Clinical trial results:
A Phase 2, Multicenter, Randomized, Placebo-controlled, Double Blind Study in Patients With Acquired Thrombotic Thrombocytopenic Purpura (aTTP) to Evaluate the Pharmacokinetics, Safety, and Efficacy of rADAMTS-13 (SHP655) Administered in Addition to Standard of Care (SoC) Treatment

Summary

EudraCT number	2018-003775-35
Trial protocol	GB DE ES IT
Global end of trial date	05 August 2021

Results information

Result version number	v1 (current)
This version publication date	20 August 2022
First version publication date	20 August 2022

Trial information

Trial identification

Sponsor protocol code	SHP655-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03922308
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Shire
Sponsor organisation address	300 Shire Way, Lexington, United States, MA 02421
Public contact	Study Director, Shire, ClinicalTransparency@shire.com
Scientific contact	Study Director, Shire, ClinicalTransparency@shire.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 August 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 August 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to assess the pharmacokinetics (PK) of ADAMTS-13 in aTTP participant treated for an acute episode by daily plasma exchange (PEX), immunosuppressant therapy, with or without SHP655 supplementation and to study the PK/ pharmacodynamic (PD) relationship between ADAMTS-13 activity levels on pathophysiological biomarkers as well as clinical efficacy parameters.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 October 2019
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	Canada: 3
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	United Kingdom: 11
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	28
EEA total number of subjects	8

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	25
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 12 investigative sites in Canada, France, Great Britain, Spain and United States from 09 October 2019 to 05 August 2021.

Pre-assignment

Screening details:

Participants with a diagnosis of acquired thrombotic thrombocytopenic purpura (aTTP) were enrolled to receive placebo, SHP655 once daily (QD) and twice daily (BID) in a ratio of 1:1:1 in this study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Subject, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Standard of Care (SoC) + Placebo

Arm description:

Participants received SoC daily plasma exchange (PEX) followed by placebo immediately and 12 +/- 1 hours after completion of PEX until remission was achieved (up to approximately 6 months).

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

SHP655 Matching Placebo intravenous (IV) infusion

Investigational medicinal product name	Standard of Care
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

PEX as SoC

Arm title	SoC + SHP655 + Placebo

Arm description:

Participants received SoC daily PEX and SHP655 40 +/- 4 international units per kilogram (IU/kg), IV injection, QD, immediately after PEX and placebo 12 +/- 1 hours after completion of PEX until remission was achieved (up to approximately 6 months).

Arm type	Experimental
Investigational medicinal product name	Standard of Care
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

PEX as SoC

Investigational medicinal product name	SHP655
Investigational medicinal product code	
Other name	rADAMTS-13
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

SHP655 IV

Arm title	SoC + SHP655

Arm description:

Participants received SoC daily PEX and SHP655 40 +/- 4 IU/kg, IV injection, BID, immediately after PEX and 12 +/- 1 hours after completion of PEX until remission was achieved (up to approximately 6 months).

Arm type	Experimental
Investigational medicinal product name	Standard of Care
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

PEX as SoC

Investigational medicinal product name	SHP655
Investigational medicinal product code	
Other name	rADAMTS-13
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

SHP655 IV

Number of subjects in period 1	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655
Started	10	9	9
Pharmacokinetic Population	10	8	9
Completed	9	6	8
Not completed	1	3	1
Not Meeting Confirmatory Inclusion Criteria	-	1	-
Lost to follow-up	1	-	-
Reason not Specified	-	2	1

Baseline characteristics

Reporting groups	
Reporting group title	Standard of Care (SoC) + Placebo
Reporting group description:	
Participants received SoC daily plasma exchange (PEX) followed by placebo immediately and 12 +/- 1 hours after completion of PEX until remission was achieved (up to approximately 6 months).	
Reporting group title	SoC + SHP655 + Placebo
Reporting group description:	
Participants received SoC daily PEX and SHP655 40 +/- 4 international units per kilogram (IU/kg), IV injection, QD, immediately after PEX and placebo 12 +/- 1 hours after completion of PEX until remission was achieved (up to approximately 6 months).	
Reporting group title	SoC + SHP655
Reporting group description:	
Participants received SoC daily PEX and SHP655 40 +/- 4 IU/kg, IV injection, BID, immediately after PEX and 12 +/- 1 hours after completion of PEX until remission was achieved (up to approximately 6 months).	

Reporting group values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655
Number of subjects	10	9	9
Age Categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	41.2	51.9	48.4
standard deviation	± 10.80	± 14.81	± 14.93
Gender categorical Units: Subjects			
Female	8	6	5
Male	2	3	4
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	0
Not Hispanic or Latino	10	8	9
Unknown or Not Reported	0	0	0
Race/Ethnicity, Customized Units: Subjects			
Race American Indian or Alaska Native	0	0	0
Race Asian	0	1	0
Race Black or African American	4	1	2
Race White	6	5	6
Race Native Hawaiian or Other Pacific Islander	0	0	0
Race Other	0	2	0
Race Missing	0	0	1

Reporting group values	Total		
Number of subjects	28		

Age Categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	19		
Male	9		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1		
Not Hispanic or Latino	27		
Unknown or Not Reported	0		
Race/Ethnicity, Customized Units: Subjects			
Race American Indian or Alaska Native	0		
Race Asian	1		
Race Black or African American	7		
Race White	17		
Race Native Hawaiian or Other Pacific Islander	0		
Race Other	2		
Race Missing	1		

End points

End points reporting groups

Reporting group title	Standard of Care (SoC) + Placebo
Reporting group description:	
Participants received SoC daily plasma exchange (PEX) followed by placebo immediately and 12 +/- 1 hours after completion of PEX until remission was achieved (up to approximately 6 months).	
Reporting group title	SoC + SHP655 + Placebo
Reporting group description:	
Participants received SoC daily PEX and SHP655 40 +/- 4 international units per kilogram (IU/kg), IV injection, QD, immediately after PEX and placebo 12 +/- 1 hours after completion of PEX until remission was achieved (up to approximately 6 months).	
Reporting group title	SoC + SHP655
Reporting group description:	
Participants received SoC daily PEX and SHP655 40 +/- 4 IU/kg, IV injection, BID, immediately after PEX and 12 +/- 1 hours after completion of PEX until remission was achieved (up to approximately 6 months).	

