

Clinical Trial Protocol

Iranian Registry of Clinical Trials

30 Jun 2026

An Exploratory Study to Evaluate the Dose Response Relationship of Pharmacodynamic Parameters of Aryoseven in Patients with Hemophilia A and B with Inhibitors

Protocol summary

Study aim

Evaluation of Dose response relationship

Design

Randomized, double blind, single dose, 5 way crossover evaluating 4 dose (10, 30, 90, 270 µg per kg) AryoSeven and one dose NovoSeven (30 µg per kg) on Pharmacodynamic (PD) parameters Thrombin Generation Assay (TGA). Patients will be randomized to a dosing sequence according to the 5 ways cross over design to receive five IV injections, each separated by a washout period of 3 days. Drug administration will be performed in an investigator and patient blinded fashion by an independent operator. Patients hospitalized prior to medication administration and sampling. Blood samples for Pharmacokinetic (PK) FVII plasma concentration (FVII:C) and PD (TGA) taken at 10 min prior to dose administration and at 10 min, 20 min, 1, 3, 5, 8, 12, 24 and 30 h after (a minimum amount of 5 ml of blood). Ddimer and Prothrombin Fragment (F1.2) will be assessed on an aliquot of the primary plasma samples at selected time points (10 min prior to dose, at 20 min, 1, 5, 12, 24 h after)

Settings and conduct

Single center study performed in Iranian Comprehensive Hemophilia Care Center. All routine tests biochemistry, hematology, virology and coagulations are performed in local laboratory. All PKPD parameters will be performed by central lab blinded to the treatment. Peripheral venous blood taken from the opposite arm to the slow injection. After blood samples centrifugation the obtained plasma will be aliquoted in dedicated cryotubes. The aliquots are placed into the patient specific Store Box and put into freezer (minus 80C). The samples are sent to the central lab periodically or at the end of patient enrollment

Participants/Inclusion and exclusion criteria

Male over 12 years, hemophilia A or B inhibitors over 5

BU, not in bleeding status. No FVII inhibitor

Intervention groups

AryoSeven, NovoSeven

Main outcome variables

Thrombin Generation Assay, DDimer, Prothrombin Fragment; FVII Plasma Concentration

General information

Reason for update

Acronym

UGA 2020-01

IRCT registration information

IRCT registration number: **IRCT20161202031193N3**

Registration date: **2021-02-01, 1399/11/13**

Registration timing: **registered_while_recruiting**

Last update: **2021-02-01, 1399/11/13**

Update count: **0**

Registration date

2021-02-01, 1399/11/13

Registrant information

Name

Amirhossein Saadatirad

Name of organization / entity

AryoGen Pharmed

Country

Iran (Islamic Republic of)

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2020-12-29, 1399/10/09
Expected recruitment end date
2021-02-20, 1399/12/02
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
An Exploratory Study to Evaluate the Dose Response Relationship of Pharmacodynamic Parameters of Aryoseven in Patients with Hemophilia A and B with Inhibitors

Public title
The Study of Dose Response Relationship Evaluation of AryoSeven in Hemophilia Patients

Purpose
Other

Inclusion/Exclusion criteria

Inclusion criteria:

Confirmed diagnosis of congenital haemophilia A or B with inhibitors to FVIII or FIX titer >5 Bethesda Units [BU] with > 2 episodes of bleeding/year requiring treatment with FVII infusions, non in bleeding episode Male adult and adolescents (>12 years) Patients informed consent has been obtained [Patients to be enrolled must also provide voluntary written informed consent to the protocol prior to screening to be eligible for the study. For adolescents, parent/legal guardian must provide consent and, wherever possible, patient assent will also be obtained. For compromised patients, their designated proxy must provide informed consent]. Patients willing and able to be hospitalized prior to time of study medication administration for plasma sampling (5 times during the study).

Exclusion criteria:

Any other type of congenital or acquired coagulopathy, such as: liver disease (hepatitis), vitamin k deficiency, uremia, malignancy. Antibodies against Factor VII Ongoing bleeding prophylaxis regimens with AryoSeven/Novoseven or planned to occur during the trial Platelet count less than 100.000 platelets/mcL (at screening visit) Any clinical sign or known history of arterial thrombotic event or deep venous- thrombosis or pulmonary embolism HIV positive with current CD4+ count of less than 200/ μ L Liver cirrhosis Factor VIII/IX immune tolerance induction regimen planned to occur during the trial Known hypersensitivity to the study medication Parallel participation in another experimental drug trial. Parallel participation in another marketed drug trial that may affect the primary end point of the study. Concomitant diseases and/or medications, or any other conditions, that render the patient unsuitable for inclusion into the study in the judgment of the investigator.

Age
From **12 years** old

Gender
Male

Phase

2

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser

Sample size

Target sample size: **12**

Randomization (investigator's opinion)

Randomized

Randomization description

Randomization will be performed using a randomization list prepared by an independent statisticians. The patient will be assigned to a specific treatment sequence. Possible sequence are planned on a balanced Latin Square design in 1:1 manner using Interactive Web Response System (IWRS).

Blinding (investigator's opinion)

Double blinded

Blinding description

Blinding will be performed by an independent third-party operator (nurse/pharmacist, unblinded), who will prepare undistinguishable syringes with patient's dosing and labelling. All people involved in the study are blind except the nurse or pharmacist who is responsible of preparing patient's treatment and an unblind CRA who is responsible for monitoring the blinding procedure.

Placebo

Not used

Assignment

Crossover

Other design features

An exploratory study to evaluate dose-response relationship of PD markers as surrogate efficacy endpoints.

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Baqiyatallah University of Medical Sciences

Street address

Shahid Nosrati st, South Sheykh Bahaee st, Mollasadra st, Vanak sq,

City

Tehran

Province

Tehran

Postal code

8174673461

Approval date

2020-12-09, 1399/09/19

Ethics committee reference number

Health conditions studied

1

Description of health condition studied

Congenital Hemophilia A with inhibitors

ICD-10 code

D66

ICD-10 code description

Hereditary factor VIII deficiency

2

Description of health condition studied

Congenital Hemophilia B with inhibitors

ICD-10 code

D67

ICD-10 code description

Hereditary factor IX deficiency

Primary outcomes

1

Description

Primary Pharmacodynamic Parameter: TGA

Timepoint

10 min prior to dose administration and at 10 min, 20 min, 1 h, 3 h, 5 h, 8 h, 12 h, 24 h and 30 h after AryoSeven or NovoSeven injection.

Method of measurement

Thrombin Generation will be measured using the ST-Genesis® Thrombin Generation System (Diagnostica Stago, Asnières sur Seine, France). Genesis® is a fully automated TG analyzer. In comparison to the CAT assay, ST Genesis® provides a normalization of each TG parameter based on a reference plasma for each test aiming to reduce the interlaboratory variability as well as the variability between differed measurement runs.

Secondary outcomes

1

Description

PD Parameters: D-Dimer, F1.2

Timepoint

10 min prior to dose administration and at 20 min, 1 h, 5 h, and 12 h and 24 h after.

Method of measurement

Validated analytical method performed by central lab

2

Description

Measurement of plasma level of factor VII clotting activity (FVII:C)

Timepoint

10 min prior to dose administration and at 10 min, 20 min, 1 h, 3 h, 5 h, 8 h, 12 h, 24 h and 30 h after

AryoSeven or NovoSeven injection

Method of measurement

Pharmacokinetic assessment of plasma level of factor VII clotting activity. (FVII:C) will be determined by commercial Staclot® VIIa-recombinant tissue factor assay (Diagnostica Stago, Asnières sur Seine, France).

Intervention groups

1

Description

Intervention group: Single dose Infusion of Biosimilar Eptacog alpha, activated (AryoSeven) 10 ug/kg in the arm that blood sampling has not taken place (after reconstitution of lyophilized powder provided)/ Product of AryoGen Pharmed

Category

Treatment - Drugs

2

Description

Intervention group: Single dose Infusion of Biosimilar Eptacog alpha, activated (AryoSeven) 30 ug/kg in the arm that blood sampling has not taken place (after reconstitution of lyophilized powder provided)/ Product of AryoGen Pharmed

Category

Treatment - Drugs

3

Description

Intervention group: Single dose Infusion of Biosimilar Eptacog alpha, activated (AryoSeven) 90 ug/kg in the arm that blood sampling has not taken place (after reconstitution of lyophilized powder provided)/ Product of AryoGen Pharmed

Category

Treatment - Drugs

4

Description

Intervention group: Single dose Infusion of Biosimilar Eptacog alpha, activated (AryoSeven) 270 ug/kg in the arm that blood sampling has not taken place (after reconstitution of lyophilized powder provided)/ Product of AryoGen Pharmed

Category

Treatment - Drugs

5

Description

Control group: Single dose Infusion of Eptacog alpha, activated (NovoSeven) 30 ug/kg in the arm that blood sampling has not taken place (after reconstitution of lyophilized powder provided)/ Product of Novo Nordisk

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Iranian Comprehensive Hemophilia Care Center

Full name of responsible person

MohammadReza Baghaipour

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Cross Zartosht Felestin st

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

AryoGen Pharmed

Full name of responsible person

Amirhossein Saadatirad

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Grant name**Grant code / Reference number****Is the source of funding the same sponsor organization/entity?**

Yes

Title of funding source

AryoGen Pharmed

Proportion provided by this source

100

Public or private sector

Private

Domestic or foreign origin

Domestic

Category of foreign source of funding

empty

Country of origin**Type of organization providing the funding**

Industry

Person responsible for general inquiries

Contact

Name of organization / entity

AryoGen Pharmed

Full name of responsible person

Amirhossein Saadatirad

Position

Project Manager of rFVIIa registration in Europe

Latest degree

Ph.D.

Other areas of specialty/work

Medical Pharmacy

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No. 140, Cross Tajbakhsh st, 24th Km Tehran Karaj
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Person responsible for scientific inquiries

Contact

Name of organization / entity

Bagheiat-allah University of Medical Sciences

Full name of responsible person

Dr. Hasan Abolghasemi

Position

Professor University CEO

Latest degree

Subspecialist

Other areas of specialty/work

Pediatrics Oncology

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Person responsible for updating data

Contact

Name of organization / entity

AryoGen Pharmed

Full name of responsible person

Amirhossein Saadatirad

Position

Project Manager of rFVIIa registration in Europe

Latest degree

Ph.D.

Other areas of specialty/work

Medical Pharmacy

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Sharing plan**Deidentified Individual Participant Data Set (IPD)**

Undecided - It is not yet known if there will be a plan to make this available

Study Protocol

Undecided - It is not yet known if there will be a plan to make this available

Statistical Analysis Plan

Undecided - It is not yet known if there will be a plan to make this available

Informed Consent Form

Undecided - It is not yet known if there will be a plan to make this available

Clinical Study Report

Undecided - It is not yet known if there will be a plan to make this available

Analytic Code

Undecided - It is not yet known if there will be a plan to make this available

Data Dictionary

Undecided - It is not yet known if there will be a plan to make this available