



## Clinical trial results:

**A Phase 3, Prospective, Randomized, Controlled, Open-Label, Multicenter, 2 Period Crossover Study With a Single Arm Continuation Evaluating the Safety and Efficacy of BAX 930 (rADAMTS13) in the Prophylactic and On-Demand Treatment of Subjects with Severe Congenital Thrombotic Thrombocytopenic Purpura (cTTP, Upshaw-Schulman Syndrome [USS], Hereditary Thrombotic Thrombocytopenic Purpura [hTTP])**

### Summary

EudraCT number	2017-000858-18
Trial protocol	GB DE ES AT FR IT PL Outside EU/EEA
Global end of trial date	30 May 2024

### Results information

Result version number	v3 (current)
This version publication date	05 February 2026
First version publication date	13 December 2024
Version creation reason	<ul style="list-style-type: none"><li>Correction of full data set</li><li>Updates to efficacy analyses and PK parameters</li></ul>

### Trial information

#### Trial identification

Sponsor protocol code	281102
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03393975
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Takeda Development Center Americas, Inc.
Sponsor organisation address	95 Hayden Avenue, Lexington, Massachusetts, United States, 02421
Public contact	Study Director, Takeda, N/A N/A, TrialDisclosures@takeda.com
Scientific contact	Study Director, Takeda, N/A N/A, TrialDisclosures@takeda.com

Notes:

### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-001160-PIP01-11
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
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Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 May 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 May 2024
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To determine the incidence of acute TTP episodes in subjects with severe cTTP receiving either standard of care (SoC) or BAX 930 as a prophylactic treatment.

Protection of trial subjects:

Each participant or legally authorized representative signed an informed consent form (ICF) before participating in the study.

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	13 October 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Japan: 5
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Poland: 6
Country: Number of subjects enrolled	United Kingdom: 12
Country: Number of subjects enrolled	United States: 11
Worldwide total number of subjects	54
EEA total number of subjects	26

Notes:

<b>Subjects enrolled per age group</b>	
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)	9
Adolescents (12-17 years)	4
Adults (18-64 years)	40
From 65 to 84 years	1
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Participants took part in the study at various investigative sites globally from 13 October 2017 to 30 May 2024.

### Pre-assignment

Screening details:

Participants with a diagnosis of cTTP were enrolled in either prophylaxis/on demand cohorts. All participants received intravenous infusion of TAK-755/standard treatment in Prophylaxis Periods 1&2,&TAK-755 in Prophylaxis Period 3(hereafter Prophylaxis Periods 1, 2,&3 are referred to simply as Periods 1, 2, and 3).

### Period 1

Period 1 title	Urgent Treatment Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	No
<b>Arm title</b>	On Demand Cohort I: TAK-755

Arm description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the TAK-755 cohort of the Urgent Treatment Period received initial dose of IV infusions 40 IU/kg [ $\pm$  4 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 1 followed by a subsequent dose IV infusion of 20 IU/kg [ $\pm$  2 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 2 and an additional daily dose IV infusions of 15 IU/kg [ $\pm$  1.5 IU/kg] TAK-755 on Day 3 until 2 days after the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

Arm type	Experimental
Investigational medicinal product name	TAK-755
Investigational medicinal product code	
Other name	BAK-930
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Daily

<b>Arm title</b>	On Demand Cohort II: SoC
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Arm description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the SoC cohort of the Urgent Treatment Period received the investigator-recommended SoC and dosing regimen until the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

Arm type	Experimental
Investigational medicinal product name	Standard of care
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Daily

Number of subjects in period 1	On Demand Cohort I: TAK-755	On Demand Cohort II: SoC
Started	2	4
Completed	2	3
Not completed	0	1
Physician decision	-	1

## Period 2

Period 2 title	Prophylaxis Period 1
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

## Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Prophylaxis Cohort I: TAK-755 Then SoC

### Arm description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in Period 1 followed by SoC for 6 months in Period 2. Thereafter participants received TAK-755 SIN dose IV infusion of 40 IU/kg Q2W for 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Arm type	Experimental
Investigational medicinal product name	TAK-755
Investigational medicinal product code	
Other name	BAX-930
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

### Dosage and administration details:

Daily

<b>Arm title</b>	Prophylaxis Cohort II: SoC Then TAK-755
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### Arm description:

Participants received SoC for 6 months in Period 1 followed by IV infusions of 40 IU/kg dose of TAK-755 ORT Q2W in Period 2 for the next 6 months. Thereafter participants received TAK-755 SIN dose IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Arm type	Experimental
Investigational medicinal product name	Standard of care
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

### Dosage and administration details:

Daily

Number of subjects in period 2	Prophylaxis Cohort I: TAK-755 Then SoC	Prophylaxis Cohort II: SoC Then TAK-755
Started	23	25
Completed	23	24
Not completed	0	1
Reason not Specified	-	1

### Period 3

Period 3 title	Prophylaxis Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Prophylaxis Cohort I: TAK-755 Then SoC

#### Arm description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in Period 1 followed by SoC for 6 months in Period 2. Thereafter participants received TAK-755 SIN dose IV infusion of 40 IU/kg Q2W for 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Arm type	Experimental
Investigational medicinal product name	Standard of care
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

#### Dosage and administration details:

Daily

<b>Arm title</b>	Prophylaxis Cohort II: SoC Then TAK-755
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#### Arm description:

Participants received SoC for 6 months in Period 1 followed by IV infusions of 40 IU/kg dose of TAK-755 ORT Q2W in Period 2 for the next 6 months. Thereafter participants received TAK-755 SIN dose IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Arm type	Experimental
Investigational medicinal product name	TAK-755
Investigational medicinal product code	
Other name	BAX-930
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

#### Dosage and administration details:

Daily

Number of subjects in period 3	Prophylaxis Cohort I: TAK-755 Then SoC	Prophylaxis Cohort II: SoC Then TAK-755
Started	23	24
Completed	23	23
Not completed	0	1
Reason not Specified	-	1

#### Period 4

Period 4 title	Prophylaxis Period 3
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

#### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Prophylaxis Cohort I: TAK-755 Then SoC

##### Arm description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in Period 1 followed by SoC for 6 months in Period 2. Thereafter participants received TAK-755 SIN dose IV infusion of 40 IU/kg Q2W for 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Arm type	Experimental
Investigational medicinal product name	Tak-755
Investigational medicinal product code	
Other name	Bax-930
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

##### Dosage and administration details:

Daily

<b>Arm title</b>	Prophylaxis Cohort II: SoC Then TAK-755
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##### Arm description:

Participants received SoC for 6 months in Period 1 followed by IV infusions of 40 IU/kg dose of TAK-755 ORT Q2W in Period 2 for the next 6 months. Thereafter participants received TAK-755 SIN dose IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Arm type	Experimental
Investigational medicinal product name	TAK-755
Investigational medicinal product code	
Other name	BAX-930
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

##### Dosage and administration details:

Daily

<b>Number of subjects in period 4</b>	Prophylaxis Cohort I: TAK-755 Then SoC	Prophylaxis Cohort II: SoC Then TAK- 755
Started	23	23
Completed	23	23



## Baseline characteristics

### Reporting groups<sup>[1]</sup>

Reporting group title	On Demand Cohort I: TAK-755
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#### Reporting group description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the TAK-755 cohort of the Urgent Treatment Period received initial dose of IV infusions 40 IU/kg [ $\pm$  4 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 1 followed by a subsequent dose IV infusion of 20 IU/kg [ $\pm$  2 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 2 and an additional daily dose IV infusions of 15 IU/kg [ $\pm$  1.5 IU/kg] TAK-755 on Day 3 until 2 days after the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

Reporting group title	On Demand Cohort II: SoC
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#### Reporting group description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the SoC cohort of the Urgent Treatment Period received the investigator-recommended SoC and dosing regimen until the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

#### Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.

Justification: The arms reported in the baseline period represent only the On Demand cohorts of this study.

Reporting group values	On Demand Cohort I: TAK-755	On Demand Cohort II: SoC	Total
Number of subjects	2	4	6
Age categorical			
Units: Subjects			
≥18 years	2	3	5
12 to <18 years	0	0	0
6 to <12 years	0	0	0
<6 years	0	1	1
Gender categorical			
Units: Subjects			
Female	1	1	2
Male	1	3	4
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	1
White	1	2	3
More than one race	0	1	1
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	2	4	6
Unknown or Not Reported	0	0	0

## End points

### End points reporting groups

Reporting group title	On Demand Cohort I: TAK-755
Reporting group description: Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the TAK-755 cohort of the Urgent Treatment Period received initial dose of IV infusions 40 IU/kg [ $\pm$ 4 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 1 followed by a subsequent dose IV infusion of 20 IU/kg [ $\pm$ 2 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 2 and an additional daily dose IV infusions of 15 IU/kg [ $\pm$ 1.5 IU/kg] TAK-755 on Day 3 until 2 days after the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.	
Reporting group title	On Demand Cohort II: SoC
Reporting group description: Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the SoC cohort of the Urgent Treatment Period received the investigator-recommended SoC and dosing regimen until the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.	
Reporting group title	Prophylaxis Cohort I: TAK-755 Then SoC
Reporting group description: Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in Period 1 followed by SoC for 6 months in Period 2. Thereafter participants received TAK-755 SIN dose IV infusion of 40 IU/kg Q2W for 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.	
Reporting group title	Prophylaxis Cohort II: SoC Then TAK-755
Reporting group description: Participants received SoC for 6 months in Period 1 followed by IV infusions of 40 IU/kg dose of TAK-755 ORT Q2W in Period 2 for the next 6 months. Thereafter participants received TAK-755 SIN dose IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.	
Reporting group title	Prophylaxis Cohort I: TAK-755 Then SoC
Reporting group description: Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in Period 1 followed by SoC for 6 months in Period 2. Thereafter participants received TAK-755 SIN dose IV infusion of 40 IU/kg Q2W for 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.	
Reporting group title	Prophylaxis Cohort II: SoC Then TAK-755
Reporting group description: Participants received SoC for 6 months in Period 1 followed by IV infusions of 40 IU/kg dose of TAK-755 ORT Q2W in Period 2 for the next 6 months. Thereafter participants received TAK-755 SIN dose IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.	
Reporting group title	Prophylaxis Cohort I: TAK-755 Then SoC
Reporting group description: Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in Period 1 followed by SoC for 6 months in Period 2. Thereafter participants received TAK-755 SIN dose IV infusion of 40 IU/kg Q2W for 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.	
Reporting group title	Prophylaxis Cohort II: SoC Then TAK-755
Reporting group description: Participants received SoC for 6 months in Period 1 followed by IV infusions of 40 IU/kg dose of TAK-755 ORT Q2W in Period 2 for the next 6 months. Thereafter participants received TAK-755 SIN dose IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.	
Subject analysis set title	Prophylaxis Cohort: TAK-755
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1	

or Period 2. Thereafter participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	On Demand Cohort I: TAK-755
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the TAK-755 cohort of the Urgent Treatment Period received initial dose of IV infusions 40 IU/kg [ $\pm$  4 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 1 followed by a subsequent dose IV infusions of 20 IU/kg [ $\pm$  2 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 2 and an additional daily dose IV infusions of 15 IU/kg [ $\pm$  1.5 IU/kg] TAK-755 on Day 3 until 2 days after the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

Subject analysis set title	Prophylaxis Cohort: TAK-755
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. Thereafter participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort: SoC
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	On Demand Cohort I: TAK-755
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the TAK-755 cohort of the Urgent Treatment Period received initial dose of IV infusions 40 IU/kg [ $\pm$  4 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 1 followed by a subsequent dose IV infusion of 20 IU/kg [ $\pm$  2 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 2 and an additional daily dose IV infusions of 15 IU/kg [ $\pm$  1.5 IU/kg] TAK-755 on Day 3 until 2 days after the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

Subject analysis set title	On Demand Cohort II: SoC
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the SoC cohort of the Urgent Treatment Period received the investigator-recommended SoC and dosing regimen until the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

Subject analysis set title	Prophylaxis Cohort: TAK-755 SIN
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.

Subject analysis set title	Prophylaxis Cohort: TAK-755 SIN
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.

Subject analysis set title	Prophylaxis Cohort: SoC (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: SoC (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: SoC (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: SoC (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: SoC (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: SoC (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: SoC (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: SoC (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: SoC (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort I: TAK-755 SIN
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received TAK-755 SIN prophylactic dose of IV infusions of 40 IU/kg for another 6 months in Period 3.

Subject analysis set title	Prophylaxis Cohort I: TAK-755 SIN
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received TAK-755 SIN prophylactic dose of IV infusions of 40 IU/kg for another 6 months in Period 3.

Subject analysis set title	Prophylaxis Cohort I: TAK-755 SIN
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received TAK-755 SIN prophylactic dose of IV infusions of 40 IU/kg for another 6 months in Period 3.

