A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multi-Center Study Evaluating the Efficacy and Safety of IPI-504 in Patients with Metastatic and/or Unresectable Gastrointestinal Stromal Tumors Following Failure of at Least Imatinib and Sunitinib

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

Summary

ID

NL-OMON34005

Source
ToetsingOnline

Brief title
RING trial: IPI-504 for GIST patients

Condition

- Soft tissue neoplasms malignant and unspecified

Synonym
Gastro Intestinal Stromal Tumor, Mesenchymal tumor of the gastrointestinal tract

Research involving
Human

Sponsors and support

Primary sponsor: Infinity Pharmaceuticals
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: GIST, Metastatic and/or Unresectable Gastrointestinal Stromal Tumor

Outcome measures

Primary outcome

The primary endpoint is progression free survival (PFS) as assessment of antitumor activity. PFS is defined as the time from randomization to the first documentation of disease progression or death due to any cause, whichever occurs first. Disease progression is defined as radiographic progression by Response Evaluation Criteria in Solid Tumors (RECIST).

Secondary outcome

The secondary efficacy endpoints are DCR (Disease Control Rate), TTP (Time to progression) en OS (Overall Survival).

Safety endpoints include assessment of adverse events (AEs), serious adverse events (SAEs), and changes in clinical laboratory and electrocardiogram (ECG) evaluations.

Study description

Background summary

Despite recent advances in the treatment of GIST, nearly all patients eventually progress with resistance to the approved TKIs, imatinib and sunitinib. Following failure of these therapies, GIST remains a fatal disease that causes significant disruption in the quality of life for patients. Therefore, novel therapies are needed for patients who have progressed on or are intolerant to the proven current therapies.

Clinical trials have shown that IPI-504 has an acceptable safety profile, encouraging biological activity in heavily pre-treated patients with GIST in whom prior therapies with imatinib and sunitinib as well as other TKIs have failed. This randomized, double-blind, placebo-controlled, multi-center, multi-national study has been designed to more fully evaluate the efficacy and safety of IPI-504 in patients with metastatic and/or unresectable GIST following failure of at least imatinib and sunitinib.

Study objective

The primary objective of this study is to compare the progression free survival (PFS) following administration of IPI-504 plus best supportive care versus placebo plus best supportive care in patients with metastatic and/or unresectable gastrointestinal stromal tumors (GIST) following failure of at least imatinib and sunitinib.

Study design

This is a Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multi-Center Study.

Intervention

First part (randomised)
Approximately 195 patients will be randomized using a 2:1 ratio to receive either IPI-504 (N=130) or placebo (N=65). Patients will receive 400 mg/m2 of IPI-504 or placebo as a 30-minute intravenous (IV) infusion twice weekly for 2 weeks followed by 1 week off treatment. Doses will be administered approximately 72 hours apart.

Second part (open-label)
After ending treatement in the first part of the study, patients receiving either IPI-504 or placebo may receive IPI-504 in the open-label portion of the study if defined inclusion criteria are met.

Study burden and risks

Patients will have blood collected at least one day before the administration of the study medicine. In addition, study medicine will be administrated twice

a week by infusion in the first two weeks of every (three-week) course of treatment.
The patients should complete a questionnaire about pain experience and quality of life (2 to 3 times per course of treatment), will have a physical examination (at the start of every course of treatment) and will have vital functions checked before every administration.

The patient may experience adverse events during or after the study. Everyone who participates in the study will be closely monitored for any possible adverse events. The care team may give medicines to the patient to reduce or prevent a number of adverse events. Earlier studies have shown that the most common side effect of treatment with IPI-504 is fatigue. Please refer to section E9 for an extensive overview of risks and adverse events.

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

o At least 18 years of age at the time of study randomisation
o Histologically confirmed metastatic and/or unresectable GIST.
o Measurable disease on CT or MRI as defined by RECIST
o Documented radiographic progression or intolerance to imatinib and sunitinib.
o Clinical failure of the most recent prior therapy for GIST. Note: There is no limit to the number of prior therapies a patient may have received
o ECOG performance status: 0 or 1.
o Hemoglobin >= 8.0 g/dL
o Absolute Neutrophil Count >= 1.5 x 109/L
o Platelets >= 100 x 109/L
o ALT and AST <= 2.5 x upper limit of normal (ULN), or <= 3.0 x ULN if considered secondary to liver metastases
o Alkaline phosphatase <= 2.5 x ULN, or <= 3.0 x ULN if considered secondary to liver metastases
o Serum bilirubin <= 1.5 x ULN
o PT and PTT <= 1.5 x ULN unless the patient is receiving warfarin. If the patient is receiving warfarin, the INR must be within therapeutic range
o Serum creatinine <= 1.5 x ULN
o Albumin >= 3.0g/dL;Please see the protocol for a detailed definition of all inclusion criteria.

Exclusion criteria

o Previous administration of other known heat shock protein 90 (Hsp90) inhibitors.
o Surgery, radiotherapy, or lesion ablative procedure to the only area of measurable disease.
o Initiation or discontinuation of concurrent medication that is a potent CYP3A inhibitor less than 2 weeks prior to administration of IPI-504 or placebo.
o History of any of the following within the last 6 months: cardiac disease such as acute coronary syndrome or unstable angina, symptomatic congestive heart failure, uncontrolled hypertension, cirrhotic liver disease, cerebrovascular accident, or any other significant co-morbid condition or disease which, in the judgment of the investigator, would place the patient at undue risk or interfere with the study.
o Grade 3 or 4 hemorrhagic event within the last 6 months.
o Known human immunodeficiency virus positivity.
o Sinus bradycardia (resting heart rate < 50 bpm) secondary to intrinsic conduction system disease.
o QTcF >= 470 milliseconds (msec), or previous history of clinically significant QTc prolongation while taking other medications.
o History of prior malignancies within the past 3 years other than non-melanomatous skin cancers that have been controlled, prostate cancer that has been treated and has not recurred, non-muscle-invasive bladder cancer, and carcinoma in situ of the cervix.
o Active or recent history (within 3 months) of keratitis or keratoconjunctivitis confirmed by ophthalmology or optometry exam.

o Presence of Left Bundle Branch Block, Right Bundle Branch Block plus left anterior hemiblock, bifascicular block, or 3rd degree heart block.This does not include patients with a history of these events with adequate control by pacemaker.
o Patients with known central nervous system (CNS) metastases.
o Women who are pregnant or lactating.;Please see the protocol for a detailed description of all exclusion criteria.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Start date (anticipated):	01-02-2009
Enrollment:	5
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	not applicable
Generic name:	Retaspimycin hydrochloride
Product type:	Medicine
Brand name:	Placebo
Generic name:	Mannitol solubilised in water

Ethics review

Approved WMO Date:	09-02-2009
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-04-2009
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2008-002396-28-NL
ClinicalTrials.gov	NCT00688766
CCMO	NL25626.078.08