Clinical trial results:
A Phase 2, uncontrolled, three-stage, dose-escalation cohort study to evaluate the safety, pharmacokinetics, pharmacodynamics, immunogenicity, and clinical activity of OMS721 in adults with thrombotic microangiopathies.

Summary

EudraCT number	2014-001032-11
Trial protocol	LT BE PL IT
Global end of trial date	16 October 2020

Results information

Result version number	v1 (current)
This version publication date	28 June 2026
First version publication date	28 June 2026

Trial information

Trial identification

Sponsor protocol code	OMS721-TMA-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02222545
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Omeros Corporation
Sponsor organisation address	201 Elliott Avenue West, Seattle, United States, 98119
Public contact	Steve Whitaker, Omeros Corporation, +1 2066765000,
Scientific contact	Steve Whitaker, Omeros Corporation, +1 2066765000,

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	31 October 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 January 2020
Global end of trial reached?	Yes
Global end of trial date	16 October 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The co-primary objectives of this study are to:
• Assess the safety and tolerability of multiple-dose administration of OMS721 in subjects with TMA
• Evaluate the clinical activity of multiple-dose administration of OMS721 in subjects with TMA

Protection of trial subjects:

N/A

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	02 November 2014
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	Poland: 20
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Bulgaria: 2
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Lithuania: 6
Country: Number of subjects enrolled	New Zealand: 6
Country: Number of subjects enrolled	Singapore: 3
Country: Number of subjects enrolled	Hong Kong: 4
Country: Number of subjects enrolled	Taiwan: 8
Country: Number of subjects enrolled	Malaysia: 6
Country: Number of subjects enrolled	Thailand: 3
Country: Number of subjects enrolled	United States: 17
Worldwide total number of subjects	84
EEA total number of subjects	37

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)	2
Adults (18-64 years)	69
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted globally at different sites between 02 Nov 2014 and 11 Aug 2020

Pre-assignment

Screening details:

At least age 18 at screening (Visit 1) and have a diagnosis of primary aHUS, persistent HSCT-associated TMA or TTP with no clinically apparent alternative explanation for thrombocytopenia and anemia.

Pre-assignment period milestones

Number of subjects started	84
Number of subjects completed	58

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Did not meet eligibility criteria: 22
Reason: Number of subjects	Physician decision: 4

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Narsoplimab Low Dose

Arm description:

Administration of narsoplimab via IV at a low dose of 0.675 mg/kg once-weekly.

Arm type	Experimental
Investigational medicinal product name	Narsoplimab
Investigational medicinal product code	
Other name	OMS721
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received narsoplimab intravenously once per week.

Arm title	Narsoplimab Medium Dose

Arm description:

Administration of narsoplimab via IV at a medium dose of 2.0 mg/kg once-weekly.

Arm type	Experimental
Investigational medicinal product name	Narsoplimab
Investigational medicinal product code	
Other name	OMS721
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received narsoplimab intravenously once per week.

Arm title	Narsoplimab High Dose

Arm description:

Administration of narsoplimab via IV at a high dose of 4.0 mg/kg once-weekly.

Arm type	Experimental
Investigational medicinal product name	Narsoplimab
Investigational medicinal product code	
Other name	OMS721
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received narsoplimab intravenously once per week.

Number of subjects in period 1[1]	Narsoplimab Low Dose	Narsoplimab Medium Dose	Narsoplimab High Dose
Started	3	3	52
Completed	2	3	27
Not completed	1	0	25
Consent withdrawn by subject	-	-	3
Adverse event, non-fatal	1	-	2
Death	-	-	9
Deaths based on LT Chart Review of HSCT patients	-	-	10
Proceeded to compassionate use of narsoplimab	-	-	1

Notes:

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

Justification: Worldwide number relates to signed informed consent.

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	58	58	
Age categorical Units: Subjects			
Adults (18-64 years)	49	49	
Adults (65+ years)	9	9	
Age continuous Units: years			
arithmetic mean	46.7		
standard deviation	± 16.3	-	
Gender categorical Units: Subjects			
Female	24	24	
Male	34	34	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	2	
Not Hispanic or Latino	56	56	
Unknown or Not Reported	0	0	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	14	14	
Black or African American	2	2	
White	40	40	
More than one race	0	0	
Unknown or Not Reported	1	1	
Native Hawaiian or Other Pacific Islander	1	1	

End points

End points reporting groups

Reporting group title	Narsoplimab Low Dose
Reporting group description: Administration of narsoplimab via IV at a low dose of 0.675 mg/kg once-weekly.	
Reporting group title	Narsoplimab Medium Dose
Reporting group description: Administration of narsoplimab via IV at a medium dose of 2.0 mg/kg once-weekly.	
Reporting group title	Narsoplimab High Dose
Reporting group description: Administration of narsoplimab via IV at a high dose of 4.0 mg/kg once-weekly.	
Subject analysis set title	OMS721-TMA-001 HSCT-TMA High Dose
Subject analysis set type	Sub-group analysis
Subject analysis set description: 28 participants entered the study with a diagnosis of HSCT-TMA	
Subject analysis set title	OMS721-TMA -001 TTP Medium Dose
Subject analysis set type	Sub-group analysis
Subject analysis set description: Patients diagnosed with TTP and treated with a medium dose	
Subject analysis set title	OMS721-TMA -001 TTP High Dose
Subject analysis set type	Sub-group analysis
Subject analysis set description: Patients diagnosed with TTP and treated in high dose arm.	
Subject analysis set title	OMS721-TMA-001 aHUS Low Dose
Subject analysis set type	Full analysis
Subject analysis set description: Patients diagnosed with aHUS within the low dose group.	
Subject analysis set title	OMS721-TMA-001 aHUS Medium Dose
Subject analysis set type	Sub-group analysis
Subject analysis set description: Patients diagnosed with aHUS within the medium dose cohort	
Subject analysis set title	OMS721-TMA-001 aHUS High Dose
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects diagnosed with aHUS within the high dose cohort.	