Subject analysis set title	Prophylaxis Cohort I: TAK-755 ORT
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT once Q2W for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort I: TAK-755 SIN
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received TAK-755 SIN prophylactic dose of IV infusions of 40 IU/kg for another 6 months in Period 3.

Subject analysis set title	Prophylaxis Cohort: TAK-755-ORT
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.

Subject analysis set title	Prophylaxis Cohort: TAK-755-SIN
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.

Subject analysis set title	Prophylaxis Cohort: SoC
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: TAK-755-ORT
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.

Subject analysis set title	Prophylaxis Cohort: TAK-755-SIN
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.

Subject analysis set title	Prophylaxis Cohort: SoC
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: TAK-755
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. Thereafter participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort: SoC
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: TAK-755
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. Thereafter participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort: SoC
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: TAK-755 ORT
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.

Subject analysis set title	Prophylaxis Cohort: SoC
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2. (except for PK-II where they did not receive SoC).

Subject analysis set title	Prophylaxis Cohort: TAK-755 ORT
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.

Subject analysis set title	Prophylaxis Cohort: SoC
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: TAK-755 ORT
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.

Subject analysis set title	Prophylaxis Cohort: TAK-755 SIN
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.

Subject analysis set title	Prophylaxis Cohort: SoC
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: TAK-755-ORT
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.

Subject analysis set title	Prophylaxis Cohort: TAK-755 SIN
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.

Subject analysis set title	Prophylaxis Cohort: SoC
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: TAK-755-ORT
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Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.	
Subject analysis set title	Prophylaxis Cohort: TAK-755 SIN
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.	
Subject analysis set title	Prophylaxis Cohort: SoC
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received SoC for 6 months in either Period 1 or Period 2.	
Subject analysis set title	Prophylaxis Cohort: TAK-755-ORT
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2..TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.	
Subject analysis set title	Prophylaxis Cohort: TAK-755 SIN
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.	
Subject analysis set title	Prophylaxis Cohort: SoC
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received SoC for 6 months in either Period 1 or Period 2.	
Subject analysis set title	Prophylaxis Cohort: TAK-755-ORT
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.	
Subject analysis set title	Prophylaxis Cohort: TAK-755 SIN
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.	
Subject analysis set title	Prophylaxis Cohort: SoC
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received SoC for 6 months in either Period 1 or Period 2.	
Subject analysis set title	Prophylaxis Cohort: TAK-755-ORT
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.	
Subject analysis set title	Prophylaxis Cohort: TAK-755 SIN
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.

Subject analysis set title	Prophylaxis Cohort: SoC
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: TAK-755-ORT
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.

Subject analysis set title	Prophylaxis Cohort: TAK-755 SIN
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.

Subject analysis set title	Prophylaxis Cohort: SoC
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: TAK-755 (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort: TAK-755 (Period 3)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort: SoC (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: TAK-755 (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort: TAK-755 (Period 3)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort: SoC (Periods 1 and 2)
Subject analysis set type	Sub-group analysis



Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: TAK-755 (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort: TAK-755 (Period 3)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort: SoC (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: TAK-755 (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort: TAK-755 (Period 3)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort: SoC (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: TAK-755 (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort: TAK-755 (Period 3)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort: SoC (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: TAK-755 (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort: TAK-755 (Period 3)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort: SoC (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: TAK-755 (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort: TAK-755 (Period 3)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort: SoC (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: TAK-755 (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort: TAK-755 (Period 3)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort: SoC (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: TAK-755 (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort: TAK-755 (Period 3)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort: SoC (Periods 1 and 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort I: TAK-755 Then SoC
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in Period 1 followed by SoC for 6 months in Period 2. Thereafter participants received TAK-755 SIN dose IV infusion of 40 IU/kg Q2W for 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort II: SoC Then TAK-755
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in Period 1 followed by IV infusions of 40 IU/kg dose of TAK-755 ORT Q2W in Period 2 for the next 6 months. Thereafter participants received TAK-755 SIN dose IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort I: TAK-755 Then SoC
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in Period 1 followed by SoC for 6 months in Period 2. Thereafter participants received TAK-755 SIN dose IV infusion of 40 IU/kg Q2W for 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort II: SoC Then TAK-755
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in Period 1 followed by IV infusions of 40 IU/kg dose of TAK-755 ORT Q2W in Period 2 for the next 6 months. Thereafter participants received TAK-755 SIN dose IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort I: TAK-755 Then SoC
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in Period 1 followed by SoC for 6 months in Period 2. Thereafter participants received TAK-755 SIN dose IV infusion of 40 IU/kg Q2W for 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort II: SoC Then TAK-755
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in Period 1 followed by IV infusions of 40 IU/kg dose of TAK-755 ORT Q2W in Period 2 for the next 6 months. Thereafter participants received TAK-755 SIN dose IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	Prophylaxis Cohort: TAK-755 ORT
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.

Subject analysis set title	Prophylaxis Cohort: TAK-755 SIN
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.

Subject analysis set title	Prophylaxis Cohort: SoC
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Subject analysis set title	Prophylaxis Cohort: TAK-755
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. Thereafter participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Subject analysis set title	On Demand Cohort I: TAK-755
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the TAK-755 cohort of the Urgent Treatment Period received initial dose of IV infusions 40 IU/kg [ $\pm$  4 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 1 followed by a subsequent dose IV infusions of 20 IU/kg [ $\pm$  2 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 2 and an additional daily dose IV infusions of 15 IU/kg [ $\pm$  1.5 IU/kg] TAK-755 on Day 3 until 2 days after the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

Subject analysis set title	On Demand Cohort II: SoC
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the SoC cohort of the Urgent Treatment Period received the investigator-recommended SoC and dosing regimen until the acute event was resolved.

Subject analysis set title	On Demand Cohort I: TAK-755
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the TAK-755 cohort of the Urgent Treatment Period received initial dose of IV infusions 40 IU/kg [ $\pm$  4 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 1 followed by a subsequent dose IV infusions of 20 IU/kg [ $\pm$  2 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 2 and an additional daily dose IV infusions of 15 IU/kg [ $\pm$  1.5 IU/kg] TAK-755 on Day 3 until 2 days after the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

Subject analysis set title	On Demand Cohort II: SoC
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the SoC cohort of the Urgent Treatment Period received the investigator-recommended SoC and dosing regimen until the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

Subject analysis set title	Prophylaxis Cohort: TAK-755
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Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. Thereafter participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.	
Subject analysis set title	Prophylaxis Cohort: SoC
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received SoC for 6 months in either Period 1 or Period 2.	
Subject analysis set title	Prophylaxis Cohort: TAK-755-ORT
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.	
Subject analysis set title	Prophylaxis Cohort: TAK-755-SIN
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received TAK-755 SIN prophylactic dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.	
Subject analysis set title	Prophylaxis Cohort: SoC
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received SoC for 6 months in either Period 1 or Period 2.	
Subject analysis set title	Prophylaxis Cohort: TAK-755-ORT
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.	
Subject analysis set title	Prophylaxis Cohort: TAK-755-SIN
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.	
Subject analysis set title	Prophylaxis Cohort: SoC
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants received SoC for 6 months in either Period 1 or Period 2.	

### **Primary: Number of Participants With Acute Thrombotic Thrombocytopenic Purpura (TTP) Events During Prophylactic Treatment**

End point title	Number of Participants With Acute Thrombotic Thrombocytopenic Purpura (TTP) Events During Prophylactic Treatment <sup>[1]</sup>
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#### **End point description:**

As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts, in a combined manner for Periods 1 and 2 for TAK-755 and SoC treatments respectively, and separately for Period 3 in which all participants received TAK-755. mFAS included all FAS participants who were treated according to their randomized treatment sequence with the exclusion of those enrolled prior to November 2017 who were treated with SoC instead of the randomized treatment of TAK-755 in period 1 because TAK-755 was not available. For participants enrolled prior to

November 2017, only the first 6 months of SoC treatment in period 1 was included in the analysis. Subjects analysed: the number of participants with data available for analyses.

End point type	Primary
End point timeframe:	
Up to 74.5 months	
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 one event was observed under SOC. Due to the sparseness of data, only summary analysis was provided.

End point values	Prophylaxis Cohort: TAK-755 (Periods 1 and 2)	Prophylaxis Cohort: TAK-755 (Period 3)	Prophylaxis Cohort: SoC (Periods 1 and 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	44	44	45	
Units: participants	0	0	1	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Acute Thrombotic Thrombocytopenic Purpura (TTP) Events Responding to TAK-755

End point title	Percentage of Acute Thrombotic Thrombocytopenic Purpura (TTP) Events Responding to TAK-755
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End point description:

Percentage of acute TTP events responding to TAK-755, was defined as not requiring the use of another human disintegrin and metalloprotease with a thrombospondin type 1 motif, member 13 (ADAMTS13)-containing agent. As per planned analysis, data for this outcome measure were collected and reported only for the TAK-755 treatment arm of both the prophylaxis (irrespective of the prophylaxis periods) and on demand cohorts. Modified Full Analysis Set (mFAS) included all Full Analysis Set participants who were treated according to their randomized treatment sequence with the exclusion of those enrolled prior to November 2017 who were treated with SoC instead of the randomized treatment of TAK-755 in period 1 because TAK-755 was not available. For participants enrolled prior to November 2017, only the first 6 months of SoC treatment in period 1 was included in the analysis. Subjects analysed: participants with acute TTP events that were confirmed by central lab data treated with TAK-755.

End point type	Secondary
End point timeframe:	
Up to 79.6 months	

End point values	Prophylaxis Cohort: TAK-755	On Demand Cohort I: TAK-755		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0 <sup>[2]</sup>	1		
Units: percentage of events				
number (not applicable)		100		

Notes:

[2] - No participants were available for analysis.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Resolution of Acute TTP Events

End point title	Time to Resolution of Acute TTP Events
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End point description:

Time to resolution of acute TTP events following initiation of treatment with TAK-755 or SoC agent was assessed. Acute TTP events were considered resolved when: (a) Platelet count was >150,000 per microliter (μL) or drop of platelet count was within 25 percent (%) of baseline, whichever occurred first, and (b) Elevation of lactate dehydrogenase (LDH) <1.5 x baseline or <1.5 x upper limit of normal (ULN). As per planned analysis, data for this outcome measure were collected and reported in a combined manner irrespective of the prophylaxis treatment Periods, partitioned per treatment received (TAK-755 and SoC) for the on demand and prophylactic cohorts. '0.999' and '999' indicates that 95% confidence interval was not estimable due to censoring in the specified category. Modified FAS. Subjects analysed is the number of participants with acute TTP events that were confirmed by central lab data.

End point type	Secondary
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End point timeframe:

Up to 79.6 months

End point values	Prophylaxis Cohort: TAK-755	Prophylaxis Cohort: SoC	On Demand Cohort I: TAK-755	On Demand Cohort II: SoC
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0 <sup>[3]</sup>	1	1	1
Units: days				
median (confidence interval 95%)	( to )	14.8 (0.999 to 999)	3.0 (0.999 to 999)	1.5 (0.99999 to 99999)

Notes:

[3] - No participants were available for analysis.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With Thrombocytopenia During Prophylactic Treatment

End point title	Number of Participants With Thrombocytopenia During Prophylactic Treatment
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End point description:

Thrombocytopenia was defined as a decrease in platelet count  $\geq 25$  % of baseline or a platelet count <150,000/μL, reported by treatment arm for the prophylactic cohort. As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts, in a combined manner for Periods 1 and 2 for TAK-755 and SoC treatments respectively, and separately for Period 3 in which all participants received TAK-755. Modified FAS included all FAS participants who were treated according to their randomized treatment sequence with the exclusion of those enrolled prior to November 2017 who were treated with SoC instead of the randomized treatment of TAK-755 in period 1

because TAK-755 was not available. For participants enrolled prior to November 2017, only the first 6 months of SoC treatment in period 1 was included in the analysis. Subjects analysed indicates the number of participants with data available for analyses.

End point type	Secondary
End point timeframe:	
Up to 79.6 months	

End point values	Prophylaxis Cohort: TAK-755 (Periods 1 and 2)	Prophylaxis Cohort: TAK-755 (Period 3)	Prophylaxis Cohort: SoC (Periods 1 and 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	44	44	45	
Units: participants	13	11	21	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Microangiopathic Hemolytic Anemia During Prophylactic Treatment

End point title	Number of Participants With Microangiopathic Hemolytic Anemia During Prophylactic Treatment
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End point description:

Microangiopathic hemolytic anemia was defined as an elevation of LDH  $>1.5*$  of baseline or  $>1.5*$ ULN (with a possible evidence of schistocytes on blood smear) and was reported by treatment arm for the prophylactic cohort. As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts, in a combined manner for Periods 1 and 2 for TAK-755 and SoC treatments respectively, and separately for Period 3 in which all participants received TAK-755. Modified FAS included all FAS participants who were treated according to their randomized treatment sequence with the exclusion of those enrolled prior to November 2017 who were treated with SoC instead of randomized treatment of TAK-755 in period 1 because TAK-755 was not available. For participants enrolled prior to November 2017, only first 6 months of SoC treatment in period 1 was included in the analysis. Subjects analysed indicates the number of participants with data available for analyses.

