Multi-center, Randomized, Open-label, Parallel-arm, Single-dose, Pharmacokinetic Study of rVIIa-FP (CSL689) in Subjects with Congenital Factor VII Deficiency

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- to evaluate the FVIIa activity PK of 2 CSL689 dose levels in subjects with congenital FVII deficiency- to determine the PK characteristics of FVIIa activity of CSL689- to evaluate the safety and tolerability of intravenous administration of CSL689...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Blood and lymphatic system disorders congenital
Study type	Interventional

Summary

ID

NL-OMON43708

Source
ToetsingOnline

Brief title
CSL689_1002 PK and safety study in patients with congenital FVII deficiency

Condition

- Blood and lymphatic system disorders congenital

Synonym
Factor VII Deficiency; Congenital coagulation factor VII deficiency

Research involving
Human

Sponsors and support

Primary sponsor: CSL Behring GmbH
Source(s) of monetary or material Support: Sponsor

Intervention

Keyword: Factor VII deficiency, Factor VIIa, Pharmacokinetics, Safety

Outcome measures

Primary outcome

- Elimination half-life of plasma factor VIIa activity

- Maximum observed plasma FVIIa activity

- Area under the curve (AUC0-t), Area under plasma factor VIIa activity versus

time curve from time 0 to last sample with quantifiable activity

Secondary outcome

- Total clearance, Total clearance of plasma factor VIIa activity

- AUC(0-inf), Area under plasma factor VIIa activity versus time curve from

time 0 extrapolated to infinity

- Incremental recovery, Incremental recovery of plasma factor VIIa activity

- Time of occurrence of maximum observed plasma FVIIa activity

- Number of subjects with antibodies against CSL689

- Number of subjects with inhibitors against CSL689

Study description

Background summary

Investigating PK, safety and tolerability of CSL689 (rVIIa-FP) in patients with congenital Factor VII deficiency

Study objective

- to evaluate the FVIIa activity PK of 2 CSL689 dose levels in subjects with congenital FVII deficiency
- to determine the PK characteristics of FVIIa activity of CSL689
- to evaluate the safety and tolerability of intravenous administration of CSL689

Study design

A multicenter, randomized, open-label, parallel-arm, phase 1 study to investigate the PK of CSL689 in subjects with congenital FVII deficiency.

Intervention

Single dose of either NovoSeven (25 µg/kg) or pdFVII (30 IU/kg) and
Single dose of CSL689 (100 or 300 µg/kg)

Study burden and risks

On Day 1, eligible subjects will receive a single dose of their routine replacement therapy (either NovoSeven rFVIIa [25 µg/kg] or pdFVII [30 IU/kg]), followed by up to 48 hr of blood sampling for PK assessments. After a washout period of >= 48 hr, subjects will be randomized to a single dose of 100 µg/kg of CSL689 or a single dose of 300 µg/kg of CSL689, followed by blood sampling for PK assessments (0 to 48 hr after administration of CSL689). Routine safety data will be collected during the study, with follow-up visits to assess potential formation of inhibitory antibodies.

Based on data from the nonclinical safety pharmacology and toxicity studies, potential risks associated with CSL689 include the development of anti drug antibodies and thromboembolic complications. Although considered unlikely based on evidence from the published literature, there is also a very low risk of patients with congenital FVII deficiency developing inhibitory antibodies against CSL689, after treatment with the replacement factor.
None of these risks were observed in the first in human study that included 30 subjects exposed to CSL689 at doses greater than those proposed for the current study (ranging 140 to 1000 µg/kg bodyweight).

Nonclinical studies, as well as the first in human study (CSL689_1001) have shown that CSL689 has a favorable PK profile when compared to the currently available products. As such, the use of a replacement factor with an extended t1/2 compared to currently available FVIIa products should provide the benefit of longer intervals between administration of treatment for patients with congenital FVII deficiency.
However, study CSL689_1001 involved healthy volunteers, and whilst the

collected PK data can be considered as representative of the CSL689 PK profile in patients with hemophilia, this extrapolation cannot be extended to patients with congenital FVII deficiency, hence the need for the current PK study.

The characterization of the CSL689 PK profile from the current study will support further clinical development of CSL689 as replacement therapy for the treatment of acute bleeding events and for prophylaxis, Given its extended t1/2, CSL689 is expected to present the possibility of less frequent treatments, with a resulting positive impact on treatment compliance and a reduced burden on patients and physicians.
The associated benefit risk balance of the study is considered acceptable for the enrolled subjects.

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

- subjects with proven congenital factor VII deficiency
- age >= 18 years.
- FVII level < 2%.
- minimum of 50 previous exposure days to plasma-derived factor VII or recombinant factor VIIa

Exclusion criteria

- History of, or risk factors for, thromboembolic events, including known deep vein thrombosis
- Inhibitor to FVII or rFVIIa, current or historic.
- Known or suspected hypersensitivity to hamster protein, to CSL689, or to any excipient of CSL689.
- Known or suspected allergy to rFVIIa or hamster protein.
- Major surgery within 1 month before screening or scheduled major and / or orthopedic surgery during the study.
- Advanced atherosclerotic disease (ie, known history of ischemic heart disease, or ischemic stroke)
- Human immunodeficiency virus (HIV)-positive subjects with cluster of differentiation 4 (CD4) + lymphocyte count of < 200/ µL at screening.
- Use of an investigational agent within 30 days before the study
- Use of concomitant therapy not permitted during the study (ie, other platelet inhibitors, desmopressin, fibrinolysis inhibitors, except if used as local treatment [eg, for oral bleeds]

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-07-2015
Enrollment:	9
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	CSL689
Generic name:	rVIIa-FP
Product type:	Medicine
Brand name:	Factor VII "Baxter" 600 I.U (plasma derived)
Generic name:	Factor VII "Baxter" 600 I.U (plasma derived)
Product type:	Medicine
Brand name:	NovoSeven
Generic name:	eptacog alfa
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	27-11-2014
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-05-2015
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-08-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-12-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO Date:	23-02-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-04-2016
Application type:	Amendment
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	EUCTR2014-002982-32-NL
CCMO	NL51207.091.14