Glivec (imatinib mesylate) in systemic sclerosis, a pilot study

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To investigate the efficacy (and the toxicity) of Glivec in systemic sclerosis by examining clinical outcomes (clinical and laboratory findings).

Ethical review	Approved WMO
Status	Pending
Health condition type	Immunodeficiency syndromes
Study type	Interventional

Summary

ID

NL-OMON30793

Source
ToetsingOnline

Brief title
Glivec in systemic sclerosis

Condition

- Immunodeficiency syndromes

Synonym
sclerodermia, systemic sclerosis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: fibroblast, Imatinib mesylate, Rodnan skin score, systemic sclerosis

Outcome measures

Primary outcome

Rodnan skin score

Secondary outcome

· Disease severity score

· Number of digital ulcers

· Pulmonary function test (CO-diffusion)

· Kidney function as measured by creatinin clearance

Study description

Background summary

Systemic sclerosis is a debilitating generalized autoimmune disorder, characterized by fibrotic arteriosclerosis of peripheral and visceral vasculature and variable degrees of extracellular matrix accumulation (mainly collagen) in both skin and viscera. The disease is associated with specific autoantibodies. Various subsets of disease with specific clinical features and variable involvement of internal organs are distinguished.
Involvement of internal organs, including gastrointestinal tract, lungs, heart and kidneys, accounts for increased morbidity and mortality. No putative antifibrotic or immunosuppressive agents have yet been shown to be of unequivocal benefit in placebo-controlled clinical trial. Treatment is for mostly supportive.
Due to its extensive proliferation and increased collagen synthesis the fibroblast is regarded as the key effector cell in fibrosis. A host of mediators has been implicated in the pathogenesis of fibrosis. Platelet derived growth factor (PDGF) is regarded as a key molecule driving the fibrotic response. Therefore the PDGF pathway may be considered an attractive pathway for pharmacological intervention of the fibrotic response in these patients. PDGF-receptors belong to the so-called receptor tyrosine kinase family. Recently, several compounds have been developed that block signal transduction of various tyrosine kinases. In the present study we would like to examine whether the tyrosine kinase inhibitor Glivec is capable of inhibiting disease progression patients with systemic sclerosis.

Study objective

To investigate the efficacy (and the toxicity) of Glivec in systemic sclerosis by examining clinical outcomes (clinical and laboratory findings).

Study design

Open label study. Purpose evaluation of effect on skin score, digital ulcers, pulmonary and renal function.
Planned treatment: Glivec 1 dd 400 mg
Treatment duration: 12 months

Intervention

Glivec 1 dd 400 mg

Study burden and risks

Treatment with Glivec has adverse effects.The presence of adverse effects will be actively sought and will be recorded on standardised forms. Adverse effects sufficient to withdraw medication will be determined after discussion with the trial coordinator (PvD). Intolerance to Glivec is an end-point of the study and will result in departure from the protocol without withdrawing the patient from the study.

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 systemic sclerosis (either diffuse or limited) refractory to standard therapy
· Adequate end organ function, defined as: total bilirubin <1.5 x ULN, SGOT and SGPT < 2.5 x ULN (or <5 x ULN if hepatic disease involvement is present), creatinine < 1.5 x ULN, ANC >1.5 x 109/L, platelets > 100 x 109/L.
· Adequate anticonception in women
· Written informed consent

Exclusion criteria

· Age < 18 years
· Previous or current malignancy
· Current treatment with endothelin receptor antagonist
· Current treatment with immunosuppressive drugs
· Life expectancy < 6 months
· Pregnancy
· Inability to adhere to the current protocol

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2007
Enrollment:	10
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Gleevec
Generic name:	Imatinib mesylate
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	03-07-2007
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-09-2007
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	EUCTR2006-007091-15-NL
CCMO	NL16016.078.07