Clinical trial results:
An Open-Label, Single-Dose, Phase 1/2 Study to Evaluate the Pharmacokinetics, Safety, and Tolerability of Human Protein C (TAK-662) for the Treatment of Congenital Protein C Deficiency in Japanese Subjects Followed by an Extension Part

Summary

EudraCT number	2022-003877-48
Trial protocol	Outside EU/EEA
Global end of trial date	31 October 2024

Results information

Result version number	v1 (current)
This version publication date	08 May 2025
First version publication date	08 May 2025

Trial information

Trial identification

Sponsor protocol code	TAK-662-1501

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04984889
WHO universal trial number (UTN)	U1111-1267-4412
Other trial identifiers	jRCT: jRCT2031210209

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	95 Hayden Avenue, Lexington, United States, MA 02421
Public contact	Study Director, Takeda, +1 877-825-3327, TrialDisclosures@takeda.com
Scientific contact	Study Director, Takeda, +1 877-825-3327, TrialDisclosures@takeda.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 December 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 October 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To measure the pharmacokinetic (PK) parameters of TAK-662 in asymptomatic participants with homozygous or double heterozygous congenital protein C deficiency in Japanese participants.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) of GCP, the principles of the Declaration of Helsinki, as well as other applicable national and local ethical and legal requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 September 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 5
Worldwide total number of subjects	5
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	2
Adolescents (12-17 years)	1
Adults (18-64 years)	2
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 4 centers in Japan from 7 September 2021 to 31 October 2024. A total of 5 Japanese participants were enrolled in this 2-part study to receive TAK-662 in Pharmacokinetic (PK) part (Part 1) followed by 3 treatment options in the Extension part (Part 2) (on-demand, short-term, or long-term prophylaxis).

Pre-assignment

Screening details:

As per planned analysis, the Extension Part data was collected, analyzed and reported as per On-demand and Short-term Prophylaxis treatments and per dose level wise data was not collected in this study.

Period 1

Period 1 title	PK Part: Up to 7 Days
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	PK Part: TAK-662

Arm description:

Participants received a single 80 IU/kg dose of TAK-662, intravenous infusion on Day 1 in PK part.

Arm type	Experimental
Investigational medicinal product name	TAK-662
Investigational medicinal product code	
Other name	Protein C Concentrate
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

TAK-662 80 IU/kg administered as intravenous infusion.

Number of subjects in period 1	PK Part: TAK-662
Started	5
Completed	5

Period 2

Period 2 title	Extension Part: Up to 35 Months
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Extension Part, On-demand Treatment (TAK-662)

Arm description:

Participants with purpura fulminans (PF), coumarin-induced skin necrosis/warfarin-induced skin necrosis (CISN/WISN), and/or other acute thromboembolic episode received a single dose of TAK-662 (100-120 IU/kg), followed by three subsequent infusions, every 6 hours at a dose of 60-80 IU/kg, and followed by subsequent infusions (45-60 IU/kg) continued every 6 or 12 hours until resolution of all non-necrotic lesions and/or stabilization of thrombi. Treatment could be terminated when an acute episode improved.

Arm type	Experimental
Investigational medicinal product name	TAK-662
Investigational medicinal product code	
Other name	Protein C Concentrate
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

TAK-662 (100-120 IU/kg), followed by three subsequent infusions, every 6 hours at a dose of 60-80 IU/kg, and followed by subsequent infusions (45-60 IU/kg) continued every 6 or 12 hours until resolution of all non-necrotic lesions and/or stabilization of thrombi.

Arm title	Extension Part, Short-term Prophylaxis Treatment (TAK-662)

Arm description:

Participants who required short-term prophylaxis of acute thrombotic episodes during surgery received TAK-662 at a dose of 100-120 IU/kg, intravenous infusion once daily, until anticoagulation therapy was successfully switched to TAK-662 prior to surgery. Fifteen minutes prior to surgery, a dose of 60-80 IU/kg was administered and continued once every 6 hours for the first 24 hours after surgery began. The frequency of infusions was reduced to 3 times daily between 24 and 48 hours, and twice daily after 48 hours at the same dose (45-60 IU/kg). Treatment with TAK-662 continued twice daily until anticoagulation therapy was initiated (if applicable) and the investigator determined that adequate level of the anticoagulation was achieved.

