A multicenter open-label study to evaluate safety and dosimetry of Lutathera in adolescent patients with somatostatin receptor positive gastroenteropancreatic neuroendocrine (GEP-NET) tumors, pheochromocytoma and paragangliomas

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Primary objectives:• Evaluate organ absorbed radiation doses from PRRT with Lutathera in adolescent patients with SSTR-positive GEP-NETs• Evaluate safety and tolerability of Lutathera in adolescents with SSTR-positive GEP-NETsSecondary objectives:•...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Endocrine neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON50857

Source
ToetsingOnline

Brief title
CAAA601A32201 (NETTER-P)

Condition

- Endocrine neoplasms malignant and unspecified

Synonym
Gastroenteropancreatic neuroendocrine, GEP-NET

Research involving
Human

Sponsors and support

Primary sponsor: Advanced Accelerator Applications
Source(s) of monetary or material Support: Industry

Intervention

Keyword: GEP-NET, Lutathera, Paraganglioma, Pheochromocytoma

Outcome measures

Primary outcome

- Target organ (e.g. kidney and bone marrow) absorbed radiation doses in adolescents with SSTR-positive GEP-NETs

- The incidence of adverse events (AEs) and laboratory toxicities after the 1st Lutathera administration in adolescents with SSTR-positive GEPNETs

Secondary outcome

- The incidence of adverse events (AEs) and laboratory toxicities until 6 months after the last Lutathera dose (short-term follow-up) in adolescents with SSTR-positive GEP-NETs

- The incidence of adverse events (AEs) and laboratory abnormalities during the long term follow-up of 5 years after the last Lutathera dose in adolescents with SSTR-positive GEP-NETs

- Calculated organ absorbed doses and PK parameters based on imaging/blood radioactivity concentration data from adolescent patients with SSTR-positive GEP-NETs compared to the predicted distribution / organ absorbed doses

Study description

Background summary

There are currently no approved therapies for GEP-NETs in the pediatric population. As observed in adults, the diagnosis of NETs in children is often delayed due to the indolent nature of the disease. It has been reported that 10% to 20% of pediatric patients present with metastatic disease at diagnosis. While surgical intervention is favored as first-line treatment for patients with early-stage disease, metastatic GEP-NETs in the pediatric population, as in adults, are often unresectable. Non-surgical treatment modalities for the pediatric population include those used in adults, namely, somatostatin analogues, chemotherapy, everolimus, and peptide receptor radionuclide therapy (PRRTs). A small number of published studies have reported data on the use of Lutathera in children and adolescents with neuroblastomas, or with 90Y-DOTATOC in pediatric GEP-NETs. There are no published studies on the use of Lutathera in pediatric GEP-NETs.
Given the limitations of approved therapeutic options for the GEP-NET and PPGL pediatric population, these diseases in adolescents constitute an area of high unmet need. This clinical study aims to address this unmet need and to accelerate access of Lutathera as a potential treatment for adolescent patients with a primary focus on GEP-NETs. Due to the rarity of pediatric data in PPGL and unmet need in this indication, an exploratory cohort will be open for enrolment of adolescent patients with somatostatin receptor positive PPGLs.

Study objective

Primary objectives:
• Evaluate organ absorbed radiation doses from PRRT with Lutathera in adolescent patients with SSTR-positive GEP-NETs
• Evaluate safety and tolerability of Lutathera in adolescents with SSTR-positive GEP-NETs

Secondary objectives:
• Evaluate cumulative safety of Lutathera in adolescents with SSTR-positive GEP-NETs
• Evaluate long-term safety of Lutathera in adolescents with SSTR-positive GEP-NETs
• Perform comparative assessment of dosimetry and pharmacokinetics (PK) between adolescent patients with GEP-NET and adult patients using the extrapolation model developed for the clinical study

Study design

This is a multicenter, open-label, single-arm study to evaluate the safety and

dosimetry of Lutathera in adolescent patients 12 to <18 years old with somatostatin receptor positive GEP-NETs and PPGLs. The study will enroll at least 8 patients in the GEP-NET cohort and as many adolescents with PPGL as possible in the exploratory PPGL cohort.The study schedule for each patient consists of the screening period (up to 2 weeks) followed by the treatment period (4 treatment administrations at 8-week intervals), and the follow-up period (5 years).

Intervention

Lutathera (7.4 GBq/200 mCi x 4 administrations every 8 weeks; cumulative dose: 29.6 GBq/800 mCi), with a concomitant administration of 2.5% Lysine - Arginine amino acid (AA) solution

Study burden and risks

Participation in the study will consist of about 6 months of treatment and 5 years of follow-up. During that time, participants will need to visit the study site about 32 times. Out of these 32 visits, some visits can be done remotely, through a phone call with the investigator. Most study visits should take about 2-3 hours. However, the visits to the study site when Lutathera is administered, as well as the visits during 1st week when radioactivity is measured, will be longer. Aside from the intervention described above, participation in this study involves blood draws at multiple visits, radiation exposure through CT, SRI, SPECT/CT and whole body planar imaging. Participants will be subjected to: questions regarding medical history, use of concomitant medications/procedures and adverse events; MRI scans; urine sampling; measurement of vital signs; physical examination; ECGs, and patient reported outcomes questionnaires.

Very common side effects related to the study drug (happens to about 1 in 10 people) include low platelet count, low white blood cell count, low red cell count, decreased all blood cell count (pancytopenia), decreased appetite, nausea, vomiting and fatigue.
The most common side effects of amino acid administration are nausea (approximately 25%) and vomiting (approximately 10%).
Possible risks related to the IV infusion are: infection, inflammation of the vein, infiltration, extravasation (where the drug leaks into the surrounding tissues outside of the vein) and embolism (obstruction in a blood vessel).
In addition, there is a risk due to increased radiation exposure from the CT, SRI, SPECT/CT and whole body planar imaging.

Considering the age of participants, additional potential safety concerns in the pediatric population will be controlled via assessment of safety biomarkers. This includes potential effects of treatment with Lutathera on endocrine (hypothalamic-pituitary) function, gonadal function, growth and bone

development that will be controlled during and after the treatment with Lutathera.
All safety effects of Lutathera will be carefully assessed in this study, and patients will be closely monitored.
As this is the first study of Lutathera in adolescents with GEP-NETs and PPGLs, its efficacy and safety has not been established in this population yet.
However, based on adult efficacy and similarities between adolescents and adults, it is expected that Lutathera administered in the study may bring therapeutic benefit to adolescents with GEP-NETs and PPGLs. This study will be essential to bring new potential therapeutic options for adolescent GEP-NET and PPGL patients.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)

Inclusion criteria

1. GEP-NET cohort: Presence of metastasized or locally advanced, inoperable (curative intent), histologically proven, G1 or G2 (Ki-67 index <=20%), well differentiated GEP-NET. PPGL cohort: presence of metastasized or locally advanced, inoperable (curative intent), histologically proven PPGL.
2. Patients from 12 to < 18 years of age at the time of enrollment.
3. Expression of somatostatin receptors confirmed by a somatostatin receptor imaging (SRI) modality within 3 months prior to enrollment, with tumor uptake observed in the target lesions more or equal to the normal liver uptake.
4. Performance status as determined by Karnofsky score >= 50 or Lansky Play-Performance Scale score >= 50.

Exclusion criteria

Laboratory parameters:
• Estimated creatinine clearance calculated by the Cockroft-Gault method < 70 mL/min
• Hb concentration <5.0 mmol/L (<8.0 g/dL); WBC <2x109/L; platelets <75x109/L.
• Total bilirubin >3 x ULN for age.
• Serum albumin <3.0 g/dL unless prothrombin time is within the normal range.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	2
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Lutathera
Generic name:	Luthathera

Ethics review

Approved WMO Date:	14-06-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	10-08-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	18-10-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	17-01-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-06-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-07-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-12-2023
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
EudraCT	EUCTR2020-002951-39-NL
CCMO	NL75659.041.21