End point type	Secondary
End point timeframe:	
Up to 79.6 months	

End point values	Prophylaxis Cohort: TAK-755 (Periods 1 and 2)	Prophylaxis Cohort: TAK-755 (Period 3)	Prophylaxis Cohort: SoC (Periods 1 and 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	44	44	45	
Units: participants	8	13	12	



## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With Neurological Symptoms During Prophylactic Treatment

End point title	Number of Participants With Neurological Symptoms During Prophylactic Treatment
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End point description:

Neurological symptoms (TTP related) (e.g., confusion, dysphonia, dysarthria, focal or general motor symptoms including seizures), were reported by treatment arm for the prophylactic cohort. As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts, in a combined manner for Periods 1 and 2 for TAK-755 and SoC treatments respectively, and separately for Period 3 in which all participants received TAK-755. Modified FAS included all FAS participants who were treated according to their randomized treatment sequence with the exclusion of those enrolled prior to November 2017 who were treated with SoC instead of the randomized treatment of TAK-755 in period 1 because TAK-755 was not available. For participants enrolled prior to November 2017, only the first 6 months of SoC treatment in period 1 was included in the analysis. Subjects analysed indicates the number of participants with data available for analyses.

End point type	Secondary
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End point timeframe:

Up to 79.6 months

End point values	Prophylaxis Cohort: TAK-755 (Periods 1 and 2)	Prophylaxis Cohort: TAK-755 (Period 3)	Prophylaxis Cohort: SoC (Periods 1 and 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	44	44	45	
Units: participants	4	9	7	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With Renal Dysfunction During Prophylactic Treatment

End point title	Number of Participants With Renal Dysfunction During Prophylactic Treatment
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End point description:

Renal dysfunction was defined as an increase in serum creatinine  $>1.5 \times$  baseline. Number of participants with renal dysfunction were reported by treatment arm for the prophylactic cohort. As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts, in a combined manner for Periods 1 and 2 for TAK-755 and SoC treatments respectively, and separately for Period 3 in which all participants received TAK-755. Modified FAS included all FAS participants who were treated according to their randomized treatment sequence with the exclusion of those enrolled prior to November 2017 who were treated with SoC instead of the randomized treatment of TAK-755 in period 1 because TAK-755 was not available. For participants enrolled prior to November 2017, only the first 6 months of SoC treatment in period 1 was included in the analysis. Subjects analysed indicates the number of participants with data available for analyses.

End point type	Secondary
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End point timeframe:

Up to 79.6 months

End point values	Prophylaxis Cohort: TAK-755 (Periods 1 and 2)	Prophylaxis Cohort: TAK-755 (Period 3)	Prophylaxis Cohort: SoC (Periods 1 and 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	44	44	45	
Units: participants	5	4	2	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Abdominal Pain During Prophylactic Treatment

End point title	Number of Participants With Abdominal Pain During Prophylactic Treatment
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End point description:

Number of participants with abdominal pain (TTP related) were reported by treatment arm for the prophylaxis cohort. As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts, in a combined manner for Periods 1 and 2 for TAK-755 and SoC treatments respectively, and separately for Period 3 in which all participants received TAK-755. Modified FAS included all FAS participants who were treated according to their randomized treatment sequence with the exclusion of those enrolled prior to November 2017 who were treated with SoC instead of the randomized treatment of TAK-755 in period 1 because TAK-755 was not available. For participants enrolled prior to November 2017, only the first 6 months of SoC treatment in period 1 was included in the analysis. Subjects analysed indicates the number of participants with data available for analyses.

End point type	Secondary
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End point timeframe:

Up to 79.6 months

End point values	Prophylaxis Cohort: TAK-755 (Periods 1 and 2)	Prophylaxis Cohort: TAK-755 (Period 3)	Prophylaxis Cohort: SoC (Periods 1 and 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	44	44	45	
Units: participants	2	2	6	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Dose Modification Not Prompted by an Acute TTP Event During Prophylactic Treatment

End point title	Number of Participants With Dose Modification Not Prompted
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## End point description:

Number of participants with dose modification not prompted by an acute TTP event were reported by treatment for the prophylactic cohort. As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts, in a combined manner for Periods 1 and 2 for TAK-755 and SoC treatments respectively, and separately for Period 3 in which all participants received TAK-755. Modified FAS included all FAS participants who were treated according to their randomized treatment sequence with the exclusion of those enrolled prior to November 2017 who were treated with SoC instead of the randomized treatment of TAK-755 in period 1 because TAK-755 was not available. For participants enrolled prior to November 2017, only the first 6 months of SoC treatment in period 1 was included in the analysis. Subjects analysed indicates the number of participants with data available for analyses.

End point type	Secondary
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End point timeframe:

Up to 79.6 months

End point values	Prophylaxis Cohort: TAK-755 (Periods 1 and 2)	Prophylaxis Cohort: TAK-755 (Period 3)	Prophylaxis Cohort: SoC (Periods 1 and 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	44	44	45	
Units: participants	0	1	3	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Supplemental Doses Prompted by Subacute TTP Event During Prophylactic Treatment

End point title	Number of Supplemental Doses Prompted by Subacute TTP Event During Prophylactic Treatment
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## End point description:

Number of supplemental doses prompted by subacute TTP events were reported by treatment for the prophylactic cohort. As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts, in a combined manner for Periods 1 and 2 for TAK-755 and SoC treatments respectively, and separately for Period 3 in which all participants received TAK-755. Modified FAS included all FAS participants who were treated according to their randomized treatment sequence with the exclusion of those enrolled prior to November 2017 who were treated with SoC instead of the randomized treatment of TAK-755 in period 1 because TAK-755 was not available. For participants enrolled prior to November 2017, only the first 6 months of SoC treatment in period 1 was included in the analysis. Subjects analysed indicates the number of participants with data available for analyses.

End point type	Secondary
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End point timeframe:

Up to 79.6 months

End point values	Prophylaxis Cohort: TAK-755 (Periods 1 and 2)	Prophylaxis Cohort: TAK-755 (Period 3)	Prophylaxis Cohort: SoC (Periods 1 and 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	44	44	45	
Units: supplemental doses				
number (not applicable)	0	5	9	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Acute TTP Events on Their Final Dose

End point title	Number of Participants With Acute TTP Events on Their Final Dose
End point description:	
Number of participants with acute TTP events on their final dose and dosing regimen for the prophylactic cohort were reported. As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts, in a combined manner for Periods 1 and 2 for TAK-755 and SoC treatments respectively, and separately for Period 3 in which all participants received TAK-755. Modified FAS included all FAS participants who were treated according to their randomized treatment sequence with the exclusion of those enrolled prior to November 2017 who were treated with SoC instead of the randomized treatment of TAK-755 in period 1 because TAK-755 was not available. For participants enrolled prior to November 2017, only the first 6 months of SoC treatment in period 1 was included in the analysis. Subjects analysed indicates the number of participants with data available for analyses.	
End point type	Secondary
End point timeframe:	
Up to 79.6 months	

End point values	Prophylaxis Cohort: TAK-755 (Periods 1 and 2)	Prophylaxis Cohort: TAK-755 (Period 3)	Prophylaxis Cohort: SoC (Periods 1 and 2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	44	44	45	
Units: participants	0	0	1	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with Treatment emergent Adverse Events (TEAEs) and Serious Treatment Emergent Adverse Events (Serious TEAEs)

End point title	Number of Participants with Treatment emergent Adverse Events (TEAEs) and Serious Treatment Emergent Adverse Events (Serious TEAEs)
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**End point description:**

AE: Any untoward medical occurrence in participants administered IP that does not necessarily have a causal relationship with treatment. TEAE: AE that has start date-time on/after start date-time of first dose of treatment participant is taking on that assessment/period or if it has start date-time before start date-time of first dose but increases in severity on/after start date-time of the first dose of treatment. SAE: An untoward medical occurrence that at any dose meets 1 or more of following criteria: death; initial/prolonged in-patient hospitalization; life threatening experience; persistent/significant disability/incapacity; congenital anomaly, medically important event (may not be immediately life threatening or result in death or require hospitalization but may require medical or surgical intervention to prevent 1 of the other outcomes). Vital signs, clinical chemistry, hematology as assessed by the investigator were reported as AE.

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End point type	Secondary
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End point timeframe:

Up to 79.6 months

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End point values	Prophylaxis Cohort: TAK-755	Prophylaxis Cohort: SoC	On Demand Cohort I: TAK-755	On Demand Cohort II: SoC
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	47	48	2	4
Units: participants				
TEAES	42	44	0	3
Serious TEAEs	6	8	0	1

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**Statistical analyses**

No statistical analyses for this end point

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**Secondary: Number of Participants With Inhibitory Antibodies to ADAMTS13**

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End point title	Number of Participants With Inhibitory Antibodies to ADAMTS13
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End point description:

Number of participants with inhibitory antibodies to ADAMTS13 were reported. As per planned analysis, data for this outcome measure were collected and reported in a combined manner irrespective of the Prophylaxis Periods and partitioned as per the treatment received during the course of the study, presented for the prophylaxis cohorts only. The Safety Analysis Set included all participants treated with at least 1 dose of TAK-755 or SoC treatment after randomization. Subjects analysed indicates the number of participants with data available for analyses.

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End point type	Secondary
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End point timeframe:

Up to 79.6 months

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End point values	Prophylaxis Cohort: TAK-755	Prophylaxis Cohort: SoC		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	4		
Units: participants	1	0		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Total Quantity of ADAMTS13 Administered During the Treatment of Acute TTP Events in Participants in TAK-755 Treatment Arm

End point title	Total Quantity of ADAMTS13 Administered During the Treatment of Acute TTP Events in Participants in TAK-755 Treatment Arm
End point description:	
Total quantity of ADAMTS13 administered during the treatment of acute TTP events (all acute TTP events irrespective of central lab confirmation were included) was assessed. Acute TTP events typically require 3 to 4 days of intensified treatment. As per planned analysis, data for this outcome measure were collected and reported only for the TAK-755 treatment arm of both the prophylaxis (irrespective of the prophylaxis periods) and on demand cohorts. The Safety Analysis Set.	
End point type	Secondary
End point timeframe:	
Up to 79.6 months	

End point values	Prophylaxis Cohort: TAK-755	On Demand Cohort I: TAK-755		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0 <sup>[4]</sup>	2		
Units: IU				
arithmetic mean (standard deviation)	()	5720.25 (± 189.858)		

Notes:

[4] - No participants were analyzed.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Incremental Recovery (IR) of ADAMTS13 Activity for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment

End point title	Incremental Recovery (IR) of ADAMTS13 Activity for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment
End point description:	
ADAMTS13 activity measured by fluorescent resonance energy transfer(FRETs) assay.IR:body weight normalized maximum increase in plasma ADAMTS13 activity level.IR of ADAMTS13 activity for SoC agent&TAK-755 in plasma was assessed.(IU/mL)/(IU/kg)=(International units per milliliter)/(International units per kilogram).PK-I,-II&-III denote crossover PK evaluation of a maximum of 14 days at start of Prophylaxis Treatment Period (PTP) 1,end of PTP2&3 respectively.Per planned	

for this outcome measure was collected&reported as per treatment(intervention)received(rADAMTS13 manufactured in Orth, Austria[TAK-755 ORT],rADAMTS13 manufactured in Singapore[TAK-755 SIN],or SoC)during course of study,only for prophylaxis cohorts.9999:mean&SD were not estimable due to values below lower limit of quantification.99999:no participants were analysed in specified category.No participants received SoC in PK-II and PK-III thus there is no data for same.n=variable for each reported category.

End point type	Secondary
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End point timeframe:

PK-I (Month 1:Day 1 up to 12), PK-II (Month 12:Day 1 up to 12), and PK-III (Month 19:Day 1 up to 12): Pre-infusion and at multiple timepoints post-infusion up to 288 hours

End point values	Prophylaxis Cohort: TAK-755 SIN	Prophylaxis Cohort: TAK-755 ORT	Prophylaxis Cohort: SoC	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	36	22	
Units: (IU/mL)/(IU/kg)				
arithmetic mean (standard deviation)				
PK-I: ADAMTS13 Activity	9999 (± 9999)	0.025 (± 0.00592)	0.0212 (± 0.0267)	
PK-II: ADAMTS13 Activity	0.0292 (± 0.00630)	0.0283 (± 0.00644)	99999 (± 99999)	
PK-III: ADAMTS13 Activity	0.0260 (± 0.00617)	99999 (± 99999)	99999 (± 99999)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: IR of ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment

End point title	IR of ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment
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End point description:

ADAMTS13 antigen measured using commercial ADAMTS13 enzyme-linked immunosorbent assay(ELISA)using ADAMTS13 antigen.IR:body weight normalized maximum increase in plasma ADAMTS13 antigen.IR of ADAMTS13 antigen for SoC agent&TAK-755 in plasma was assessed.(µg/mL)/(µg/kg)is(microgram per milliliter)/(microgram per kilogram).PK-I,PK-II,&PK-III denote crossover PK evaluation of a maximum of 14 days at start of PTP 1,end of PTP 2&3 respectively.Per planned analysis,data for this outcome measure was collected&reported as per treatment(intervention)received(rADAMTS13 manufactured in Orth,Austria[TAK-755 ORT],rADAMTS13 manufactured in Singapore[TAK-755 SIN],or SoC)during course of study,only for prophylaxis cohorts.9999:mean&SD were not estimable due to values below lower limit of quantification.99999:no participants analysed in specified category.No participants received SoC in PK-II and PK-III thus there is no data for same.Subjects analyzed is variable for each reported category.

End point type	Secondary
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End point timeframe:

PK-I (Month 1:Day 1 up to 12), PK-II (Month 12:Day 1 up to 12), and PK-III (Month 19:Day 1 up to 12): Pre-infusion and at multiple timepoints post-infusion up to 288 hours

End point values	Prophylaxis Cohort: TAK-755 SIN	Prophylaxis Cohort: TAK-755 ORT	Prophylaxis Cohort: SoC	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	24	37	23	
Units: (µg/mL)/ (µg/kg)				
arithmetic mean (standard deviation)				
PK-I: ADAMTS13 Antigen	9999 (± 9999)	0.0299 (± 0.00638)	0.0186 (± 0.00605)	
PK-II: ADAMTS13 Antigen	0.0324 (± 0.00668)	0.0339 (± 0.0080)	99999 (± 99999)	
PK-III: ADAMTS13 Antigen	0.0264 (± 0.0102)	99999 (± 99999)	99999 (± 99999)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Area Under the Plasma Curve [AUC]all of ADAMTS13 Activity for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment

End point title	Area Under the Plasma Curve [AUC]all of ADAMTS13 Activity for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment
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End point description:

h\*IU/mL denotes for hours\*international units per milliliters. PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '99999' indicates that no participants were analysed in the specified category. PK Analysis Set. Number of subjects analysed was variable for each category. Number analyzed (n) is variable for each reported category.

End point type	Secondary
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End point timeframe:

PK-I (Month 1:Day 1 up to 12), PK-II (Month 12:Day 1 up to 12), and PK-III (Month 19:Day 1 up to 12): Pre-infusion and at multiple timepoints post-infusion up to 288 hours

End point values	Prophylaxis Cohort: TAK-755 SIN	Prophylaxis Cohort: TAK-755 ORT	Prophylaxis Cohort: SoC	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	33	31	
Units: h*IU/mL				
arithmetic mean (standard deviation)				
PK-I: ADAMTS13 Activity	99999 (± 99999)	44.15 (± 11.197)	10.56 (± 8.263)	
PK-II: ADAMTS13 Activity	52.98 (± 13.358)	52.83 (± 11.940)	99999 (± 99999)	
PK-III: ADAMTS13 Activity	65.65 (± 23.587)	99999 (± 99999)	99999 (± 99999)	



## Statistical analyses

No statistical analyses for this end point

### Secondary: AUCall of ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment

End point title	AUCall of ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment
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End point description:

h\*µg/mL denotes for hours\*microgram per milliliters. PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '99999' indicates that no participants were analysed in the specified category. PK Analysis Set. Number of subjects analysed was variable for each category.

End point type	Secondary
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End point timeframe:

PK-I (Month 1:Day 1 up to 12), PK-II (Month 12:Day 1 up to 12), and PK-III (Month 19:Day 1 up to 12): Pre-infusion and at multiple timepoints post-infusion up to 288 hours

End point values	Prophylaxis Cohort: TAK-755 SIN	Prophylaxis Cohort: TAK-755 ORT	Prophylaxis Cohort: SoC	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	24	34	31	
Units: h*µg/mL				
arithmetic mean (standard deviation)				
PK-I: ADAMTS13 Antigen	99999 (± 99999)	34.12 (± 9.646)	7.590 (± 6.134)	
PK-II: ADAMTS13 Antigen	38.95 (± 11.137)	38.79 (± 8.835)	99999 (± 99999)	
PK-III: ADAMTS13 Antigen	49.74 (± 19.147)	99999 (± 99999)	99999 (± 99999)	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Terminal Half-Life (t<sub>1/2</sub>) of ADAMTS13 Activity and ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment

End point title	Terminal Half-Life (t <sub>1/2</sub> ) of ADAMTS13 Activity and ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During
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## End point description:

PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '99999' indicates that no participants were analysed in the specified category. PK Analysis Set. Number of subjects analysed were variable for each reported category.

End point type	Secondary
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## End point timeframe:

PK-I (Month 1:Day 1 up to 12), PK-II (Month 12:Day 1 up to 12), and PK-III (Month 19:Day 1 up to 12): Pre-infusion and at multiple timepoints post-infusion up to 288 hours

End point values	Prophylaxis Cohort: TAK-755 ORT	Prophylaxis Cohort: TAK-755 SIN	Prophylaxis Cohort: SoC	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	34	24	22	
Units: hours				
arithmetic mean (standard deviation)				
PK-I: ADAMTS13 Activity	47.14 (± 11.573)	99999 (± 99999)	62.88 (± 28.927)	
PK-I: ADAMTS13 Antigen	53.59 (± 13.354)	99999 (± 99999)	58.70 (± 23.575)	
PK-II: ADAMTS13 Activity	52.51 (± 15.579)	45.77 (± 10.231)	99999 (± 99999)	
PK-II: ADAMTS13 Antigen	54.15 (± 16.553)	49.72 (± 15.942)	99999 (± 99999)	
PK-III: ADAMTS13 Activity	99999 (± 99999)	35.38 (± 5.286)	99999 (± 99999)	
PK-III: ADAMTS13 Antigen	99999 (± 99999)	39.85 (± 3.243)	99999 (± 99999)	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Residence Time Extrapolated to Infinity (MRT0-inf) of ADAMTS13 Activity and ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment

End point title	Mean Residence Time Extrapolated to Infinity (MRT0-inf) of ADAMTS13 Activity and ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment
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## End point description:

PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '9999' indicates that Mean & SD were not estimable as values were below lower limit of quantification.

'99999' indicates that no participants were analysed in the specified category. PK Analysis Set. Number of subjects analysed were variable for each reported category.

End point type	Secondary
End point timeframe:	
PK-I (Month 1:Day 1 up to 12), PK-II (Month 12:Day 1 up to 12), and PK-III (Month 19:Day 1 up to 12): Pre-infusion and at multiple timepoints post-infusion up to 288 hours	

End point values	Prophylaxis Cohort: TAK-755-ORT	Prophylaxis Cohort: TAK-755 SIN	Prophylaxis Cohort: SoC	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	31	23	2	
Units: hours				
arithmetic mean (standard deviation)				
PK-I: ADAMTS13 Activity	64.35 (± 17.498)	99999 (± 99999)	9999 (± 9999)	
PK-I: ADAMTS13 Antigen	71.20 (± 16.538)	99999 (± 99999)	9999 (± 9999)	
PK-II: ADAMTS13 Activity	65.89 (± 13.472)	61.56 (± 11.762)	99999 (± 99999)	
PK-II: ADAMTS13 Antigen	72.36 (± 19.224)	66.30 (± 18.738)	99999 (± 99999)	
PK-III: ADAMTS13 Activity	99999 (± 99999)	41.67 (± 6.171)	99999 (± 99999)	
PK-III: ADAMTS13 Antigen	99999 (± 99999)	46.30 (± 4.266)	99999 (± 99999)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Clearance (CL) of ADAMTS13 Activity and ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment

End point title	Clearance (CL) of ADAMTS13 Activity and ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment
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End point description:

PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '9999' indicates that Mean & SD were not estimable as values were below lower limit of quantification. '99999' indicates that no participants were analysed in the specified category. PK Analysis Set. Number of subjects analysed were variable for each reported category.

End point type	Secondary
End point timeframe:	
PK-I (Month 1:Day 1 up to 12), PK-II (Month 12:Day 1 up to 12), and PK-III (Month 19:Day 1 up to 12): Pre-infusion and at multiple timepoints post-infusion up to 288 hours	

End point values	Prophylaxis Cohort: TAK-755-ORT	Prophylaxis Cohort: TAK-755 SIN	Prophylaxis Cohort: SoC	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	31	23	2	
Units: liters per hour (L/h)				
arithmetic mean (standard deviation)				
PK-I: ADAMTS13 Activity	0.0618 ( $\pm$ 0.0144)	99999 ( $\pm$ 99999)	9999 ( $\pm$ 9999)	
PK-I: ADAMTS13 Antigen	0.0456 ( $\pm$ 0.0117)	99999 ( $\pm$ 99999)	99999 ( $\pm$ 99999)	
PK-II: ADAMTS13 Activity	0.0530 ( $\pm$ 0.0134)	0.0549 ( $\pm$ 0.0117)	99999 ( $\pm$ 99999)	
PK-II: ADAMTS13 Antigen	0.0409 ( $\pm$ 0.0109)	0.0480 ( $\pm$ 0.0133)	99999 ( $\pm$ 99999)	
PK-III: ADAMTS13 Activity	99999 ( $\pm$ 99999)	0.0553 ( $\pm$ 0.0177)	99999 ( $\pm$ 99999)	
PK-III: ADAMTS13 Antigen	99999 ( $\pm$ 99999)	0.0462 ( $\pm$ 0.0110)	99999 ( $\pm$ 99999)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Volume at Steady State (Vss) of ADAMTS13 Activity and ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment

End point title	Volume at Steady State (Vss) of ADAMTS13 Activity and ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment
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End point description:

PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '9999' indicates that Mean &SD were not estimable as values were below lower limit of quantification. '99999' indicates that no participants were analysed in the specified category. PK Analysis Set. Number of subjects analysed was variable for each category.

End point type	Secondary
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End point timeframe:

PK-I (Month 1:Day 1 up to 12), PK-II (Month 12:Day 1 up to 12), and PK-III (Month 19:Day 1 up to 12): Pre-infusion and at multiple timepoints post-infusion up to 288 hours

End point values	Prophylaxis Cohort: TAK-755-ORT	Prophylaxis Cohort: TAK-755 SIN	Prophylaxis Cohort: SoC	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	31	23	2	
Units: liters				
arithmetic mean (standard deviation)				
PK-I: ADAMTS13 Activity	3.852 (± 0.916)	99999 (± 99999)	9999 (± 9999)	
PK-I: ADAMTS13 Antigen	3.124 (± 0.650)	99999 (± 99999)	9999 (± 9999)	
PK-II: ADAMTS13 Activity	3.401 (± 0.715)	3.304 (± 0.635)	99999 (± 99999)	
PK-II: ADAMTS13 Antigen	2.812 (± 0.479)	3.007 (± 0.613)	99999 (± 99999)	
PK-III: ADAMTS13 Activity	99999 (± 99999)	2.265 (± 0.669)	99999 (± 99999)	
PK-III: ADAMTS13 Antigen	99999 (± 99999)	2.172 (± 0.698)	99999 (± 99999)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Maximum Concentration (Cmax) of ADAMTS13 Activity for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment

End point title	Maximum Concentration (Cmax) of ADAMTS13 Activity for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment
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End point description:

IU/mL stands for International units per milliliter. PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth,Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '9999' indicates that Mean & SD were not estimable as values were below lower limit of quantification. '99999' indicates that no participants were analysed in the specified category. PK Analysis Set. Number of subjects analysed was variable for each category.

End point type	Secondary
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End point timeframe:

PK-I (Month 1:Day 1 up to 12), PK-II (Month 12:Day 1 up to 12), and PK-III (Month 19:Day 1 up to 12): Pre-infusion and at multiple timepoints post-infusion up to 288 hours

End point values	Prophylaxis Cohort: TAK-755-ORT	Prophylaxis Cohort: TAK-755 SIN	Prophylaxis Cohort: SoC	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	36	22	41	
Units: IU/mL				
arithmetic mean (standard deviation)				
PK-I: ADAMTS13 Activity	1.003 (± 0.235)	9999 (± 9999)	0.192 (± 0.102)	

PK-II: ADAMTS13 Activity	1.130 ( $\pm$ 0.253)	1.162 ( $\pm$ 0.250)	99999 ( $\pm$ 99999)	
PK-III: ADAMTS13 Activity	99999 ( $\pm$ 99999)	1.036 ( $\pm$ 0.253)	99999 ( $\pm$ 99999)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cmax of ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment

End point title	Cmax of ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment
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End point description:

µg/mL stands for microgram per milliliter. PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '99999' indicates that Mean & SD were not estimable as values were below lower limit of quantification. '99999' indicates that no participants were analysed in the specified category. PK Analysis Set. Number of subjects analysed was variable for each category.

