Clinical Trial Protocol
Iranian Registry of Clinical Trials

10 Jun 2026

A Randomized, Multi-center, Single Dose, Cross over Study Comparing the Pharmacokinetic of Bio-similar EPTACOG Alfa with NOVOSEVEN®, in Patients with Congenital Factor VII Deficiency

Protocol summary

Study aim

Evaluatiation of pharmacokinetic(PK) of biosimilar eptacog alfa(AryoSeven)and NovoSeven in phase A(PK)and monitoring inhibiting antibody formation,lack of efficacy,collection of safety data in the following 12 months(Phase B)

Design

A phase III multicenter double-blind cross-over study with 24 sample size who based on 1:1 randomization receive either single dose of AryoSeven and NovoSeven 30 mcg per kg separated by 3days washout period.Patients hospitalized at time of medication administration and plasma sampling.Plasma sampling atleast 5ml at 10min before,10,20min,1,3,6,8,12,24,30h post drug administration.Phase B:At end of PK phase all patients receive AryoSeven on demand for every bleeding episode that occurs during 12 months or prophylaxis.The treatment modality(on demand at study center or home,or prophylaxis)decided by Investigator.Sampling for determination of antibody taken every 3 months.

Settings and conduct

Multicenter Iran and Turkey.First phase 1 week with infusion of single dose aryoseven and novoseven randomly.Second phase 1year receiving aryoseven for all bleedings.Blinding by an independent third party nurse or pharmacist unblinded who prepares undistinguishable syringes with patient dosing and labelling

Participants/Inclusion and exclusion criteria

Inclusion:Aḏult and children more than12 years with confirmed diagnosis of severe Factor VII Deficiency(less than 1%)with more than 2 episodes of bleeding per year requiring treatment with FVII infusions Exclusion:inhibitor against FVII is positive at time of study entry.Active hepatitis and liver cirrhosis

Intervention groups

Intervention group are congenital FVII deficient patients who receive AryoSeven 30 mcg per kg Control group are congenital FVII deficient patients who receive NovoSeven 30 mcg per kg

Main outcome variables

similar pharmacokinetic profile

General information

Reason for update

Trial completion date is recorded wrong and needs correction.

Acronym

IRCT registration information

IRCT registration number: **IRCT2016120231193N1**
Registration date: **2016-12-25, 1395/10/05**
Registration timing: **prospective**

Last update: **2022-02-27, 1400/12/08**
Update count: **2**

Registration date

2016-12-25, 1395/10/05

Registrant information

Name
Amirhossein Saadatirad
Name of organization / entity
AryoGen Pharmed
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Iran (Islamic Republic of)
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Recruitment status

Recruitment complete

Funding source

Aryogen Pharmed Company

Expected recruitment start date

2016-12-21, 1395/10/01

Expected recruitment end date

2017-09-23, 1396/07/01

Actual recruitment start date

2017-06-24, 1396/04/03

Actual recruitment end date

2018-09-01, 1397/06/10

Trial completion date

2019-09-14, 1398/06/23

Scientific title

A Randomized, Multi-center, Single Dose, Cross over Study Comparing the Pharmacokinetic of Bio-similar EPTACOG Alfa with NOVOSEVEN®, in Patients with Congenital Factor VII Deficiency

Public title

The pharmacokinetic study of AryoSeven with Novoseven in Patients with Congenital Factor VII Deficiency

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Patients with a confirmed diagnosis of congenital, severe Factor VII deficiency (FVII <1%), with >2 episodes of bleeding/year requiring treatment with FVII infusions, in non-bleeding status. Male and female 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. Patients in the Pharmacokinetic (PK) phase will be hospitalized at time of study medication administration and plasma sampling (2 times during the study).

Exclusion criteria:

Any other type of congenital or acquired coagulopathy (except congenital Factor VII deficiency), such as: liver disease (hepatitis), vitamin k deficiency, uremia, malignancy. Antibodies against Factor VII Patients entering the PK Phase who have not suspended prophylactic regime with Novoseven or AryoSeven 3 days before starting the trial (receiving first dose of study medication). Platelet count less than 100.000 platelets/mcL (at screening visit) 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) 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 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 to **99 years** old

Gender

Both

Phase

3

Groups that have been masked

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

Sample size

Target sample size: **24**

Actual sample size reached: **24**

Randomization (investigator's opinion)

Randomized

Randomization description

The eligible patients are administered randomly in a 1:1 manner with either AryoSeven or NovoSeven. Allocation of treatment in this study is performed randomly using block randomization. Randomization sequence is prepared using R-CAN software version 4.0.1 in a blocks of 2 or 4 for 24 patients. Randomization list is prepared by an independent statisticians based on a balanced Latin Square design and the code is allocated to a patient by a third party in the study site based on the order of enrollment.

