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 wayscross 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 (10min prior to dose,at 20min,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/µL 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

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Province

Tehran

Postal code

8174673461

Approval date

2020-12-09, 1399/09/19

Ethics committee reference number

IR.BMSU.REC.1399.502

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-Genesia® Thrombin Generation System (Diagnostica Stago, Asniéres sur Seine, France). Genesia® is a fully automated TG analyzer. In comparison to the CAT assay, ST Genesia® 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, Asniéres 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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Sponsors / Funding sources

1

Sponsor

Name of organization / entity
AryoGen Pharmed

Full name of responsible person
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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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Person responsible for scientific inquiries

Contact

Name of organization / entity
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Full name of responsible person
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Subspecialist

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Person responsible for updating data

Contact

Name of organization / entity
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Full name of responsible person
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Position
Project Manager of rFVIIa registration in Europe
Latest degree
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Other areas of specialty/work
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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