End point type	Secondary
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End point timeframe:

PK-I (Month 1:Day 1 up to 12), PK-II (Month 12:Day 1 up to 12), and PK-III (Month 19:Day 1 up to 12): Pre-infusion and at multiple timepoints post-infusion up to 288 hours

End point values	Prophylaxis Cohort: TAK-755-ORT	Prophylaxis Cohort: TAK-755 SIN	Prophylaxis Cohort: SoC	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	37	24	41	
Units: µg/mL				
arithmetic mean (standard deviation)				
PK-I: ADAMTS13 Antigen	0.713 ( $\pm$ 0.145)	9999 ( $\pm$ 9999)	0.141 ( $\pm$ 0.0710)	
PK-II: ADAMTS13 Antigen	0.804 ( $\pm$ 0.185)	0.844 ( $\pm$ 0.168)	99999 ( $\pm$ 99999)	
PK-III: ADAMTS13 Antigen	99999 ( $\pm$ 99999)	0.715 ( $\pm$ 0.203)	99999 ( $\pm$ 99999)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Assessment of Von Willebrand Factor:Antigen (VWF:Ag) During Prophylactic Treatment

End point title	Change from Baseline in Assessment of Von Willebrand Factor:
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## End point description:

VWF:Ag is a measure of total VWF protein & was assessed using a sandwich ELISA employing polyclonal anti-human-VWF antibodies. Assessments of VWF:Ag at baseline and following infusion of SoC agent and TAK-755 treatment during initial PK assessment were reported. PK-I, PK-II, and PK-III denote crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '99999' indicates that no participants were analysed in the specified category. PD Analysis Set. Number of subjects analysed was variable for each category.

End point type	Secondary
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## End point timeframe:

PK-I (Month 1:Day 12), PK-II (Month 12:Day 12), and PK-III (Month 19:Day 12): Post-infusion at 288 hours

End point values	Prophylaxis Cohort: TAK-755-ORT	Prophylaxis Cohort: TAK-755 SIN	Prophylaxis Cohort: SoC	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	23	21	19	
Units: percentage of VWF:Ag				
arithmetic mean (standard deviation)				
VWF:Ag : PK-I	-0.11 (± 17.064)	99999 (± 99999)	3.67 (± 19.705)	
VWF:Ag : PK-II	0.48 (± 34.798)	-1.31 (± 22.259)	99999 (± 99999)	
VWF:Ag : PK-III	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Assessment of Von Willebrand Factor:Ristocetin Cofactor Activity (VWF:RCo) During Prophylactic Treatment

End point title	Change from Baseline in Assessment of Von Willebrand Factor:Ristocetin Cofactor Activity (VWF:RCo) During Prophylactic Treatment
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## End point description:

VWF:RCo provides a measure of ability of VWF to bind platelet glycoprotein Ib. Stabilized platelets are agglutinated in presence of VWF & antibiotic Ristocetin. Assessments of VWF:RCo at baseline & following infusion of SoC agent & TAK-755 treatment during initial PK assessment was reported. PK-I, PK-II, & PK-III denote crossover PK evaluation of a maximum of 14 days at start of Prophylaxis Treatment Period 1 & end of Prophylaxis Treatment Periods 2 & 3 respectively. As per planned analysis, data for this outcome measure were collected & reported as per treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during course of study, only for prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for same. '99999' indicates that no participants were analysed in specified category. PD Analysis Set. Number of subjects analysed was variable for each category.

End point type	Secondary
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## End point timeframe:

PK-I (Month 1:Day 12), PK-II (Month 12:Day 12), and PK-III (Month 19:Day 12): Post-infusion at 288

End point values	Prophylaxis Cohort: TAK-755-ORT	Prophylaxis Cohort: TAK-755 SIN	Prophylaxis Cohort: SoC	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	23	21	24	
Units: percentage of VWF:RCo				
arithmetic mean (standard deviation)				
VWF:RCo- PK-I	3.63 ( $\pm$ 42.178)	99999 ( $\pm$ 99999)	9.99 ( $\pm$ 33.230)	
VWF:RCo- PK-II	7.45 ( $\pm$ 31.917)	3.60 ( $\pm$ 30.678)	99999 ( $\pm$ 99999)	
VWF:RCo- PK-III	99999 ( $\pm$ 99999)	99999 ( $\pm$ 99999)	99999 ( $\pm$ 99999)	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Assessment of ADAMTS13 Activity Expressed as Pre-Infusion ADAMTS13 Levels

End point title	Assessment of ADAMTS13 Activity Expressed as Pre-Infusion ADAMTS13 Levels
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End point description:

PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '9999' indicates that Mean & SD were not estimable as values were below lower limit of quantification. '99999' indicates that no participants were analysed in the specified category. PD Analysis Set. Number of subjects analysed was variable for each category.

End point type	Secondary
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End point timeframe:

PK-I (Month 1:Day 1), PK-II (Month 12:Day 1), and PK-III (Month 19:Day 1): Pre-infusion (within 1 hour)

End point values	Prophylaxis Cohort: TAK-755 ORT	Prophylaxis Cohort: TAK-755 SIN	Prophylaxis Cohort: SoC	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	36	22	44	
Units: IU/mL				
arithmetic mean (standard deviation)				
ADAMTS13 Activity: PK-I	9999 ( $\pm$ 9999)	9999 ( $\pm$ 9999)	9999 ( $\pm$ 9999)	



ADAMTS13 Activity: PK-II	9999 (± 9999)	9999 (± 9999)	99999 (± 99999)	
ADAMTS13 Activity: PK-III	99999 (± 99999)	9999 (± 9999)	99999 (± 99999)	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Assessment of Select VWF Parameters Expressed as Pre-Infusion Levels of VWF:RCo

End point title	Assessment of Select VWF Parameters Expressed as Pre-Infusion Levels of VWF:RCo
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End point description:

PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '99999' indicates that no participants were analysed in the specified category. PD Analysis Set. Number of subjects analysed was variable for each category.

End point type	Secondary
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End point timeframe:

PK-I (Month 1:Day 1), PK-II (Month 12:Day 1), and PK-III (Month 19:Day 1): Pre-infusion (within 1 hour)

End point values	Prophylaxis Cohort: TAK-755-ORT	Prophylaxis Cohort: TAK-755-SIN	Prophylaxis Cohort: SoC	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	36	25	43	
Units: percentage of VWF:RCo				
arithmetic mean (standard deviation)				
PK-I: VWF:RCo	145.54 (± 54.698)	137.62 (± 52.978)	148.46 (± 51.415)	
PK-II: VWF:RCo	155.76 (± 63.032)	154.98 (± 74.444)	99999 (± 99999)	
PK-III: VWF:RCo	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Assessment of Select VWF Parameters Expressed as Pre-Infusion Levels of VWF:Ag

End point title	Assessment of Select VWF Parameters Expressed as Pre-Infusion Levels of VWF:Ag
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End point description:

PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '9999' indicates that Mean &SD were not estimable as values were below lower limit of quantification. '99999' indicates that no participants were analysed in the specified category. PD Analysis Set. Number of subjects analysed was variable for each category.

End point type	Secondary
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End point timeframe:

PK-I (Month 1:Day 1), PK-II (Month 12:Day 1), and PK-III (Month 19:Day 1): Pre-infusion (within 1 hour)

End point values	Prophylaxis Cohort: TAK-755-ORT	Prophylaxis Cohort: TAK-755-SIN	Prophylaxis Cohort: SoC	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	37	25	35	
Units: percentage of VWF:Ag				
arithmetic mean (standard deviation)				
PK-I: VWF:Ag	110.38 (± 45.205)	9999 (± 9999)	105.07 (± 40.539)	
PK-II: VWF:Ag	120.48 (± 49.224)	116.66 (± 60.338)	99999 (± 99999)	
PK-III: VWF:Ag	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Assessment of Select VWF Parameters Expressed as Pre-Infusion Levels of VWF:mm Low Resolution (Res.) Intermediate

End point title	Assessment of Select VWF Parameters Expressed as Pre-Infusion Levels of VWF:mm Low Resolution (Res.) Intermediate
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End point description:

PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '9999' indicates that Mean &SD were not estimable as values were below lower limit of quantification. '99999' indicates that no participants were analysed in the specified category. PD Analysis Set. Number of subjects analysed was variable for each category.

End point type	Secondary
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End point timeframe:

PK-I (Month 1:Day 1), PK-II (Month 12:Day 1), and PK-III (Month 19:Day 1): Pre-infusion (within 1 hour)

End point values	Prophylaxis Cohort: TAK-755-ORT	Prophylaxis Cohort: TAK-755-SIN	Prophylaxis Cohort: SoC	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	38	25	39	
Units: % of VWF:mm Low Res.Intermediate				
arithmetic mean (standard deviation)				
PK-I: VWF:mm Low Res. Intermediate	32.14 (± 3.375)	9999 (± 9999)	31.22 (± 2.955)	
PK-II: VWF:mm Low Res. Intermediate	30.87 (± 3.754)	31.10 (± 3.616)	99999 (± 99999)	
PK-III: VWF:mm Low Res. Intermediate	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Assessment of Select VWF Parameters Expressed as Pre-Infusion Levels of VWF:mm Low Res. Large

End point title	Assessment of Select VWF Parameters Expressed as Pre-Infusion Levels of VWF:mm Low Res. Large
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End point description:

PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '9999' indicates that Mean &SD were not estimable as values were below lower limit of quantification. '99999' indicates that no participants were analysed in the specified category. PD Analysis Set. Number of subjects analysed was variable for each category.

End point type	Secondary
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End point timeframe:

PK-I (Month 1:Day 1), PK-II (Month 12:Day 1), and PK-III (Month 19:Day 1): Pre-infusion (within 1 hour)

End point values	Prophylaxis Cohort: TAK-755-ORT	Prophylaxis Cohort: TAK-755-SIN	Prophylaxis Cohort: SoC	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	38	25	39	
Units: % of VWF:mm Low Res. Large				
arithmetic mean (standard deviation)				
PK-I: VWF:mm Low Res. Large	45.98 (± 5.920)	9999 (± 9999)	46.03 (± 5.043)	

PK-II: VWF:mm Low Res. Large	46.17 ( $\pm$ 5.670)	44.93 ( $\pm$ 7.319)	99999 ( $\pm$ 99999)	
PK-III: VWF:mm Low Res. Large	99999 ( $\pm$ 99999)	99999 ( $\pm$ 99999)	99999 ( $\pm$ 99999)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Assessment of Select VWF Parameters Expressed as Pre-Infusion Levels of VWF:mm Low Res. Small

End point title	Assessment of Select VWF Parameters Expressed as Pre-Infusion Levels of VWF:mm Low Res. Small
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End point description:

PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '9999' indicates that Mean & SD were not estimable as values were below lower limit of quantification. '99999' indicates that no participants were analysed in the specified category. PD Analysis Set. Number of subjects analysed was variable for each category.

End point type	Secondary
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End point timeframe:

PK-I (Month 1:Day 1), PK-II (Month 12:Day 1), and PK-III (Month 19:Day 1): Pre-infusion (within 1 hour)

End point values	Prophylaxis Cohort: TAK-755-ORT	Prophylaxis Cohort: TAK-755-SIN	Prophylaxis Cohort: SoC	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	38	25	39	
Units: % of VWF:mm Low Res. Small				
arithmetic mean (standard deviation)				
PK-I: VWF:mm Low Res. Small	21.66 ( $\pm$ 4.230)	9999 ( $\pm$ 9999)	22.77 ( $\pm$ 5.161)	
PK-II: VWF:mm Low Res. Small	22.96 ( $\pm$ 3.047)	23.96 ( $\pm$ 5.320)	99999 ( $\pm$ 99999)	
PK-III: VWF:mm Low Res. Small	99999 ( $\pm$ 99999)	99999 ( $\pm$ 99999)	99999 ( $\pm$ 99999)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Total Binding Antibodies to ADAMTS13 During Prophylactic Treatment

End point title	Number of Participants With Total Binding Antibodies to
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## End point description:

Total binding antibodies to ADAMTS13 were measured by an ELISA-based assay, detecting total immunoglobulins (IgG, IgA, and IgM). As per planned analysis, data for this outcome measure were collected and reported per sequence (Prophylaxis Cohort I: TAK-755 Then SoC and Prophylaxis Cohort II: SoC Then TAK-755) for the prophylaxis cohorts only. The Safety Analysis Set included all participants treated with at least 1 dose of TAK-755 or SoC treatment after randomization. 2 participants randomized to Prophylaxis Cohort I received actual treatment as per Prophylaxis Cohort II and are presented per actual treatment arm.

End point type	Secondary
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End point timeframe:

Up to 79.6 months

End point values	Prophylaxis Cohort I: TAK-755 Then SoC	Prophylaxis Cohort II: SoC Then TAK-755		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21	27		
Units: participants	0	2		

## Statistical analyses

No statistical analyses for this end point

**Secondary: Number of Participants With Neutralizing Antibodies to ADAMTS13 During Prophylactic Treatment**

End point title	Number of Participants With Neutralizing Antibodies to ADAMTS13 During Prophylactic Treatment
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## End point description:

Neutralizing antibodies were measured by a Bethesda method with Nijmegen modification using the ADAMTS13 FRETS-VWF73 activity assay. As per planned analysis, data for this outcome measure were collected and reported per sequence (Prophylaxis Cohort I: TAK-755 Then SoC and Prophylaxis Cohort II: SoC Then TAK-755) for the prophylaxis cohorts only. The Safety Analysis Set included all participants treated with at least 1 dose of TAK-755 or SoC treatment after randomization. 2 participants randomized to Prophylaxis Cohort I received actual treatment as per Prophylaxis Cohort II and are presented per actual treatment arm.

End point type	Secondary
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End point timeframe:

Up to 79.6 months

End point values	Prophylaxis Cohort I: TAK-755 Then SoC	Prophylaxis Cohort II: SoC Then TAK-755		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21	27		
Units: participants	0	1		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With Anti-Chinese Hamster Ovary (Anti-CHO) Protein Antibodies During Prophylactic Treatment

End point title	Number of Participants With Anti-Chinese Hamster Ovary (Anti-CHO) Protein Antibodies During Prophylactic Treatment
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End point description:

Total immunoglobulin antibodies (Immunoglobulin G [IgG], A [IgA], and M [IgM]) against CHO protein were analyzed using ELISA assay. As per planned analysis, data for this outcome measure were collected and reported per sequence (Prophylaxis Cohort I: TAK-755 Then SoC and Prophylaxis Cohort II: SoC Then TAK-755) for the prophylaxis cohorts only. The Safety Analysis Set included all participants treated with at least 1 dose of TAK-755 or SoC treatment after randomization. 2 participants randomized to Prophylaxis Cohort I received actual treatment as per Prophylaxis Cohort II and are presented per actual treatment arm.

End point type	Secondary
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End point timeframe:

Up to 79.6 months

End point values	Prophylaxis Cohort I: TAK-755 Then SoC	Prophylaxis Cohort II: SoC Then TAK-755		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21	27		
Units: participants	0	2		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in cTTP-Patient Experience Questionnaire (cTTP-PEQ) Total Score

End point title	Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in cTTP-Patient Experience Questionnaire (cTTP-PEQ) Total Score
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End point description:

cTTP-PEQ has 26 questions that assess participant's experience of fatigue, joint, muscle, abdominal & chest pain in previous 24 hours, neurologic manifestations, bruising, feelings of depression & mood alterations, & activity limitation in past 7 days, & participant's attitudes, experienced side effects, work/school absences & travel impact associated with treatment received for TTP during previous 2 weeks. cTTP PEQ is focused on measuring symptoms & impacts of disease. Total scores range: 0-162. Higher score indicates greater burden & poor quality of life. Per planned analysis, for prophylaxis cohorts data for this endpoint was collected & reported by categorizing as per Prophylaxis Periods & per age groups,  $\geq 12$  years, 12-18 years,  $\geq 18$  years for both on demand & prophylaxis cohorts. 999999: SD was not estimable for single

participant.99999:no participants were analysed in specified category.No participants in OD Cohorts had cTTP-PEQ data available for analysis at scheduled post-baseline visit.n:variable for each category.

End point type	Secondary
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End point timeframe:

Baseline, Urgent Treatment Period: Day 7, End of Period 1 (Month 6), End of Period 2 (Month 12), and End of Period 3. Modified FAS. Number of subjects analysed was variable for each category.

End point values	Prophylaxis Cohort: TAK-755	Prophylaxis Cohort: SoC	On Demand Cohort I: TAK-755	On Demand Cohort II: SoC
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	12	0 <sup>[5]</sup>	0 <sup>[6]</sup>
Units: score on a scale				
arithmetic mean (standard deviation)				
≥12 years: Total Score, End of Period 1	-2.6 (± 24.17)	-2.2 (± 12.47)	()	()
≥12 years: Total Score, End of Period 2	-10.4 (± 18.13)	-1.4 (± 18.38)	()	()
≥12 years: Total Score, End of Period 3	-10.6 (± 13.13)	99999 (± 99999)	()	()
12 to < 18 years: Total Score, End of Period 1	99999 (± 99999)	12.0 (± 999999)	()	()
12 to < 18 years: Total Score, End of Period 2	13.0 (± 999999)	99999 (± 99999)	()	()
12 to < 18 years: Total Score, End of Period 3	-6.0 (± 996999)	99999 (± 99999)	()	()
≥18 years: Total Score, End of Period 1	-2.6 (± 24.17)	-3.5 (± 12.22)	()	()
≥18 years: Total Score, End of Period 2	-12.5 (± 17.37)	-1.4 (± 18.38)	()	()
≥18 years: Total Score, End of Period 3	-10.9 (± 13.41)	99999 (± 99999)	()	()
≥12 years: Total Score, Urgent Treatment Period Da	99999 (± 99999)	99999 (± 99999)	()	()
≥18years:Total Score,Urgent Treatment Period Day7	99999 (± 99999)	99999 (± 99999)	()	()
12 to < 18 years: Total Score, Urgent Treatment D7	99999 (± 99999)	99999 (± 99999)	()	()

Notes:

[5] - No participants in the on demand cohorts had post-baseline data.

[6] - No participants in the on demand cohorts had post-baseline data.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in Physical and Mental Component Scores of the 36-Item Short Form Health Survey Version 2 (SF-36v2)

End point title	Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in Physical and Mental Component Scores of the 36-Item Short Form Health Survey Version 2 (SF-36v2)
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End point description:

SF-36v2:questionnaire to evaluate participant's health related quality of life,has 36 questions related to 8 health dimensions:physical functioning,role-physical(role limitations due to physical health problems),bodily pain,general health,vitality(energy/fatigue),social functioning,role-emotional(role limitations due to emotional problems),&mental health(MH).Physical component score(between 0

using physical functioning,role-physical,bodily pain,general health scales.Higher scores=better quality of life.Mental component score(between 0-100)was generated using vitality,social functioning,role-emotional,&MH scales.Higher scores=better quality of life.Per planned analysis,prophylaxis cohorts(PC) data was collected&reported by categorizing as per Prophylaxis Periods&per component scores for both on demand&PC.99999:no participants analysed in specified category.ModifiedFAS.No post-baseline SF-36v2 data was available for OD Cohort participants.n=variable for each category.

End point type	Secondary
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End point timeframe:

Baseline, Urgent Treatment Period: Day 7, End of Period 1 (Month 6), End of Period 2 (Month 12), and End of Period 3 (Month 19)

End point values	Prophylaxis Cohort I: TAK-755 Then SoC	Prophylaxis Cohort II: SoC Then TAK-755	On Demand Cohort I: TAK-755	On Demand Cohort II: SoC
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	21	11	0 <sup>[7]</sup>	0 <sup>[8]</sup>
Units: score on a scale				
arithmetic mean (standard deviation)				
Physical Component Score: End of Period 1	3.934 (± 10.1098)	-0.532 (± 4.8297)	()	()
Physical Component Score: End of Period 2	3.121 (± 6.3196)	2.625 (± 6.4219)	()	()
Physical Component Score: End of Period 3	1.019 (± 4.8970)	99999 (± 99999)	()	()
Mental Component Score: End of Period 1	-7.263 (± 7.4244)	5.418 (± 5.0244)	()	()
Mental Component Score: End of Period 2	2.880 (± 5.2646)	-4.853 (± 9.9302)	()	()
Mental Component Score: End of Period 3	3.852 (± 7.4066)	99999 (± 99999)	()	()
Physical Component Score: Urgent Treatment D7	99999 (± 99999)	99999 (± 99999)	()	()
Mental Component Score: Urgent Treatment D7	99999 (± 99999)	99999 (± 99999)	()	()

Notes:

[7] - No participants in the on demand cohorts had post-baseline data.

[8] - No participants in the on demand cohorts had post-baseline data.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in Abbreviated 9-item Treatment Satisfaction Questionnaire for Medication (TSQM-9) Domain Scores

End point title	Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in Abbreviated 9-item Treatment Satisfaction Questionnaire for Medication (TSQM-9) Domain Scores
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End point description:

TSQM is a treatment satisfaction measure used to assess the overall level of participant's satisfaction or dissatisfaction with their medications. TSQM-9 is a 9-item, validated, self-administered instrument used to assess participant's satisfaction with medication. The three domains assessed are treatment effectiveness, convenience, and global satisfaction. The score of each of the 3 domains is based on an algorithm to create a score of 0 to 100. Higher score indicates greater satisfaction in that domain. As per planned analysis, for the prophylaxis cohorts data for this outcome measure were collected and reported by categorizing as per Prophylaxis Periods and per domain scores for both on demand and prophylaxis cohorts. '99999' indicates that no participants were analysed in the specified category.



Modified FAS. Number of subjects analysed was variable for each category. No participants in the OD Cohorts had TSQM-9 data available for analysis at scheduled post-baseline visits.

End point type	Secondary
End point timeframe:	
Baseline, Urgent Treatment Period: Day 7, End of Period 1 (Month 6), End of Period 2 (Month 12), and End of Period 3 (Month 19)	

End point values	Prophylaxis Cohort I: TAK-755 Then SoC	Prophylaxis Cohort: SoC	On Demand Cohort I: TAK-755	On Demand Cohort II: SoC
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	10	0 <sup>[9]</sup>	0 <sup>[10]</sup>
Units: score on a scale				
arithmetic mean (standard deviation)				
Treatment Effectiveness Score: End of Period 1	26.8519 (± 36.07548)	4.4444 (± 13.55778)	()	()
Treatment Effectiveness Score: End of Period 2	25.0000 (± 17.42119)	12.9630 (± 17.09330)	()	()
Treatment Effectiveness Score: End of Period 3	22.2222 (± 20.11626)	99999 (± 99999)	()	()
Convenience Score: End of Period 1	36.1111 (± 16.75900)	1.6667 (± 11.43059)	()	()
Convenience Score: End of Period 2	27.7778 (± 15.27076)	14.8148 (± 27.81479)	()	()
Convenience Score: End of Period 3	21.0526 (± 29.48919)	99999 (± 99999)	()	()
Global Satisfaction Score: End of Period 1	28.5714 (± 9.03508)	5.0000 (± 16.85270)	()	()
Global Satisfaction Score: End of Period 2	23.5714 (± 16.85270)	14.2857 (± 21.66536)	()	()
Global Satisfaction Score: End of Period 3	22.9323 (± 16.07433)	99999 (± 99999)	()	()
Treatment Effectiveness Score: Urgent Treatment D7	99999 (± 99999)	99999 (± 99999)	()	()
Convenience Score: Urgent Treatment Period Day 7	99999 (± 99999)	99999 (± 99999)	()	()
Global Satisfaction Score: Urgent Treatment D7	99999 (± 99999)	99999 (± 99999)	()	()

Notes:

[9] - No participants in the on demand cohorts had post-baseline data.

[10] - No participants in the on demand cohorts had post-baseline data.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in EuroQoL 5 Dimensions Questionnaire 3-Level (EQ-5D-3L) Domain Scores

End point title	Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in EuroQoL 5 Dimensions Questionnaire 3-Level (EQ-5D-3L) Domain Scores
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End point description:

EQ-5D-3L health questionnaire is a participant-answered questionnaire scoring 5 dimensions(domains) - mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension is scored on an ordinal scale with 3 available levels of response and scores ranging from 1 to 3, "no problems,"

"some problems," and "extreme problems," respectively. Lower scores for the domains in the EQ-5D-3L indicate improvement. As per planned analysis, for the prophylaxis cohorts data for this outcome measure were collected and reported by categorizing as per Prophylaxis Periods and per domain scores for both on demand and prophylaxis cohorts. '99999' indicates that no participants were analysed in the specified category. Modified FAS. Number of subjects analysed was variable for each category. No participants in the OD Cohorts had EQ-5D-3L data available for analysis at scheduled post-baseline visits.