Primary: Assess the Safety and Tolerability of Multiple-dose Administration of OMS721 in Participants With TMA

End point title	Assess the Safety and Tolerability of Multiple-dose Administration of OMS721 in Participants With TMA[1]
End point description: Incidence of treatment-emergent adverse events (AEs): clinically significant changes in vital signs, ECG, and laboratory tests were reported as AEs. 28 participants entered the study with a diagnosis of HSCT-TMA; all participants were in the High Dose Arm.	
End point type	Primary
End point timeframe: Day 1 to 37 days after end of treatment, approximately up to 31 weeks	

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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	OMS721-TMA-001 HSCT-TMA High Dose			
Subject group type	Subject analysis set			
Number of subjects analysed	28[2]			
Units: Participants	27			

Notes:

[2] - 28 subjects entered the study with a diagnosis of HSCT-TMA; all subjects were in the high dose arm

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With HSCT-TMA Who Respond to OMS721

End point title	Number of Participants With HSCT-TMA Who Respond to OMS721[3]

End point description:

Response defined as: Improvement in TMA laboratory markers of platelet count and lactate dehydrogenase (LDH) and improvement in clinical status. Only subjects with HSCT-TMA were analyzed; 28 subjects with HSCT were in the Full Analysis Set (FAS).

End point type	Primary

End point timeframe:

Day 1 to up to 2 years following the first dose of OMS721

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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	OMS721-TMA-001 HSCT-TMA High Dose			
Subject group type	Subject analysis set			
Number of subjects analysed	28[4]			
Units: Participants	17			

Notes:

[4] - Only subjects with HSCT-TMA were analyzed; 28 subjects with HSCT were in the full analysis set.

Statistical analyses

No statistical analyses for this end point

Secondary: Participants With HSCT-TMA Treated With OMS721: 100-day Survival

End point title	Participants With HSCT-TMA Treated With OMS721: 100-day Survival

End point description:

Number of participants alive from the date of TMA diagnosis. Only participants with HSCT-TMA were analyzed; all 28 HSCT-TMA participants were in the OMS721 high dose arm.

End point type	Secondary

End point timeframe:

Study Day of HSCT-TMA diagnosis to 100 days later

End point values	OMS721-TMA-001 HSCT-TMA High Dose			
Subject group type	Subject analysis set			
Number of subjects analysed	28[5]			
Units: Participants	19			

Notes:

[5] - Only subjects with HSCT-TMA were analyzed; all 28 HSCT-TMA subjects were in the OMS721 high dose arm

Statistical analyses

No statistical analyses for this end point

Secondary: Participants With HSCT-TMA Treated With OMS721: Overall Survival

End point title	Participants With HSCT-TMA Treated With OMS721: Overall Survival

End point description:

Survival days from the day of TMA diagnosis

End point type	Secondary

End point timeframe:

Study Day of HSCT-TMA diagnosis to up to 2 years following first dose of OMS721

End point values	OMS721-TMA-001 HSCT-TMA High Dose			
Subject group type	Subject analysis set			
Number of subjects analysed	28[6]			
Units: days				
median (confidence interval 95%)	274 (103 to 835)			

Notes:

[6] - Only subjects with HSCT-TMA wee analyzed; all 28 HSCT-TMA subjects were in the OMS721 high dose arm

Statistical analyses

No statistical analyses for this end point

Secondary: Participants With HSCT-TMA Treated With OMS721: Duration of Response

End point title	Participants With HSCT-TMA Treated With OMS721: Duration of Response

End point description:

Number of days from the first response date to the first relapse date. Only participants with HSCT-TMA and responded to OMS721 were analyzed.

End point type	Secondary

End point timeframe:

Study Day 1 to up to 2 years following first dose of OMS721

End point values	OMS721-TMA-001 HSCT-TMA High Dose			
Subject group type	Subject analysis set			
Number of subjects analysed	17[7]			
Units: days				
number (confidence interval 95%)	561 (185 to 757)			

Notes:

[7] - Only participants with HSCT-TMA and responded to OMS721 were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Participants With HSCT-TMA Treated With OMS721: Freedom From Platelet Transfusion

End point title	Participants With HSCT-TMA Treated With OMS721: Freedom From Platelet Transfusion

End point description:

Number of participants with absence of platelet transfusions. Only participants with HSCT-TMA who were receiving platelet transfusions were analyzed; all were in the OMS721 high dose arm.

End point type	Secondary

End point timeframe:

Study Day -14 to 4 weeks following the last platelet transfusion

End point values	OMS721-TMA-001 HSCT-TMA High Dose			
Subject group type	Subject analysis set			
Number of subjects analysed	18[8]			
Units: Participants	8			

Notes:

[8] - Only participants with HSCT-TMA who were receiving platelet transfusions at baseline were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Freedom From Red Blood Cell (RBC) Transfusion

End point title	Freedom From Red Blood Cell (RBC) Transfusion

End point description:

Number of participants with absence of RBC transfusions. Only participants with HSCT-TMA who were receiving RBC transfusions at baseline were analyzed; all were in the OMS721 high dose arm.