Primary: ADAMTS-13 Activity Levels

End point title	ADAMTS-13 Activity Levels[1]
End point description:	
ADAMTS-13 Activity Levels was assessed by fluorescence resonance energy transfer (FRETS) ADAMTS13 activity, with or without SHP655 Supplementation. Schedule A (Days 1, 2, 3, 4, 6, 8, 11, and every 3 days thereafter) or Schedule B (Days 1, 2, 3, 5, 7, 9, 12, and every 3 days thereafter). Data is reported for multiple timepoints: within(≤)15 minutes pre-PEX & post-PEX;≤15 minutes 0.5-3 hours,4-6 hours post end of investigational product(IP) infusion 1;≤15 minutes,0.5-3 hours post end IP infusion 2;30 minutes pre-IP infusion 2 of Schedule A & Schedule B (up to Day 11 or 12).Pharmacokinetic (PK) Set:all enrolled participants with confirmed aTTP diagnosis who received at least 1 dose of investigational product and who had at least 1 evaluable post-dose PK value (ADAMTS-13 antigen and ADAMTS-13 activity).Overall number:participants available for analyses. 'n':participants with data available.9999: Data not estimable for 1 participant.99999:Data not estimable due to less participants.	
End point type	Primary
End point timeframe:	
Up to Days 11 or 12	

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: No Statistical data was collected for this outcome measure.

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: international units(IU)/ml				
arithmetic mean (standard deviation)				
Day 1: ≤15min Pre-PEX(n=8,7,8)	0.1439 (± 0.19247)	99999 (± 99999)	99999 (± 99999)	
Day 1: ≤15 min Post-PEX(n=9,8,9)	0.5418 (± 0.18345)	0.5011 (± 0.19236)	0.3029 (± 0.29020)	
Day 1: ≤15 min Post End of IP1(n=10,7,9)	0.4571 (± 0.19125)	2.012 (± 0.82832)	1.352 (± 0.93502)	
Day 1: 0.5-3 hr Post End of IP 1(n=10,7,9)	0.4420 (± 0.20895)	1.905 (± 0.83349)	1.266 (± 0.98904)	

Day 1: 4-6 hr Post End of IP 1(n=10,5,9)	0.3197 (± 0.20545)	1.163 (± 0.61343)	0.7912 (± 0.69403)	
Day 1: ≤30 min Pre-IP 2(n=10,6,9)	0.2108 (± 0.19731)	1.027 (± 0.55951)	0.4949 (± 0.54891)	
Day 1: ≤15 min Post End of IP 2(n=9,8,9)	0.2267 (± 0.18660)	1.022 (± 0.52060)	1.545 (± 1.0854)	
Day 1: 0.5-3 hr Post End of IP 2(n=8,7,9)	0.2007 (± 0.20012)	1.015 (± 0.56462)	1.300 (± 1.1114)	
Day 2: ≤15 min Pre-PEX(n=10,7,8)	0.1691 (± 0.15909)	0.7650 (± 0.61929)	0.9482 (± 0.99771)	
Day 2: ≤15 min Post-PEX(n=10,7,9)	0.5801 (± 0.16107)	0.7808 (± 0.36544)	0.8426 (± 0.54317)	
Day 2: ≤15 min Post End of IP 1(n=10,6,9)	0.5433 (± 0.20267)	1.965 (± 0.72122)	1.977 (± 0.98427)	
Day 2: 0.5-3 hr Post End of IP 1(n=10,8,9)	0.5281 (± 0.24842)	2.105 (± 1.0656)	2.153 (± 1.3856)	
Day 2: 4-6 hr Post End of IP 1(n=9,8,9)	0.4170 (± 0.25202)	1.622 (± 0.78046)	1.411 (± 0.75100)	
Day 2: ≤30 min Pre-IP 2(n=10,8,9)	0.3117 (± 0.24934)	1.309 (± 0.48787)	1.044 (± 0.55923)	
Day 2: ≤15 min Post End of IP 2(n=10,8,9)	0.2998 (± 0.24960)	1.283 (± 0.52550)	1.960 (± 0.99952)	
Day 2: 0.5-3 hr Post End of IP 2(n=10,8,9)	0.2833 (± 0.23999)	1.398 (± 0.47591)	2.129 (± 1.4547)	
Day 3: ≤15 min Pre-PEX(n=9,6,5)	0.2468 (± 0.23669)	1.044 (± 0.54178)	1.129 (± 1.0570)	
Day 3: ≤15 min Post-PEX(n=10,8,6)	0.5342 (± 0.22251)	0.7786 (± 0.16455)	0.7020 (± 0.40432)	
Day 3: ≤15 min Post End of IP 1(n=10,8,6)	0.5215 (± 0.23522)	2.210 (± 0.96057)	1.911 (± 1.6633)	
Day 3: 0.5-3 hr Post End of IP 1(n=10,8,6)	0.4970 (± 0.23979)	2.086 (± 0.85567)	1.785 (± 1.1566)	
Day 3: 4-6 hr Post End of IP 1(n=10,8,7)	0.4670 (± 0.30646)	1.680 (± 0.46457)	1.271 (± 0.71567)	
Day 3: ≤30 min Pre-IP 2(n=10,7,7)	0.3424 (± 0.29275)	1.196 (± 0.44550)	1.041 (± 0.84152)	
Day 3: ≤15 min Post End of IP 2(n=10,7,6)	0.3514 (± 0.31264)	1.263 (± 0.38468)	1.478 (± 1.0343)	
Day 3: 0.5-3 hr Post End of IP 2(n=10,7,7)	0.3227 (± 0.28191)	1.267 (± 0.43580)	1.902 (± 1.4522)	
Day4 or 5:≤15min Pre-PEX(n=7,6,5)	0.2378 (± 0.30513)	1.094 (± 0.67793)	1.378 (± 1.1964)	
Day4 or 5:≤15min Post-PEX(n=7,8,5)	0.4554 (± 0.26405)	0.8222 (± 0.21072)	0.8725 (± 0.57834)	
Day4 or 5:≤15min Post End of IP1(n=7,8,5)	0.7599 (± 1.0062)	2.257 (± 0.95791)	1.679 (± 1.3803)	
Day4 or 5:0.5-3hr Post End of IP1(n=7,8,5)	0.6699 (± 0.76875)	2.425 (± 1.4869)	1.405 (± 1.0118)	
Day4 or 5:4-6hr Post End of IP1(n=7,7,5)	0.5663 (± 0.69581)	1.741 (± 0.84171)	1.214 (± 1.0280)	
Day4 or 5:≤30min Pre-IP2(n=6,6,5)	0.5045 (± 0.60730)	1.290 (± 0.64745)	1.255 (± 0.98796)	
Day4 or 5:≤15min Post End of IP2(n=6,6,5)	0.4596 (± 0.58498)	1.288 (± 0.63801)	2.306 (± 1.6006)	
Day4 or 5:0.5-3hr Post End of IP2(n=6,6,5)	0.4129 (± 0.49574)	1.106 (± 0.59034)	2.009 (± 1.4354)	
Day6 or 7:≤15 min Pre-PEX(n=4,2,2)	0.1246 (± 0.24910)	99999 (± 99999)	99999 (± 99999)	
FRETS:Day6 or 7:≤15min Post-PEX(n=4,3,2)	0.2587 (± 0.30131)	0.7311 (± 0.48855)	99999 (± 99999)	
Day6 or 7:≤15min Post End of IP1(n=4,3,2)	0.2150 (± 0.26924)	1.481 (± 0.89773)	99999 (± 99999)	

