ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
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Study Identification

Unique Protocol ID:	87RI18_0007 (DFG HEP)
Brief Title:	Description of the Evolution of Plasma and Urinary Concentrations of Iohexol in a Cirrhotic Patient Population (DFG HEP)
Official Title:	Description of the Evolution of Plasma and Urinary Concentrations of Iohexol in a Cirrhotic Patient Population: "Pilot Study on 9 Patients"
Secondary IDs:	

Study Status

Record Verification:	September 2018
Overall Status:	Not yet recruiting
Study Start:	December 18, 2018 [Anticipated]
Primary Completion:	December 25, 2019 [Anticipated]
Study Completion:	December 25, 2019 [Anticipated]

Sponsor/Collaborators

Sponsor:	University Hospital, Limoges
Responsible Party:	Sponsor
Collaborators:	

Oversight

U.S. FDA-regulated Drug:	No
U.S. FDA-regulated Device:	No
U.S. FDA IND/IDE:	No
Human Subjects Review:	Board Status: Approved Approval Number: 18-LIMO-01 Board Name: CPP Sud-Est V Board Affiliation: CPP Phone: + 33 4 76 76 57 83 Email: cppsudest5@chu-grenoble.fr Address: CHU de Grenoble C 10217 38043 GRENOBLE Cedex 9 04 76 76 57 83

Data Monitoring:	No
FDA Regulated Intervention:	No

Study Description

Brief Summary:

Background: It is important to accurately assess the glomerular filtration rate (GFR) of patients with liver diseases, particularly cirrhosis, to deliver care and adjust the drugs' posology.

Purpose: The frequency of chronic renal failure is underestimated in patients with advanced liver disease and the difficulty to assess kidney failure justifies the investigator's study, which aims to describe, by means of a population pharmacokinetic model, the evolution of plasma and urinary concentrations of iohexol, an effective non-ionic, water-soluble contrast agent which is used in radiographic procedures, in cirrhotic patients.

Detailed Description:

Cirrhosis is often complicated by kidney failure and the prognostic value of renal function (serum creatinine) during cirrhosis is included in the MELD model. In addition, chronic kidney disease (15%) after liver transplantation is also an independent mortality factor.

The most commonly used methods to estimate GFR are based on creatinine, but in patients suffering from advanced hepatic disease, such as cirrhosis, this parameter is incorrect, due to the low creatinine production and potentially to elevated serum bilirubin and decreased albumin levels. Furthermore, ascites can interfere with serum creatinine concentration. In this condition, all creatinine-based evaluations of GFR overestimate gold standard-measured GFR. Specific eGFR equations for liver disease or new approaches for estimating GFR may be necessary.

The plasma clearance of iohexol is a recognized technique for the measurement of the glomerular filtration rate (GFR).

Conditions

Conditions:	Cirrhosis Renal
Keywords:	Cirrhosis Renal GFR renal function Bayesian model plasma clearance iohexol

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 4
Interventional Study Model:	Single Group Assignment
Number of Arms:	1
Masking:	None (Open Label)
Allocation:	N/A
Enrollment:	9 [Anticipated]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Iohexol administration After injecting a loading dose of 5ml of Iohexol Inj 300 MG/ML bolus, blood samples will be taken at given times for 24 hours. The urinary samples will be taken at each urination, with measurement of the exact volume and times	Drug: Iohexol Inj 300 MG/ML After injecting a loading dose of 5ml of iohexol bolus, blood samples will be taken at given times for 24 hours. The urinary samples will be taken at each urination, with measurement of the exact volume and times

Outcome Measures

Primary Outcome Measure:

1. Change of plasma concentrations of iohexol in a population of 9 cirrhotic patients from rich kinetics.
   Plasma concentration curves for iohexol according to the time.

   [Time Frame: 0 minute, 15 minute, 30 minute, 1 hour, 90 minute, 2 hours, 3 hours, 4 hours, 6 hours, 8 hours, 12 hours, 24 hours]

2. Change of urinary concentrations of iohexol in a population of 9 cirrhotic patients from rich kinetics.
   Urine concentration curves for iohexol according to the time.

   [Time Frame: 0 minute, 4 hours, 8 hours, 12 hours, 24 hours]

Secondary Outcome Measure:

3. Calculate the renal clearance of iohexol.
   Renal clearance of iohexol obtained by noncompartmental analysis.

   [Time Frame: 0 minute, 15 minute, 30 minute, 1 hour, 90 minute, 2 hours, 3 hours, 4 hours, 6 hours, 8 hours, 12 hours, 24 hours]

4. Calculate the plasma clearance of iohexol.
   Urinary clearance of iohexol obtained by noncompartmental analysis.

   [Time Frame: 0 minute, 15 minutes, 30 minutes, 1 hour, 90 minutes, 2 hours, 3 hours, 4 hours, 6 hours, 8 hours, 12 hours, 24 hours]

5. Develop a pharmacokinetic model for the estimation of renal clearance from plasma clearance.
   The evaluation of the performance of the model will be based on its ability to predict iohexol concentrations, expressed through (%) and accuracy (root of mean bias squared = RMSE) between urinary concentrations and predicted plasma levels and urinary concentrations and observed plasma levels.

   [Time Frame: 0 minute, 15 minutes, 30 minutes, 1 hour, 90 minutes, 2 hours, 3 hours, 4 hours, 6 hours, 8 hours, 12 hours, 24 hrs]

6. Evaluate the correlation between plasma clearance of iohexol obtained by the model and The GFR estimated by (CKD-EPI formula B, MDRD4 and MDRD6 formulas C, renal clearance of cystatine C)
   Linear Correlation Coefficients and Point Clouds between the plasma clearance of iohexol estimated by model and the DFGs calculated by the different methods. Bland Altman curves will also be drawn.

   [Time Frame: 0 minute, 24 hours]

7. Determine in the model of plasmatic clearance the relevant covariates.
   Evaluation of covariates by multiple linear regression and point clouds (continuous covariates) or Mann Whitney and box plots (categorical covariates). Inclusion of covariates characterized by a P <0.01 in the model. Looking for covariates that will influence the relationship between plasma clearance and renal clearance : grade of intensity of ascites. 2 grades: minimal, (ultrasound) or moderate and bulky, age, weight (of the day and H24), sex, diuresis of 24 hours, albumin, natriuresis, taking diuretics (nature and dose), other drugs that can influence GFR, biological stigmata of hepatic insufficiency or portal hypertension: bilirubin, albumin, INR, phosphatases, Child Pugh score, MELD score.

   [Time Frame: 0 minute, 24 hours]

Eligibility

Minimum Age:	18 Years
Maximum Age:	70 Years
Sex:	All
Gender Based:	No
Accepts Healthy Volunteers:	No
Criteria:	Inclusion Criteria:

- Patients with advanced liver disease, with potential indication for liver transplantation, with or without ascites :
  - No ascites: 3 patients.
  - Grade 1 (mild): ascites only detectable by ultrasound examination. 3 patients.
  - Grade 2 (moderate) and Grade 3 (wide): clinically significant ascites, causing moderate symmetrical distension of the abdomen, or causing severe abdominal distension. 3 patients.
- Patients will be over 18 years, affiliated to a social security scheme and give their informed consent.

Exclusion Criteria:

- Hypersensitivity to the active substance to the products of iodinated contrasts or to any of the excipients mentioned in Composition section
- History of major or cutaneous immediate reaction delayed injection of iodinated contrast medium (Omnipaque)
- Patients with thyrotoxicosis
- Asthmatic patients
- Patient with a history of dysthyroidism
- Patients with severe cardiovascular disease
- Patients with central nervous system disorders especially vascular
- Patients with pheochromocytoma
- Patients with myasthenia
- Patients with sickle cell disease
- Patients with autoimmune disease
- Patients treated with metformin
- Patients requiring anesthesia on the first day of levies
- Patients with an injection of iodine contrast during hospitalization and in both previous weeks. Gadolinium injections are not not contraindicated
- Patients under guardianship or curatorship or incapacitated give informed consent

Contacts/Locations

Central Contact Person:	PAUL CARRIER, PH Telephone: + 335 55 05 66 84 Email: pcarrier@hotmail.fr
Central Contact Backup:	
Study Officials:	
Locations:	

IPDSharing

Plan to Share IPD:

References

Citations:

Links:

Available IPD/Information: