A single arm, phase II, open-label study to determine the efficacy of 100mg twice daily oral dosing of Midostaurin administered to patients with Agressive Systemic Mastocytosis or Mast Cell Leukemia +/- an Associated Hematological Clonal Non-Mast Cell Lineage Disease

Published: 10-06-2008
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Objective of this study is to determine the efficacy of midostaurin in patients with ASM or MCL with/without an associated hematological clonal non-mast cell lineage disease.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON37318

Source
ToetsingOnline

Brief title
AgressiveSystemicMastocytosis (ASM) or MastCell Leukemia (MCL), midostaurin

Condition

- Leukaemias

Synonym

Agressive Systemic Mastocytosis

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma B.V.

Intervention

Keyword: Agressive Systemic Mastocytosis, Mast Cell Leukemia, midostaurin

Outcome measures

Primary outcome

To determine the efficacy of midostaurin in patients with ASM or MCL with or without an AHNMD when administered orally at a dose of 100 mg b.i.d. continuously as measured by overall response rate.

Secondary outcome

To evaluate the duration of response

To evaluate the time to response

To evaluate overall survival

To evaluate the safety and tolerability of midostaurin in patients with ASM or MCL (with or without an associated hematological clonal non-mast cell lineage disease).

To characterize t he KIT mutational status at baseline and after 6 cycles of therapy and evaluate potential associations with efficacy outcomes.

Study description

Background summary

Aggressive Systemic Mastocytosis (ASM) and Mast Cell Leukemia (MCL) are myeloproliferative neoplasms with limited treatment options and generally poor prognosis. Both are diseases in which the body produces excessive amounts of a particular type of white blood cell named mast cell. To date, there have been limited treatment options for ASM and MCL. Existing treatments such as interferon-alpha, steroids, and cladribine exhibit variable response rates in advanced mast cell disease and these are usually partial in nature.

Study objective

Objective of this study is to determine the efficacy of midostaurin in patients with ASM or MCL with/without an associated hematological clonal non-mast cell lineage disease.

Study design

Na het doorlopen van de screeningsfase zal de patient, indien hij/zij aan de in-/exclusie criteria voldoet, starten met midostaurin behandeling. Patienten zullen 2 maal daags midostaurin innemen. Patienten kunnen met de behandeling doorgaan zolang midostaurin goed verdragen wordt of totdat de ziekte verergert.

After the screenings period the patient will, in case patient meets all in-/exclusion criteria, start with midostaurin treatment. Midostaurin will be dosed twice daily. Treatment can be continued till progressive disease or unacceptable toxicity (whichever comes first).

Intervention

Patients will be treated with twice daily 100 mg midostaurin.
A cycles is 28 days.
Patients take their medication continuously.

Study burden and risks

After the screeningsperiod the patient will be hospitalized during cycle 1 for 3 days, to closely monitor for any potential side effects, adverse events and to obtain pharmacokinetic drug levels.
For the following visits the patient is asked to come to the clinic weekly during the first month, biweekly during the second month, then once every month for the following 10 months and subsequently every 3 months thereafter.

Evaluation of response will be done via bonemarrow assessments, bonescans and DEXA scans.

Contacts

Public
Novartis

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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

Adult patients with diagnosis of one major plus at least one minor criterion, or the presence of at least 3 minor criteria according to WHO criteria for Systemic Mastocytosis (Valent et al. 2001);Patient must present with at least one measurable C-Finding.;For patients with MCL: bone marrow aspirate smears must show 20% or more immature mast cells.

Exclusion criteria

Patients who have demonstrated relapse to more than two prior regimen of SM treatment-regardless of treatment regimen for supportive care (e.g. symptom limiting therapies);Patients who have aggressive systemic mastocytosis with eosinophilia and known positivity for the FIP1L1-PDGFR fusion unless they have demonstrated relapse or disease

progression on prior imatinib therapy;Patients on imatinib therapy and known to be KIT D816V negative unless they have demonstrated relapse, resistance or intolerance to imatinib.;Patients with any pulmonary infiltrate including those suspected to be of infectious origin.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-01-2009
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nvt
Generic name:	midostaurin

Ethics review

Approved WMO Date:	10-06-2008
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	01-09-2008

Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-12-2008
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-01-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-07-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	27-12-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-12-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-05-2012
Application type:	Amendment
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:	08-02-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	01-03-2013

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-05-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-02-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-02-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-09-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-10-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-10-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-10-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-01-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-03-2017

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-07-2017
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	EUCTR2008-0002800-4-NL
CCMO	NL23439.042.08