Day 6 or 7:0.5-3hr Post End of IP1(n=4,3,2)	0.2194 (± 0.24929)	1.673 (± 1.0721)	99999 (± 99999)	
Day6 or 7:4-6hr Post End of IP1(n=4,3,2)	0.1443 (± 0.24485)	1.467 (± 1.1232)	99999 (± 99999)	
Day6 or 7:≤30min Pre-IP2(n=4,2,2)	0.1272 (± 0.25440)	99999 (± 99999)	99999 (± 99999)	
Day6 or 7:≤15min Post End of IP2(n=4,2,2)	0.1422 (± 0.28435)	99999 (± 99999)	99999 (± 99999)	
Day6 or 7:0.5-3hr Post End of IP2(n=4,2,1)	0.1336 (± 0.26710)	99999 (± 99999)	9999 (± 9999)	
Day8 or 9:≤15min Pre-PEX(n=0,1,0)	0 (± 0)	9999 (± 9999)	0 (± 0)	
Day8 or 9:≤15min Post-PEX(n=0,2,0)	0 (± 0)	99999 (± 99999)	0 (± 0)	
Day8 or 9:≤15min Post End of IP1(n=0,1,0)	0 (± 0)	9999 (± 9999)	0 (± 0)	
Day8 or 9:0.5-3hr Post End of IP1(n=0,1,0)	0 (± 0)	9999 (± 9999)	0 (± 0)	
Day8 or 9:4-6hr Post End of IP Infusion1(n=0,1,0)	0 (± 0)	9999 (± 9999)	0 (± 0)	
Day8 or 9:≤30min Pre-IP2(n=0,1,0)	0 (± 0)	9999 (± 9999)	0 (± 0)	
Day8 or 9:≤15min Post End of IP2(n=0,1,0)	0 (± 0)	9999 (± 9999)	0 (± 0)	
Day8 or 9:0.5-3hr Post End of IP2(n=0,1,0)	0 (± 0)	9999 (± 9999)	0 (± 0)	
Day 11 or 12:≤15 min Pre-PEX(n=0,1,0)	0 (± 0)	9999 (± 9999)	0 (± 0)	
Day11 or 12: ≤15min Post-PEX(n=0,1,0)	0 (± 0)	9999 (± 9999)	0 (± 0)	
Day11 or 12: ≤15min Post End of IP1(n=0,1,0)	0 (± 0)	0 (± 0)	0 (± 0)	
Day11 or 12:0.5-3hr Post End of IP1(n=0,1,0)	0 (± 0)	0 (± 0)	0 (± 0)	
Day11 or 12:4-6hr Post End of IP1(n=0,1,0)	0 (± 0)	0 (± 0)	0 (± 0)	
Day11 or 12:≤30min Pre-IP2(n=0,1,0)	0 (± 0)	9999 (± 9999)	0 (± 0)	
Day11 or 12: ≤15min Post End of IP2(n=0,1,0)	0 (± 0)	9999 (± 9999)	0 (± 0)	
Day11 or 12:0.5-3hr Post End of IP2(n=0,1,0)	0 (± 0)	9999 (± 9999)	0 (± 0)	

Statistical analyses

No statistical analyses for this end point

Primary: Platelet Count

End point title	Platelet Count[2]

End point description:

The platelet counts are reported in units of 10^9 per liter blood. SAS included all participants randomized, who received any dose of investigational product. Overall number analyzed are the number of participants with data evaluable for analyses. Number analyzed is the number of participants available for analysis.

End point type	Primary

End point timeframe:

Baseline and end of study (EOS) (up to approximately 15 months)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No Statistical data was collected for this outcome measure.

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	9	9	
Units: 10^9 platelets/L				
arithmetic mean (standard deviation)				
Baseline (n=10,9,8)	35.80 (± 32.076)	27.67 (± 17.571)	15.38 (± 7.463)	
EOS (n=9,7,9)	278.89 (± 79.592)	267.00 (± 86.906)	286.22 (± 109.264)	

Statistical analyses

No statistical analyses for this end point

Primary: Lactate Dehydrogenase (LDH) Levels

End point title	Lactate Dehydrogenase (LDH) Levels[3]

End point description:

The lactate dehydrogenase levels are reported. The lactate dehydrogenase levels are reported.

End point type	Primary

End point timeframe:

Baseline and EOS (up to approximately 15 months)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No Statistical data was collected for this outcome measure.

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	9	8	
Units: international units (IU)/L				
arithmetic mean (standard deviation)				
Baseline (n=10,9,8)	634.6 (± 378.37)	616.3 (± 478.14)	787.8 (± 188.39)	
EOS (n=8,6,8)	197.3 (± 42.00)	208.8 (± 75.20)	220.4 (± 69.93)	

Statistical analyses

No statistical analyses for this end point

Secondary: Dose(s) of SHP655 Needed to Achieve and Maintain Adequate Plasma

Levels of rADAMTS-13

End point title	Dose(s) of SHP655 Needed to Achieve and Maintain Adequate Plasma Levels of rADAMTS-13

End point description:

Dose(s) of SHP655 needed to achieve and maintain adequate plasma levels of rADAMTS-13 in order to support induction of remission and to reduce the number of PEX procedures needed for the treatment of acute aTTP episodes was assessed.

End point type	Secondary

End point timeframe:

From start of study drug administration up to 13 weeks (following remission up to 6 months)

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[4]	0[5]	0[6]	
Units: participants				

Notes:

[4] - Data not analyzed due to sparse sample collections and confounding dosing inputs.

[5] - Data not analyzed due to sparse sample collections and confounding dosing inputs.

[6] - Data not analyzed due to sparse sample collections and confounding dosing inputs.

Statistical analyses

No statistical analyses for this end point

Secondary: PK/PD Temporal Relationship of Safety and Efficacy Parameter as a Function of ADAMTS-13 Activity

End point title	PK/PD Temporal Relationship of Safety and Efficacy Parameter as a Function of ADAMTS-13 Activity

End point description:

Parameters included platelet and LDH counts.