Arm type	Experimental
Investigational medicinal product name	TAK-662
Investigational medicinal product code	
Other name	Protein C Concentrate
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

TAK-662 at a dose of 100-120 IU/kg, intravenous infusion once daily, until anticoagulation therapy was successfully switched to TAK-662 prior to surgery. Fifteen minutes prior to surgery, a dose of 60-80 IU/kg was administered and continued once every 6 hours for the first 24 hours after surgery began. The frequency of infusions was reduced to 3 times daily between 24 and 48 hours, and twice daily after 48 hours at the same dose (45-60 IU/kg).

Number of subjects in period 2	Extension Part, On-demand Treatment (TAK-662)	Extension Part, Short-term Prophylaxis Treatment (TAK-662)
Started	4	1
Completed	4	1

Baseline characteristics

Reporting groups	
Reporting group title	PK Part: TAK-662
Reporting group description:	
Participants received a single 80 IU/kg dose of TAK-662, intravenous infusion on Day 1 in PK part.	

Reporting group values	PK Part: TAK-662	Total	
Number of subjects	5	5	
Age Categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	15.2		
standard deviation	± 8.87	-	
Gender categorical Units: Subjects			
Male	4	4	
Female	1	1	
Race/Ethnicity, Customized Units: Subjects			
Japanese	5	5	

End points

End points reporting groups

Reporting group title	PK Part: TAK-662

Reporting group description:

Participants received a single 80 IU/kg dose of TAK-662, intravenous infusion on Day 1 in PK part.

Reporting group title	Extension Part, On-demand Treatment (TAK-662)

Reporting group description:

Participants with purpura fulminans (PF), coumarin-induced skin necrosis/warfarin-induced skin necrosis (CISN/WISN), and/or other acute thromboembolic episode received a single dose of TAK-662 (100-120 IU/kg), followed by three subsequent infusions, every 6 hours at a dose of 60-80 IU/kg, and followed by subsequent infusions (45-60 IU/kg) continued every 6 or 12 hours until resolution of all non-necrotic lesions and/or stabilization of thrombi. Treatment could be terminated when an acute episode improved.

Reporting group title	Extension Part, Short-term Prophylaxis Treatment (TAK-662)

Reporting group description:

Participants who required short-term prophylaxis of acute thrombotic episodes during surgery received TAK-662 at a dose of 100-120 IU/kg, intravenous infusion once daily, until anticoagulation therapy was successfully switched to TAK-662 prior to surgery. Fifteen minutes prior to surgery, a dose of 60-80 IU/kg was administered and continued once every 6 hours for the first 24 hours after surgery began. The frequency of infusions was reduced to 3 times daily between 24 and 48 hours, and twice daily after 48 hours at the same dose (45-60 IU/kg). Treatment with TAK-662 continued twice daily until anticoagulation therapy was initiated (if applicable) and the investigator determined that adequate level of the anticoagulation was achieved.

Subject analysis set title	Extension Part, Long-term Prophylaxis Treatment (TAK-662)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who required long-term prophylaxis were planned to receive TAK-662 at a dose of 45-60 IU/kg, intravenous infusion, twice daily. The dose was to be adjusted by referring to the latest protein C activity at the investigator’s discretion. No participants received TAK-662 for long-term prophylaxis during the study.

Primary: PK Part: Protein C Activity Level of TAK-662

End point title	PK Part: Protein C Activity Level of TAK-662[1]

End point description:

Protein C is a vitamin K-dependent plasma protein and is an important component of the coagulation system. Protein C activity level was measured by chromogenic assays. Protein C activity level of TAK-662 was reported. The PK population included all study participants who took at least 1 dose of TAK-662 and had enough number of quantifiable blood levels for TAK-662 collected post-dose without important protocol deviations (PDs)/violations or events thought to substantially affect the PK.

