Distribution of NIlotinib in semen in men treated for chronic Myeloid leukaemiA

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Leukaemias
Study type	Observational invasive

Summary

ID

NL-OMON47098

Source
ToetsingOnline

Brief title
DANIMA

Condition

- Leukaemias

Synonym
cancer of the white bloodcells, Chronic Myeloid leukaemie

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ziekenhuisapotheek

Intervention

Keyword: nilotinib, semen

Outcome measures

Primary outcome

The primary endpoint of the study is the percentage of nilotinib present in

seminal fluid in relation to the plasma concentration.

Secondary outcome

The secondary endpoint is the calculated maximal concentration nilotinib

absorbed by the partner, using the volume of distribution of the tyrosine

kinase inhibitors and the percentage in seminal fluid found in this study.

Study description

Background summary

Treatment of cancer has developed enormously during the last decade. Especially for chronic myeloid leukaemia (CML), the advent of TKI*s, such as nilotinib has dramatically changed prospects of patients with 8 year overall survival rates increasing from 50% to 90% in approximately 10 years. Many anticancer agents are known for their reprotoxicity, genotoxicity and mutagenicity. For the TKIs that are used in CML, teratogenicity is well known when taken by a pregnant mother. Hypospadias, vertebral-, abdominal wall- and skull abnormalities have occurred in clearly higher frequencies than the normal background rate. However, children of men taking TKIs seem not to have an increased risk of teratogenicity. Whether nilotinib in seminal fluid would pose any risk to the developing fetus when a pregnant woman has sexual intercourse with a man taking nilotinib is unknown. During unprotected sexual intercourse the seminal fluid comes in contact with mucosal tissue of the partner and may be absorbed.
A few studies investigated the risk for women of men on anticancer agents such as, lenalidomide and thalidomide. Here, detectable amounts of the anti-cancer drugs in the seminal fluid of men using either lenalidomide or thalidomide could be demonstrated.
No data is available on nilotinib and the amount present in seminal fluid. Information is necessary to provide adequate information to male users and

their partners.

Study objective

This study is designed to determine the level of nilotinib detectable in seminal fluid of men treated with this tyrosine kinase inhibitor and in order to form an advise on the use of physical barriers like, condoms, to protect sexual partners from exposure to nilotinib..

Study design

The study is an open-label non-intervention single-centre study. At two different time points, subjects will collect seminal fluid and blood samples. The blood samples will be collected by dried blood spots (DBS). This biosampling method which can be performed at home by the subjects themselves uses a few drops of blood collected by a finger sting blotted on filter paper to determine the plasma level of nilotinib.

Study burden and risks

Chronic myeloid leukaemia requires life-long treatment with nilotinib in most patients. As at least 25% of patients is below 40 years and life expectancy seems normal in well responding patients, pregnancy related issues are of major importance. Currently, use of condoms is advised for any male patient, in order to protect their sexual partners against nilotinib exposure. If this study shows very low and acceptable nilotinib levels in seminal fluid, condoms may no longer be required in cases where contraception is not needed.
The patients burden consists of two extra blood samples by Dried Blood Spot (DBS) and the effort of collecting and delivery of seminal fluid at two different time points. Patients may feel embarrassment with participation in the study.
There are no physiological or physical risk during the study. All patients receive nilotinib as standard care.

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

male patients
aged >18 years
use of nilotinib for a minimal period of 1 month in chronic phase of chronic myeloid leukaemia
willing and capable of donating a semen sample for pharmacological analysis

Exclusion criteria

Refractory chronic myeloid leukaemia with persistent leukocytosis

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-03-2018
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO Date:	09-08-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-08-2018
Application type:	Amendment
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	NL56589.029.16