End point type	Secondary

End point timeframe:

Up to 6 months

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[7]	0[8]	0[9]	
Units: participants				

Notes:

[7] - Data not analyzed due to sparse sample collections and confounding dosing inputs.

[8] - Data not analyzed due to sparse sample collections and confounding dosing inputs.

[9] - Data not analyzed due to sparse sample collections and confounding dosing inputs.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With ADAMTS-13 Binding Antibodies Per Titer

End point title	Number of Participants With ADAMTS-13 Binding Antibodies Per Titer

End point description:

Antibody titer indicates the level of the antibodies in a blood sample, defined as the greatest dilution (or lowest concentration) of the blood sample at which an antibody assay (such as ELISA for e.g.), still produces a detectable positive result. Data is presented per titer. SAS included all participants randomized, who received any dose of investigational product. Overall number analyzed are the number of ADA positive participants. 'n' indicates number analyzed is the number of participants available for analysis. Data is presented per titer for ADA positive participants only.

End point type	Secondary

End point timeframe:

Baseline and EOS (up to approximately 15 months)

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	8	8	
Units: participants				
Baseline- 1:20 (n=7,8,8)	2	3	1	
Baseline- 1:40 (n=7,8,8)	3	2	2	
Baseline- 1:80 (n=7,8,8)	2	0	1	
Baseline- 1:160 (n=7,8,8)	0	1	2	
Baseline- 1:320 (n=7,8,8)	0	2	0	
Baseline- 1:640 (n=7,8,8)	0	0	1	
Baseline- 1:1280 (n=7,8,8)	0	0	1	
EOS- 1:20 (n=3,2,5)	0	1	0	
EOS- 1:40 (n=3,2,5)	2	0	1	
EOS- 1:80 (n=3,2,5)	1	0	2	
EOS- 1:2560 (n=3,2,5)	0	1	0	
EOS- 1:5120 (n=3,2,5)	0	0	1	
EOS- 1:81920 (n=3,2,5)	0	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Inhibitory Autoantibody (Nab) Levels by Time

End point title	Inhibitory Autoantibody (Nab) Levels by Time

End point description:

SAS included all participants randomized, who received any dose of investigational product. Overall number analyzed are the number of participants with data evaluable for analyses. 'n' indicates number analyzed is the number of participants available for analysis.

End point type	Secondary

End point timeframe:

Baseline and EOS (up to approximately 15 months)

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	9	9	
Units: days				
median (full range (min-max))				
Baseline (n=10,9,9)	1.25 (0.6 to 3.4)	1.25 (1.0 to 1.8)	1.80 (0.6 to 4.0)	
EOS (n=9,7,8)	0.60 (0.6 to 0.6)	0.70 (0.7 to 1.7)	4.00 (4.0 to 4.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: ADAMTS-13 Activity Levels in Participants Receiving Additional SHP655 for up to 30 Days After Resolution by Using FRETS

End point title	ADAMTS-13 Activity Levels in Participants Receiving Additional SHP655 for up to 30 Days After Resolution by Using FRETS

End point description:

ADAMTS-13 activity levels in participants receiving additional SHP655 for up to 30 days after the resolution of the thrombotic thrombocytopenic purpura (TTP) episode were assessed. Resolution was defined as a normal platelet count and LDH <2 ULN for at least 48 hours following initial normalization of platelet count (acute episode period). PK Set included all enrolled participants with confirmed aTTP diagnosis who received at least 1 dose of investigational product and who had at least 1 evaluable post-dose PK value (ADAMTS-13 antigen and ADAMTS-13 activity). Overall number analyzed are the number of participants available for analyses. 'n' indicates number analyzed is the number of participants with data available for analyses at given time point. 9999: Mean and SD was not estimable due to low number of evaluable participants.

End point type	Secondary

End point timeframe:

At Days 3, 7, 10, 21, 28, 42, 56 and 84

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	7	6	
Units: IU/mL				
arithmetic mean (standard deviation)				
Day 3 (n=6,2,6)	0.4602 (± 0.14328)	-99999 (± 99999)	0.1171 (± 0.28688)	
Day 7 (n=4,2,7)	0.3037 (± 0.26921)	0.3180 (± 0.34714)	-99999 (± 99999)	
Day 10 (n=3,4,5)	0.9021 (± 0.20520)	0.5518 (± 0.33962)	0.4904 (± 0.46441)	

Day 21 (n=4,5,5)	0.8102 (± 0.52773)	0.6264 (± 0.60971)	0.5320 (± 0.51432)	
Day 28 (n=4,5,4)	0.8830 (± 0.51516)	0.8931 (± 0.41323)	0.8632 (± 0.62848)	
Day 42 (n=4,4,4)	0.9968 (± 0.36745)	0.8842 (± 0.39784)	1.055 (± 0.36080)	
Day 56 (n=3,4,3)	1.088 (± 0.25524)	0.9923 (± 0.33663)	1.092 (± 0.19961)	
Day 84 (n=7,6,6)	0.9708 (± 0.43831)	1.021 (± 0.65715)	0.6051 (± 0.48113)	

Statistical analyses

No statistical analyses for this end point

Secondary: Relationship Between ADAMTS-13 Activity and End-organ Disease Status

End point title	Relationship Between ADAMTS-13 Activity and End-organ Disease Status

End point description:

Data could not be analyzed due to sparse sample collections and confounding dosing inputs with daily sequential PEX + SHP655 dosing.

End point type	Secondary

End point timeframe:

Up to 6 months

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[10]	0[11]	0[12]	
Units: participants				

Notes:

[10] - Data not analyzed due to sparse sample collections and confounding dosing inputs.

[11] - Data not analyzed due to sparse sample collections and confounding dosing inputs.

[12] - Data not analyzed due to sparse sample collections and confounding dosing inputs.

Statistical analyses

No statistical analyses for this end point

Secondary: Predose Concentration (Cpre) to Maximum Plasma Concentration (Cmax) Ratio

End point title	Predose Concentration (Cpre) to Maximum Plasma Concentration (Cmax) Ratio

End point description:

PK Set included all enrolled participants with confirmed aTTP diagnosis who received at least 1 dose of investigational product and who had at least 1 evaluable post-dose PK value (ADAMTS-13 antigen and ADAMTS-13 activity). Overall number analyzed are the number of participants available for analyses. 'n' indicates number analyzed is the number of participants with data available for analyses at given time point. 9999: Mean and SD was not estimable due to low number of evaluable participants. 99999: Mean and SD was not estimable for 1 participant.