End point type	Secondary
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End point timeframe:

Baseline, Urgent Treatment Period: Day 7, End of Period 1 (Month 6), End of Period 2 (Month 12), and End of Period 3 (Month 19)

End point values	Prophylaxis Cohort I: TAK-755 Then SoC	Prophylaxis Cohort: SoC	On Demand Cohort I: TAK-755	On Demand Cohort II: SoC
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	10	0 <sup>[11]</sup>	0 <sup>[12]</sup>
Units: score on a scale				
arithmetic mean (standard deviation)				
Mobility: End of Period 1	0.3 (± 0.46)	-0.1 (± 0.32)	()	()
Mobility: End of Period 2	-0.1 (± 0.30)	0.0 (± 0.00)	()	()
Mobility: End of Period 3	-0.1 (± 0.23)	99999 (± 99999)	()	()
Self-Care: End of Period 1	0.1 (± 0.35)	0.0 (± 0.00)	()	()
Self-Care: End of Period 2	0.0 (± 0.00)	0.0 (± 0.00)	()	()
Self-Care: End of Period 3	-0.1 (± 0.23)	99999 (± 99999)	()	()
Usual Activities: End of Period 1	0.0 (± 0.53)	-0.2 (± 0.42)	()	()
Usual Activities: End of Period 2	0.0 (± 0.45)	0.0 (± 0.63)	()	()
Usual Activities: End of Period 3	-0.1 (± 0.40)	99999 (± 99999)	()	()
Pain/Discomfort: End of Period 1	0.3 (± 0.46)	-0.2 (± 0.63)	()	()
Pain/Discomfort: End of Period 2	-0.3 (± 0.65)	0.2 (± 0.41)	()	()
Pain/Discomfort: End of Period 3	-0.2 (± 0.54)	99999 (± 99999)	()	()
Anxiety/Depression: End of Period 1	0.1 (± 0.64)	0.0 (± 0.00)	()	()
Anxiety/Depression: End of Period 2	-0.1 (± 0.30)	0.0 (± 0.00)	()	()
Anxiety/Depression: End of Period 3	-0.1 (± 0.46)	99999 (± 99999)	()	()
Mobility: Urgent Treatment Period Day 7	99999 (± 99999)	99999 (± 99999)	()	()
Self-Care: Urgent Treatment Period Day 7	99999 (± 99999)	99999 (± 99999)	()	()
Usual Activities: Urgent Treatment Period Day 7	99999 (± 99999)	99999 (± 99999)	()	()
Pain/Discomfort: Urgent Treatment Period Day 7	99999 (± 99999)	99999 (± 99999)	()	()
Anxiety/Depression: Urgent Treatment Period Day 7	99999 (± 99999)	99999 (± 99999)	()	()

Notes:

[11] - No participants in the on demand cohorts had post-baseline data.

[12] - No participants in the on demand cohorts had post-baseline data.

## Statistical analyses

## Secondary: Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in EQ-5D-youth (EQ-5D-Y) Domain Scores

End point title	Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in EQ-5D-youth (EQ-5D-Y) Domain Scores
End point description:	
EQ-5D-Y:health questionnaire;participant aged from 8 to 16 years answered on 5 dimensions (domains)-mobility,self-care,usual activities,pain/discomfort&anxiety/depression.EQ-5D-Y:includes 5 descriptive items:Mobility,self-care,doing usual activities,having pain/discomfort,& feeling anxiety/depressed.Each dimension is scored at 3 levels:1=No problems,2=some problems,&3=a lot of problems.Lower scores indicate improvement.As per planned analysis,for prophylaxis cohorts data for this outcome measure was collected&reported by categorizing as per Prophylaxis Periods per domain scores for both on demand&prophylaxis cohorts.'999999':SD was not estimable for a single participant.'999999':no participants were analysed in specified category.Modified FAS.Number of subjects analysed was variable for each category.No participants in OD Cohorts had EQ-5D-Y data available for analysis at scheduled post-baseline visits.	
End point type	Secondary
End point timeframe:	
Baseline, Urgent Treatment Period: Day 7, End of Period 1 (Month 6), End of Period 2 (Month 12), and End of Period 3 (Month 19)	

End point values	Prophylaxis Cohort I: TAK-755 Then SoC	Prophylaxis Cohort: SoC	On Demand Cohort I: TAK-755	On Demand Cohort II: SoC
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	3	0 <sup>[13]</sup>	0 <sup>[14]</sup>
Units: score on a scale				
arithmetic mean (standard deviation)				
Mobility: End of Period 1	0.0 (± 999999)	0.0 (± 0.00)	()	()
Mobility: End of Period 2	0.0 (± 0.00)	0.0 (± 999999)	()	()
Mobility: End of Period 3	0.0 (± 0.00)	99999 (± 99999)	()	()
Self-Care: End of Period 1	0.0 (± 999999)	0.0 (± 0.00)	()	()
Self-Care: End of Period 2	0.0 (± 0.00)	0.0 (± 999999)	()	()
Self-Care: End of Period 3	0.0 (± 0.00)	99999 (± 99999)	()	()
Usual Activities: End of Period 1	0.0 (± 999999)	0.0 (± 0.00)	()	()
Usual Activities: End of Period 2	0.0 (± 0.00)	0.0 (± 999999)	()	()
Usual Activities: End of Period 3	0.0 (± 0.00)	99999 (± 99999)	()	()
Pain/Discomfort: End of Period 1	1.0 (± 999999)	-0.7 (± 0.58)	()	()
Pain/Discomfort: End of Period 2	-0.7 (± 0.58)	0.0 (± 999999)	()	()
Pain/Discomfort: End of Period 3	-0.3 (± 0.96)	99999 (± 99999)	()	()
Anxiety/Depression: End of Period 1	0.0 (± 999999)	0.0 (± 0.00)	()	()
Anxiety/Depression: End of Period 2	0.3 (± 0.58)	0.0 (± 999999)	()	()
Anxiety/Depression: End of Period 3	0.0 (± 0.00)	99999 (± 99999)	()	()
Mobility: Urgent Treatment Period Day 7	99999 (± 99999)	99999 (± 99999)	()	()
Self-Care: Urgent Treatment Period Day 7	99999 (± 99999)	99999 (± 99999)	()	()
Usual Activities: Urgent Treatment Period Day 7	99999 (± 99999)	99999 (± 99999)	()	()

Pain/Discomfort: Urgent Treatment Period Day 7	99999 (± 99999)	99999 (± 99999)	()	()
Anxiety/Depression: Urgent Treatment Period Day 7	99999 (± 99999)	99999 (± 99999)	()	()

Notes:

[13] - No participants in the on demand cohorts had post-baseline data.

[14] - No participants in the on demand cohorts had post-baseline data.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in Pediatric Quality of Life Inventory (Peds QL) Scale Total Scores

End point title	Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in Pediatric Quality of Life Inventory (Peds QL) Scale Total Scores
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End point description:

PedsQL:generic health related quality of life instrument designed specifically for pediatric population&captures domains like physical functioning,emotional functioning,social functioning,school functioning,psychosocial summary,physical health&total score.Peds-QL total score consists 23 items of all domains.This modular instrument uses 5-point scale:0(never)-4(almost always).Items are reversed scored&linearly transformed to 0-100 scale as follows:0=100,1=75,2=50,3=25,4=0.Higher scores:better quality of life.Per planned analysis,prophylaxis cohorts data for this endpoint were collected&reported by categorizing as per Prophylaxis Periods&per age groups,2-<5years,5-<8years,8-<13years,&13-<18years,for both on demand&prophylaxis cohorts.999999:SD was not estimable for a single participant.999999:no participants were analysed in specified category.No participants in OD Cohorts had Peds QL data available for analysis at scheduled post-baseline visits.n=variable for each reported category.

End point type	Secondary
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End point timeframe:

Baseline, Urgent Treatment Period: Day 7, End of Period 1 (Month 6), End of Period 2 (Month 12), and End of Period 3 (Month 19)

End point values	Prophylaxis Cohort I: TAK-755 Then SoC	Prophylaxis Cohort: SoC	On Demand Cohort I: TAK-755	On Demand Cohort II: SoC
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	5	0 <sup>[15]</sup>	0 <sup>[16]</sup>
Units: score on a scale				
arithmetic mean (standard deviation)				
2 to< 5 years,End of Period 1	25.0000 (± 47.14045)	99999 (± 99999)	()	()
2 to< 5 years, End of Period 2	99999 (± 99999)	27.3810 (± 47.14045)	()	()
2 to< 5 years, End of Period 3	24.4048 (± 49.66583)	99999 (± 99999)	()	()
5 to< 8 years, End of Period 1	29.3478 (± 999999)	-16.3043 (± 999999)	()	()
5 to< 8 years, End of Period 2	-6.5217 (± 999999)	32.6087 (± 999999)	()	()
5 to< 8 years, End of Period 3	17.9348 (± 19.21486)	99999 (± 99999)	()	()
8 to< 13 years, End of Period 1	-2.1739 (± 999999)	15.2174 (± 13.83470)	()	()
8 to < 13 years, End of Period 2	8.6957 (± 23.05783)	1.0870 (± 999999)	()	()

8 to< 13 years, End of Period 3	5.7971 (± 7.39876)	99999 (± 99999)	()	()
13 to< 18 years, End of Period 1	99999 (± 99999)	99999 (± 99999)	()	()
13 to< 18 years, End of Period 2	99999 (± 99999)	99999 (± 99999)	()	()
13 to< 18 years, End of Period 3	99999 (± 99999)	99999 (± 99999)	()	()
2 to < 5 years: Urgent Treatment Period Day 7	99999 (± 99999)	99999 (± 99999)	()	()
5 to< 8 years: Urgent Treatment Period Day 7	99999 (± 99999)	99999 (± 99999)	()	()
8 to < 13 years: Urgent Treatment Period Day 7	99999 (± 99999)	99999 (± 99999)	()	()

Notes:

[15] - No participants in the on demand cohorts had post-baseline data.

[16] - No participants in the on demand cohorts had post-baseline data.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Resource Utilization: Annualized Length of Hospital Stay for Acute TTP Events for Prophylaxis Cohorts

End point title	Resource Utilization: Annualized Length of Hospital Stay for Acute TTP Events for Prophylaxis Cohorts
End point description:	
The annualized number of days participants stayed in hospital for acute TTP events were assessed. As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts in a combined manner for Periods 1 and 2 for SoC treatment and for Periods 1, 2, and 3 for TAK-755 treatment respectively. Modified FAS.	
End point type	Secondary
End point timeframe:	
Up to 79.6 months	

End point values	Prophylaxis Cohort: TAK-755	Prophylaxis Cohort: SoC		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44	45		
Units: days/year				
median (full range (min-max))	0.00 (0.0 to 0.0)	0.00 (0.0 to 3.4)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Resource Utilization: Annualized Number of Acute Care Visits for Prophylaxis Cohorts

End point title	Resource Utilization: Annualized Number of Acute Care Visits for Prophylaxis Cohorts
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End point description:

Annualized number of acute care visits was calculated as the number of acute care visits  $\times$  365.25/(End date - treatment start date + 1). As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts in a combined manner for Periods 1 and 2 for SoC treatment and for Periods 1, 2, and 3 for TAK-755 treatment respectively. Modified FAS.

End point type	Secondary
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End point timeframe:

Up to 79.6 months

End point values	Prophylaxis Cohort: TAK-755	Prophylaxis Cohort: SoC		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44	45		
Units: acute care visits per year				
arithmetic mean (standard deviation)	0.60 ( $\pm$ 1.391)	0.14 ( $\pm$ 0.498)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Resource Utilization: Annualized Number of Days Missed From School or Work for Prophylaxis Cohorts

End point title	Resource Utilization: Annualized Number of Days Missed From School or Work for Prophylaxis Cohorts
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End point description:

Annualized number of days missed from school or work were assessed. As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts in a combined manner for Periods 1 and 2 for SoC treatment and for Periods 1, 2, and 3 for TAK-755 treatment respectively. Modified FAS.

End point type	Secondary
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End point timeframe:

Up to 79.6 months

End point values	Prophylaxis Cohort: TAK-755	Prophylaxis Cohort: SoC		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44	45		
Units: days/year				
median (full range (min-max))	0.00 (0.0 to 180.3)	0.00 (0.0 to 294.5)		

## Statistical analyses



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug up to end of study (79.6 months)

Adverse event reporting additional description:

Safety Analysis Set=all participants treated with at least 1 dose of TAK-755/SoC treatment after randomization.As per planned analysis,data for AEs were collected & reported in a combined manner irrespective of Prophylaxis Periods & partitioned as per treatment received during course of study,presented for on demand & prophylaxis cohorts.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.1
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### Reporting groups

Reporting group title	Prophylaxis Cohort: TAK-755
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Reporting group description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. Thereafter participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

Reporting group title	On Demand Cohort I: TAK-755
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Reporting group description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the TAK-755 cohort of the Urgent Treatment Period received initial dose of IV infusions 40 IU/kg [+/- 4 IU/kg] TAK-755 ORT or TAK-755 SIN infusion on Day 1 followed by a subsequent dose IV infusions of 20 IU/kg [+/- 2 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 2 and an additional daily dose IV infusions of 15 IU/kg [+/- 1.5 IU/kg] TAK-755 on Day 3 until 2 days after the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

Reporting group title	On Demand Cohort II: SoC
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Reporting group description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the SoC cohort of the Urgent Treatment Period received the investigator-recommended SoC and dosing regimen until the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

Reporting group title	Prophylaxis Cohort: SoC
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Reporting group description:

Participants received SoC for 6 months in either Period 1 or Period 2.