End point type	Primary

End point timeframe:

Pre-infusion, 0.5, 1, 2, 4, 8, 12, 24, and 36 hours post-infusion

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	PK Part: TAK-662			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: international unit per milliliter(IU/ml)				
arithmetic mean (standard deviation)				
Pre-infusion	0.000 (± 0.000)			

0.5 hour	1.746 (± 0.557)			
1 hour	1.616 (± 0.523)			
2 hours	1.458 (± 0.519)			
4 hours	1.168 (± 0.441)			
8 hours	0.844 (± 0.295)			
12 hours	0.632 (± 0.257)			
24 hours	0.304 (± 0.150)			
36 hours	0.148 (± 0.095)			

Statistical analyses

No statistical analyses for this end point

Primary: PK Part: Percentage of In-vivo Recovery (IVR) of TAK-662

End point title	PK Part: Percentage of In-vivo Recovery (IVR) of TAK-662[2]

End point description:

IVR corrected for plasma was determined using the formula: IVR (percentage [%])= (Maximum observed plasma concentration (Cmax) [IU/mL] – Concentration (C) pre-infusion [IU/mL]) * Plasma volume pre-infusion (PV) millilitre (mL)/ Dose (international unit [IU])*100 where Cmax was the observed Cmax value before baseline correction. IVR of TAK-662 measured in terms of percentage was reported. The PK population included all study participants who took at least 1 dose of TAK-662 and had enough number of quantifiable blood levels for TAK-662 collected post-dose without important PDs/violations or events thought to substantially affect the PK.

End point type	Primary

End point timeframe:

Pre-infusion, 0.5, 1, 2, 4, 8, 12, 24, and 36 hours post-infusion

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	PK Part: TAK-662			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: percentage of IVR				
arithmetic mean (standard deviation)	95.71 (± 31.22)			

Statistical analyses

No statistical analyses for this end point

Primary: PK Part: Terminal Phase Elimination Half-life (t1/2) of TAK-662

End point title	PK Part: Terminal Phase Elimination Half-life (t1/2) of TAK-

End point description:

t1/2 of TAK-662 was reported. The PK population included all study participants who took at least 1 dose of TAK-662 and had enough number of quantifiable blood levels for TAK-662 collected post-dose without important PDs/violations or events thought to substantially affect the PK.

End point type	Primary

End point timeframe:

Pre-infusion, 0.5, 1, 2, 4, 8, 12, 24, and 36 hours post-infusion

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	PK Part: TAK-662			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: hour				
median (full range (min-max))	11.6 (7.68 to 13.0)			

Statistical analyses

No statistical analyses for this end point

Primary: PK Part: Incremental Recovery (IR) of TAK-662

End point title	PK Part: Incremental Recovery (IR) of TAK-662[4]

End point description:

IR of TAK-662 was reported measured in terms of international unit per millilitre/ international unit per kilogram (IU/mL)/(IU/kg). The PK population included all study participants who took at least 1 dose of TAK-662 and had enough number of quantifiable blood levels for TAK-662 collected post-dose without important PDs/violations or events thought to substantially affect the PK.

End point type	Primary

End point timeframe:

Pre-infusion, 0.5, 1, 2, 4, 8, 12, 24, and 36 hours post-infusion

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	PK Part: TAK-662			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: (IU/mL)/(IU/kg)				
arithmetic mean (standard deviation)	0.02063 (± 0.006588)			

Statistical analyses

No statistical analyses for this end point

Primary: PK Part: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of the Last Quantifiable Concentration (AUClast) of TAK-662

End point title	PK Part: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of the Last Quantifiable Concentration (AUClast) of TAK-662[5]

End point description:

AUClast of TAK-662 was reported measured in terms of international unit*hour per millilitre (IU*h/ml). The PK population included all study participants who took at least 1 dose of TAK-662 and had enough number of quantifiable blood levels for TAK-662 collected post-dose without important PDs/violations or events thought to substantially affect the PK.