End point type	Secondary

End point timeframe:

Pre-PEX and post-PEX at multiple timepoints at Days 1, 2, 3, 4 or 5, 6 or 7, 8 or 9, and 11 or 12

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	7	9	
Units: ratio				
arithmetic mean (standard deviation)				
FRETS: Day 1 (n=5,2,1)	2.744 (± 3.3837)	99999 (± 99999)	9999 (± 9999)	
FRETS: Day 2 (n=4,7,7)	2.587 (± 0.92176)	3.534 (± 2.4373)	3.675 (± 2.3380)	
FRETS: Day 3 (n=4,7,6)	1.669 (± 0.34045)	2.134 (± 0.45392)	2.268 (± 1.0679)	
FRETS: Day 4 or 5 (n=2,5,5)	99999 (± 99999)	2.543 (± 0.59576)	1.972 (± 0.91248)	
FRETS: Day 6 or 7 (n=1,2,1)	9999 (± 9999)	99999 (± 99999)	9999 (± 9999)	
FRETS: Day 8 or 9 (n=0,1,0)	0 (± 0)	9999 (± 9999)	0 (± 0)	
FRETS: Day 11 or 12 (n=0,0,0)	0 (± 0)	0 (± 0)	0 (± 0)	

Statistical analyses

No statistical analyses for this end point

Secondary: AUC Overall: Area Under the Plasma Concentration Time Curve ADAMTS13 Activity by Using FRETS

End point title	AUC Overall: Area Under the Plasma Concentration Time Curve ADAMTS13 Activity by Using FRETS

End point description:

Pharmacokinetic (PK) Set included all enrolled participants with confirmed aTTP diagnosis who received at least 1 dose of investigational product and who had at least 1 evaluable post-dose PK value (ADAMTS-13 antigen and ADAMTS-13 activity). 'n' indicates number analyzed are the number of participants available for analysis at the specific time point. 9999: Mean and SD was not estimable due to low number of evaluable participants.

End point type	Secondary

End point timeframe:

Within 15 min pre-PEX and at multiple timepoints Post PEX at Days 1, 2, 3, 4 or 5 and 6 or 7

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: h*IU/mL				
arithmetic mean (standard deviation)				
Day 1(n=9,7,8)	3.563 (± 2.5551)	19.87 (± 9.1150)	12.80 (± 8.4633)	
Day 2(n=10,8,9)	4.461 (± 3.9480)	24.16 (± 9.0323)	21.97 (± 11.135)	
Day 3(n=9,7,6)	5.590 (± 4.7232)	22.75 (± 5.6549)	23.49 (± 9.2589)	
Day 4 or 5(n=5,6,5)	9.507 (± 11.592)	24.10 (± 11.357)	22.05 (± 14.192)	
Day 6 or 7(n=2,2,2)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Systemic and Antibody Induced Clearance

End point title	Systemic and Antibody Induced Clearance

End point description:

Data could not be analyzed due to sparse sample collections and confounding dosing inputs with daily sequential PEX + SHP655 dosing.

End point type	Secondary

End point timeframe:

15 minutes pre-PEX,15 minutes post-PEX,15 minutes, 0.5-3 hours, 4-6 hours post end of IP infusion 1,30 minutes pre-IP infusion 2,15 minutes, 0.5-3 hours post-IP infusion 2 of Schedule A or Schedule B (up to 6 months)

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[13]	0[14]	0[15]	
Units: participants				

Notes:

[13] - Data not analyzed due to sparse sample collections and confounding dosing inputs.

[14] - Data not analyzed due to sparse sample collections and confounding dosing inputs.

[15] - Data not analyzed due to sparse sample collections and confounding dosing inputs.

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax: Maximum ADAMTS-13 Activity Between PEX or SHP655 Infusions by Using FRETS

End point title	Cmax: Maximum ADAMTS-13 Activity Between PEX or SHP655 Infusions by Using FRETS

End point description:

PK Set included all enrolled participants with confirmed aTTP diagnosis who received at least 1 dose of investigational product and who had at least 1 evaluable post-dose PK value (ADAMTS-13 antigen and ADAMTS-13 activity). 'n' indicates number analyzed is the number of participants available for analyses at given time point. 9999: Mean and SD was not estimable for 1 participant. 99999: Mean and SD was not estimable due to low number of evaluable participants.

End point type	Secondary

End point timeframe:

Pre-PEX and post-PEX at multiple timepoints at Days 1, 2, 3, 4 or 5, 6 or 7, 8 or 9, and 11 or 12

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: IU/mL				
arithmetic mean (standard deviation)				
Day 1 (n=10,7,9)	0.4157 (± 0.17075)	2.011 (± 0.79036)	1.653 (± 1.0655)	
Day 2 (n=10,7,9)	0.4951 (± 0.27178)	2.153 (± 1.1404)	2.458 (± 1.4369)	
Day 3 (n=10,8,7)	0.4307 (± 0.28420)	2.228 (± 0.93968)	2.222 (± 1.5080)	
Day 4 or 5 (n=7,7,5)	0.6438 (± 0.97767)	2.633 (± 1.4955)	2.377 (± 1.5934)	
Day 6 or 7 (n=4,3,2)	0.1362 (± 0.095283)	1.625 (± 1.0126)	9999 (± 9999)	
Day 8 or 9 (n=0,1,0)	0 (± 0)	9999 (± 9999)	0 (± 0)	
Day 11 or 12 (n=0,0,0)	0 (± 0)	0 (± 0)	0 (± 0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Levels of ADAMTS-13 Prior PEX ADAMTS13 Activity by Using FRETS

End point title	Trough Levels of ADAMTS-13 Prior PEX ADAMTS13 Activity by Using FRETS

End point description:

PK Set included all enrolled participants with confirmed aTTP diagnosis who received at least 1 dose of investigational product and who had at least 1 evaluable post-dose PK value (ADAMTS-13 antigen and ADAMTS-13 activity). Overall number analyzed are the number of participants available for analyses. 'n' number analyzed are the number of participants with data available for analysis at the specific time point. 9999: Mean and SD was not estimable due to low number of evaluable participants.

