Safety, efficacy and exposure of subcutaneously administered NNC0365-3769 (Mim8) prophylaxis in children with haemophilia A with or without FVIII inhibitors

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Primary objective: To investigate the safety of Mim8 prophylaxis in children with haemophilia A with or without FVIII inhibitors.Secondary objectives• To investigate the efficacy of Mim8 prophylaxis in children with haemophilia A with or without...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Coagulopathies and bleeding diatheses (excl thrombocytopenic)
Study type	Interventional

Summary

ID

NL-OMON51874

Source
ToetsingOnline

Brief title
Frontier 3

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
blood clothing disorder, Haemophilia A

Research involving
Human

Sponsors and support

Primary sponsor: Novo Nordisk
Source(s) of monetary or material Support: Novo Nordisk

Intervention

Keyword: Haemophilia A with and without inhibitors, Mim8, NNC0365-3769

Outcome measures

Primary outcome

Number of treatment emergent adverse events from treatment initiation to follow-up visit (week 0 to week 72)

Secondary outcome

• Number of treated bleeds from treatment initiation to end of treatment (week 0 to week 52)

• Number of treated spontaneous bleeds from treatment initiation to end of treatment (week 0 to week 52)

• Number of treated traumatic bleeds from treatment initiation to end of treatment (week 0 to week 52)

• Number of treated joint bleeds from treatment initiation to end of treatment (week 0 to week 52)

• Number of treated target joint bleeds from treatment initiation to end of treatment (week 0 to week 52)

• Number of injection site reactions from treatment initiation to end of treatment (week 0 to week 52)

• Consumption of factor product per bleed treatment from run-in initiation to end of treatment (week -26 to week 52)

• Occurrence of anti-Mim8 antibodies from treatment initiation to end of treatment (week 0 to week 52)

• Mim8 plasma concentration from treatment initiation to end of treatment (week 0 to week 52)

• Change in physical function domain of PEDS-QL Generic Core Scales from treatment initiation to end of treatment (week 0 to week 52)

• Treatment preference for Mim8 versus previous treatment using Caregiver H-PPQ, once during treatment (week 26)

• Change in patients* treatment burden using the Hemo-TEM from treatment initiation to end of treatment (week 0 to week 52)

Study description

Background summary

Mim8 has been evaluated in a nonclinical programme comprising PK, toxicology, efficacy and safety pharmacology. Collectively, the nonclinical safety studies support progression of Mim8 in clinical development.
The FRONTIER1 First Human Dose (FHD) study, administering single ascending doses (SAD) to healthy participants followed by multiple ascending doses (MAD) to participants with haemophilia A (NN7769-4513), was initiated in January 2020 and is ongoing. Therefore, no clinical results are available now. Before initiating the FRONTIER3 study, a safety and PK/PD summary of the available SAD and MAD data from the FRONTIER1 study will be prepared. This summary will be submitted to regulatory authorities, if and as required. No risks have been identified.

Study objective

Primary objective:
To investigate the safety of Mim8 prophylaxis in children with haemophilia A with or without FVIII inhibitors.

Secondary objectives
• To investigate the efficacy of Mim8 prophylaxis in children with haemophilia

A with or without FVIII inhibitors.
• To evaluate the consumption of coagulation factor replacement product per bleed treatment (number of injections) with Mim8 prophylaxis in children with haemophilia A with or without FVIII inhibitors.
• To evaluate the development of anti-Mim8 antibodies with Mim8 prophylaxis in children with haemophilia A with or without FVIII inhibitors.
• To investigate exposure of Mim8 after once-weekly and once-monthly subcutaneous dosing in children with haemophilia A with or without FVIII inhibitors.
• To evaluate treatment burden with Mim8 prophylaxis in children with haemophilia A with or without FVIII inhibitors, as reported by their caregivers.
• To investigate treatment preference among caregivers of previously treated children with haemophilia A with or without FVIII inhibitors.
• To evaluate aspects of physical functioning with Mim8 prophylaxis in children with haemophilia A with or without FVIII inhibitors.

Study design

This is a prospective, multinational, multicentre, open label, non-controlled and one-arm phase 3 study with no randomisation. The treatment period will be 52 weeks. The study includes a run-in period of at least 26 weeks duration for participants previously treated on prophylaxis. There is no run-in period for previously untreated patients (PUPs) and participants on immune tolerance induction (ITI). The run-in period is optional for participants treated on demand.
The treatment period is composed of a part 1 and part 2 with 26 weeks of once-weekly treatment (part 1) followed by 26 weeks of once-weekly or once-monthly treatment (part 2). For part 2, the participant and parent(s)/caregiver(s) will be able to choose either weekly or monthly dosing frequency.

Intervention

Subcutaneous injections of Mim8.

Study burden and risks

Based on the findings from nonclinical studies, on the identified potential risks described in the protocol, and the possible clinical benefit in participants with haemophilia A with or without FVIII inhibitors, it is evaluated that the anticipated benefits outweigh the potential risks of Mim8 in this phase 3 study. The clinical study may only be conducted (in minors) if it subjects the person concerned to as little burden, and other foreseeable risks, as possible.

Contacts

Public
Novo Nordisk

Flemingweg 8
Alphen aan den Rijn 2408AV
NL
Scientific
Novo Nordisk

Flemingweg 8
Alphen aan den Rijn 2408AV
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)
Babies and toddlers (28 days-23 months)

Inclusion criteria

-Informed consent obtained before any study-related activities. Study-related activities are any procedures that are carried out as part of the study, including activities to determine suitability for the study.
- Male and female participants with the diagnosis of congenital haemophilia A of any severity based on medical records.
- Aged 1*11 years (both inclusive) at the time of signing informed consent.
- For previously treated participants :
a. Participant has been prescribed treatment with FVIII concentrate or bypassing agent in the
last 26 weeks prior to screening.
b. Participant with endogenous FVIII activity >=1%, based on medical records, must have at

least 1 treated bleed during the previous 26 weeks before screening for which factor VIII
concentrate or bypassing agent has been prescribed (No requirements for participants with
FVIII activity <1%).
- For previously untreated participants :
a. Diagnosis of severe haemophilia A (endogenous FVIII activity < 1%) based on medical
records.
- Child and parent(s)/caregiver(s) willingness and ability to comply with scheduled visits and
study procedures, including the completion of diary and patient-reported outcomes
questionnaires.

Exclusion criteria

- Known or suspected hypersensitivity to study product or related products.
- Previous participation in this study. Participation is defined as signed informed consent.
- Exposure to non-factor haemostatic products for bleeding prophylaxis within 6 months (or 5 half-lives of the medicinal product, whichever is shorter) prior to planned first dose, for participants not included in the run-in.
- Known congenital or acquired coagulation disorders other than haemophilia A.
- Other conditions (e.g. autoimmune disease) or laboratory abnormality that may increase risk of bleeding or thrombosis, as evaluated by the investigator.
- Any disorder, except for conditions associated with haemophilia A, that in the investigator*s opinion might jeopardise the participant*s safety or compliance with the protocol.
- Mental incapacity, unwillingness to cooperate or a language barrier precluding adequate understanding and cooperation.
- Lack of adequate parental/caregiver support to enter accurately and timely information regarding treatment and bleeding episodes into an (electronic) diary.
- Previous or current treatment for thromboembolic disease (with the exception of previous catheter-associated thrombosis for which anti-thrombotic treatment is not currently ongoing) or signs of thromboembolic disease.
- Major surgery planned to take place after screening.
- Immune tolerance induction planned to take place after treatment initiation.
- Hepatic dysfunction defined as aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT) >3 times the upper limit of normal combined with total bilirubin >1.5 times the upper limit of normal measured at screening.
- Serum creatinine above 1.5 x upper limit of normal (ULN), measured at screening.

- Pregnancy (female participants).

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	29-07-2022
Enrollment:	4
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nog niet bekend
Generic name:	NNC0365-3769 (Mim 8)

Ethics review

Approved WMO Date:	20-09-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-11-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO Date:	13-06-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-07-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-07-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-08-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-12-2022
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	19-01-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam

	020 566 7389
	mecamc@amsterdamumc.nl
Approved WMO Date:	06-03-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam)
	Kamer G4-214
	Postbus 22660
	1100 DD Amsterdam
	020 566 7389
	mecamc@amsterdamumc.nl

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	EUCTR2020-003467-26-NL
CCMO	NL78852.018.21