End point type	Secondary

End point timeframe:

Study Day -14 to 4 weeks following the last RBC transfusion

End point values	OMS721-TMA-001 HSCT-TMA High Dose			
Subject group type	Subject analysis set			
Number of subjects analysed	22[9]			
Units: Participants	11			

Notes:

[9] - Only participants with HSCT-TMA who were receiving RBC transfusions at baseline were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Participants With HSCT-TMA Treated With OMS721: Change From Baseline in Platelet Count

End point title	Participants With HSCT-TMA Treated With OMS721: Change From Baseline in Platelet Count

End point description:

Changes from baseline in Platelet count (10^9 cells per liter). Only participants with HSCT-TMA were analyzed; all were in the OMS721 high dose arm

End point type	Secondary

End point timeframe:

Study Day 1 to Day 97, approximately 13 weeks

End point values	OMS721-TMA-001 HSCT-TMA High Dose			
Subject group type	Subject analysis set			
Number of subjects analysed	28[10]			
Units: Platelet count				
arithmetic mean (confidence interval 95%)	29.5 (13.5 to 45.6)			

Notes:

[10] - Only participants with HSCT-TMA were analyzed; all were in the high dose arm.

Statistical analyses

No statistical analyses for this end point

Secondary: Participants With HSCT-TMA: Pharmacokinetics (PK) of Multiple-dose Administration of OMS721

End point title	Participants With HSCT-TMA: Pharmacokinetics (PK) of Multiple-dose Administration of OMS721

End point description:

PK parameters including clearance rate. PK parameters were reported for all groups combined

End point type	Secondary

End point timeframe:

Pre-dose and up to 204 days post-dose

End point values	OMS721-TMA-001 HSCT-TMA High Dose			
Subject group type	Subject analysis set			
Number of subjects analysed	28[11]			
Units: L/H				
arithmetic mean (standard deviation)	0.1422 (± 0.0918)			

Notes:

[11] - Only participants with HSCT-TMA were analyzed; all were in the high dose arm.

Statistical analyses

No statistical analyses for this end point

Secondary: Participants With HSCT-TMA (ADA)

End point title	Participants With HSCT-TMA (ADA)

End point description:

Presence of ADA response. Immunogenicity of multiple-dose administration of OMS721 in subjects with TMA

End point type	Secondary

End point timeframe:

Pre-dose and up to 204 days post-dose

End point values	OMS721-TMA-001 HSCT-TMA High Dose	OMS721-TMA -001 TTP Medium Dose	OMS721-TMA -001 TTP High Dose	OMS721-TMA-001 aHUS Low Dose
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28	1	4	3
Units: Participants	3	0	1	1

End point values	OMS721-TMA-001 aHUS Medium Dose	OMS721-TMA-001 aHUS High Dose		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2	20		
Units: Participants	0	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Participants With HSCT-TMA Treated With OMS721: Change From Baseline in LDH

End point title	Participants With HSCT-TMA Treated With OMS721: Change From Baseline in LDH

End point description:

Changes from baseline in LDH

End point type	Secondary

End point timeframe:

Study Day 1 to Day 97, approximately 13 weeks

End point values	OMS721-TMA-001 HSCT-TMA High Dose			
Subject group type	Subject analysis set			
Number of subjects analysed	28[12]			
Units: U/L				
arithmetic mean (confidence interval 95%)	-111.9 (-190.7 to -33.1)			

Notes:

[12] - Only participants with HSCT-TMA were analyzed; all were in the OMS721 high dose arm

Statistical analyses

No statistical analyses for this end point

Secondary: Participants With HSCT-TMA Treated With OMS721: Change From Baseline in Creatinine

End point title	Participants With HSCT-TMA Treated With OMS721: Change From Baseline in Creatinine

End point description:

Changes from baseline in creatinine

End point type	Secondary

End point timeframe:

Study Day 1 to Day 97, approximately 13 weeks

End point values	OMS721-TMA-001 HSCT-TMA High Dose			
Subject group type	Subject analysis set			
Number of subjects analysed	28[13]			
Units: mg/dL				
arithmetic mean (confidence interval 95%)	-0.18 (-0.43 to 0.07)			

Notes:

[13] - Only participants with HSCT-TMA were analyzed; all were in the OMS721 high dose arm

Statistical analyses

No statistical analyses for this end point

Secondary: Participants With HSCT-TMA Treated With OMS721: Change From Baseline in Haptoglobin

End point title	Participants With HSCT-TMA Treated With OMS721: Change From Baseline in Haptoglobin
End point description: Changes from baseline in Haptoglobin	
End point type	Secondary
End point timeframe: Study Day 1 to Day 97, approximately 13 weeks	

End point values	OMS721-TMA-001 HSCT-TMA High Dose			
Subject group type	Subject analysis set			
Number of subjects analysed	27[14]			
Units: mg/dL				
arithmetic mean (confidence interval 95%)	67.7 (40.2 to 95.2)			

Notes:

[14] - Only participants with HSCT-TMA were analyzed; all were in the OMS721 high dose arm

Statistical analyses

No statistical analyses for this end point

Secondary: Participants With HSCT-TMA Treated With OMS721: Change From Baseline in Hemoglobin

End point title	Participants With HSCT-TMA Treated With OMS721: Change From Baseline in Hemoglobin
End point description: Changes from baseline in Hemoglobin	
End point type	Secondary
End point timeframe: Study Day 1 to Day 97, approximately 13 weeks	

End point values	OMS721-TMA-001 HSCT-TMA High Dose			
Subject group type	Subject analysis set			
Number of subjects analysed	22[15]			
Units: g/dL				
arithmetic mean (confidence interval 95%)	0.38 (-0.17 to 0.92)			

Notes:

[15] - Only participants with HSCT-TMA were analyzed; Some patients were excluded due to transfusions

Statistical analyses

No statistical analyses for this end point

Secondary: Participants With HSCT-TMA: Pharmacokinetics (PK) of Multiple-dose Administration of OMS721

End point title	Participants With HSCT-TMA: Pharmacokinetics (PK) of Multiple-dose Administration of OMS721

End point description:

PK parameters Apparent volume of the central compartment (V1)

End point type	Secondary

End point timeframe:

Pre-dose and up to 204 days post-dose

End point values	OMS721-TMA-001 HSCT-TMA High Dose			
Subject group type	Subject analysis set			
Number of subjects analysed	28[16]			
Units: L				
arithmetic mean (standard deviation)				
Apparent volume of the central compartment (V1)	11.6 (± 3.8)			
Apparent volume of the peripheral compartment (V2)	5.6 (± 3.2)			

Notes:

[16] - Only participants with HSCT-TMA were analyzed; all were in the OMS721 high dose arm.

Statistical analyses

No statistical analyses for this end point

Secondary: Participants With HSCT-TMA: Pharmacokinetics (PK) of Multiple-dose Administration of OMS721

End point title	Participants With HSCT-TMA: Pharmacokinetics (PK) of Multiple-dose Administration of OMS721

End point description:

PK parameters Concentration of OMS721 that achieves half maximum elimination rate (KM) (ug/mL)

End point type	Secondary

End point timeframe:

Pre-dose and up to 204 days post-dose

End point values	OMS721-TMA-001 HSCT-TMA High Dose			
Subject group type	Subject analysis set			
Number of subjects analysed	28[17]			
Units: ug/mL				
arithmetic mean (standard deviation)	14.2 (± 15.2)			

Notes:

[17] - Only participants with HSCT-TMA were analyzed; all were in the OMS721 high dose arm

Statistical analyses

No statistical analyses for this end point

Secondary: Participants With HSCT-TMA: Pharmacodynamics (PD)

End point title	Participants With HSCT-TMA: Pharmacodynamics (PD)

End point description:

PD measure is expressed as percentage inhibition of C4d to assess ex-vivo lectin pathway activation

End point type	Secondary

End point timeframe:

Pre-dose and up to 204 days post-dose

End point values	OMS721-TMA-001 HSCT-TMA High Dose			
Subject group type	Subject analysis set			
Number of subjects analysed	28[18]			
Units: Percentage				
arithmetic mean (standard deviation)				
Baseline	26.3 (± 31.8)			
Maximum	95.9 (± 1.21)			

Notes:

[18] - PD was analyzed only in HSCT-TMA participants

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From the signing informed consent form to end of follow up	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0
Reporting groups	
Reporting group title	HSCT-TMA-001 High Dose
Reporting group description: 28 participants entered the study with a diagnosis of HSCT-TMA	
Reporting group title	aHUS OMS721-TMA-001 Low Dose
Reporting group description: 3 participants entered the study with a diagnosis of aHUS and were enrolled in the low dose cohort	
Reporting group title	aHUS OMS721-TMA-001 Medium Dose
Reporting group description: 2 participants entered the study with a diagnosis of aHUS and were enrolled in the medium dose cohort	
Reporting group title	aHUS OMS721-TMA-001 High Dose
Reporting group description: 20 participants entered the study with a diagnosis of aHUS and were enrolled in the high dose cohort	
Reporting group title	TTP OMS721-TMA-001 Medium Dose
Reporting group description: 1 participant entered the study with a diagnosis of TTP and were enrolled in the medium dose cohort	
Reporting group title	TTP OMS721-TMA-001 High Dose
Reporting group description: 4 participants entered the study with a diagnosis of TTP and were enrolled in the high dose cohort	

Serious adverse events	HSCT-TMA-001 High Dose	aHUS OMS721-TMA-001 Low Dose	aHUS OMS721-TMA-001 Medium Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 28 (60.71%)	2 / 3 (66.67%)	1 / 2 (50.00%)
number of deaths (all causes)	16	2	0
number of deaths resulting from adverse events	11	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Diffuse large B-cell lymphoma			

subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (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
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (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
Blood pressure inadequately controlled			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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
Hypertensive crisis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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
Hypertensive emergency			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 28 (3.57%)	2 / 3 (66.67%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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

Disease progression			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Immune system disorders			
Graft-versus-host disease in gastrointestinal tract			
subjects affected / exposed	4 / 28 (14.29%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Graft-versus-host disease			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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
Graft versus host disease in gastrointestinal tract			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary alveolar haemorrhage			

subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (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
Psychiatric disorders			
Confusional state			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (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
Psychotic disorder			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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			
Post procedural haematoma			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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
Post procedural haemorrhage			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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			
Acute myocardial infarction			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (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			
Haemorrhage intracranial			

subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (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
Lethargy			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (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
Seizure			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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			
Haemolytic uraemic syndrome			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (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
Neutropenia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (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
Thrombotic microangiopathy			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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
Atypical haemolytic uraemic syndrome			

subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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
Leukopenia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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
Thrombotic thrombocytopenic purpura			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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			
Vomiting			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (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
Nausea			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (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
Ascites			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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
Diarrhoea			

subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	1 / 2 (50.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic cirrhosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
End stage renal disease			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (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
Chronic kidney disease			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (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			
Neutropenic sepsis			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Septic shock			

subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Fungal infection			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (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			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (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
Pneumonia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Respiratory tract infection viral			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (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
Urosepsis			

subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (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
Staphylococcal infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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
Clostridium difficile colitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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
Orchitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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
Pneumonia bacterial			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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
Renal graft infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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
Urinary tract infection bacterial			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (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
Pneumonia viral			

subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (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
Gastrointestinal candidiasis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pseudomonal sepsis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 28 (3.57%)	0 / 3 (0.00%)	0 / 2 (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