End point type	Secondary

End point timeframe:

Within 15 min pre-PEX and at multiple timepoints Post PEX at Days 2, 3, 4 or 5 and 6 or 7

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	8	9	
Units: IU/mL				
arithmetic mean (standard deviation)				
Day 2(n=7,8,9)	0.1667 (± 0.17308)	0.8493 (± 0.62139)	0.9274 (± 0.93426)	
Day 3(n=7,7,7)	0.2579 (± 0.26836)	1.110 (± 0.52612)	1.174 (± 0.93910)	
Day 4 or 5(n=4,7,5)	0.3138 (± 0.38416)	1.180 (± 0.65905)	1.378 (± 1.1976)	
Day 5 or 6(n=3,3,2)	0.1660 (± 0.28752)	1.070 (± 0.98879)	9999 (± 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With ADAMTS-13 Activity Trough Levels >10%

End point title	Percentage of Participants With ADAMTS-13 Activity Trough Levels >10%

End point description:

PK Set included all enrolled participants with confirmed aTTP diagnosis who received at least 1 dose of investigational product and who had at least 1 evaluable post-dose PK value (ADAMTS-13 antigen and ADAMTS-13 activity). Overall number analyzed are the particiapnts from PK set, which included number of participants available for analysis. 'n' indicates number analyzed are the number of participants available with ADAMTS activity absolute Ctrough values at given time point.

End point type	Secondary

End point timeframe:

Pre-dose at Days 2, 3 4 or 5, 6 or 7, 8 or 9, and 11 or 12

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	8	9	
Units: percentage of participants				
number (not applicable)				
Day 2 (n=7,8,9)	57.1	100.0	77.8	
Day 3 (n=7,7,7)	57.1	100.0	85.7	
Day 4 or 5 (n=4,6,5)	50.0	100.0	100.0	
Day 6 or 7 (n=3,3,2)	33.3	66.7	50.0	
Day 8 or 9 (n=0,1,0)	0	100.0	0	
Day 11 or 12 (n=0,1,0)	0	100.0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Achieved Remission Following Normalization of Platelet Count

End point title	Number of Participants who Achieved Remission Following Normalization of Platelet Count

End point description:

Remission was defined as the time taken to achieve platelet count ≥150,000/µL, which was confirmed by a second normal platelet count ≥150,000/µL and LDH <2 ULN 48 hours following initial normalization. FAS included all enrolled participants with confirmed aTTP diagnosis who were treated with a study product and had an ADAMTS-13 activity reading from at least one post infusion sample.

End point type	Secondary

End point timeframe:

From start of study drug administration up to 13 weeks (following remission up to 6 months)

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: participants	9	8	8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Remission

End point title	Percentage of Participants Achieving Remission

End point description:

Remission was defined as a normal platelet count and LDH <2 upper limit of normal (ULN) for at least 48 hours following initial normalization of platelet count (acute episode period). Normalization of platelet count was defined ≥150,000/µL, which was confirmed by a second normal platelet count ≥150,000/µL and LDH <2 ULN. Overall number analyzed are the number of participants with data available for analysis. FAS included all enrolled participants with confirmed aTTP diagnosis who were treated with a study product and had an ADAMTS-13 activity reading from at least one post infusion sample.

End point type	Secondary

End point timeframe:

From start of study drug administration up to 13 weeks (following remission up to 6 months)

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	8	
Units: percentage of participants				
number (confidence interval 95%)	100.0 (69.15 to 100.00)	100.0 (63.06 to 100.00)	88.9 (51.75 to 99.72)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Exacerbation

End point title	Time to First Exacerbation

End point description:

Exacerbation was defined as recurrent thrombocytopenia following a response and requiring a reinitiation of daily plasma exchange treatment after ≥1 day but ≤30 days of no plasma exchange treatment. Data is reported based on Kaplan-Meier estimates. Data was reported for time to first exacerbation in categories for participants enrolled before protocol amendment 4 (from study start up to 11 months) and after protocol amendment 4 (from 11 months up to the EOS). FAS included all enrolled participants with confirmed aTTP diagnosis who were treated with a study product and had an ADAMTS-13 activity reading from at least one post infusion sample. 99999: The median and upper limit of confidence interval (CI) was not evaluable due to no events in participants.

End point type	Secondary

End point timeframe:

From start of study drug administration up to EOS (up to approximately 15 months)

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: days				
median (confidence interval 50%)				
From Study Start up to 11 Months	99999 (2.00 to 99999)	99999 (99999 to 99999)	8.0 (5.00 to 99999)	
From 11 Months up to EOS(up to approx. 15 months)	99999 (4.00 to 99999)	99999 (99999 to 99999)	99999 (6.00 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Relapse

End point title	Time to Relapse

End point description:

Relapse was determined by platelet count or the occurrence after remission of a major clinical event (e.g., Myocardial Infraction (MI), stroke, death) deemed by the investigator to be related to aTTP. Data was reported for time to relapse in categories for participants enrolled before protocol amendment 4 (from study start up to 11 months) and after protocol amendment 4 (from 11 months up to the EOS). FAS included all enrolled participants with confirmed aTTP diagnosis who were treated with a study product and had an ADAMTS-13 activity reading from at least one post infusion sample. 99999: The median, lower and upper limit of CI was not evaluable due to no events in participants.

End point type	Secondary

End point timeframe:

From start of study drug administration up to EOS (up to approximately 15 months)

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: days				
median (confidence interval 50%)				
From Study Start up to 11 Months(n=10,8,9)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	
'From 11 Months up to EOS(up to approx. 15 months)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Exacerbation

End point title	Percentage of Participants With Exacerbation

End point description:

Exacerbation was determined by platelet count or the occurrence after remission of a major clinical event (e.g., myocardial infarction (MI), stroke, death) deemed by the investigator to be related to aTTP. Data was reported for percentage of participants with exacerbation in categories for participants enrolled before protocol amendment 4 (from study start up to 11 months) and after protocol amendment 4 (from 11 months up to the EOS). FAS included all enrolled participants with confirmed aTTP diagnosis who were treated with a study product and had an ADAMTS-13 activity reading from at least one post infusion sample.

End point type	Secondary

End point timeframe:

From start of study drug administration up to EOS (up to approximately 15 months)

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: percentage of participants				
number (confidence interval 95%)				
From Study Start up to 11 Months	50.0 (6.76 to 93.24)	0.0 (0.00 to 60.24)	60.0 (14.66 to 94.73)	
'From 11 Months up to EOS(up to approx. 15 months)	33.3 (4.33 to 77.72)	0.0 (0.00 to 60.24)	33.3 (0.84 to 90.57)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Relapse

End point title	Percentage of Participants With Relapse

End point description:

Relapse was determined by platelet count or the occurrence after remission of a major clinical event (e.g., Myocardial Infraction (MI), stroke, death) deemed by the investigator to be related to aTTP. Data was reported for percentage of participants with exacerbation in categories for participants enrolled before protocol amendment 4 (from study start up to 11 months) and after protocol amendment 4 (from 11 months up to the EOS).

End point type	Secondary

End point timeframe:

From start of study drug administration up to EOS (up to approximately 15 months)

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: percentage of participants				
number (confidence interval 95%)				
From Study Start up to 11 Months	0.0 (0.0 to 60.24)	0.0 (0.0 to 60.24)	0.0 (0.0 to 52.18)	
'From 11 Months up to EOS(up to approx. 15 months)	0.0 (0.0 to 45.93)	0.0 (0.0 to 60.24)	0.0 (0.0 to 70.76)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Major Clinical Events Related to Thrombotic Thrombocytopenic Purpura (TTP)

End point title	Percentage of Participants With Major Clinical Events Related to Thrombotic Thrombocytopenic Purpura (TTP)

End point description:

Major clinical events related to TTP included Death, Stroke, MI and organ dysfunction not normalized within the 90-day observation period which consisted of chronic renal insufficiency, neurologic impairment and neurocognitive deficits. FAS included all enrolled participants with confirmed aTTP diagnosis who were treated with a study product and had an ADAMTS-13 activity reading from at least one post infusion sample.

End point type	Secondary

End point timeframe:

From start of study drug administration up to EOS (up to approximately 15 months)

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: percentage of participants				
number (not applicable)				
Renal Insufficiency	90.0	100.0	88.9	
Neurologic Deficits	60.0	100.0	77.8	
Brain Injury	50.0	62.5	66.7	
Death, Stroke and MI	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Major Clinical Events Related to PEX

End point title	Number of Participants With Major Clinical Events Related to PEX

End point description:

Major clinical events included clinically relevant bleeding (modified ITP score) or thrombosis at the site of line insertion, adverse reactions to plasma, including citrate reactions, allergic reactions, and transfusion-related acute lung injury (TRALI). Data is reported by summarizing the data for all parameters. FAS included all enrolled participants with confirmed aTTP diagnosis who were treated with a study product and had an ADAMTS-13 activity reading from at least one post infusion sample.

End point type	Secondary

End point timeframe:

Up to 6 months

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: participants	6	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Anti-drug Antibody (ADA) Titer of Binding Relative to Baseline

End point title	Number of Participants with Anti-drug Antibody (ADA) Titer of Binding Relative to Baseline

End point description:

SAS included all participants randomized, who received any dose of investigational product. Overall number analyzed are the number of participants available for analyses. Number analyzed are the number of participants with data available for analysis at the specific time point.

End point type	Secondary

End point timeframe:

Baseline and EOS (at approximately Month 15)

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	9	9	
Units: participants				
Baseline (n=10,9,9)	7	8	8	
EOS at Month 15 (n=9,7,8)	3	2	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With at Least One Positive Identification of Antibodies to SHP655

End point title	Percentage of Participants With at Least One Positive Identification of Antibodies to SHP655

End point description:

Percentages are based on the total number of participants per treatment group that have at least one ADA sample analyzed. Full Analysis Set (FAS) included all enrolled participants with confirmed aTTP diagnosis who were treated with a study product and had an ADAMTS-13 activity reading from at least one post infusion sample.

End point type	Secondary

End point timeframe:

Up to 6 months

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: percentage of participants				
number (not applicable)				
ADA Positive: up to 3 Months	80.0	62.5	88.9	
ADA Positive: up to 6 Months	20.0	75.0	33.3	
Nab Positive: up to 3 Months	40.0	37.5	33.3	
Nab Positive: up to 6 Months	30.0	37.5	22.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Inhibitory Antibodies Relative to Baseline

End point title	Number of Participants with Inhibitory Antibodies Relative to Baseline

End point description:

SAS included all participants randomized, who received any dose of investigational product. Overall number analyzed are the number of participants available for analyses. Number analyzed are the number of participants with data available for analysis at the specific time point.

End point type	Secondary

End point timeframe:

Baseline and EOS (at approximately Month 15)

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	9	9	
Units: participants				
Baseline (n=10,9,9)	6	4	7	
EOS at Month 15 (n=9,7,8)	3	3	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment Emergent Adverse Events (TEAEs), Specifically Product-Related TEAEs and Serious TEAEs

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs), Specifically Product-Related TEAEs and Serious TEAEs

End point description:

AE:any untoward medical occurrence in a participants administered IP that does not necessarily have a causal relationship with the treatment.TEAE:an adverse event with an onset that occurs after receiving study drug. SAE:an AE with any untoward clinical manifestation of signs, symptoms/outcomes which results in death, requires inpatient hospitalization/prolongation of hospitalization, results in persistent or significant disability/incapacity, congenital abnormality/birth defect, important medical event, bronchospasm associated with anaphylaxis, reviewed & confirmed seroconversion for human immunodeficiency virus (HIV), hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis E virus (HEV), or parvovirus B19 (B19V). Product related AE:any event emerging/manifesting at or after the initiation of treatment with an IP/medicinal product or any existing event that worsens. SAS:all participants randomized, who received any dose of investigational product.

End point type	Secondary

End point timeframe:

From first dose of study drug until the EOS (up to approximately 15 months)

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	9	9	
Units: participants				
Any TEAEs	10	9	8	
Specifically Product-Related TEAEs	0	1	0	
Serious TEAEs	4	1	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinically Relevant Changes in Vital Signs

End point title	Number of Participants with Clinically Relevant Changes in Vital Signs

End point description:

Vital signs were assessed based on blood pressure, pulse rate, respiratory rate and body temperature. SAS included all participants randomized, who received any dose of investigational product.

End point type	Secondary

End point timeframe:

From first dose of study drug until the EOS (up to approximately 15 months)

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	9	9	
Units: participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinically Relevant Changes in Clinical Chemistry

End point title	Number of Participants with Clinically Relevant Changes in Clinical Chemistry

End point description:

Clinical chemistry assessed alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, alkaline phosphatase, blood urea nitrogen, creatinine, and glucose. SAS included all participants randomized, who received any dose of investigational product.

End point type	Secondary

End point timeframe:

From first dose of study drug until the EOS (up to approximately 15 months)

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	9	9	
Units: participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Clinically Relevant Changes in Hematology

End point title	Number of Participants with Clinically Relevant Changes in Hematology

End point description:

Hematology consisted of complete blood count and leukocytes with differential (basophils, eosinophils, lymphocytes, monocytes, neutrophils), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC) and platelet count. SAS included all participants randomized, who received any dose of investigational product.

