Effects of bosentan in a homogeneous population of SSc subjects with a predefined restriction of blood flow in the hands

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The primary objectives are:- To demonstrate the relationship of blood flow in the hands and the extent of digital ulcera in patients with systemic scleroderma;- Evaluate the effect of bosentan on the blood flow in the hands from baseline to 12 weeks...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Connective tissue disorders (excl congenital)
Study type	Interventional

Summary

ID

NL-OMON36236

Source
ToetsingOnline

Brief title
HOME

Condition

- Connective tissue disorders (excl congenital)
- Skin vascular abnormalities
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Systemic Connective Tissue Disease, Systemic Scleroderma

Research involving
Human

Sponsors and support

Primary sponsor: Actelion Pharmaceuticals
Source(s) of monetary or material Support: Actelion Pharmaceuticals Nederland bv

Intervention

Keyword: Blood perfusion, Bosentan, Digital Ulcera, Systemic Scleroderma

Outcome measures

Primary outcome

- Relationship between blood flow in the hands, as measured by laser Doppler imaging, and extent of digital ulcera assessed by the mean blood flow restriction in four distinct groups of patients: patients without current digital ulcera (pitting scars allowed), patients with new digital ulcera (less than 3 months old), patients with persistent digital ulcera (more than 3 months old) and patients with significant tip-necrosis;

- Change in blood flow in the hands after 12 weeks of bosentan treatment compared to the blood flow at 0 weeks, as measured by laser Doppler imaging.

Secondary outcome

- Change in blood flow in different regions of the hands after 4 and 12 weeks of bosentan treatment compared to the blood flow after 0 weeks, as measured by laser Doppler imaging;

- Change in modified Rodnan Skin Score (mRSS) from 0 weeks to 12 weeks, 26 weeks and 52 weeks of bosentan treatment;

- Change in selected components of the Scleroderma Health Assessment

Questionnaire from 0 weeks to 12 weeks, 26 weeks and 52 weeks of bosentan

treatment;

- Changes in EQ 5D from 0 weeks to 12 weeks, 26 weeks and 52 weeks of bosentan

treatment;

- Total number of new DU and pitting scars developed from 0 weeks to 12 weeks,

26 weeks and 52 weeks of bosentan treatment.

Study description

Background summary

The effect of bosentan on digital ulcers (DU) was studied in two randomized placebo-controlled trials (RAPIDS-1 and RAPIDS-2). A limitation of these studies was the heterogeneous study population. More importantly, there were no endpoints that assessed changes in vasculopathy and / or perfusion. Laser Doppler imaging has been shown to effectively demonstrate blood flow restrictions in the hands of patients with Systemic Scleroderma (SSc) (Rosato et al, 2010).

This study has been set up to demonstrate the relation between the blood flow in the hands and the extent of the digital ulcera in patients with systemic scleroderma.

In addition, the impact of bosentan on the blood flow in the hands, in a defined cohort of systemic scleroderma patients with a history of digital ulcera within the past 2 years and a clinically relevant reduction of blood flow in the hands, will be assessed.

Study objective

The primary objectives are:
- To demonstrate the relationship of blood flow in the hands and the extent of digital ulcera in patients with systemic scleroderma;

- Evaluate the effect of bosentan on the blood flow in the hands from baseline to 12 weeks, measured by laser Doppler imaging, in systemic scleroderma patients with a history of digital ulcera in the past 2 years and a clinically relevant reduction of blood flow at baseline.

The secondary objectives are:
- To evaluate the effect of bosentan on the blood flow in different regions of the hands from 0 weeks to 4 weeks and 12 weeks;
- To evaluate the effect of bosentan on the hand function, pain perception and quality of life from 0 weeks to 12 weeks, 26 weeks and 52 weeks;
- To evaluate the effect of bosentan on the modified Rodnan Skin Score from 0 weeks to 12 weeks, 26 weeks and 52 weeks;
- To evaluate the effect of bosentan on the development of new digital ulcera and pitting scars from 0 weeks to 12 weeks, 26 weeks and 52 weeks.

Study design

Open label, non comparative study.

Intervention

Patients that will be included in the study will start bosentan treatment as described in the summary of product characteristics. After 12 weeks of treatment the investigator/treating physician decides, together with the patient, if the bosentan treatment will be continued (for as long as needed).

Study burden and risks

The patients will visit the hospital 5 times (after 0, 4, 12, 26 and 52 weeks) as a result of participating in this study. During visit 1, 2 and 3 the blood flow in the hands will be measured by laser Doppler imaging. During visit 1, 3, 4 and 5 the patient will be asked to complete 2 questionnaires (selected components of the SHAQ and the EQ 5D) and the investigator completes 1 questionnaire (modified Rodnan Skin Score).

Next to the known risks of treatment with bosentan there are no significant risks to participation in this study and the burden is minimal, compared to the advantage the patient might experience from treatment with bosentan.

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

1. Male and female subjects > 18 years diagnosed with systemic sclerosis;
2. Reduction of blood flow measured by laser Doppler imaging, of at least 50%, distally to the proximal interphalangeal joint, compared to historical healthy controls;
3. Women of childbearing potential must have a negative pregnancy test and use a reliable form of contraception;
4. A history of 1 or more DUs within 2 years prior to inclusion;
5. No use of bosentan in the past;
6. Subjects willing and able to sign informed consent.

Exclusion criteria

1. Parenteral Prostanoid treatment for DU < 3 months ago;
2. Chronic treatment with PDE-5 inhibitor or ERA;
3. History of bosentan use;
4. Irreversible significant limitation of the hand function, e.g. amputation of more than one finger;
5. Other types of system- or connective tissue diseases;

6. Significant peripheral (macro-) vascular disease due to e.g. diabetes, hyperlipidemia, uncontrolled systemic hypertension, coagulopathy;
7. Any serious medical co morbidity (eg, active malignancy) such that the subjects life expectancy is < 12 months;
8. Known AST and/or ALT elevations higher than 3 times Upper Limit Normal (ULN);
9. Moderate to severe liver function disorder;
10. Pregnancy or breastfeeding;
11. Treatment with Glibenclamide, Fluconazole, Cyclosporin A, Tacrolimus or other calcineurin inhibitors;
12. Hypersensitivity for bosentan or one of its components;
13. Subjects not able to follow the protocol.

Study design

Design

Study phase:	4
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-04-2011
Enrollment:	106
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Tracleer
Generic name:	Bosentan
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	10-12-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-03-2011
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2010-023908-27-NL
CCMO	NL34698.091.10