End point type	Primary

End point timeframe:

Pre-infusion, 0.5, 1, 2, 4, 8, 12, 24, and 36 hours post-infusion

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	PK Part: TAK-662			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: IU*h/ml				
geometric mean (geometric coefficient of variation)	19.24 (± 47.0)			

Statistical analyses

No statistical analyses for this end point

Primary: PK Part: Area Under the Plasma Concentration-time Curve From Time 0 to Infinity (AUC0-infinity) of TAK-662

End point title	PK Part: Area Under the Plasma Concentration-time Curve From Time 0 to Infinity (AUC0-infinity) of TAK-662[6]

End point description:

AUC0-infinity of TAK-662 was reported. The PK population included all study participants who took at least 1 dose of TAK-662 and had enough number of quantifiable blood levels for TAK-662 collected post-dose without important PDs/violations or events thought to substantially affect the PK.

End point type	Primary

End point timeframe:

Pre-infusion, 0.5, 1, 2, 4, 8, 12, 24, and 36 hours post-infusion

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	PK Part: TAK-662			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: IU*h/ml				
geometric mean (geometric coefficient of variation)	21.88 (± 47.1)			

Statistical analyses

No statistical analyses for this end point

Primary: PK Part: Maximum Observed Plasma Concentration (Cmax) of TAK-662

End point title	PK Part: Maximum Observed Plasma Concentration (Cmax) of TAK-662[7]

End point description:

Cmax of TAK-662 was reported. The PK population included all study participants who took at least 1 dose of TAK-662 and had enough number of quantifiable blood levels for TAK-662 collected post-dose without important PDs/violations or events thought to substantially affect the PK.

End point type	Primary

End point timeframe:

Pre-infusion, 0.5, 1, 2, 4, 8, 12, 24, and 36 hours post-infusion

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	PK Part: TAK-662			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: IU/ml				
geometric mean (geometric coefficient of variation)	1.679 (± 31.7)			

Statistical analyses

No statistical analyses for this end point

Primary: PK Part: Time to Reach the Maximum Plasma Concentration (Tmax) of TAK-662

End point title	PK Part: Time to Reach the Maximum Plasma Concentration (Tmax) of TAK-662[8]

End point description:

Tmax of TAK-662 was reported. The PK population included all study participants who took at least 1 dose of TAK-662 and had enough number of quantifiable blood levels for TAK-662 collected post-dose without important PDs/violations or events thought to substantially affect the PK.

End point type	Primary

End point timeframe:

Pre-infusion, 0.5, 1, 2, 4, 8, 12, 24, and 36 hours post-infusion

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	PK Part: TAK-662			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: hour				
median (full range (min-max))	0.53 (0.43 to 0.60)			

Statistical analyses

No statistical analyses for this end point

Secondary: Extension Part: Percentage of Surgical Episodes During Short-Term Prophylaxis That is Free of Presentations of PF or Thromboembolic Complications

End point title	Extension Part: Percentage of Surgical Episodes During Short-Term Prophylaxis That is Free of Presentations of PF or Thromboembolic Complications

End point description:

Percentage of surgical episodes for which TAK-662 was utilized as short-term prophylaxis that is free of presentations of PF or thromboembolic complications was reported. Efficacy Analysis Set in Short-term Prophylaxis included all participants who took at least 1 dose of TAK-662 during short-term prophylaxis in the extension part.