End point type	Secondary

End point timeframe:

From first dose of study drug until the EOS (up to approximately 15 months)

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	9	9	
Units: participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Receiving Rescue Therapy

End point title	Percentage of Participants Receiving Rescue Therapy

End point description:

Rescue therapy was defined as any product with a known interruption to the pharmacokinetic/ pharmacodynamic (PK/PD) relationship between ADAMTS-13 activity, von Willebrand factor (VWF) activity, and platelet count. If rescue therapy was initiated, the administration of IP (SHP655 or placebo) was suspended for the duration of the study. Number of participants experiencing occurrence of receiving rescue therapy was assessed. FAS included all enrolled participants with confirmed aTTP diagnosis who were treated with a study product and had an ADAMTS-13 activity reading from at least one post infusion sample.

End point type	Secondary

End point timeframe:

From first dose of study drug until the EOS (up to approximately 15 months)

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: percentage of participants				
number (not applicable)	20.0	0	22.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Meeting Rescue Criteria

End point title	Percentage of Participants Meeting Rescue Criteria

End point description:

Rescue therapy was defined as any product with a known interruption to the PK/PD relationship between ADAMTS-13 activity, VWF activity, and platelet count. If rescue therapy was initiated, the administration of IP (SHP655 or placebo) was suspended for the duration of the study. Number of participants experiencing occurrence in meeting rescue therapy criteria was assessed. Percentage of participants

with rescue therapy initiated are based on laboratory criteria and adverse events. FAS included all enrolled participants with confirmed aTTP diagnosis who were treated with a study product and had an ADAMTS-13 activity reading from at least one post infusion sample.

End point type	Secondary

End point timeframe:

From first dose of study drug until the EOS (up to approximately 15 months)

End point values	Standard of Care (SoC) + Placebo	SoC + SHP655 + Placebo	SoC + SHP655	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: percentage of participants				
number (not applicable)	10.0	0.0	11.1	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of study drug administration up to end of the study (up to approximately 15 months)

Adverse event reporting additional description:

At each visit the investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of the relation to study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24

Reporting groups

Reporting group title	Standard of Care (SoC) + Placebo

Reporting group description:

Participants received SoC daily plasma exchange (PEX) followed by placebo immediately and 12 +/- 1 hours after completion of PEX until remission was achieved (up to approximately 6 months).

Reporting group title	SoC + SHP655

Reporting group description:

Participants received SoC daily PEX and SHP655 40 +/- 4 IU/kg, IV injection, BID, immediately after PEX and 12 +/- 1 hours after completion of PEX until remission was achieved (up to approximately 6 months).

Reporting group title	SoC + SHP655 + Placebo

Reporting group description:

Participants received SoC daily PEX and SHP655 40 +/- 4 international units per kilogram (IU/kg), IV injection, QD, immediately after PEX and placebo 12 +/- 1 hours after completion of PEX until remission was achieved (up to approximately 6 months).

Serious adverse events	Standard of Care (SoC) + Placebo	SoC + SHP655	SoC + SHP655 + Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 10 (40.00%)	3 / 9 (33.33%)	1 / 9 (11.11%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombotic thrombocytopenic purpura			
subjects affected / exposed	3 / 10 (30.00%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (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
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (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			
Pulmonary embolism			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (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	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Standard of Care (SoC) + Placebo	SoC + SHP655	SoC + SHP655 + Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)	6 / 9 (66.67%)	9 / 9 (100.00%)
Vascular disorders			
Hot flush			
subjects affected / exposed	2 / 10 (20.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Flushing			

subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	4	0	0
Deep vein thrombosis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
General disorders and administration site conditions			
Catheter site bruise			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	2	0	1
Chest discomfort			
subjects affected / exposed	2 / 10 (20.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	3	1	0
Catheter site related reaction			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Catheter site pain			
subjects affected / exposed	2 / 10 (20.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
Fatigue			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Feeling abnormal			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Feeling cold			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			

subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Medical device site discomfort			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Peripheral swelling			
subjects affected / exposed	2 / 10 (20.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	2	0	2
Swelling face			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	3 / 10 (30.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	3	1	1
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Dry throat			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	2 / 10 (20.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	5	0	1
Dyspnoea exertional			
subjects affected / exposed	3 / 10 (30.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
Epistaxis			
subjects affected / exposed	2 / 10 (20.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Oropharyngeal pain			

subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Orthopnoea			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Pleural effusion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Suffocation feeling			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Throat irritation			
subjects affected / exposed	2 / 10 (20.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
Wheezing			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract congestion			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Delirium			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Confusional state			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Anxiety			
subjects affected / exposed	2 / 10 (20.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	5	1	0
Insomnia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0

Restlessness			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Procedural anxiety			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Panic attack			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 10 (10.00%)	1 / 9 (11.11%)	2 / 9 (22.22%)
occurrences (all)	1	1	2
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 10 (10.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Heart rate increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
Blood pressure increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	3
Blood glucose increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Oxygen saturation decreased			

subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Neutrophil count increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
White blood cell count abnormal			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Anal injury			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Citrate toxicity			
subjects affected / exposed	2 / 10 (20.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
Contusion			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Infusion related reaction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
Transfusion related complication			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Extrasystoles			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Palpitations			

subjects affected / exposed	2 / 10 (20.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Ventricular tachycardia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Nervous system disorders			
Autonomic nervous system imbalance			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	2 / 10 (20.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	5	1	1
Hypoaesthesia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	7
Taste disorder			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Syncope			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Sensory disturbance			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Restless legs syndrome			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Tremor			

subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Neutrophilia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Thrombotic thrombocytopenic purpura			
subjects affected / exposed	1 / 10 (10.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Eye disorders			
Eye pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Abdominal distension			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Constipation			
subjects affected / exposed	1 / 10 (10.00%)	1 / 9 (11.11%)	3 / 9 (33.33%)
occurrences (all)	1	1	4
Abdominal pain upper			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	2 / 9 (22.22%)
occurrences (all)	1	0	3
Gingival bleeding			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Stomatitis			

subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Paraesthesia oral			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	2
Nausea			
subjects affected / exposed	3 / 10 (30.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	5	0	0
Skin and subcutaneous tissue disorders			
Ecchymosis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Papule			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Pruritus			
subjects affected / exposed	3 / 10 (30.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	3	0	1
Rash			
subjects affected / exposed	1 / 10 (10.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	1	1	2
Rash pruritic			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Skin tightness			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Skin weeping			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0

Urticaria			
subjects affected / exposed	2 / 10 (20.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	7	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 10 (20.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Dysuria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	1	1	1
Back pain			
subjects affected / exposed	2 / 10 (20.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	7	0	1
Muscular weakness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Myopathy			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	2 / 10 (20.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Pain in jaw			

subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	2 / 10 (20.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Oral herpes			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Tooth infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hyperlactacidaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Abnormal weight gain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Hypoglycaemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Hypokalaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
Hypomagnesaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported