A randomized, multi-center, open-label, active-controlled Phase 3 trial to assess the efficacy and safety of octreotide subcutaneous depot (CAM2029) versus octreotide LAR or lanreotide ATG in patients with gastroenteropancreatic neuroendocrine tumors

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This study has been transitioned to CTIS with ID 2023-508723-12-00 check the CTIS register for the current data. Primary Objective• To assess superiority of treatment with CAM2029 compared to treatment with octreotide long-acting release (LAR) or…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON54375

Source
ToetsingOnline

Brief title
HS-19-657 / SORENTO

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym

gastroenteropancreatic neuroendocrine tumors, neuroendocrine tumor which started in pancreas or other parts gastrointestinal tract

Research involving
Human

Sponsors and support

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

Intervention

Keyword: CAM2029, gastroenteropancreatic neuroendocrine tumor, GEP-NET

Outcome measures

Primary outcome

Primary Endpoint

• PFS, defined as the time from the date of randomization to the date of the first documented disease progression as per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1) or death due to any cause, whichever occurs first, as assessed by a Blinded Independent Review Committee (BIRC)

Secondary outcome

Secondary Endpoints

• PFS using RECIST 1.1 as assessed by local Investigators

• Overall survival

• ORR, defined as the proportion of patients with best overall response of complete response (CR) or partial response (PR) as per RECIST 1.1

• DCR, defined as the proportion of patients with best overall response of CR, PR or stable disease (SD) as per RECIST 1.1

• Time to response and duration of response as per RECIST 1.1

• Average number of injections of octreotide rescue medication per month for

each patient during the trial

• Total dosage and dose intensity of rescue medication

• Octreotide plasma concentrations over time

• Correlation between octreotide concentration and other endpoints or measures as appropriate

• Proportion of patients/partners declared competent by trial personnel to administer CAM2029 out of those trying

• Change from baseline in Quality of Life Questionnaire - Neuroendocrine Carcinoid Module (QLQ-GINET21), Short Form-36 (SF-36), and the global health status/quality of life scale score of the European Organization for Research and Treatment of Cancer*s Core Quality of Life Questionnaire (EORTC QLQ-C30)

• Treatment Satisfaction Questionnaire for Medication (TSQM) scores over time using all 4 domains of TSQM (effectiveness, side effects, convenience, and global satisfaction)

• Adverse events (AEs) (including local tolerability)

• Changes in laboratory values, vital signs, electrocardiogram readings and gallbladder imaging

Exploratory Endpoints

• Progression-free survival in the Extension Treatment Period (PFS-ext), defined as time from date of randomization to the date of documented disease progression as per RECIST 1.1 or death from any cause, whichever occurs first, in the Open-label Extension Treatment Period, as assessed by a BIRC

• PFS2, defined as time from date of randomization to the date of documented

progression as per RECIST 1.1 on next-line therapy or death from any cause,

whichever occurs first

• Number of patients hospitalized

• Total number and length of hospitalizations

• Describe patients* experiences with the trial regimen and trial activities

using data from patient exit interviews

• Explore the minimal important difference for EORTC QLQ-C30 using patient exit

interviews

• To explore the minimal important difference for EORTC QLQ-C30 using the

Patient Global Impression of Severity (PGI-S) and patient exit interviews

• Time to deterioration of ECOG performance status

• Qualification and quantification of anti-octreotide antibodies

Study description

Background summary

CAM2029 is an experimental drug, which means it is not approved by Health Authorities (such as Ministerie van volksgezondheid, welzijn en sport) for the treatment of GEP-NET. However, other drugs that contain the active substance (octreotide) that is used in CAM2029 are currently approved by health authorities for the treatment of GEP-NET and other diseases and conditions. CAM2029 is a long-acting product with octreotide (a hormone drug that is used to treat some tumors) which is administered under the skin (subcutaneously) to create a depot. The octreotide is slowly released from this depot, which may lead to stable therapeutic levels in the blood; stable level may be achieved after 2nd injection. CAM2029 is provided in a ready-to-use syringe or pen at the dose of 20 mg. Both the syringe and pen have a thin needle and the volume of the dose is small. It also offers an option for a potentially easier and convenient way of administration as the drug can be given by you or your partner/caregiver.

Octreotide LAR and lanreotide ATG are both approved by Health Authorities in

The Netherlands for the treatment of GEP-NET. The products containing these two formulations may be sold under many different brand names in your country (such as Sandostatin LAR, Somatuline, etc.).

Neuroendocrine tumors (NET) are rare tumors that develop in cells of the neuroendocrine system. There is a number of different types of NET. The type of NET depends on the particular cells where the tumor starts. You have been diagnosed with NET that is believed to have started in the pancreas or other parts of the gastrointestinal tract. The current standard of care treatment for GEP-NET is a medicine called somatostatin analogues (SSAs). SSAs are drugs that stop the body from making too much hormone. The SSAs stop or reduce the increase of NET cells that may produce such hormones. Some NET make large amounts of hormone. Octreotide LAR and lanreotide ATG are classified as SSAs and work similarly to natural somatostatin.

Study objective

This study has been transitioned to CTIS with ID 2023-508723-12-00 check the CTIS register for the current data.

Primary Objective
• To assess superiority of treatment with CAM2029 compared to treatment with octreotide long-acting release (LAR) or lanreotide autogel (ATG) on progression-free survival (PFS) in patients with unresectable/metastatic and well-differentiated gastroenteropancreatic neuroendocrine tumors (GEP-NET)

Secondary Objectives
• To assess superiority of treatment with CAM2029 compared to treatment with octreotide LAR or lanreotide ATG with respect to PFS based on local Investigator assessment
• To compare the 2 treatment groups with respect to overall survival
• To evaluate the 2 treatment groups with respect to overall response rate (ORR) and disease control rate (DCR)
• To describe time to tumor response and duration of response in the 2 treatment groups
• To evaluate the need for rescue medication for symptom control in the 2 treatment groups
• To assess the pharmacokinetics (PK) of octreotide after CAM2029 administration
• To assess octreotide exposure-response relationship for CAM2029
• To assess supervised self- or partner-administration of CAM2029
• To evaluate patient-reported outcomes (PROs) for health-related quality of life in the 2 treatment groups
• To evaluate the 2 treatment groups with respect to patient satisfaction with the treatment
• To confirm the safety and tolerability of CAM2029 in patients with unresectable/metastatic and well-differentiated GEP-NET

Exploratory Objectives
• To describe the effect of intensified treatment with CAM2029 in the Open-label Extension Treatment Period
• To compare the 2 treatment groups with respect to progression-free survival 2 (PFS2) based on local Investigator assessment
• To assess hospital resource utilization
• To evaluate the 2 treatment groups with respect to treatment experience
• To evaluate the 2 treatment groups with respect to patients* impression of disease severity
• To evaluate the 2 treatment groups with respect to Eastern Cooperative Oncology Group (ECOG) performance status
• To assess the immunogenicity of octreotide in patients with metastatic/inoperable and well-differentiated GEP-NET

Study design

Trial Design and Schedule
This is a prospective, multi-center, randomized, open-label, parallel-group, Phase 3 trial comparing the efficacy of treatment with CAM2029 20 mg every 2 weeks to treatment with the Investigator*s choice of comparator, i.e. octreotide LAR 30 mg or lanreotide ATG 120 mg every 4 weeks (the comparator treatment group) in patients with advanced, well-differentiated GEP-NET.

Approximately 300 patients will be randomized to 1 of 2 treatment groups in the Open-label Randomized Treatment Period. The patients will be followed until disease progression and the primary PFS analysis will be performed after 194 events (i.e. disease progression) during the Randomized Treatment Period.

Patients who experience progressive disease (PD) during the Randomized Treatment Period may enter an optional Open-label Extension Treatment Period, during which they will be treated with CAM2029 20 mg once weekly.

After the primary PFS analysis (based on the BIRC assessment of PD), the trial will remain open. Patients still being followed on the trial will continue as per the schedule of assessments. Patients who are still ongoing in the comparator treatment group at the time of the primary PFS analysis will have the possibility to be switched to receive treatment with CAM2029 20 mg every 2 weeks, if the trial meets the primary objective.

The overall survival follow-up will end at the latest 2 years after the primary PFS analysis. At that time, the final analysis of trial data will be conducted. All available data from all patients up to that cut-off date will be analyzed.

A Data Monitoring Committee will be established, which will conduct periodic reviews of safety data from the trial.

Intervention

Screening Period
The Screening Period will have a duration of up to 28 days. During this period, eligibility will be evaluated.

Open-label Randomized Treatment Period
Eligible patients will be randomized in a 1:1 ratio to 1 of the 2 treatment groups on Day 1:
• CAM2029 treatment group (CAM2029 20 mg, administered every 2 weeks)
• Comparator treatment group (Investigator*s choice of octreotide LAR 30 mg or lanreotide ATG 120 mg, administered every 4 weeks)

During the Randomized Treatment Period, tumor progression will be evaluated every 12 weeks. Safety will be evaluated continuously and plasma samples for assessment of octreotide concentration will be taken in patients who receive CAM2029 or octreotide LAR. Patient-reported treatment satisfaction will be assessed using a general questionnaire and will be compared between CAM2029 and the comparator products. Health-related quality of life parameters will also be assessed by PROs.

Patients will continue to receive the randomized investigational medicinal product (IMP) treatment (CAM2029/comparator) as scheduled, until they experience any of the following:
• Disease progression as confirmed by the BIRC
• Unacceptable toxicity that precludes further treatment
• Discontinuation of treatment at the discretion of the Investigator or patient
• Lost to follow-up
• Death

If the patient discontinues the randomized IMP treatment, the patient will be asked to return for an End-of-treatment Visit.

End-of-treatment Visit
The End-of-treatment Visit should be performed within 28 days after the date the IMP treatment is discontinued in the Randomized Treatment Period. The End-of-treatment Visit is not considered the end of the trial. Next-line therapy may be started after this visit at the Investigator*s discretion.

If the patient discontinued the randomized IMP treatment due to PD, patients in both treatment groups will have the option to start treatment with CAM2029 20 mg once weekly in an Extension Treatment Period.

Open-label Extension Treatment Period (optional)
After the BIRC confirms PD during treatment with the IMP (CAM2029/comparator) in the Randomized Treatment Period, patients in both treatment groups may be

switched to receive treatment with CAM2029 20 mg once weekly in an Extension Treatment Period, if the Investigator considers it beneficial for the patient.
The End-of-treatment Visit may be the same visit as the first visit in the Extension Treatment Period. During this period, tumor progression will be evaluated every 12 weeks. Safety will be evaluated continuously and plasma samples for assessment of octreotide concentration will be taken.
Patient-reported treatment satisfaction will be assessed using a general questionnaire and health-related quality of life parameters will be assessed by PROs.

Treatment with CAM2029 will continue until the patients experience any of the following:
• Disease progression as confirmed by the BIRC
• Unacceptable toxicity that precludes further treatment
• Discontinuation of treatment at the discretion of the Investigator or patient
• Lost to follow-up
• Death

After discontinuation of the CAM2029 once-weekly treatment, the patient will be asked to return for an End-of-extension-treatment Visit.

End-of-extension-treatment Visit
The End-of-extension-treatment Visit should be performed within 28 days after the date the CAM2029 treatment is discontinued in the Extension Treatment Period. The End-of-extension-treatment Visit is not considered the end of the trial. Next-line therapy may be started after this visit at the Investigator*s discretion.

After end of treatment: safety follow-up, efficacy follow-up and survival follow-up

Study burden and risks

- The risks associated with the study medications CAM2029, Octreotide LAR and Lanreotide ATG
- The discomforts linked to the procedures, such as blood draws, CT scans (adn contrast used), MRI (and constrast used), PET-CT scan, ECG, bone scan
- The burden of additional visits to the study center, additional procedures and questionnaires
These risks are included in the patient information sheet, and in the section additional remarks of this form

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

Main Inclusion Criteria for the Trial
• Male or female patient >=18 years old
• Histologically confirmed, advanced (unresectable and/or metastatic), and well-differentiated NET of GEP or presumed GEP origin
• At least 1 measurable, somatostatin receptor-positive*, lesion according to RECIST 1.1 determined by multiphasic CT or MRI (performed within 28 days before randomization)
*Somatostatin-receptor imaging must be performed within 12 months before randomization. Somatostatin receptor-positive lesions are defined as lesions with a visual assessment of uptake greater than the liver
• Results from FDG-PET CT for patients with well-differentiated Grade 3 NET (if performed) must show that FDG avid areas of disease also are avid on somatostatin-receptor imaging
• ECOG performance status of 0 to 2

Main Inclusion Criteria for the Extension Treatment Period
• Disease progression confirmed by the BIRC
• At least 6 months of treatment with IMP (CAM2029/comparator) in the Randomized Treatment Period before documented disease progression

Exclusion criteria

Main Exclusion Criteria for the Trial
• Documented evidence of disease progression while on treatment (including SSAs) for locally advanced unresectable or metastatic disease
• Known central nervous system metastases
• Consecutive treatment with long-acting SSAs for more than 6 months before randomization
• Carcinoid symptoms that are refractory to treatment (according to the Investigator's judgement) with conventional doses of octreotide LAR or lanreotide ATG and/or to treatment with daily doses of <=600 µg of octreotide IR
• Previous treatment with more than 1 cycle (where 1 cycle means <=28 days on treatment) of targeted therapies such as mammalian target of rapamycin (mTOR) inhibitors (e.g. sirolimus, temsirolimus, or everolimus) or vascular endothelial growth factor inhibitors (e.g. sunitinib, lenvatinib, or cabozantinib), or more than 1 cycle of chemotherapy or interferon for GEP-NET
• Treatment of GEP-NET with trans-arterial chemoembolization or trans-arterial embolization within 12 months before screening
• Previously received radioligand therapy (peptide receptor radionuclide therapy) at any time
• Hepatic/pancreatic-related exclusion criteria:
*Active hepatitis. Patients with no significant viral load, no acute signs of inflammation, and no clinical necessity for therapy are allowed, at the Investigator*s discretion
* Symptomatic cholelithiasis
* Clinically active or chronic liver disease, including liver cirrhosis of Child-Pugh class B or C
• Patients with poorly controlled diabetes, as evidenced by hemoglobin A1c (HbA1c) >8.0%
• Cardiac history 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:
* History of myocardial infarction, unstable angina pectoris, or coronary artery bypass graft within 6 months before screening
* Uncontrolled congestive heart failure
• 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)
• Long QT syndrome, family history of idiopathic sudden death or congenital long QT syndrome, or any of the following:

* Risk factors for Torsades de Pointes, including uncorrected hypokalemia or hypomagnesemia, history of cardiac failure, or history of clinically significant/symptomatic bradycardia
*Treatment with concomitant medication(s) with a "known risk of Torsades de Pointes" per www.crediblemeds.org that cannot be discontinued or replaced with safe alternative medication at least 7 days or 5 half-lives (whichever is longer) before start of IMP treatment
* Patients with a QTc interval corrected by Fridericia's formula >450 msec for males and >470 msec for females at screening
• Any other contraindicated serious medical condition that, in the Investigator's opinion, may prevent the patient from safely participating in the trial

Main Exclusion Criteria for the Extension Treatment Period
• Unresolved, drug-related serious adverse event that, in the Investigator's opinion, contraindicates treatment with CAM2029
• Clinically significant symptoms, medical conditions, rapid clinical deterioration, or other circumstances that, in the Investigator's opinion, would preclude compliance with the protocol, adequate cooperation in the trial, or may prevent the patient from safely participating in the trial

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	31-07-2022
Enrollment:	21
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	CAM2029 (Octreotide subcutaneous depot) - pen
Generic name:	not applicable
Product type:	Medicine
Brand name:	CAM2029 (Octreotide subcutaneous depot) - syringe
Generic name:	not applicable
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	lanreotide acetate
Generic name:	lanreotide acetate
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	09-09-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	15-12-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	04-02-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-04-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-11-2022
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	14-11-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-02-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-03-2023
Application type:	Amendment
Review commission:	METC NedMec

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	CTIS2023-508723-12-00
EudraCT	EUCTR2021-000849-40-NL
CCMO	NL78414.031.21