End point type	Secondary

End point timeframe:

Extension Part: From the first dose of TAK-662 short-term prophylaxis treatment in the Extension Part up to 35 months

End point values	Extension Part, Short-term Prophylaxis Treatment (TAK-662)			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: percentage of episode				
number (confidence interval 95%)	100.0 (2.50 to 100.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Extension Part: Number of Episode Rated as Effective, Effective With

Complications, or Not Effective on Efficacy Rating Scale During On-Demand Treatment

End point title	Extension Part: Number of Episode Rated as Effective, Effective With Complications, or Not Effective on Efficacy Rating Scale During On-Demand Treatment

End point description:

The treatment of episodes of PF, CISN/ WISN, and/or other vascular thromboembolic events were rated as "effective", "effective with complications", or "not effective" according to the efficacy rating scale, as judged by investigators on the basis of following criteria, Effective: stabilization and regression of skin lesions/stabilization of thrombi; Effective with complications: treatment was effective but caused an adverse drug reaction that interfered with the regimen (resulted in change of dose or frequency of dosing) or forcing discontinuation of treatment or introducing pathogenic viral infection; Not effective: all other cases. Efficacy Analysis Set in On-Demand Treatment included all participants who took at least 1 dose of TAK-662 on-demand in the extension part.

End point type	Secondary

End point timeframe:

Extension Part: From the first dose of TAK-662 on-demand treatment in the Extension Part up to 35 months

End point values	Extension Part, On-demand Treatment (TAK-662)			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: treatment episodes				
number (not applicable)				
Effective	19			
Effective With Complications	0			
Not Effective	0			

Statistical analyses

No statistical analyses for this end point

Secondary: PK and Extension Parts: Number of Participants With Treatment-Related Adverse Experiences (AEs)

End point title	PK and Extension Parts: Number of Participants With Treatment-Related Adverse Experiences (AEs)

End point description:

A treatment-related AE was defined as an adverse event that followed a reasonable temporal sequence from administration of a drug (including the course after withdrawal of the drug), or for which possible involvement of the drug was not able to be ruled out, although factors other than the drug, such as underlying diseases, complications, concomitant medications and concurrent treatments, might also be responsible. Number of participants with treatment-related AEs as assessed by the Investigator were reported. The safety population included all enrolled participants in the study who took at least 1 dose of TAK-662.

End point type	Secondary

End point timeframe:

PK Part: From the start of study drug administration up to Day 7; Extension Part: From the first dose of study drug administration in the Extension Part up to 35 months

End point values	PK Part: TAK-662	Extension Part, On-demand Treatment (TAK-662)	Extension Part, Short-term Prophylaxis Treatment (TAK-662)	Extension Part, Long-term Prophylaxis Treatment (TAK-662)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	5	4	1	0[9]
Units: participants	1	0	0	

Notes:

[9] - No participants received TAK-662 for long-term prophylaxis treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Extension Part: Number of Episodes of PF and/or Thrombotic Episodes During Long-Term Prophylaxis

End point title	Extension Part: Number of Episodes of PF and/or Thrombotic Episodes During Long-Term Prophylaxis

End point description:

Number of Episodes of PF and/or Thrombotic Episodes During Long-Term Prophylaxis was planned to be reported. Efficacy Analysis Set in long-term prophylaxis included all study participants who took at least 1 dose of TAK-662 during long-term prophylaxis in the extension part. The "Number of Participants Analysed" is zero because no participants received TAK-662 for long-term prophylaxis; therefore, no data was collected and reported.

End point type	Secondary

End point timeframe:

Extension Part: From the first dose of TAK-662 long-term prophylaxis treatment in the Extension Part up to 35 months

End point values	Extension Part, Long-term Prophylaxis Treatment (TAK-662)			
Subject group type	Subject analysis set			
Number of subjects analysed	0[10]			
Units: episode				
number (not applicable)				

Notes:

[10] - No participants received TAK-662 for long-term prophylaxis treatment.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

PK Part: From start of study drug administration up to Day 7; Extension part: From first dose of study drug administration in Extension Part up to up to 35 months

Adverse event reporting additional description:

No participant received TAK-662 for long-term prophylaxis and therefore, no safety data could be collected and reported for 'Extension Part, Long-term Prophylaxis treatment (TAK-662) arm.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	PK Part: TAK-662

Reporting group description:

Participants received a single 80 international unit per kilogram (IU/kg) dose of TAK-662, intravenous infusion on Day 1 in PK part.

