A SINGLE ARM OPEN LABEL INTERNATIONAL MULTI CENTER STUDY OF THE EFFICACY AND SAFETY OF SUNITINIB MALATE (SU011248, SUTENT®) IN PATIENTS WITH PROGRESSIVE ADVANCED METASTATIC WELL DIFFERENTIATED UNRESECTABLE PANCREATIC NEUROENDOCRINE TUMORS.

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Evaluating the efficacy and safety of sunitinib in patients with progressive, advanced/metastatic well-differentiated, unresectable pancreatic neuroendocrine tumors.

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

Summary

ID

NL-OMON37660

Source
ToetsingOnline

Brief title
A6181202

Condition

- Neoplastic and ectopic endocrinopathies
- Endocrine neoplasms malignant and unspecified

Synonym
progressive advanced metastatic well differentiated unresectable pancreatic neuroendocrine tumors; Pancreatic NET

Research involving
Human

Sponsors and support

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

Intervention

Keyword: - EFFICACY AND SAFETY, - PHASE 4, - PROGRESSIVE ADVANCED METASTATIC WELL DIFFERENTIATED UNRESECTABLE PANCREATIC NEUROENDOCRINE TUMORS, - SUNITINIB MALATE

Outcome measures

Primary outcome

Progression Free Survival (PFS)

Secondary outcome

Objective Response Rate (ORR)

Overall Survival (OS)

Study description

Background summary

The purpose of this study is to evaluate the efficacy and safety of sunitinib in patients with progressive, advanced/metastatic well-differentiated, unresectable pancreatic neuroendocrine tumors. Pancreatic neuroendocrine tumors (NET) are rare malignancies and because of the relatively indolent nature of this disease, the majority of patients are diagnosed with disseminated metastases. The resistance to traditional treatment modalities distinguishes well differentiated neuroendocrine tumors from poorly differentiated carcinoma and small cell carcinoma.

With the exception of surgery for localized disease, there was a lack of

available therapies with meaningful, clinical benefit for well differentiated pancreatic NET until recently. Available treatment options for unresectable disease have included the use of somatostatin analogs, which may relieve symptoms related to hormonal hypersecretion, but there is little evidence to support a direct antitumor effect.

Since 2010, Sunitinib (Sutent®) is registered in the Netherlands for the treatment of progressive, advanced/metastatic well-differentiated, unresectable pancreatic neuroendocrine tumors. This indicates that the Dutch government has the opinion that prescribing sunitinib for this indication is well-considered. However, experience with sunitinib as first line treatment is still limited. This research will be done to collect more data on the efficacy and safety of the drug as a first line treatment of this type of pancreatic cancer in an advanced stage. This study is conducted to meet regulatory post-marketing commitments of the FDA.

Study objective

Evaluating the efficacy and safety of sunitinib in patients with progressive, advanced/metastatic well-differentiated, unresectable pancreatic neuroendocrine tumors.

Study design

The patient participates in the study approximately 1 year on average; in this period the patient will visit the hospital every 2 weeks (first month) or 4 weeks (after first month), 16 visits in total. During these visits the following procedures will be performed:
* Discuss medical history, treatments, and drug use complaints.
* Measurement of blood pressure, pulse, temperature and weight and any further physical examination.
* Blood tests (about 20 ml each time) to examine:
- Overall health status (including thyroid) assessment.
- The amount of sunitinib in the blood.
- the pancreas, the severity of the disease and the possible impact of the study treatment thereon.
* Urinalysis to assess the general health status.
* Pregnancy test (if applicable).
* Assessment of the tumor with a CT scan and possibly a bone scan.
* ECG ("ECG").
* Measurement of the pumping power of the heart with an echocardiogram or MUGA scan
* Completion of two questionnaires on health and daily activities. .

Four weeks after treatment, there is a final visit. After treatment with study medication, the patient in the follow-up phase will be called every 8 weeks, up

to 5 years once all patients are included.

Intervention

- oral intake of 37.5 mg study medication once a day on a continuous daily dosing regimen (CDD)
- laboratory assessments (blood and urine)
- questionnaires

Study burden and risks

All medicines have side effects, as well sunitinib. Side effects often disappear when the drug is stopped. They can also remain for a longer period or permanently. Side effects can be mild, but also severe and even life threatening. However, there may be not previously reported, potentially serious, side effects. Furthermore, the patient may also experience an allergic reaction to the drug.
40% or more of patients experienced: diarrhea, fatigue, nausea.
10-40% of patients experienced: vomiting, blisters and/or rash on hands and feet that may be painful, decreases in red blood cells (oxygen carrying cells), decreases in platelets (which help stop and prevent you from bleeding), high blood pressure, inflammation of mucous membranes (including mouth sores), taste disturbances, constipation, decreases in white blood cells (infection-fighting cells), upset stomach, decreased appetite (including anorexia), abdominal pain, shortness of breath, headache, rash, cough, fever, back pain, swelling, pain in extremities (hand and feet), skin, hair, and nail color changes, nosebleed, joint pain, decreased thyroid function, dry skin, inability to sleep.
5-10% of patients experienced: weight loss, dizziness, muscle aches, chest pain, hair loss, dehydration, dry mouth, skin redness, bloating, flatulence, throat pain, heartburn and indigestion, itching, burning sensation of the tongue, chills, swelling in the face, infection, watering of the eye, increased levels of liver enzymes, skin peeling, depression.

RISK OF PROCEDURES
A blood draw may cause faintness, inflammation of the vein, pain, bruising, or bleeding at the site of puncture

In a CT or bone scan, the patient is subject to additional radiation. In this study there are no more scans performed than during treatment of the disease outside a research setting. The patient is not exposed to more radiation because of study participation. The injection of contrast may hurt. Occasionally patients experience a hypersensitivity reaction.

In a MUGA scan, radioactive material is injected. The amount of radiation is less than 2 times the amount to which we are exposed in everyday life in one year . Cardiac function may also be assessed by an echocardiogram. In that

case, no radioactivity is used.

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. Histologically or cytologically proven diagnosis of well differentiated pancreatic neuroendocrine tumor (according to WHO 2000 classification) with available Ki-67 index.;2. Unresectable (as assessed by the investigator) or metastatic disease documented on a scan (CT, MRI, or Octreoscan) taken within 28 days of study enrollment. Disease progression (per RECIST 1.0) within 12 months prior to study enrollment. ;3. Disease that is not amenable to surgery, radiation, or combined modality therapy with curative intent.;4. Presence of at least one measurable target lesion for further evaluation according to RECIST 1.0 (contrast enhancing lesion with the largest diameter larger or equal to 20 mm, based on conventional CT scan (or larger or equal to 10 mm with spiral CT scan) done within 3 weeks before the

start of treatment).

Exclusion criteria

1. Patients with poorly-differentiated pancreatic neuroendocrine tumors (according to WHO 2000 classification). ;2. Prior treatment with any tyrosine kinase inhibitors, anti-VEGF angiogenesis inhibitors, non-VEGF-targeted angiogenesis inhibitors, or mTOR inhibitors.;3. Diagnosis of any second malignancy within the last 5 years, except for adequately treated basal cell or squamous cell skin cancer, or in situ carcinoma of the cervix uteri.;4. Treatment with strong CYP3A4 inhibitors and inducers within 7 and 12 days, respectively, prior to study drug administration.

Study design

Design

Study phase:	4
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-06-2012
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	SUTENT
Generic name:	sunitinib malate
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	24-01-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-06-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-06-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-09-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-10-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-05-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-02-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	13-02-2014
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	EUCTR2011-004363-74-NL
ClinicalTrials.gov	NCT01525550
CCMO	NL39081.042.12