Serious adverse events	aHUS OMS721-TMA-001 High Dose	TTP OMS721-TMA-001 Medium Dose	TTP OMS721-TMA-001 High Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 20 (60.00%)	0 / 1 (0.00%)	2 / 4 (50.00%)
number of deaths (all causes)	3	0	0
number of deaths resulting from adverse events	3	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Vascular disorders			
Orthostatic hypotension			

subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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 pressure inadequately controlled			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive emergency			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Pyrexia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Sudden death			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (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 / 1	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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			

Graft-versus-host disease in gastrointestinal tract			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Graft-versus-host disease			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Hypersensitivity			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (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
Graft versus host disease in gastrointestinal tract			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Pulmonary oedema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Pulmonary alveolar haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Psychiatric disorders			
Confusional state			

subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Delirium			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Psychotic disorder			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (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
Injury, poisoning and procedural complications			
Post procedural haematoma			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (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
Post procedural haemorrhage			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Lethargy			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Seizure			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (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
Blood and lymphatic system disorders			
Haemolytic uraemic syndrome			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Neutropenia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Thrombotic microangiopathy			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Pancytopenia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical haemolytic uraemic syndrome			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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	0 / 20 (0.00%)	0 / 1 (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
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Colitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Nausea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Ascites			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (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
Diarrhoea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Hepatobiliary disorders			
Hepatic cirrhosis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (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

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
End stage renal disease			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Chronic kidney disease			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (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
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Infections and infestations			
Neutropenic sepsis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Septic shock			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Bacteraemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Escherichia sepsis			

subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Fungal infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Gastroenteritis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Pneumonia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory tract infection viral			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Urosepsis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Staphylococcal infection			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			

subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orchitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal graft infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (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
Urinary tract infection bacterial			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (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
Pneumonia viral			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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 candidiasis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Pseudomonal sepsis			

subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (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

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

Non-serious adverse events	HSCT-TMA-001 High Dose	aHUS OMS721-TMA-001 Low Dose	aHUS OMS721-TMA-001 Medium Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 28 (96.43%)	3 / 3 (100.00%)	1 / 2 (50.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	1 / 2 (50.00%)
occurrences (all)	4	0	1
Orthostatic hypotension			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	5	0	0
Blood pressure inadequately controlled			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Venous thrombosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Removal of renal transplant			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1

General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	9 / 28 (32.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	12	0	0
Fatigue			
subjects affected / exposed	6 / 28 (21.43%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	10	0	0
Chills			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	4	0	0
Oedema peripheral			
subjects affected / exposed	3 / 28 (10.71%)	1 / 3 (33.33%)	0 / 2 (0.00%)
occurrences (all)	3	1	0
Gait disturbance			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
General physical health deterioration			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Graft versus host disease in gastrointestinal tract			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Hypersensitivity			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Epistaxis			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Acute respiratory failure			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Dyspnoea			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Catatonia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Investigations			
Weight decreased			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	6	0	0
Alanine aminotransferase increased			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Blood pressure decreased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Blood pressure increased			

subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Injury, poisoning and procedural complications			
Allergic transfusion reaction			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Headache			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Aphasia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Ataxia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Polyneuropathy			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	7 / 28 (25.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	9	0	0

Anaemia			
subjects affected / exposed	4 / 28 (14.29%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	7	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Blindness transient			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Retinal neovascularisation			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	8 / 28 (28.57%)	0 / 3 (0.00%)	1 / 2 (50.00%)
occurrences (all)	10	0	1
Vomiting			
subjects affected / exposed	8 / 28 (28.57%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	14	0	0
Nausea			
alternative assessment type: Non-systematic			
subjects affected / exposed	7 / 28 (25.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	10	0	0
Abdominal pain			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	4	0	0
Haemorrhoids			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Colitis			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0

Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Ascites			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gastric disorder			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Umbilical hernia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Dry skin			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Ecchymosis			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	4	0	0
Urticaria			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Leukocyturia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 3 (33.33%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Euthyroid sick syndrome			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue			

disorders			
Back pain			
subjects affected / exposed	5 / 28 (17.86%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	7	0	0
Bone pain			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Muscular weakness			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Neck pain			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Pain in extremity			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Cytomegalovirus infection			
subjects affected / exposed	4 / 28 (14.29%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	5	0	0
Lower respiratory tract infection			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Upper respiratory tract infection			
subjects affected / exposed	3 / 28 (10.71%)	1 / 3 (33.33%)	0 / 2 (0.00%)
occurrences (all)	3	1	0
Pneumonia klebsiella			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Staphylococcal bacteraemia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0

Nasopharyngitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Staphylococcal infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Clostridium difficile colitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Oral fungal infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pneumonia bacterial			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection bacterial			
subjects affected / exposed	0 / 28 (0.00%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	6 / 28 (21.43%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	8	0	0
Hyperglycaemia			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Hypoalbuminaemia			

subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Hypocalcaemia			
subjects affected / exposed	3 / 28 (10.71%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	5	0	0
Hyperkalaemia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Hypernatraemia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Metabolic acidosis			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Vitamin D deficiency			
subjects affected / exposed	2 / 28 (7.14%)	0 / 3 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0

Non-serious adverse events	aHUS OMS721-TMA-001 High Dose	TTP OMS721-TMA-001 Medium Dose	TTP OMS721-TMA-001 High Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 20 (95.00%)	0 / 1 (0.00%)	3 / 4 (75.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	7 / 20 (35.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	10	0	0
Orthostatic hypotension			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood pressure inadequately controlled			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	5	0	0
Venous thrombosis			

subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Surgical and medical procedures			
Removal of renal transplant			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Fatigue			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Gait disturbance			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
General physical health deterioration			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Immune system disorders			
Graft versus host disease in gastrointestinal tract			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypersensitivity			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Reproductive system and breast			

disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Epistaxis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Acute respiratory failure			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Catatonia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Investigations			
Weight decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			

subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Blood pressure decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hepatic enzyme increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Allergic transfusion reaction			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	2
Aphasia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Ataxia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Polyneuropathy			

subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Anaemia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	4	0	0
Thrombocytopenia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Blindness transient			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Periorbital oedema			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Retinal neovascularisation			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 20 (20.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	5	0	0
Vomiting			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	6	0	0
Nausea			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 20 (15.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	4	0	0
Abdominal pain			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	4	0	0

Haemorrhoids			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Colitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Gastric disorder			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Umbilical hernia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Dry skin			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			

Leukocyturia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Euthyroid sick syndrome			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Infections and infestations			
Cytomegalovirus infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			

subjects affected / exposed	4 / 20 (20.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	4	0	0
Pneumonia klebsiella			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Staphylococcal infection			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Bronchitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Clostridium difficile colitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Oral fungal infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pneumonia bacterial			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pneumonia cytomegaloviral			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection bacterial			

subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Hypocalcaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hyperkalaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hypernatraemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Metabolic acidosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 20 (0.00%)	0 / 1 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 March 2014	Amendment #1: - Change to Section 10.4 Safety Monitoring to address FDA's issue in IND review * Added text that if Grade 3 or higher adverse events occur in any subject in a cohort then safety information will be provided to FDA for review prior to proceeding with dose escalation * Added text on how dose selection will occur for Stage 2 * Added text to provide stopping rules for the study
31 March 2014	Amendment #2: - Change to Section 10.4 Safety Monitoring to address FDA's issues in IND review: * The safety data will be reviewed by a clinical study monitoring team * Added text that AEs of Grade 3 or higher will be reviewed carefully with respect to number and causality when determining if dose escalation is appropriate * Added text on how dose selection will occur for Stage 2 * Added text to provide stopping rules for the study
04 April 2014	Amendment #3: - Change to Section 19.1 Study Schedule of Events to correct superscript and footnotes and associations for #5-11: * Removed Pre-dose and Screening ECG * Replaced Post-dose ECG with ECG * Corrected footnote associations for superscripts 6-11
16 April 2014	Amendment #4: - Change to Section 7.4 has been amended to remove the limitation on the stopping rule to “treatment-related” adverse events and now includes all adverse events. Rationale: The inclusion of all adverse events in safety evaluations was agreed with FDA in prior discussions. The “treatment-related” qualifier was inadvertently retained.

20 July 2015	Amendment #8: - Changes to Sections 2, 7.1, 7.2, 7.4, 10.1, added third stage to the study allowing patients with response to therapy to continue on study treatment for an additional 4 weeks or 12 weeks depending on the disease type. Rationale: Stage 3 was added for extension of drug treatment should subjects show response to therapy - Changes to Section 2: Increase Number of Study Centers from 35 to 50. Rationale: With such a rare patient population, this is to help reach enrollment of 89 subjects - Changes to Sections 2, 7.1.2: Increase duration of the Study from 20 months to 48 months. Rationale: Current feasibility shows enrollment <1 subject/site/year. Increasing study duration helps with reaching enrollment goal of 89 subjects and to accommodate for increasing treatment period of aHUS subjects and the addition of Stage 3 - Changes to Sections 2, 10.2: Increase number of subjects to be enrolled from 29 to 89. Rationale: Addition of patients to continue treatment will increase the total exposure and provide more knowledge about OMS721 - Changes to Sections 2, 7.2, 10: Increased stage 2 treatment period for aHUS subjects from 4 weeks to 12 weeks. Rationale: Typically, aHUS is a chronically treated disease. Chronic toxicity evaluation has been completed without significant findings. The increased treatment duration will provide longer treatment that will be provide more benefit to subjects who receive from treatment. - Changes to Sections 2, 13.1: Added detection of AEs that occur at an incidence of at least 7.5% in the separate cohorts. Rationale: Provides level of AE detection for amended sample size - Changes to Sections 5.3.1.3, 10.4.2: Added periodic review by Data Monitoring Committee. Rationale: Provide additional safety monitoring
20 July 2015	Amendment #8 (Cont'd) - Changes to Sections 2, 5.1.2, 7.1, 8.1, 10.2.1.1, 13.1: Expand TTP patient population by removing refractory criteria and the failure to attain a treatment response criteria related to refractory TTP. Rationale: The inclusion criterion of "refractory TTP" was changed to "TTP" following discussions with several hematologists who informed us that patients meeting the original refractory criterion were extremely rare. Several large centers (e.g., University of Iowa, University or Wisconsin, St. Louis University and University of Pittsburgh told us they have not had any patients meeting the original criterion for several years. Also, no subjects have been screened that meet the refractory criterion. Therefore, it appears that the refractory criterion describes a patient population that is very rare and likely not feasible to study. Hematologists also indicated that, if safe, effective and approved, they envision use of OMS721 as first-line treatment either with or without plasma therapy. Although allowing use of OMS721 as first-line treatment in combination with plasma therapy will complicate determination of efficacy in this study, the hematologists believe that observation of time to response either with or without rituximab can provide adequate proof of principle to justify further placebo-controlled trials in the TTP population. - Changes to Sections 2, 8.1: Remove timeframe criteria of "in the week immediately" for plasma therapy treatments for the Plasma therapy-resistant aHUS patients. Rationale: Subjects with chronic aHUS may have been demonstrated to be plasma therapy resistant in the past. It is not ethical to retreat plasma therapy resistant patients in order to enroll in the study. Therefore, the timing of failed plasma therapy has been deleted. - Changes to Sections 10.1.1.1, 10.1.2.1: Included screening for mycobacterial or significant fungal infection. Rationale: This was added to screen for potential latent infections.
20 July 2015	Amendment #8 (Cont'd) - Changes to Section 7.2.1, Increased OMS721 upper limit half-life range from 35 to 79. Rationale: Corrected incorrect data point
20 April 2017	Amendment #9 - Change to Section 2: Investigational Product, Dosage, and Mode of Administration: Added a second formulation of OMS721, 'Drug Product, OMS721 185 mg/mL. Rationale: To add another formulation of OMS721 for use in the study.

12 October 2018	Amendment #10 - Change to Section 2: Methodology: Enrollment of aHUS and TTP subjects is closed. Rationale: Stage 1 of the protocol is complete. For Stage 2 and 3 enrollment of aHUS and TTP subjects is closed. Enrollment of HSCT-TMA patients is ongoing. - Change to Section 2: Methodology: Changed the dose to 370 mg IV weekly (from 4.0 mg/kg IV weekly). Rationale: Updated the Stage 2 and 3 dose for HSCT-TMA patients to 370 mg IV weekly. Subjects in the middle of a treatment cycle at the time of implementation of Amendment 10 should continue with their original dose. - Change to Section 2: Investigational Product: As of Amendment 10 the 100 mg/mL Injection Solution formulation is no longer being used. Updated to reflect that Drug Product, OMS721 185 mg/mL will be the formulation used. Rationale: The 100 mg/mL Injection Solution is no longer being used, and all subjects will be dosed with Drug Product OMS721 185 mg/mL moving forward. Subjects in the middle of a treatment cycle at the time of implementation of Amendment 10 should stay on their original dose and formulation. - Change to Section 2: Statistical Methods: Efficacy: The description of primary and secondary endpoint analysis was changed to state that all study endpoint will be summarized descriptively by cohort and visit (if applicable). Rationale: Updating the description of efficacy analysis. - Change to Section 5.2.1: The nonclinical experience section was updated to include the most up to date information. Includes reproductive and development studies. Rationale: Provide updated nonclinical study information. - Change to Section 7.2.1: Updated rationale for selection of doses to reflect the change to 370 mg dose. Included 3 new figures showing that there is no correlation between body weight parameters and clearance of OMS721. Rationale: Provided rationale for change of dose to 370 mg.
08 May 2020	Amendment #11: - Change to Sections 2, 6.1: Objectives: Revised the co-primary objective from "evaluate the clinical activity of multiple-dose administration of OMS721 in subjects with TMA" to "Evaluate the efficacy of OMS721 in patients with HSCT-TMA by response defined as improvement in TMA laboratory markers of platelet count and LDH, and improvement in clinical status." Rationale: To provide more detail on the definition of clinical activity and response in HSCT-TMA patients - Change to Sections 2, 7.1, 19.4: Added that "for patients with HSCT-TMA enrolled under Amendment 10 or earlier versions of this protocol, additional data will be collected. These data will include supplemental data on patient demographics and baseline conditions, donor characteristics, the transplant procedure, concomitant medications, TMA-related laboratory measures, transfusions, transplant complications, and outcomes. These data will be derived from medical records from the time of transplant conditioning through the last available patient contact with the site, or up to 2 years (104 weeks) following the first dose of OMS721, whichever comes first." Also added that "as of Amendment 11, enrollment in the study has been completed, and the additional data will be collected until a predetermined data cutoff date for those patients who have not reached 2 years after first OMS721 dose" Rationale: These data were requested by regulatory authorities because patients who have undergone HSCT typically have complicated post-transplant courses, and these additional data will provide the needed information to draft patient narratives, including the full patient profile, and allow for better understanding of OMS721 response and outcomes.

08 May 2020	Amendment #11 (Cont'd) - Change to Sections 2, 13.2.10: Added "The coronavirus associated lockdown situation in various countries has created uncertainty in the ability to collect all follow-up data and resolve all queries on a few patients enrolled in the study. When adequate data on the primary and secondary endpoints is available, the database will be locked for interim analyses and creation of an interim CSR to enable regulatory submission for drug approval. Efforts will continue to collect additional follow-up data and resolve any outstanding queries." Rationale: An interim database lock is planned to enable regulatory submission of the data. Due to the coronavirus situation in many countries, there may be some queries that have not been resolved by the time of the interim database lock, however efforts will continue to resolve those before final database lock. - Change to Sections 2, 7.1: Revised the number of patients planned from 89 to approximately 60. Rationale: "To reflect that enrollment is closed, with the planned total sample size for HSCT-TMA patients of 28"
08 May 2020	Amendment #11 (Cont'd) - Change to Sections 2, 7.3.1: Revised the primary endpoint from "clinical activity assessed by platelet count" to: "For HSCT-TMA patients, response to OMS721 treatment. A responder is defined as a patient with HSCT-TMA who demonstrates improvement in laboratory TMA markers (platelet count and LDH) and clinical benefit (either improvement in organ function or reduction in transfusion burden). The specific criteria are defined as follows: Improvement in laboratory TMA markers: * Platelet count: ** For patients with baseline platelet count = 20,000/µL: tripling of baseline platelet count AND post-baseline platelet count > 30,000/µL AND no platelet transfusions 2 days before and on the day of the platelet count collection. ** For patients with baseline platelet count > 20,000/µL: increase in platelet count = 50% AND post-baseline platelet count > 75,000/µL AND no platelet transfusions 2 days before and on the day of the platelet count collection. * LDH: is defined as LDH < 1.5 times ULN.
08 May 2020	Amendment #11 (Cont'd) - Improvement in clinical status: • Improvement in organ function as evidenced by any of the following criteria: o Improvement in renal function as evidenced by any of the following: 1) a reduction of creatinine > 40%; 2) creatinine < ULN and reduction of creatinine > 20%; or 3) discontinuation of renal replacement therapy (RRT). o Improvement in pulmonary function as evidenced by either of the following criteria: 1) extubation and discontinuation of ventilator support; or 2) discontinuation of noninvasive mechanical ventilation (continuous positive pressure ventilation). o Improvement in neurological function as evidenced by either of the following criteria: 1) improvement in reversible neurological conditions (e.g., cessation of seizures); or 2) stabilization of irreversible neurological conditions (e.g., stability of neurological deficits following stroke without further deterioration or subsequent strokes). o Improvement in gastrointestinal function (gastrointestinal HSCT-TMA requires diagnosis by tissue biopsy) as measured by improvement in the gastrointestinal measures in the Mount Sinai Acute Graft Versus Host Disease (GVHD) International Consortium (MAGIC) criteria OR • Freedom from transfusion (no transfusions for at least 4 weeks from the last transfusion except for patients who died within 4 weeks of the last transfusion; only evaluated in patients who received transfusions within the 2 weeks prior to or on the first OMS721 dose date) Rationale: To provide more detail on the definition of clinical activity and response in HSCT-TMA patients.

08 May 2020	Amendment #11 (Cont'd) - Revised and added to the secondary endpoints to include: • Duration of response, defined as the number of days from the first response date to the first relapse date • 100-day survival, from the date of TMA diagnosis • Overall survival, from the date of TMA diagnosis • Freedom from platelet transfusion defined as no platelet transfusions for at least 4 weeks following the last platelet transfusion except for patients who died within 4 weeks of the last platelet transfusion (only evaluated in patients who had platelet transfusions in the 2 weeks prior to or on the first OMS721 dose date) • Freedom from RBC transfusion defined as no RBC transfusions for at least 4 weeks following the last RBC transfusion except for patients who died within 4 weeks of the last RBC transfusion (only evaluated in patients who had RBC transfusions in the 2 weeks prior to or on the first OMS721 dose date) • Change from baseline in platelet count (post baseline platelet counts without platelet transfusions 2 days before and on the day of the platelet count collection will be used) over time using central laboratory values • Change from baseline in LDH over time using central laboratory values • Change from baseline in haptoglobin over time using central laboratory values • Change from baseline in Hgb (post baseline Hgb without RBC and whole blood transfusions 6 days before and on the day of the Hgb collection will be used) over time using central laboratory values • Change from baseline in creatinine over time using central laboratory values • The PK of multiple-dose administration of OMS721 (this will be assessed in patients with HSCT-TMA as well as patients with aHUS and TTP) • The PD of multiple-dose administration of OMS721(this will be assessed in patients with HSCT-TMA as well as patients with aHUS and TTP)
08 May 2020	Amendment #11 (Cont'd) - Revised and added to the secondary endpoints to include: • The immunogenicity of multiple-dose administration of OMS721 (this will be assessed in patients with HSCT-TMA as well as patients with aHUS and TTP) • Rationale: To provide for the collection of data for further evaluation of the benefit and risk of OMS721 for the treatment of HSCT-TMA - Changes to Section 6.2: Updated the Secondary Study Objectives to match the revised Secondary Endpoints. Rationale: To provide consistency throughout the protocol amendment - Changes to Section 6.3: Added the exploratory objective "Describe the effect of OMS721 on TMA laboratory markers in patients with aHUS and TTP". Rationale: This is a primary endpoint in HSCT-TMA patients but will also be examined as an exploratory objective for aHUS and TTP patients
08 May 2020	Amendment #11 (Cont'd) - Changes to Section 7.3.3: Revised the exploratory endpoints from MBL and MASP-2 concentration to: • Assess the effect of baseline circulating MBL levels on PK and PD measures in patients with HSCT-TMA, aHUS, and TTP • Assess the effect of baseline circulating MASP-2 levels on PK and PD measures in patients with HSCT-TMA, aHUS, and TTP • Describe the effect of OMS721 on TMA laboratory markers in patients with aHUS and TTP • Rationale: To expand on and provide more detail on the exploratory endpoints

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/35439028