Assessment of concentrations of belimumab in body fluids of patients with systemic lupus erythematosus

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To determine the concentration of belimumab in blood, saliva and seminal fluid in patients with SLE, treated with intravenous or subcutaneous belimumab.

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

Summary

ID

NL-OMON49577

Source
ToetsingOnline

Brief title
Concentrations of belimumab in SLE patients

Condition

- Connective tissue disorders (excl congenital)
- Foetal complications

Synonym
lupus, systemische lupus erythematosus

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Belimumab, Body fluids, SLE

Outcome measures

Primary outcome

Our main endpoint is the concentration of belimumab in seminal fluid in men

with SLE, treated with (intravenous and subcutaneous) belimumab.

Secondary outcome

Our secondary endpoints are:

- the concentration of belimumab in blood in male and female patients with SLE,

treated with belimumab (intravenously or subcutaneously);

- the seminal fluid : blood concentration ratio of belimumab in male patients

with SLE treated with belimumab (intravenously or subcutaneously);

- the concentration of belimumab in saliva in male and female patients with

SLE, treated with belimumab (intravenously or subcutaneously).

Study description

Background summary

The biological agent belimumab (Benlysta®) has recently been introduced for the treatment of severe systemic lupus erythematosus (SLE), a systemic autoimmune disease affecting women and men aged 20 to 45 years, the period of life during which pregnancies are usually planned. The introduction of belimumab for the treatment of SLE has improved the disease course in many of these patients importantly. Female patients treated with belimumab are advised against pregnancy because insufficient data on the safety of its use during pregnancy with regard to potential embryotoxic effects are available. Men treated with belimumab are currently advised not to induce a pregnancy because no data on belimumab concentrations in seminal fluid and on the safety of peri-conceptual paternal exposure to belimumab with regard to pregnancy outcome and embryotoxic effects are available. A study on belimumab concentrations in blood of healthy

subjects and SLE patients treated with belimumab demonstrated that steady state levels of belimumab in blood are rapidly reached in intravenously treated individuals, while a steady state level of belimumab in blood of subcutaneously treated individuals is not achieved before 11 weeks of treatment (1). No data are currently available on the distribution of belimumab to other body fluids. In particular, it is unknown whether belimumab is detectable in the seminal fluid of men treated with belimumab. Therefore, it is unknown whether men treated with belimumab should indeed be adviced to avoid inducing a pregnancy. Belimumab may be transported by body fluids (seminal fluid, saliva, blood) of the man in the recipient woman. Previous studies on other chemical agents have demonstrated that the concentration of those chemical agents in seminal fluid is in general equal to or lower than the blood concentration of that particular chemical agent (2). In addition, it is assumed that total absorption of a seminal dose of a chemical with a high seminal fluid : blood concentration ratio is at least three orders of magnitude lower than that in the man (2). However, the seminal fluid : blood concentration ratio of belimumab is unknown.

The present study is designed to provide more insight in the distribution of intravenously or subcutaneously administered belimumab to three body fluids by assessment of belimumab concentrations in blood, saliva and seminal fluid, and assessment of the seminal fluid : blood concentration ratio of belimumab in males treated with belimumab. The results of this study will provide information which is necessary for better counselling of male SLE patients treated with belimumab in the future on safety issues regarding inducing a pregnancy during belimumab therapy. Furthermore, the results of this study will provide insight in sex differences in belimumab concentrations in blood and saliva.

REFERENCES

1. Pons-Estel GJ, Alarcon GS, Scofield L, Reinlib L, Cooper GS. Understanding the epidemiology and progression of systemic lupus erythematosus. Semin Arthritis Rheum. 2010;39(4):257-68.
2. Klemmt L, Scialli AR. The transport of chemicals in semen. Birth Defects Res B Dev Reprod Toxicol. 2005;74(2):119-31.

Study objective

To determine the concentration of belimumab in blood, saliva and seminal fluid in patients with SLE, treated with intravenous or subcutaneous belimumab.

Study design

Study design: A single centre, cohort study in a maximum of 10 patients with SLE, treated with belimumab

Intervention: For patients treated with intravenous belimumab at the day care in our hospital: withdrawal of blood directly before (10 ml) and directly after (10 ml) infusion of belimumab; withdrawal of saliva directly before (4 ml) and directly after (4 ml) infusion of belimumab. This will be done during 3 separate visits to the day clinic for belimumab treatment. Men treated with intravenous belimumab are asked if they can intercept seminal fluid at three random time points at home (3 x 4 ml).

For patients treated with subcutaneous belimumab (self-administration at home): withdrawal of blood (10 ml) and withdrawal of saliva (4 ml) at the day of a visit at the outpatient clinic of the department of rheumatology. This will be done during 3 separate visits to the outpatient clinic during belimumab treatment. Men treated with subcutaneous belimumab are asked if they can intercept seminal fluid at three random time points at home (3 x 4 ml).

Only in case of withdrawal of belimumab treatment, the withdrawal of blood and saliva and (for male patients only) the interception of seminal fluid will be done again during 3 separate visits to the outpatient clinic after cessation of belimumab treatment.

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: During treatment with belimumab, withdrawal of blood (20 ml for patients treated with intravenous belimumab and 10 ml for patients treated with subcutaneous belimumab), withdrawal of saliva (8 ml for patients treated with intravenous belimumab and 4 ml for patients treated with subcutaneous belimumab) and interception of seminal fluid (12 ml) will take place up to three times. If treatment with belimumab is stopped, withdrawal of blood, withdrawal of saliva and interception of seminal fluid will take place up to three times.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Diagnosis with SLE according to the American College of Rheumatology (ACR) revised criteria for the classification of SLE
- Age 18 years or older
- Current treatment with belimumab (intravenous or subcutaneous administration)
- Signed informed consent form

Exclusion criteria

None

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-07-2020
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	17-06-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC

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
CCMO	NL69878.029.19