Een gerandomiseerde, open-label, multicenter studie om de effectiviteit van nilotinib te vergelijken met de beste ondersteunende behandeling met of zonder een tyrosine kinase remmer (keus van de onderzoeker) bij volwassen patiënten met gastrointestinale stromacel tumoren die resistent zijn voor zowel imatinib en sunitinib.

Geen registraties gevonden.

Ethische beoordeling	Goedgekeurd WMO
Status	Werving gestopt
Type aandoening	Maagdarmstelselneoplasmata maligne en niet-gespecificeerd
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON30672

Bron
ToetsingOnline

Verkorte titel
Onderzoeken van de effectiviteit van nilotinib bij patiënten met GIST

Aandoening

- Maagdarmstelselneoplasmata maligne en niet-gespecificeerd

Synoniemen aandoening
GIST

Betreft onderzoek met
Mensen

Ondersteuning

Primaire sponsor: Novartis
Overige ondersteuning: Novartis Pharma BV

Onderzoeksproduct en/of interventie

Trefwoord: Gastrointestinale stromacel tumor, Nilotinib

Uitkomstmaten

Primaire uitkomstmaten

Primair eindpunt

* Progressie vrije overleving

Secundaire uitkomstmaten

Secundair

* Response, tijd tot response, en overall overleving

* Veiligheid en verdraagbaarheid

Toelichting onderzoek

Achtergrond van het onderzoek

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
.

Doel van het onderzoek

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.

Onderzoeksopzet

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.

Onderzoeksproduct en/of interventie

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.

Inschatting van belasting en risico

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.

Contactpersonen

Publiek

Novartis

Raapopseweg 1
6824 DP Arnhem
NL

Wetenschappelijk

Novartis

Raapopseweg 1
6824 DP Arnhem
NL

Locaties

Landen waar het onderzoek wordt uitgevoerd

Netherlands

Deelname eisen

Leeftijd
Volwassenen (18-64 jaar)

65 jaar en ouder

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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

Onderzoeksopzet

Opzet

Fase onderzoek:	3
Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Actieve controle groep
Doel:	Behandeling / therapie

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-12-2006
Aantal proefpersonen:	10
Type:	Verwachte startdatum

In onderzoek gebruikte producten en hulpmiddelen

Soort:	Geneesmiddel
Merknaam:	Tasigna
Generieke naam:	nilotinib

Ethische beoordeling

Goedgekeurd WMO

Datum:	16-10-2006
Soort:	Eerste indiening
Toetsingscommissie:	METC Leids Universitair Medisch Centrum (Leiden)

Goedgekeurd WMO

Datum:	02-04-2007
Soort:	Amendement
Toetsingscommissie:	METC Leids Universitair Medisch Centrum (Leiden)

Goedgekeurd WMO

Datum:	01-05-2007
Soort:	Amendement
Toetsingscommissie:	METC Leids Universitair Medisch Centrum (Leiden)
Goedgekeurd WMO Datum:	08-08-2008
Soort:	Amendement
Toetsingscommissie:	METC Leids Universitair Medisch Centrum (Leiden)
Goedgekeurd WMO Datum:	24-05-2011
Soort:	Amendement
Toetsingscommissie:	METC Leids Universitair Medisch Centrum (Leiden)

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
EudraCT	EUCTR2006-002267-11-NL
CCMO	NL14252.058.06