Serious adverse events	Prophylaxis Cohort: TAK-755	On Demand Cohort I: TAK-755	On Demand Cohort II: SoC
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 47 (12.77%)	0 / 2 (0.00%)	1 / 4 (25.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Platelet count decreased			



subjects affected / exposed	0 / 47 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Shoulder fracture			
subjects affected / exposed	0 / 47 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 47 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 47 (2.13%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 47 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombotic thrombocytopenic purpura			
subjects affected / exposed	1 / 47 (2.13%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed	0 / 47 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 47 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 47 (2.13%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	1 / 47 (2.13%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adnexal torsion			
subjects affected / exposed	1 / 47 (2.13%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Sinus disorder			
subjects affected / exposed	0 / 47 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 47 (2.13%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			

subjects affected / exposed	1 / 47 (2.13%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis clostridial			
subjects affected / exposed	1 / 47 (2.13%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	Prophylaxis Cohort: SoC		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 48 (16.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Platelet count decreased			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Shoulder fracture			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 48 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Headache			

subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	2 / 48 (4.17%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Thrombotic thrombocytopenic purpura			
subjects affected / exposed	0 / 48 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 48 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 48 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adnexal torsion			

subjects affected / exposed	0 / 48 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Sinus disorder			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 48 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 48 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis clostridial			
subjects affected / exposed	0 / 48 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	Prophylaxis Cohort: TAK-755	On Demand Cohort I: TAK-755	On Demand Cohort II: SoC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 47 (82.98%)	0 / 2 (0.00%)	3 / 4 (75.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 47 (6.38%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Haematoma			

subjects affected / exposed occurrences (all)	3 / 47 (6.38%) 4	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 47 (6.38%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Fatigue			
subjects affected / exposed	5 / 47 (10.64%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	5	0	0
Malaise			
subjects affected / exposed	3 / 47 (6.38%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Pyrexia			
subjects affected / exposed	6 / 47 (12.77%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	11	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	3 / 47 (6.38%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	4	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	5 / 47 (10.64%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	8	0	0
Rhinorrhoea			
subjects affected / exposed	5 / 47 (10.64%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	5	0	0
Cough			
subjects affected / exposed	8 / 47 (17.02%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	10	0	0
Epistaxis			
subjects affected / exposed	3 / 47 (6.38%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	4	0	0
Investigations			
Platelet count decreased			
subjects affected / exposed	4 / 47 (8.51%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	7	0	0

Blood lactate dehydrogenase increased subjects affected / exposed occurrences (all)	4 / 47 (8.51%) 4	0 / 2 (0.00%) 0	1 / 4 (25.00%) 2
Injury, poisoning and procedural complications Immunisation reaction subjects affected / exposed occurrences (all)  Allergic transfusion reaction subjects affected / exposed occurrences (all)	3 / 47 (6.38%) 4  0 / 47 (0.00%) 0	0 / 2 (0.00%) 0  0 / 2 (0.00%) 0	0 / 4 (0.00%) 0  1 / 4 (25.00%) 1
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)  Headache subjects affected / exposed occurrences (all)  Hypoaesthesia subjects affected / exposed occurrences (all)  Lethargy subjects affected / exposed occurrences (all)  Migraine subjects affected / exposed occurrences (all)  Paraesthesia subjects affected / exposed occurrences (all)  Syncope subjects affected / exposed occurrences (all)	5 / 47 (10.64%) 13  15 / 47 (31.91%) 106  4 / 47 (8.51%) 4  5 / 47 (10.64%) 12  7 / 47 (14.89%) 18  1 / 47 (2.13%) 1  4 / 47 (8.51%) 4	0 / 2 (0.00%) 0  0 / 2 (0.00%) 0  0 / 2 (0.00%) 0  0 / 2 (0.00%) 0  0 / 2 (0.00%) 0  0 / 2 (0.00%) 0	0 / 4 (0.00%) 0  1 / 4 (25.00%) 1  1 / 4 (25.00%) 1  0 / 4 (0.00%) 0  1 / 4 (25.00%) 1  0 / 4 (0.00%) 0

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 47 (6.38%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Thrombocytopenia			
subjects affected / exposed	3 / 47 (6.38%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences (all)	5	0	1
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	3 / 47 (6.38%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	8 / 47 (17.02%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	16	0	0
Vomiting			
subjects affected / exposed	8 / 47 (17.02%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	8	0	0
Nausea			
subjects affected / exposed	8 / 47 (17.02%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences (all)	15	0	1
Diarrhoea			
subjects affected / exposed	9 / 47 (19.15%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	14	0	0
Skin and subcutaneous tissue disorders			
Petechiae			
subjects affected / exposed	0 / 47 (0.00%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	2 / 47 (4.26%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Pruritus			
subjects affected / exposed	2 / 47 (4.26%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences (all)	3	0	1
Urticaria			
subjects affected / exposed	2 / 47 (4.26%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0



Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	2 / 47 (4.26%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Arthralgia			
subjects affected / exposed	3 / 47 (6.38%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	5	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	8 / 47 (17.02%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	8	0	0
Influenza			
subjects affected / exposed	3 / 47 (6.38%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	5	0	0
Nasopharyngitis			
subjects affected / exposed	8 / 47 (17.02%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	18	0	0
Upper respiratory tract infection			
subjects affected / exposed	6 / 47 (12.77%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	7	0	0
Tooth abscess			
subjects affected / exposed	1 / 47 (2.13%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Rhinitis			
subjects affected / exposed	7 / 47 (14.89%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	8	0	0
Pharyngitis			
subjects affected / exposed	3 / 47 (6.38%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Oral herpes			
subjects affected / exposed	3 / 47 (6.38%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	5	0	0
Viral infection			
subjects affected / exposed	4 / 47 (8.51%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	5	0	0
Metabolism and nutrition disorders			

Iron deficiency subjects affected / exposed occurrences (all)	3 / 47 (6.38%) 3	0 / 2 (0.00%) 0	0 / 4 (0.00%) 0
<b>Non-serious adverse events</b>	Prophylaxis Cohort: SoC		
Total subjects affected by non-serious adverse events subjects affected / exposed	37 / 48 (77.08%)		
Vascular disorders Hypertension subjects affected / exposed occurrences (all)  Haematoma subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0  2 / 48 (4.17%) 3		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)  Fatigue subjects affected / exposed occurrences (all)  Malaise subjects affected / exposed occurrences (all)  Pyrexia subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1  7 / 48 (14.58%) 10  2 / 48 (4.17%) 2  2 / 48 (4.17%) 4		
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)  Rhinorrhoea	4 / 48 (8.33%) 6		

subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0		
Cough subjects affected / exposed occurrences (all)	3 / 48 (6.25%) 3		
Epistaxis subjects affected / exposed occurrences (all)	4 / 48 (8.33%) 8		
Investigations Platelet count decreased subjects affected / exposed occurrences (all)	5 / 48 (10.42%) 8		
Blood lactate dehydrogenase increased subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1		
Injury, poisoning and procedural complications Immunisation reaction subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 2		
Allergic transfusion reaction subjects affected / exposed occurrences (all)	7 / 48 (14.58%) 8		
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	3 / 48 (6.25%) 3		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0		
Headache subjects affected / exposed occurrences (all)	10 / 48 (20.83%) 70		
Hypoaesthesia subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0		

Lethargy subjects affected / exposed occurrences (all)	3 / 48 (6.25%) 6		
Migraine subjects affected / exposed occurrences (all)	2 / 48 (4.17%) 4		
Paraesthesia subjects affected / exposed occurrences (all)	2 / 48 (4.17%) 4		
Syncope subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	2 / 48 (4.17%) 2		
Thrombocytopenia subjects affected / exposed occurrences (all)	3 / 48 (6.25%) 9		
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	6 / 48 (12.50%) 7		
Vomiting subjects affected / exposed occurrences (all)	6 / 48 (12.50%) 8		
Nausea subjects affected / exposed occurrences (all)	2 / 48 (4.17%) 4		
Diarrhoea subjects affected / exposed occurrences (all)	2 / 48 (4.17%) 3		
Skin and subcutaneous tissue disorders			

Petechiae			
subjects affected / exposed	0 / 48 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	4 / 48 (8.33%)		
occurrences (all)	5		
Pruritus			
subjects affected / exposed	3 / 48 (6.25%)		
occurrences (all)	5		
Urticaria			
subjects affected / exposed	7 / 48 (14.58%)		
occurrences (all)	9		
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	3 / 48 (6.25%)		
occurrences (all)	3		
Arthralgia			
subjects affected / exposed	3 / 48 (6.25%)		
occurrences (all)	4		
Infections and infestations			
COVID-19			
subjects affected / exposed	3 / 48 (6.25%)		
occurrences (all)	3		
Influenza			
subjects affected / exposed	0 / 48 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	6 / 48 (12.50%)		
occurrences (all)	13		
Upper respiratory tract infection			
subjects affected / exposed	3 / 48 (6.25%)		
occurrences (all)	3		
Tooth abscess			
subjects affected / exposed	0 / 48 (0.00%)		
occurrences (all)	0		
Rhinitis			

subjects affected / exposed	2 / 48 (4.17%)		
occurrences (all)	2		
Pharyngitis			
subjects affected / exposed	0 / 48 (0.00%)		
occurrences (all)	0		
Oral herpes			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences (all)	1		
Viral infection			
subjects affected / exposed	2 / 48 (4.17%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Iron deficiency			
subjects affected / exposed	2 / 48 (4.17%)		
occurrences (all)	2		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 March 2017	The following changes were made as per Amendment 1: 1. Replaced hereditary thrombotic thrombocytopenic purpura (hTTP) with congenital thrombotic thrombocytopenic purpura (cTTP). 2. Adapted pharmacokinetic (PK) infusion numbers. 3. Removed PK test from dosing visits.
09 May 2017	The following changes were made as per Amendment 2: 1. ADAMTS13 trough levels were re-defined as pre-infusion ADAMTS13. 2. Defined severe TTP signs. 3. Specified that participants enrolling in the on-demand cohort and moving to the prophylaxis cohort were analysed separately and were not counted towards the 40 participants cap on the prophylaxis cohort. 4. Updated criteria for enrolling adolescent participants.
06 December 2018	The following changes were made as per Amendment 5: 1. Changed hereditary TTP to congenital TTP. 2. Added SHP655, as the new name given to BAX 930. 3. Numbers of participants for planned enrolment (i.e., sample size changed from 60 to 62), enrolment of pediatric participants, duration of time for participants in the prophylaxis cohort, and planned study period dates and study duration were amended. 4. PK/PD points were added to reflect the PK comparability study. 5. Period 3 treatment phase was added.
06 March 2020	The following changes were made as per Amendment 9: 1. Added TAK-755, as the new name given to SHP655. 2. 6 more participants were added to the study, in the prophylaxis cohort. 3. Health Related Quality of Life and Resource Utilization were included under secondary objectives.
23 February 2021	The following changes were made as per Amendment 11: 1. The estimated study completion date was changed from June 2023 to January 2024. 2. The total duration of the study was increased from 60 months to 70 months. 3. After 30 September 2021, screened participants in the prophylactic cohort could initiate the study with TAK-755 SIN. 4. Secondary efficacy outcome measures text was changed from "number and incidence of acute TTP episodes..." to "proportion of acute TTP episodes...".
18 April 2021	The following changes were made as per Amendment 13: 1. Participants receiving a COVID-19 vaccination during the study period were monitored frequently by telephonic health checks and for thrombocytopenia for 14 consecutive days following vaccination, as deemed appropriate by the investigator.
18 November 2021	The following changes were made as per Amendment 15: 1. Study completion dates were updated as: Study Primary Completion date changed from Feb 2023 to Nov 2023 and Study Completion from Jan 2024 to Mar 2024. 2. Sentence was removed: "Participants who switch from the on-demand to the prophylaxis cohort upon resolution of the acute event will be excluded from the primary efficacy analysis." 3. Secondary outcome measure 8 was revised to "Incidence of supplemental doses prompted by subacute TTP events".

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported