A multicentre, randomised, dose-confirmation, factorial phase II study to evaluate the optimal dose of 68Ga-OPS202 as a PET imaging agent in subjects with gastroenteropancreatic neuroendocrine tumour (GEP-NET)

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Primary Study Objective:*To define the optimal dose range for peptide mass and radioactivity of 68Ga-OPS202 based on detected lesions in adult subjects with somatostatin receptor 2 (sstr2) positive gastroenteropancreatic neuroendocrine tumour (GEP-...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON45307

Source
ToetsingOnline

Brief title
OPS202

Condition

- Other condition

Synonym
GEP-NET

Health condition

gastroenteropancreatic neuroendocrine tumour (GEP-NET)

Research involving
Human

Sponsors and support

Primary sponsor: Ipsen Pharmaceuticals
Source(s) of monetary or material Support: Ipsen Pharma

Intervention

Keyword: - 68Ga-OPS202, - dose confirmation, - Gastroenteropancreatic neuroendocrine tumour (GEP-NET), - PET imaging agent

Outcome measures

Primary outcome

Primary Endpoint and Evaluation:

*For each combination of injected peptide/radioactivity dose ranges,

differences in

relative lesion counts derived from a 2 × 3 factorial analysis measuring the

ratio of

the number of lesions detected by 68Ga-OPS202 to the number of lesions assessed

by

standard-of-truth (descriptive analyses).

The standard-of-truth in the present study is the CT scan images acquired at

Visit 2 and

Visit 3.

Secondary outcome

Secondary endpoints and evaluations:

Key secondary endpoint:

*For each combination of injected peptide/radioactivity dose ranges,

differences in

image quality derived from a 2 × 3 factorial analysis measuring the

tumour-to-background ratio in each of the major anatomic sites (i.e. descriptive

analyses for liver, lymph nodes, bone and lung)

A qualitative analysis of the image assessed by the independent blinded readers

will be

performed to back up the quantitative quality measured by tumour-to-background

analysis.

Study description

Background summary

Gastroenteropancreatic neuroendocrine tumours (GEP-NETs) constitute a heterogeneous group of tumours with their origin in neuroendocrine cells of the embryological gut. Most commonly, the primary lesion is located in the gastric mucosa, the small and large intestine, the rectum or pancreas. Importantly, approximately 80% of newly diagnosed patients present with metastasis, requiring an effective systemic treatment to prolong survival.
Most GEP-NETs overexpress somatostatin receptors (sstr), located on their cell surfaces. Somatostatin-based radiolabeled agonistic peptides have been successfully introduced into the clinic for targeted imaging of sstr-positive NETs, especially of the clinically most relevant subtype sstr2.
OPS202 is a new generation somatostatin analogue (antagonist) compound with potential superior tumour detection as a consequence of the availability of more binding sites, both active and inactive sstr2. 68Ga-OPS202 as a PET radiopharmaceutical is a candidate being developed for integration in standard diagnostic tumour imaging.
The present dose-confirmation phase II study aims to define the optimal dose range for peptide mass and radioactivity based on detected number of lesions and tumour-to-background ratio in subjects with sstr2-positive GEP-NET.

Study objective

Primary Study Objective:

*To define the optimal dose range for peptide mass and radioactivity of 68Ga-OPS202 based on detected lesions in adult subjects with somatostatin receptor 2 (sstr2) positive gastroenteropancreatic neuroendocrine tumour (GEP-NET).

Secondary Study Objectives:
*To further refine the optimal dose range for peptide mass and radioactivity of 68Ga-OPS202 based on quantitative maximum standardized uptake value (SUVmax) and other quality parameters.
*To describe the safety and tolerability of diagnostic 68Ga-OPS202 in subjects with sstr2-positive GEP-NET.

To characterize the pharmacokinetics (PK) of OPS202 in subjects with GEP NET.

Exploratory Objectives:
*To provide preliminary estimates of the sensitivity of 68Ga-OPS202 positron emission tomography/computed tomography (PET/CT) scan imaging, as well as SUV ratio [SUVmax lesion/ SUVmax reference tissue] and signal-to-noise ratios (SNR).

Study design

This is a multicentre, multinational, randomised, open-label, reader-blinded, dose-confirmation, 2 × 3 factorial phase II study, with an approximate 7-week duration.

Two target peptide mass dose ranges (5-20 µg and 30-45 µg), and three radioactivity dose ranges (40-80 megabecquerels [MBq], 100-140 MBq and 160-200 MBq activity of 68Ga) of 68Ga-OPS202 will be investigated to provide information on different possible peptide/radioactivity dose range combinations .

This is an open-label study. Independent readers will evaluate 68Ga-OPS202 PET/CT images and will be blinded to the investigator site and clinical status of the subject, including pathology, laboratory, and history/physical exam findings. Furthermore, the independent readers will be blinded to peptide mass dose, radioactivity dose, and the temporal sequence of dosing.

Intervention

i.v. injections of two different peptide/radioactivity dose of 68Ga-OPS202 followed by PET/CT scan imaging 1 hour post dosing (up to 80 min)

Study burden and risks

Subjects to be recruited in the phase 2 68Ga-OPS202 dose-confirmation study are

patients with
a histologically confirmed well-differentiated gastro-entero-pancreatic neuroendocrine tumour
(GEP-NET) having had a somatostatin receptor (sstr) scan within the last 6 months that indicates the presence of sstr subtype 2 (sstr2) lesions.
NETs are diagnostically challenging because these tumours are not only very rare, but also
comprise a heterogeneous disease entity with variable morphological and functional
characteristics. The ability to label somatostatin analogues with 68Ga has optimized the role of
PET for the diagnosis and staging of patients with GEP-NETs. To date, only sstr agonists
have been used for diagnostic imaging. However, in vivo studies showed that potent sstr
antagonists (such as 68Ga-OPS202) can visualize tumours equally well or even better as
compared with their agonist counterparts.
Every subject enrolled in this study will receive a 68Ga-OPS202 PET/CT scan which is expected to provide better diagnostic images compared to the previous sstr scintigraphy. the dose of the applied radioactivity is within the safe ranges defined by the clinical guidelines, and the radioactive isotope (68Ga) used has a short half-life (68 min).
Considering that the peptide mass doses used in this study are also in the range of microdoses,
and that OPS202 is an sstr2 antagonist, no or very limited effect on biological functions is
expected.

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

(1) Men or women aged 18 years or older;(2) Subjects with pathologically confirmed, well differentiated functioning or non-functioning metastatic GEP-NET (Grade I and II as per WHO classification 2010);(3) Subjects with a confirmed presence of somatostatin receptors (type 2) on technically evaluable tumour lesions documented by a positive Somatostatin Receptor Scan acquired within 6 months prior to screening (Visit 1) and showing minimally two lesions in at least one of the key organs namely liver, lymph nodes, bone or lungs; these images shall be available to be sent to the ICL electronically to ascertain quality and admissibility;(4) Eastern Cooperative Oncology Group (ECOG) performance status * 2;(5) Subjects with body weight between 50 kg (110 lb) and 110 kg (243 lb), inclusive;(6) Adequate bone marrow, liver and renal function, with:;* Calculated Glomerular filtration rate (GFR) * 45 mL/min
* Albumin: > 30 g/L
* Alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (AP): * 5 times upper limit of normal (ULN)
* Bilirubin: * 3 times ULN (3 × 1.1 mg/dL)
* Leukocytes: * 3*109/L and neutrophils * 1*109/L
* Erythrocytes: * 3.5*1012/L
* Platelets: * 90*109/L;(7) Signed written informed consent prior to any study-related procedures

Exclusion criteria

(1) Subjects with fewer than five lesions in total and more than 25 lesions/organ detected by the previous somatostatin receptor positive scan in key organs: liver, lymph nodes, bone or lung;(2) Subject who have received treatment of any somatostatin analogue, including Somatuline® Autogel® /Depot®, Sandostatin® LAR within 28 days, and Sandostatin® within 24 hours prior to first 68Ga-OPS202 administration.;(3) Presence of active infection at screening or history of serious infection within the previous 6 weeks prior to the first 68Ga-

OPS202 administration;(4) Prior or planned administration of a radiopharmaceutical within 8 half-lives of the radionuclide;(5) Clinically relevant trauma within 2 weeks prior to first 68Ga-OPS202 administration;(6) Known hypersensitivity to NODAGA, to Gallium-68, to JR11 or to any of the excipients of 68Ga-OPS202;(7) History of, or current active allergic or autoimmune disease, including asthma or any condition requiring long-term use of systemic corticosteroids;(8) Known human immunodeficiency virus (HIV) or positive serology for HIV, hepatitis B and C;(9) Any condition that precludes the proper performance of PET and/or CT scan:
a) Subjects who are not able to tolerate the CT contrast agent,
b) Subjects with metal implants or arthroplasty, or any other objects that might interfere with the PET and/or CT analysis
c) Subjects unable to raise arms for prolonged imaging purposes
d) Subjects unable to lie still for the entire imaging time
e) Subjects weighing greater than 110 kg (243 lb);(10) Administration of another investigational medicinal product within 30 days prior to first 68Ga-OPS202 administration;(11) Female subjects who are pregnant, breast feeding or of childbearing potential not willing to practice effective contraceptive techniques during the study treatment period and for 30 days after the last dose of 68Ga-OPS202 administration; pregnancy test must be performed at the start of the study and prior to each 68Ga-OPS202 administration;(12) Subjects who have any severe and/or uncontrolled medical conditions or other conditions that could affect their participation in the study, including any mental condition rendering the subject unable to understand the nature, scope and possible consequences of the study, and/or evidence of an uncooperative attitude;(13) Subject who experienced a previous cancer (except basocellular carcinoma of the skin and/or in situ carcinoma of the cervix/uterus and/or subjects treated with curative intent and free from disease for more than 5 years) other than NET

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	6
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	68Ga-OPS202
Generic name:	satoreotide trizoxetan

Ethics review

Approved WMO Date:	19-04-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-10-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-01-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-02-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-03-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	29-05-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2016-004928-39-NL
CCMO	NL61372.042.17