Blinding (investigator's opinion)

Double blinded

Blinding description

Blinding is performed by an independent third party operator (nurse/pharmacist, unblinded), who will prepared undistinguishable syringes with patient’s dosing and labelling.

Placebo

Not used

Assignment

Crossover

Other design features

Secondary Ids

1

Registry name

clinicaltrials.gov

Secondary trial Id

NCT03079063

Registration date

2017-03-14, 1395/12/24

Ethics committees

1

Ethics committee

Name of ethics committee

Iran University of Medical science

Street address

Iran University of Medical Sciences ,Shahid Hemmat Highway

City

Tehran

Province

Tehran

Postal code
1449614535
Approval date
2016-09-25, 1395/07/04
Ethics committee reference number
IR.IUMS.REC.1395.28155

2

Ethics committee
Name of ethics committee
Added at 2017-01-07: Shiraz University of Medical Sciences
Street address
Added at 2017-01-07: Shiraz University of Medical Sciences
City
Added at 2017-01-07: Shiraz
Province
Fars
Postal code
Added at 2017-01-07:
Approval date
2016-12-14, 1395/09/24
Ethics committee reference number
IR.SUMS.REC.1395.158

Health conditions studied

1

Description of health condition studied
Hereditary deficiency of factor VII
ICD-10 code
D68.2
ICD-10 code description
Hereditary deficiency of other clotting factors

Primary outcomes

1

Description
PK-parameters: the area under the plasma activity-time curve from time 0 to last quantifiable activity (AUClast)
Timepoint
10 min before drug administration,10 min, 20 min, 1 h, 3 h, 6 h, 8 h and 12 h and 24 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, Asniéres sur Seine, France)., performed by a central lab blinded to the patient's treatment.

2

Description
PK-parameters: maximum plasma activity Cmax
Timepoint
10 min before drug administration,10 min, 20 min, 1 h, 3 h, 6 h, 8 h and 12 h and 24 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, Asniéres sur Seine, France)., performed by a central lab blinded to the patient's treatment.

Secondary outcomes

1

Description
Secondary Pharmacokinetic parameters: AUCinf, Vd, Thalf, Tmax, Clearance, Mean Residence Time, λz.
Timepoint
For secondary PK parameters:10 min before drug administration,10 min, 20 min, 1 h, 3 h, 6 h, 8 h and 12 h and 24 h after AryoSeven or NovoSeven injection.
Method of measurement
PK Parameters: Measurement of plasma level of factor VII clotting activity (FVII:C) performed by a central lab.

2

Description
Immunogenicity assessment.
Timepoint
At screening visit, after the second dose/second drug administration (visit 3) and then every 3 months for a year.
Method of measurement
Immunogenicity by PT-based bethesda assay by local lab and confirmatory test by the modified Nijmegen method of the Bethesda assay by central lab

3

Description
Clinical response in treatment of bleeding
Timepoint
2h , 6h and 12 h after last dose of Aryoseven injection at every bleeding
Method of measurement
4 point scale (Excellent, Good, Moderate, None) by investigator

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
Biosimilar eptacog alfa (AryoSeven) product of AryoGen Pharmed, intravenous, single dose of 30 mcg per kg
Category
Treatment - Drugs

2

Description
Novo Nordisk eptacog alfa (Novoseven), intravenous, single dose of 30 mcg per kg
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
No. 3,Cross Zartosht and Felestin St, Tehran, Iran
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1415863675
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2

Recruitment center
Name of recruitment center
Added at 2017-01-07: Hematology research center
Full name of responsible person
Added at 2017-01-07: Dr. Mohammad Reza Bordbar
Street address
Added at 2017-01-07: Hematology research center, 6th floor, Mohammad Rasoul allah research building,Khalili street, Shiraz, Iran
City
Added at 2017-01-07: Shiraz
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۷۱۴۵۸۳۷۴۹
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Sponsors / Funding sources

1

Sponsor
Name of organization / entity
AryoGen Pharmed
Full name of responsible person
Amrhossein Saadatirad
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No 140, Corner of Tajbakhsh street, 24th Km of Tehran Karaj Makhsous road
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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

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Person responsible for updating data

Contact

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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