Phase II single arm open pilot study to demonstrate the efficacy of midostaurin in symptom improvement and decrease of mast cell burden in patients with indolent or smoldering systemic mastocytosis

Published: 31-01-2013
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Primary: To study the efficacy and tolerability of Midostaurin in patients with indolent or smoldering systemic mastocytosis on mediator symptom reduction.Secondary: 1) To study whether Midostaurin can reduce mast cell infiltration and 2) to assess...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Haematopoietic neoplasms (excl leukaemias and lymphomas)
Study type	Interventional

Summary

ID

NL-OMON39686

Source
ToetsingOnline

Brief title
Midostaurin in Indolent Systemic Mastocytosis

Condition

- Haematopoietic neoplasms (excl leukaemias and lymphomas)

Synonym
mastocytosis; mast cell disease

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W,Novartis

Intervention

Keyword: mast cell, systemic mastocytose, therapy, tyrosine kinase inhibitor

Outcome measures

Primary outcome

Percent change in the Sumscore of all symptoms assessed by the Mastocytosis Symptom Assessment Form (MSAF) after 12 weeks.

Secondary outcome

Persistence of improvement symptom score at 6 months. Percent change in the mast cell burden (bone marrow infiltrate, skin infiltrate, serum tryptase levels) after 6 months. Number and grading of CTC adverse events during the 6 months of therapy.

Study description

Background summary

Patients with indolent or smoldering systemic mastocytosis can have severe disabling symptoms. Almost all patients have fatigue, a compromised quality of life, hampering normal functioning. Since this form of mastocytosis is not considered life-threatening, mast cell eradication has never been applied and patients receive only symptomatic therapy with histamine blockers. Midostaurin, a c-KIT inhibitor has shown activity regarding symptom control and decrease of malignant mast cells in patients with a rare subset of systemic mastocytosis, the aggressive form.

Study objective

Primary: To study the efficacy and tolerability of Midostaurin in patients with indolent or smoldering systemic mastocytosis on mediator symptom reduction.
Secondary: 1) To study whether Midostaurin can reduce mast cell infiltration and 2) to assess its safety in this group of patients.

Study design

Single arm, open label pilot phase II study.

Intervention

treatment with Midostaurin, twice daily 100 mg orally for 6 months continuously.

Study burden and risks

Risks and burden: Patients will take an experimental drug with thus far as frequent adverse event nausea and vomiting (<3% CTC grade 3-4) that can be well controlled by antiemetic drugs. Other adverse events mentioned are all at a CTC grade 3-4 frequency of less than 2%. Patients have to fill in a 2 page symptoms score weekly. They will undergo an abdominal ultrasound and bone marrow examination twice (pre and post treatment), unless the pre-sample is a recent one. They will visit the UMCG 9 times including the pre-visit. At each visit blood tests will be taken (chemistry control, hemogram, tryptase levels).

Benefit: this is the first time that a potentially effective mast-cell eradicative therapy with very promising results regarding symptom improvement is offered to patients with symptomatic systemic mastocytosis for whom guidelines thus far do not prescribe such eradicative therapy. If successful with a managable adverse events pattern, a large majority of patients with this subset of mastocytosis (the predominant form) will benefit.

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

* Patients with ISM or SSM according to the WHO criteria
* Presence of the D816V c-KIT mutation
* Serum tryptase > 20 mg/l
* Serious mediator-related symptoms that cannot be controlled by H1 and H2 blocking drugs. Symptoms will be scored by an adapted MSAF (mastocytosis symptom assessment form15) with at least
o a pre-study score of 4 or more on 3 non-related items,
o or a pre-study score of 5 or more on 2 non-related items.
o one item from the scoring list can be replaced by flushes 7 or more per week or anaphylactic attacks 1 or more per week
* Age >18 years
* Willingness to apply optimal contraceptive measures (double barrier method, both men and women) if applicable, e.g. women below the age of 55, men at all ages; for both: if sexually active.
* Written informed consent

Exclusion criteria

- Aggressive systemic mastocytosis, mast cell leukemia, or ASM with or without accompanying non-clonal related non-mast cell disorder (SM-ANHMD).
* Any known other present malignancy, non-melanoma skin cancers excluded
* History of malignancy within the last 5 years, non-melanoma skin cancers excluded
* Any serious comorbidity interfering with therapy compliance and follow-up compliance
* Pregnancy

* Patients not willing or who are not able to comply with contraceptive measures

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):	13-09-2013
Enrollment:	20
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	31-01-2013
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-07-2013
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO Date:	11-07-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	29-07-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-01-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-01-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	29-08-2014
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	EUCTR2012-004868-22-NL

Register	ID
CCMO	NL41973.042.12