First International Randomized Study in MAlignant Progressive Pheochromocytoma and Paraganglioma

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Primary objective: To determine the efficacy of Sunitinib on the progression-free survival at 12 months in subjects with progressive malignant pheochromocytoma and paraganglioma treated with sunitinib at a starting dose of 37.5 mg daily (continuous...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Neoplastic and ectopic endocrinopathies
Study type	Interventional

Summary

ID

NL-OMON37272

Source
ToetsingOnline

Brief title
FIRSTMAPPP

Condition

- Neoplastic and ectopic endocrinopathies
- Endocrine neoplasms malignant and unspecified

Synonym
pheochromocytoma/paraganglioma

Research involving
Human

Sponsors and support

Primary sponsor: Institut Gustave Roussy
Source(s) of monetary or material Support: Europese Unie,Pfizer

Intervention

Keyword: Neuroendocrine tumors, Paraganglioma, Pheochromocytoma, Sunitinib

Outcome measures

Primary outcome

- Progression-free survival at 12 months

Secondary outcome

- Objective Response Rates (ORR)

- Duration of response (DR)

- Overall Time to Progression (TTP)

- Overall survival (OS)

- Number of Adverse Events assessed using NCI -CTC V4 criteria

- Number and description of adverse events and number of patients with adverse

events according to NCI -CTC V4 criteria

- Number of patients with cardiovascular toxicity tolerance assessed by

specific organisation for blood pressure monitoring

- Bone Pain evaluation on the Visual Analog Scale

Study description

Background summary

Pheochromocytomas and paragangliomas (PPGLs) arise respectively from the chromaffin cells of the adrenal medulla (80 to 90%) and paraganglia of the sympathetic or parasympathetic nervous system. These tumors belong within the larger family of neuroendocrine tumors. Malignant PPGLs are defined by the presence of metastases at sites where chromaffin cells are normally absent (i.e., liver, lungs, bones, lymph nodes). Surgery currently remains the single option for cure in patients with malignant PPGLs. Systemic therapy in most patients with progressive disease is usually considered. Data on targeted

molecular therapy are largely lacking in malignant PPGLs. Sunitinib is an oral multitargeted receptor tyrosine kinase inhibitor with antiangiogenic and antitumor activity with proven efficacy in the treatment of progressive gastrointestinal stromal tumors and metastatic renal cell carcinoma. The safety and efficacy of sunitinib for the treatment of pheochromocytoma and paragangliomas has not yet been determined.

Study objective

Primary objective:
To determine the efficacy of Sunitinib on the progression-free survival at 12 months in subjects with progressive malignant pheochromocytoma and paraganglioma treated with sunitinib at a starting dose of 37.5 mg daily (continuous dosing).

Secondary objectives:
- To determine overall survival and progression free survival.
- To determine time to progression.
- To determine objective response rate at one year.
- To determine time to and duration of tumor response.
- To assess safety profile including a dedicated cardiovascular management (home-blood pressure monitoring, ECG and echocardiography).

Exploratory objectives:
- Identification of predictors of response as well as surrogate markers of overall survival is anticipated.

Study design

Randomized, double-blind, phase II, international, multicenter study

Intervention

Patients are randomized for sunitinib 37.5 mg per day versus Placebo. For the patients randomized in the Placebo, cross over is allowed if progression. Treatment duration: 24 months.

Study burden and risks

In case of participation the patient has to visit the study center at least 18 times;
- twice during screening phase
- 1,2 and 3 weeks after start treatment
- 1 and 2 months after start treatment
- every 3 months during the treatment phase (2 years)
- every 3 months during follow up (1 year)

NB: Most visits are part of regulatory controls by the physican.

Participation will comprise the following examinations and procedures:
- Medical history, current and/or previous treatments, physical examination including dental examination, measurement of vital signs: every visit
- Blood and urinary samples: every visit
- Pregnancy test: once, before start of treatment
- Computerized tomography (CT) scan and/or Magnetic Resonance Imaging (MRI) (with intravenous injection of contrast fluid): before start of treatment and every 3 months from the 3rd month during treatment and follow up
- FDG-PET and/or MIBG-scan (with intravenous injection of radioactive isotopes): both before start of treatment, an FDG-PET or MIBG-scan every 3 months from the 3rd month during treatment and follow up
- Electrocardiogram (ECG): before start of treatment, 1 month after the beginning of treatment every 3 months and during follow-up
- Echocardiography: before start of treatment, every 3 months from the 3rd month during treatment and follow up

Furthermore, the patient is asked to:
- Estiminate pain on a visual scale (VAS score): every 3 months
- Answer a questionnaire of thirty questions about quality of life: after 3, 6 and 24 months of the beginning of treatment as well after ending the study
- Measure their blood pressure at home (6 times/day during 7 days): every week during a month, one week a month during 3 months, and then every 3 months.

The investigated drug Sunitinib may cause side effects. As with all blood drawing for the purpose of obtaining samples, there is a risk of bruising, pain, infection or bleeding at the site of the blood draw. The scans which involve exposure to radiation. The amount of radiation exposure is considered small, and will not adversely affect the patients health.

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

-Diagnosis of malignant PPGL,
-Metastatic disease not amenable to surgical resection
-Pre-treated or not
-Whatever the genetic status (sporadic or inherited)
-Evaluable disease according to RECIST 1.1 criteria
-ECOG performance status 0-2
-Life expectancy >= 6 months as prognosticated by the physician
-Age >= 18 years, no superior limit
-Adequate bone marrow reserve (Hb > 8, neutrophils >= 1500/mm^3 and platelets >=80.000/mm^3)
-Ability to comply with the protocol procedures
-Ability to take oral medication

Exclusion criteria

-Large or small cell-poorly differentiated neuroendocrine carcinoma according to WHO 2000 classification
-History of prior malignancy,
-Severe renal or hepatic insufficiency
-Patients with cardiac events
-Hypertension
-Brain metastases
-Previous treatment with the drug under study. Prior systemic treatment with any tyrosine kinase inhibitors or anti VEGF angiogenic inhibitors.
-Major surgery for any cause or local radiotherapy within one month prior to visit 1

-Liver embolisation therapy within the last 3 months prior visit 1

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:	Recruiting
Start date (anticipated):	24-09-2013
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Sutent
Generic name:	Sunitinib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	07-02-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date:	26-03-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-12-2017
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
EudraCT	EUCTR2010-024621-20-NL
CCMO	NL40621.091.12