A randomized, open-label, multi-center study to evaluate the efficacy of nilotinib versus best supportive care with or without a tyrosine kinase inhibitor (investigator's choice) in adult patients with gastrointestinal stromal tumors resistant to both imatinib and sunitinib.

Published: 16-10-2006
Last updated: 10-05-2024

Primary* To evaluate whether the efficacy of nilotinib is superior to the control arm (as measured by progression free survivalSecondary* To compare the response rate, and time to response, duration of response, and time to tumor progression of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON30672

Source
ToetsingOnline

Brief title
Evaluation of efficay of nilotinib in patients with GIST

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
GIST

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma BV

Intervention

Keyword: Gastrointestinal stromal tumors, Nilotinib

Outcome measures

Primary outcome

Primary endpoints

* Progression free survival (PFS)

Secondary outcome

Secondary endpoints

* Response, time-to response, and overall survival

* Safety and tolerability

Study description

Background summary

Nilotinib is a second generation inhibitor of the Bcr-Abl tyrosine kinase which, like imatinib. Nilotinib also inhibits the stem cell factor receptor c-Kit tyrosine kinase, which is often associated with gastrointestinal stromal tumors (GIST).

In this study, as of 15 August, 2006, 53 patients (48 imatinib-resistant and 5 imatinib-intolerant) were enrolled. 18 patients received nilotinib alone (400 mg bid), 19 patients escalating doses of nilotinib (200 mg qd, 400 mg qd, or 400 mg bid) in combination with imatinib (400 mg bid), and 16 patients nilotinib 400 mg bid plus imatinib 400 mg for 8 to 337 days (median 113 days). The median duration of treatment in patients who received nilotinib alone was 186 days (8-337 days).

39 patients had prior failure of second-line therapies in addition to progression on imatinib. Thirteen of the 18 patients treated with nilotinib alone had failed other therapies in addition to imatinib, including sunitinib, AMG-706, RAD-001or dasatinib.
Of the 18 patients who received nilotinib alone one patient achieved a partial response lasting approximately 6 months and thirteen patients exhibited disease stabilization. The median duration of response, including stable disease, was 5.3 months. The estimated median progression free survival (PFS) was approximately 6 months
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Study objective

Primary
* To evaluate whether the efficacy of nilotinib is superior to the control arm (as measured by progression free survival
Secondary
* To compare the response rate, and time to response, duration of response, and time to tumor progression of nilotinib with the control arm
* To compare overall survival of nilotinib with the control arm
* To assess the safety and tolerability of nilotinib as measured by rate and severity of adverse events.

Study design

Changed in Amendment 1 into:
This is a randomized, open-label, parallel group, two-arm study with an Extension study. At Day 1 patients will be randomized in a 2:1 ratio to nilotinib 400 mg bid arm or the control arm. The control arm includes the following three options:
Best supportive care or best supportive care plus imatinib or sunitinib at last tolerated dose.
The choice of one of these options will be at the investigator*s discretion and patients will not be permitted to switch treatment within this arm.

Intervention

Amendment 1

Arm 1:
2 x daily 400 mg nilotinib (AMN107)

Arm 2 (control arm):
The control arm includes the following three options:
Best supportive care OR
Best supportive care plus imatinib OR

Best supportive care plus sunitinib
The choice of one of these options will be at the investigator*s discretion and patients will not be permitted to switch treatment within this arm.

Study burden and risks

Toxicity of nilotinib, or imatinib or sunitinib depending on the treatment arm.
Radiation exposure of PET and CT-scan and/or an allergic reaction on the contrast fluid.
When a biopsy is done, bleeding and pain. The risk of taking blood may include pain, faint and/or bruisin.

Contacts

Public
Novartis

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NL
Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Amendment 1
* Age * 18 years
* Histologically confirmed diagnosis of GIST that is unresectable and/or metastatic and therefore not amenable to surgery or combined modality with curative intent
* Radiological confirmation of disease progression during imatinib therapy at a dose at least 400 mg daily and radiological confirmation of disease progression during sunitinib therapy that was started at 50 mg daily dose OR documented intolerance to imatinib or sunitib, is defined as patients who discontinued imatinib or sunitinib due to any * Grade 3 adverse events that cannot be managed by appropriate supportive care or medical intervention or persist after dose reduction In addition any * grade 2 Adverse event that persist * 1 month in spite of dose interruption and optimal supportive care.
* At least one measurable site of disease (RECIST) a Visit 2
* WHO Performance Status of 0, 1 or 2 at Visit 1 and Visit 2
* Patients must have normal organ, electrolytes, and marrow function at Visit 1 and Visit 2
See also Amendment 1 page 17 - section 2.8 for changes

Exclusion criteria

Amendment 1
* Prior treatment with nilotinib or any other tyrosine kinase inhibitors other than imatinib or sunitinib.
* Treatment with any cytotoxic and/or investigational cytotoxic drug * 4 weeks (6 weeks for nitrosurea or mitomycin C) prior to Visit 1 with the exception of imatinib and sunitinib
* Prior or concomitant malignancies
* Impaired cardiac function at Visit 1 or 2 (LVEF < 45%), significant impaired conduction of the heart, use of a cardiac pacemaker, congenital long QT syndrome, history of or presence of significant ventricular or atrial tachyarrhythmias or clinically significant resting bradycardia (< 50bpm), QTc > 450 msec, right bundle branch block plus left anterio hemiblock, bifascicular block, myocardial infarction within 12 months prior to Visit 1, unstable angina diagnosed or treated during the past 12 months prior to Visit 1, other clinically significant heart disease
* Patients with severe and/or uncontrolled concurrent medical disease that could cause unacceptable safety risks or compromise compliance with the protocol
* Use of therapeutic coumarin derivatives
* Use of any medications that prolong the QT interval and CYP3A4 inhibitors
* Patients who are pregnant or breast feeding
See also Amendment 1 page 17 section 2.9 for detail on changes

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-12-2006
Enrollment:	10
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Tasigna
Generic name:	nilotinib

Ethics review

Approved WMO Date:	16-10-2006
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	02-04-2007
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	01-05-2007
Application type:	Amendment

Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	08-08-2008
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	24-05-2011
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2006-002267-11-NL
CCMO	NL14252.058.06