

Clinical Trial Protocol

Iranian Registry of Clinical Trials

18 Sep 2026

A Randomized, Multicenter, Double blind, Single doses Study Comparing the Pharmacodynamic, Pharmacokinetic and Safety of Biosimilar EPTACOG Alfa with Novoseven®, in Patient with Hemophilia A or B with Inhibitors

Protocol summary

Study aim

Bioequivalence according to Pharmacokinetic, Pharmacodynamic parameters. Clinical response in controlling acute bleeding. Immunogenicity, ADRs

Design

Patients enrolled are randomized to receive injections of either doses of AryoSeven or NovoSeven, separated by washout period of 3 days. Blood samples for the PKPD phase (at least 5 ml) is collected 10 min prior dose administration and at 10, 20 min, 1, 3, 5, 8, 12, 24 and 30 h after administration. For plasma sample stability study and only for maximum 10 patients, 9 ml blood instead of 5 ml will be drawn during Visit 2 and 3 at time points 1 h and 12 h. Before second dose blood is taken for immunogenicity test. Patients hospitalized at time of study medication administration and plasma sampling. Patients will be followed for 12 months to receive AryoSeven for bleedings at center or home (by patient at home or caregiver) with dose and duration of treatment decided by Investigator. Plasma sampling for determination of antibody formation against FVII will be taken every 3 months at the center.

Settings and conduct

Multicenter (Tehran, Shiraz, Zahedan, Istanbul, Adana, Bursa) Randomized, Double blind, crossover. Blinding is performed by independent third party who prepares and labels undistinguishable syringes according to randomization.

Participants/Inclusion and exclusion criteria

Over 12 years with congenital Hemophilia A or B with inhibitors over 5 BU with over 2 episodes of bleeding per year requiring treatment with FVII, not in bleeding episode. without inhibitor to FVII and any other type of congenital or acquired coagulopathy

Intervention groups

AryoGen Eptacog alfa (AryoSeven), IV 90 or 270 mcg per kg. NovoNordisk Eptacog alfa (Novoseven), IV 90 or 270 mcg per kg

Main outcome variables

PK: Area Under Curve inf (AUC_{inf}) PD: Thrombin Generation Assay, D-Dimer, F1.2 prothrombin fragments.

General information

Reason for update

registering patient recruitment start patient recruitment end trial completion date

Acronym

UGA 2014-01

IRCT registration information

IRCT registration number: **IRCT2017021831193N2**
Registration date: **2017-08-05, 1396/05/14**
Registration timing: **prospective**

Last update: **2022-03-02, 1400/12/11**

Update count: **4**

Registration date

2017-08-05, 1396/05/14

Registrant information

Name

Amirhossein Saadatirad

Name of organization / entity

AryoGen Pharmed

Country

Iran (Islamic Republic of)

Phone

+98 26 3610 6480

Email address

saadatirada@aryogen.com

Recruitment status

Recruitment complete

Funding source

AryoGen Pharmed

Expected recruitment start date

2018-09-17, 1397/06/26

Expected recruitment end date

2019-05-31, 1398/03/10

Actual recruitment start date

2018-09-17, 1397/06/26

Actual recruitment end date

2020-10-31, 1399/08/10

Trial completion date

2021-09-23, 1400/07/01

Scientific title

A Randomized, Multicenter, Double blind, Single doses Study Comparing the Pharmacodynamic, Pharmacokinetic and Safety of Biosimilar EPTACOG Alfa with Novoseven®, in Patient with Hemophilia A or B with Inhibitors

Public title

Pharmacodynamic, Pharmacokinetic Study of AryoSeven with Novoseven®, in Patient with Hemophilia A or B with Inhibitors

Purpose

Treatment

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 subjects -Adult and children (>12 years) -Patients to be enrolled must also provide voluntary written informed consent to the protocol to be eligible for the study. For minor patients, parent/legal guardian will provide consent and, when possible, patient assent will also be obtained. For compromised patients, their designated proxy must provide informed consent. -For the PK/PD phase, patients will be hospitalized at time of study medication administration for plasma sampling (2 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 Novoseven or planned to occur during the trial. -Patients who have received routine (prophylactic) treatment with rFVIIa in the period between screening visit (visit 1) and visit 2 of this study (first dose administration). -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.

Age

From 12 years old

Gender

Male

Phase

3

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data and Safety Monitoring Board

Sample size

Target sample size: 48

Actual sample size reached: 48

Randomization (investigator's opinion)

Randomized

Randomization description

1:1 manner stratified by center

Blinding (investigator's opinion)

Double blinded

Blinding description

Blinding is performed by an independent third party operator (pharmacist or nurse, unblinded), who will prepare undistinguishable syringes with patient's dosing and labelling. As soon as the patient is registered (centrally) and randomization code assigned, the central randomization office will inform the pharmacist or nurse through email of the treatment assigned to the patient; the pharmacist or nurse will prepare the study treatment on the basis of the treatment assigned and body weight of patient (defined as weight on the date of admission). The third party operator (pharmacist or nurse) will label the study treatment syringes with labels supplied by AryoGen.

Placebo

Not used

Assignment

Crossover

Other design features**Secondary Ids****1****Registry name**

clinicaltrials.gov

Secondary trial Id

NCT03935334

Registration date

2019-05-02, 1398/02/12

2**Registry name**

clinicaltrialsregister.eu

Secondary trial Id

2019-002854-22

Registration date

2020-01-03, 1398/10/13

Ethics committees

1

Ethics committee

Name of ethics committee

Shiraz University of Medical Sciences

Street address

Shiraz University of Medical Sciences

City

Shiraz

Province

Fars

Postal code

7134814336

Approval date

2017-06-19, 1396/03/29

Ethics committee reference number

IR.SUMS.REC.1396.43

2

Ethics committee

Name of ethics committee

Iran University of Medical Sciences

Street address

Iran University of Medical Sciences ,Shahid Hemmat
Highway

City

Tehran

Province

Tehran

Postal code

1449614535

Approval date

2018-03-06, 1396/12/15

Ethics committee reference number

IR.IUMS.REC 1396.9-33058

3

Ethics committee

Name of ethics committee

Zahedan University of Medical Sciences

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Zahedan University of Medical Sciences, Dr. Hesabi
sq. Zahedan, Iran

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Zahedan

Province

Sistan-va-Balouchestan

Postal code

9816737789

Approval date

2018-12-19, 1397/09/28

Ethics committee reference number

IR.ZAUMS.REC.1397.356

Health conditions studied

1

Description of health condition studied

Hemophilia A with inhibitor

ICD-10 code

D66

ICD-10 code description

Deficiency factor VIII (with functional defect)

2

Description of health condition studied

Hemophilia B with inhibitor

ICD-10 code

D67

ICD-10 code description

Hereditary factor IX deficiency (with functional defect)

Primary outcomes

1

Description

Pharmacokinetic parameter: the area under the plasma concentration time curve from time 0 to infinity, based on the last observed concentration (AUCinf)

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

Measurement of plasma level of factor VII clotting activity (FVII:C) determined by commercial Staclot® VIIa-recombinant tissue factor assay (Diagnostica Stago, Asnières sur Seine, France)performed by a central lab.

2

Description

Pharmacodynamic parameters:Thrombin Generation Assay (TGA), D-Dimer, F1.2 prothrombin fragments

Timepoint

Thrombin Generation Assay:10 min prior to dose administration and at 10 min,20 min,1h,3 h,5 h,8 h,12 h,24 h and 30 h after AryoSeven or NovoSeven injection.D-dimer and F1.2 prothrombin fragments- 10 min- prior to dose administration and at 20 min, 1 h, 5 h, and 12 h and 24 h after on the same samples obtained for TGA

Method of measurement

Validated analytical method performed by central lab

Secondary outcomes

1

Description

Secondary PK parameters:AUClast, Cmax,tmax, AUCextra;First order rate constant associated with the terminal (log-linear) portion of the curve (λ_z);Elimination half-life; MRT; CL; Vss

Timepoint

10 min- prior to dose administration and at 10 min, 20

min, 1 h, 3 h, 5 h, 8 h and 12 h, 24 h and 30 h after AryoSeven or NovoSeven injection

Method of measurement

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

2

Description

Clinical parameters in controlling acute bleeding after treatment with AryoSeven.

Timepoint

2 h, 6 h and 12 h post infusion (last AryoSeven dose).

Method of measurement

4 point scale (Excellent, Good, Moderate, None) by the investigator

3

Description

Immunogenicity assessment.

Timepoint

At screening visit, after the second drug administration (visit 3) and then every 3 months for a year.

Method of measurement

PT based Bethesda assay

4

Description

Adverse events

Timepoint

at any time during the study

Method of measurement

Adverse events grading for severity, seriousness, expected or unexpected, relationship to the study drug, action taken, outcome.

Intervention groups

1

Description

AryoGen eptacog alfa (AryoSeven 1.2 mg), intravenous 90 microgram per kg single dose. Lyophilized powder for solution with provided solvent

Category

Treatment - Drugs

2

Description

AryoGen eptacog alfa (AryoSeven 1.2 mg), intravenous 270 microgram per kg single dose. Lyophilized powder for solution with provided solvent

Category

Treatment - Drugs

3

Description

Novo Nordisk eptacog alfa (Novoseven 1 mg), intravenous 90 microgram per kg Lyophilized powder for solution with provided solvent

Category

Treatment - Drugs

4

Description

Novo Nordisk eptacog alfa (Novoseven 1 mg), intravenous 270 microgram per kg Lyophilized powder for solution with provided solvent

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Iran Comprehensive Hemophilia Care Center

Full name of responsible person

Dr. Mohammadreza Baghaipour

Street address

Tehran, No. 3, N Felestin St

City

Tehran

Province

Tehran

Postal code

1415863675

Phone

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Email

mrbaghaipour@yahoo.com

2

Recruitment center

Name of recruitment center

Hemophilia Ward Shahid Dastgheib Hospital

Full name of responsible person

Dr. Mohammad Reza Bordbar

Street address

Building no.7, Shahid Dastgheib Hospital, Hafez avenue, Shiraz, Iran

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Shiraz

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714563769

Phone

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3

Recruitment center

Name of recruitment center

Ali Asghar Hospital

Full name of responsible person

Dr. Majid Naderi

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Sistan-va-Balouchestan

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Email

majid_naderi2000@yahoo.com

Sponsors / Funding sources

1

Sponsor**Name of organization / entity**

AryoGen Pharmed

Full name of responsible person

Amirhossein Saadatirad

Street address

No 140, Corner of Tajbakhsh street, 24th Km of
Tehran Karaj Makhsoos road

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Province

Alborz

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Email

saadatirada@aryogen.com

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

Street address

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Fax**Email**

saadatirada@aryogen.com

Web page address

Person responsible for scientific inquiries

Contact**Name of organization / entity**

Baqiyatallah Hospital

Full name of responsible person

Dr. Hasan Abolghasemi

Position

Full professor

Latest degree

Subspecialist

Other areas of specialty/work

Pediatrics

Street address

Mollasadra str, south Sheykh Bahaii str, Tehran

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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

No - There is not 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