3$  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 azothiaprime, 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**

Belgium

England

United Kingdom

**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

**Sponsor details**

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New York  
United States of America  
NY 10013  
+1 646 747 1000  
TBeecherJones@interceptpharma.com

**Sponsor type**

Industry

**Website**

<http://www.interceptpharma.com>

**ROR**

<https://ror.org/01sx6jc36>

## **Funder(s)**

**Funder type**

Industry

**Funder Name**

Intercept Pharmaceuticals Inc

# Results and Publications

## Publication and dissemination plan

Added 23/03/2018:

Results presented at the 49th Annual Meeting of the European Association for the Study of the Liver in April 2014 ([http://www.professionalabstracts.com/ilc2014/planner/index.php?go=abstract&action=abstract\\_show&absno=3124&](http://www.professionalabstracts.com/ilc2014/planner/index.php?go=abstract&action=abstract_show&absno=3124&))

## Intention to publish date

## 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?
<a href="#">Basic results</a>			28/05/2020	No	No