A randomized, placebo-controlled, double-blind, multi-center Phase 2/3 trial to assess efficacy and safety of octreotide subcutaneous depot (CAM2029) in patients with symptomatic polycystic liver disease

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This study has been transitioned to CTIS with ID 2023-505313-24-00 check the CTIS register for the current data. To evaluate the treatment effect of CAM2029 compared to placebo on liver volume in patients with polycystic liver disease (PLD)

Ethical review	Approved WMO
Status	Pending
Health condition type	Hepatobiliary neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON51354

Source
ToetsingOnline

Brief title
CAM2029

Condition

- Hepatobiliary neoplasms malignant and unspecified

Synonym
Polycystic liver disease; genetic disorder

Research involving

Human

Sponsors and support

Primary sponsor: Camurus AB
Source(s) of monetary or material Support: Camurus AB

Intervention

Keyword: Fluid Crystal, Octreotide, Polycystic liver disease

Outcome measures

Primary outcome

Change from baseline to Week 53 in height-adjusted total liver volume (htTLV)

as determined by magnetic resonance imaging (MRI) volumetry

Secondary outcome

Change from baseline to Week 53 in the Polycystic Liver Disease Symptoms

(PLD-S) measure score

Study description

Background summary

Polycystic liver disease (PLD) is a rare genetic disorder defined by the formation of multiple fluid-filled cysts in the liver. In adults, PLD can occur independently in the liver as in autosomal dominant PLD (ADPLD) (also commonly referred to as PCLD), but it is also a common accompanying condition to autosomal dominant polycystic kidney disease (ADPKD).
Liver transplantation is currently the only cure for PLD but only a minority of patients with the most severe symptoms qualify for this intervention. Other surgical treatments such as percutaneous sclerotherapy, transarterial embolization, cyst fenestration and hepatic resection are indicated to specific groups of patients with PLD. Although surgical therapies may be successful in reducing liver volume in selected patients, they can also cause signi*cant morbidity and mortality. Most surgical interventions are also only partially effective and associated with a high rate of reoccurrence, and most importantly, are unable to change the natural course of the disease.

There is currently no approved pharmacological treatment for PLD, but different drugs have been tested. Somatostatin analogues (SSAs), including lanreotide and octreotide, have been shown to inhibit the growth of hepatic cysts by reducing cAMP in experimental animal studies.
CAM2029 (*octreotide subcutaneous depot*) is a novel and long-acting subcutaneous (SC) injection depot based on the active substance octreotide and formulated with Camurus* proprietary FluidCrystal® injection depot technology. It is provided as a pre-filled pen with no need for reconstitution and offers the option of self- or partner-administration at home.
Therefore, compared to the currently available long-acting octreotide product Sandostatin LAR, which is administered as an intramuscular injection with a syringe and which needs reconstitution before injection, CAM2029 may be easier to handle and to administer, thereby potentially improving patient convenience and care. In addition, the bioavailability of octreotide has been shown to be higher for CAM2029 than for Sandostatin LAR (31).

Study objective

This study has been transitioned to CTIS with ID 2023-505313-24-00 check the CTIS register for the current data.

To evaluate the treatment effect of CAM2029 compared to placebo on liver volume in patients with polycystic liver disease (PLD)

Study design

This is a Phase 2/3, randomized, placebo-controlled, double-blind, multi-center trial designed to evaluate the efficacy and safety of 2 treatment regimens of CAM2029 versus placebo in patients with PLD.

The trial consists of a 4-week Screening Period followed by a 52-week (12-month) Treatment Period for which approximately 69 patients will be randomized in a 1:1:1 ratio to 1 of the 3 treatment arms:
• Arm 1: CAM2029 10 mg once weekly
• Arm 2: CAM2029 10 mg once every 2 weeks (weekly alternation with placebo)
• Arm 3: Placebo once weekly

Following completion of the Treatment Period, all patients will continue to a 24-week, open-label, single-arm, Extension Period with CAM2029 10 mg once weekly, followed by a 4-week Safety Follow-Up Period.

Intervention

CAM2029
During the Treatment Period, CAM2029 10 mg (0.5 mL) will be administered as an SC injection using a pre-filled pen once weekly in treatment arm 1 and every 2

weeks in treatment arm 2 (weekly alternation with placebo). During the Extension Period, CAM2029 10 mg (0.5 mL) will be administered as an SC injection using a pre-filled pen once weekly. Injections will be administered in the abdomen, thigh or buttock. Self- or partner-administration of CAM2029 will be encouraged after appropriate training, including at least 1 self- or partner-administration under the supervision of trial personnel who has been adequately trained.

Comparator Product (Placebo)
During the Treatment Period, placebo (0.5 mL) will be administered as an SC injection using a pre-filled pen every 2 weeks in treatment arm 2 (weekly alternation with CAM2029) and once weekly in treatment arm 3. Injections will be administered in the abdomen, thigh or buttock. Self- or partner-administration of CAM2029 will be encouraged after appropriate training, including at least 1 self- or partner-administration under the supervision of trial personnel who has been adequately trained.

Study burden and risks

The side effects reported during the clinical studies with CAM2029 in healthy volunteers and patients were similar to those listed for octreotide hereunder:
• Diarrhea
• Abdominal pain
• Nausea (feeling sick)
• Constipation
• Flatulence (the presence of excessive gas)
• Headache
• Gall bladder stones
• Increased blood sugar levels
• Injection site reactions

Some of the tests and procedures performed during this study may cause side effects that are not related to the study treatment:
Blood drawing; ECG; Discomfort due to completion of study questionnaires and assessments; MRI scans;

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Male or female patient, >=18 years at screening
- Diagnosis of PLD (associated with ADPKD or isolated as in ADPLD) as defined by htTLV >=2500 mL/m at screening
- Presence of at least 1 of the following PLD-related symptoms within 2 weeks before screening: bloating, fullness in abdomen, lack of appetite, feeling full quickly after beginning to eat, acid reflux, nausea, rib cage pain or pressure, pain in side, abdominal pain, back pain, shortness of breath after physical exertion, limited in mobility, concern about abdomen getting larger, dissatisfied by the size of abdomen
- Not a candidate for, or not willing to undergo, surgical intervention for hepatic cysts during the trial
- Female patients of childbearing potential must be willing to use an acceptable method of contraception from screening and during the entire trial
- Male patients must be willing to use condom as method of contraception from screening and throughout the trial unless they have been sterilized by vasectomy (with an appropriate post-vasectomy documentation of the absence of sperm in the ejaculate)

Exclusion criteria

• Surgical intervention for PLD within 3 months before screening
• Treatment with a somatostatin analogue (SSA) within 3 months before screening
• Non-responsive to previous treatment of PLD with an SSA as per the Investigator*s assessment
• Cholelithiasis within 3 months before screening or previous medical history of cholelithiasis induced by SSAs unless treated with cholecystectomy
• Presence of extrahepatic cysts that, in the Investigator*s opinion, may prevent the patient from safely participating in the trial
• Severe kidney disease, as defined by eGFR <30 mL/min/1.73 m2
• Severe liver disease defined as liver cirrhosis of Child-Pugh class C
Use of oral contraceptives or estrogen supplementation within 3 months before screening
• Poorly controlled diabetes (hemoglobin A1c >=10%) at screening
• Patients with a known history of hypothyroidism, unless they have been on adequate and stable replacement thyroid hormone therapy for at least 3 months before the first dose of the IMP.
• Uncontrolled hypertension defined by a systolic blood pressure of >160 mmHg and/or diastolic blood pressure of >100 mmHg at screening
• History of significant cardiac disease or current diagnosis of cardiac disease indicating significant risk of safety for patients participating in the trial, such as uncontrolled or significant cardiac disease, including any of the following:
a. History of myocardial infarction, angina pectoris or coronary artery bypass graft within 6 months before screening
b. Clinically significant cardiac arrhythmias (e.g. ventricular tachycardia), complete left bundle branch block or high-grade atrioventricular block (e.g. bifascicular block, Mobitz type II and third-degree atrioventricular block)
c. Long QT syndrome, family history of idiopathic sudden death or congenital long QT syndrome, or any of the following:
i. Risk factors for Torsades de Pointes including uncorrected hypokalemia or hypomagnesemia, history of cardiac failure or history of clinically significant/symptomatic bradycardia
ii. Treatment with concomitant medication(s) with a "Known risk of Torsades de Pointes" that cannot be discontinued or replaced by safe alternative medication at least 5 half-lives or 7 days (whichever is longer) before the first dose of IMP
iii. Patients with a baseline QTc interval corrected by Fridericia's formula >450 msec for males and >470 msec for females at screening
Patients with vascular compromise, including, but not limited to, mesenteric thrombosis, portal hypertension and thrombocytopenia (platelet counts less than 100x109/L)
• Pregnant, lactating or planning to be pregnant during the trial
• History of solid organ transplantation
• Contraindications to, or interference with, MRI assessments, as dictated by

local hospital regulations

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2022
Enrollment:	25
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	CAM2029
Generic name:	octreotide

Ethics review

Approved WMO Date:	12-04-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-09-2022

Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-03-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-05-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2023-505313-24-00
EudraCT	EUCTR2021-003764-27-NL
CCMO	NL79984.091.22