Reporting group title	Extension Part, On-demand Treatment (TAK-662)

Reporting group description:

Participants with purpura fulminans (PF), coumarin-induced skin necrosis/warfarin-induced skin necrosis (CISN/WISN), and/or other acute thromboembolic episode received a single dose of TAK-662 (100-120 IU/kg), followed by three subsequent infusions, every 6 hours at a dose of 60-80 IU/kg, and followed by subsequent infusions (45-60 IU/kg) continued every 6 or 12 hours until resolution of all non-necrotic lesions and/or stabilization of thrombi. Treatment could be terminated when an acute episode improved.

Reporting group title	Extension Part, Short-term Prophylaxis Treatment (TAK-662)

Reporting group description:

Participants who required short-term prophylaxis of acute thrombotic episodes during surgery received TAK-662 at a dose of 100-120 IU/kg, intravenous infusion once daily, until anticoagulation therapy was successfully switched to TAK-662 prior to surgery. Fifteen minutes prior to surgery, a dose of 60-80 IU/kg was administered and continued once every 6 hours for the first 24 hours after surgery began. The frequency of infusions was reduced to 3 times daily between 24 and 48 hours, and twice daily after 48 hours at the same dose (45-60 IU/kg). Treatment with TAK-662 continued twice daily until anticoagulation therapy was initiated (if applicable) and the investigator determined that adequate level of the anticoagulation was achieved.

Serious adverse events	PK Part: TAK-662	Extension Part, On-demand Treatment (TAK-662)	Extension Part, Short-term Prophylaxis Treatment (TAK-662)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 1 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	PK Part: TAK-662	Extension Part, On-demand Treatment (TAK-662)	Extension Part, Short-term Prophylaxis Treatment (TAK-662)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 5 (40.00%)	3 / 4 (75.00%)	0 / 1 (0.00%)
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Purpura			
subjects affected / exposed	1 / 5 (20.00%)	1 / 4 (25.00%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 April 2021	Protocol Amendment 1.0: •Regarding inclusion criteria 1 and 2, actions to be taken when consent was not able to be obtained from the participant were added. •The collection of AEs was changed by the follow-up on Day 7.
02 September 2021	Protocol Amendment 2.0: •The rationale, study design, objectives and endpoints, dosage regimen and dose adjustment, inclusion/exclusion criteria, assessments, blood sampling volume, acceptable concomitant treatment, and handling of SAE for the extension part were added. Justification: based on investigator's careful evaluation on participant's medical condition, on-demand therapy, short-term prophylaxis and/or long-term prophylaxis were allowed to be conducted as the extension part in the participants who had completed PK part. •The injection rate was added. Justification: to align the injection time with the current US package insert to assure participant's safety. •The handling of the vials was changed. Justification: in order to align with the pharmacy manual. •The instruction of self-injection was added. Justification: self-injection was allowed in the extension part. •Description of planned interim analysis was added in Section 9.2. Justification: to clarify the timing of the primary analysis because the extension part was added. •Section 9.7 was simplified including deletion of Table 4. Justification: to describe the detail of PK analyses in the CPAP. •Correction of inconsistencies within the Protocol Amendment 1.0.
08 September 2022	Protocol Amendment 3.0: •The description of "Planned Interim Analysis, Adaptive Design, and Data Monitoring Committee" of statistical analysis in Section 1.1 and Section 9.2 was changed to use the safety and efficacy data of the extension part for the first interim analysis. •The supporting description on the procedure of on-demand treatment at home after the first infusion for the second and subsequent acute episode was added in the footnote (f) of Table 3 in Section 1.3 and in Section 8.1.2.3.1. •Editorial correction of the Protocol Amendment 2.0.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported