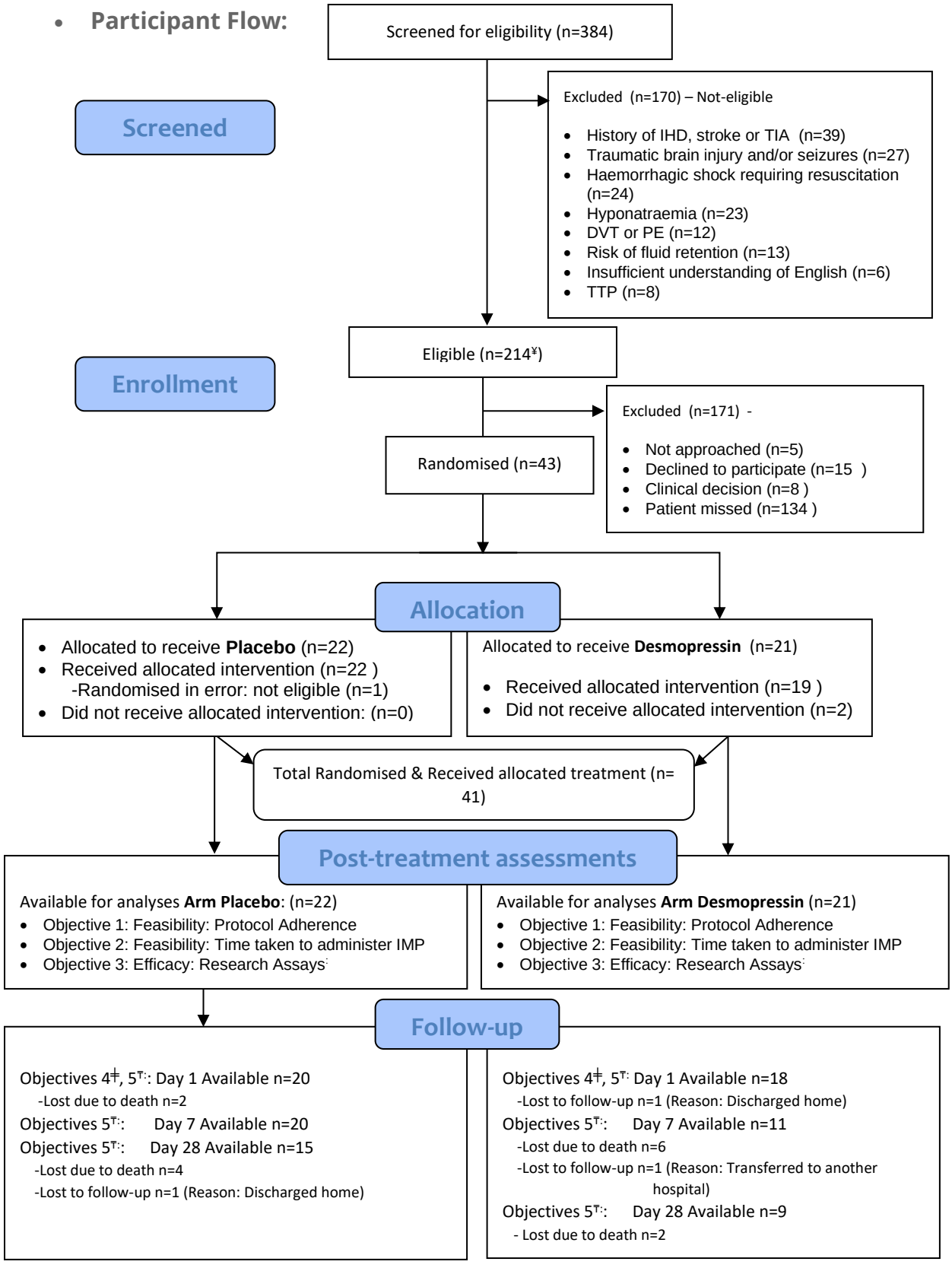
- **Participant Flow:**



Other[1]: Pregnant or breast feeding (n=2),Congenital bleeding disorder (n=1),Rare disorder (n=1); Palliative care or withdrawal of care (n=5), Not eligible due to platelet count or other haematology input (n=3), unplanned procedure (n=1),ischaemic leg (n=1) on aspiring for carotid dissection renal wedge infarct (n=1), ct 14/11/17 = SAH (n=1), pulmonary haemorrhage (n=1), severe superior mesenteric artery thrombosis (n=1)
¥: 1 participant in Placebo was not eligible and was recruited and randomised in error.
Objective 4ǂ Bleeding assessment; ; Objective 5T: Thromboembolic event monitoring

- **Baseline Characteristics:**

Baseline characteristics for all randomised participants – n (%) for categorical variables

	Placebo (N=22)	Desmopressin (N=21)	Overall (N=43)
Sex: male	13 (59.1)	12 (57.1) ¥	25 (58.1)
Planned procedure elective or emergency: elective	20 (90.9)	20 (95.2)	40 (93.0)
ICU Admission Reason (National Audit and Research Centre Codes – ICNARC):		ǂ	
Bowel obstruction	1 (4.5)	1 (4.8)	2 (4.7)
Haemorrhage	0 (0.0)	2 (9.5)	2 (4.7)
Infection	15 (68.2)	11 (52.4)	26 (60.5)
Liver cirrhosis	2 (9.1)	1 (4.8)	3 (7.0)
Malignancy	0 (0.0)	3 (14.3)	3 (7.0)
Trauma	2 (9.1)	0 (0.0)	2 (4.7)
Other*	2 (9.1)	1 (4.8)	3 (7.0)
Procedure Type:		¥	
Arterial line insertion	1 (4.5)	2 (9.5)	3 (7.0)
Central venous catheter insertion	6 (27.3)	3 (14.3)	9 (20.9)
Vascath insertion	2 (9.1)	2 (9.5)	4 (9.3)
Drain insertion	1 (4.5)	1 (4.8)	2 (4.7)
Lumbar puncture	1 (4.5)	0 (0.0)	1 (2.3)
Pulmonary artery catheter insertion	0 (0.0)	1 (4.8)	1 (2.3)
Arterial Line Removal	2 (9.1)	3 (14.3)	5 (11.6)
Central venous catheter removal	5 (22.7)	4 (19.0)	9 (20.9)
Vascath removal	3 (13.6)	3 (14.3)	6 (14.0)
Arterial line & Central venus catheter insertion	0 (0.0)	1 (4.8)	1 (2.3)
Drain removal	1 (4.5)	0 (0.0)	1 (2.3)
Initial consent given by:		¥	
patient	3 (13.6)	2 (9.5)	5 (11.6)
patient's representative – personal	7 (31.8)	5 (23.8)	12 (27.9)
patient's representative – professional	0 (0.0)	1 (4.8)	1 (2.3)

	Placebo (N=22)	Desmopressin (N=21)	Overall (N=43)
emergency waiver	12 (54.5)	12 (57.1)	24 (55.8)
ICU admission route:		¥	
ED	6 (27.3)	8 (38.1)	14 (32.6)
ward	7 (31.8)	5 (23.8)	12 (27.9)
hospital transfer	1 (4.5)	0 (0.0)	1 (2.3)
theatre	7 (31.8)	6 (28.6)	13 (30.2)
Other***	1 (4.5)	1 (4.8)	2 (4.7)
Renal failure:		ǂ	
none	10 (45.5)	7 (33.3)	17 (39.5)
acute	12 (54.5)	10 (47.6)	22 (51.2)
chronic	0 (0.0)	2 (9.5)	2 (4.7)
Antiplatelet drugs given within 7 days of randomisation	0 (0.0)	1 (4.8)ǂ	1 (2.3)
Anticoagulant drugs given within 7 days of randomisation	9 (40.9)	6 (28.6)ǂ	15 (34.9)
Procoagulant drugs given within 7 days of randomisation	6 (27.3)	6 (28.6)ǂ	12 (27.9)

***ICU Admission Reason "Other": Intrauterine death, Metabolic coma or encephalopathy, Self-harm;**

*****ICU Admission Route "Other": Endoscopy, Horton hospital CCU (ITU); ¥: Missing (n=1) ; ǂ: Missing (n=2)**

Baseline characteristics for all randomised for continuous variables

Baseline Characteristic	Treatment Arm	N	Q1	Median	Q3	Min	Max
Age (years)	Placebo	22	46.0	**60.0**	66.0	28.0	87.0
	Desmopressin	20	50.5	**58.0**	68.5	22.0	78.0
Weight (kg)	Placebo	22	60.0	**70.5**	84.0	39.0	136.0
	Desmopressin	20	70.0	**75.0**	79.8	49.0	110.0
Nadir platelet count at screening ($\times 10^9$/L)	Placebo	22	47.0	**62.0**	73.0	6.0	174.0
	Desmopressin	21	36.0	**44.0**	60.0	10.0	92.0
GCS – lowest score during first 24 hours of ICU admission, before intubation or sedation	Placebo	21	3.0	**14.0**	15.0	3.0	15.0
	Desmopressin	19	3.0	**14.0**	15.0	3.0	15.0
APACHE II score	Placebo	22	21.0	**26.5**	35.0	12.0	45.0
	Desmopressin	19	16.0	**26.0**	35.0	10.0	46.0
Serum creatinine (µmol/L)	Placebo	21	63.0	**146.0**	224.0	39.0	552.0
	Desmopressin	19	72.0	**101.0**	224.0	41.0	634.0
Platelet count ($\times 10^9$/L)	Placebo	22	50.0	**61.5**	73.0	0.0	174.0
	Desmopressin	19	32.0	**44.0**	60.0	10.0	163.0
Haemoglobin (g/L)	Placebo	22	80.0	**92.0**	102.0	66.0	127.0
	Desmopressin	19	74.0	**81.0**	102.0	67.0	136.0
Haematocrit (L/L)	Placebo	21	0.2	**0.3**	0.3	0.2	0.4
	Desmopressin	19	0.2	**0.2**	0.3	0.2	0.4

- **Outcome Measures:**

Primary Outcome

	Overall
Number of eligible patients, excluding those randomised in error	213
Number who were randomised and received the IMP, excluding those randomised in error,	40
% of eligible patients who were randomised and received the IMP, with 95% CI	18.8 (13.8-24.7)

There were 214 patients who were eligible on screening. The primary outcome analysis was based on 213 participants who were eligible at the time of randomisation, after excluding the participant who was found ineligible after randomisation took place (randomised in error).

Secondary Outcomes

Feasibility – n (%) for categorical variables

	Placebo (N=21)	Desmopressin (N=21)	Overall (N=42)
IMP administered as allocated	21 (100.0)	19 (90.5)	40 (95.2)
IMP infusion started	21 (100.0)	19 (90.5)	40 (95.2)
IMP infusion completed (not stopped early)	21 (100.0)	18 (85.7)	39 (92.9)
Pre-treatment blood sample provided <= 120 minutes before start of IMP infusion	20 (95.2)	18 (85.7)	38 (90.5)
30 minutes post-treatment blood sample provided between 30 and 60 minutes after end of IMP infusion	21 (100.0)	17 (81.0)	38 (90.5)
Planned interventional procedure carried out between 30 and 120 minutes after end of IMP infusion	19 (90.5)	15 (71.4)	34 (81.0)
120 minutes post-treatment blood sample provided between 90 and 150 minutes after end of IMP infusion	14 (66.7)	14 (66.7)	28 (66.7)
Overall adherence to protocol	14 (66.7)	11 (52.4)	25 (59.5)

Feasibility: Median for continuous variables

Feasibility	Treatment Arm	N	Q1	Median	Q3	Min	Max
Time from randomisation to start of IMP infusion (minutes)	Placebo	22	10.0	**18.0**	29.0	5.0	225.0
	Desmopressin	19	10.0	**19.0**	30.0	10.0	105.0

Platelet function, PFA-200 closure time

Research Assay	Treatment Arm	Testing Period	N	Q1	Median	Q3	Min	Max
PFA-200 closure time with ADP/collagen cartridge (seconds)	Placebo	Pre-treatment	6	112.0	**149.0**	173.0	87.0	195.0
		30 min Post-treatment	4	74.0	**124.5**	172.5	65.0	179.0
		120 min Post-treatment	3	73.0	**155.0**	201.0	73.0	201.0
	Desmopressin	Pre-treatment	2	125.0	**153.5**	182.0	125.0	182.0
		30 min Post-treatment	2	79.0	**126.5**	174.0	79.0	174.0
		120 min Post-treatment	1	106.0	**106.0**	106.0	106.0	106.0
PFA-200 closure time with P2Y cartridge (seconds)	Placebo	Pre-treatment	6	83.0	**150.5**	248.0	49.0	248.0
		30 min Post-treatment	8	87.5	**109.0**	162.5	43.0	186.0
		120 min Post-treatment	4	57.5	**82.5**	107.0	46.0	118.0
	Desmopressin	Pre-treatment	3	71.0	**139.0**	152.0	71.0	152.0
		30 min Post-treatment	4	70.0	**109.0**	145.0	57.0	155.0
		120 min Post-treatment	2	142.0	**220.0**	298.0	142.0	298.0

Platelet function, thrombin generation peak

Research Assay	Treatment Arm	Testing Period	N	Q1	Median	Q3	Min	Max
Thrombin generation peak (nM) with 1 pM TF	Placebo	Pre-treatment	9	172.0	**178.0**	263.0	89.0	358.0
		30 min Post-treatment	8	153.5	**202.0**	248.5	110.0	315.0
		120 min Post-treatment	3	195.0	**250.0**	265.0	195.0	265.0
	Desmopressin	Pre-treatment	6	99.0	**183.5**	292.0	31.0	424.0
		30 min Post-treatment	5	87.0	**182.0**	376.0	56.0	404.0
		120 min Post-treatment	3	174.0	**350.0**	415.0	174.0	415.0
Thrombin generation peak (nM) with 5 pM TF	Placebo	Pre-treatment	9	183.0	**207.0**	304.0	165.0	337.0
		30 min Post-treatment	8	187.5	**220.0**	282.0	158.0	343.0
		120 min Post-treatment	3	181.0	**269.0**	274.0	181.0	274.0
	Desmopressin	Pre-treatment	6	159.0	**255.5**	335.0	42.0	337.0
		30 min Post-treatment	5	177.0	**228.0**	331.0	79.0	343.0
		120 min Post-treatment	3	166.0	**313.0**	332.0	166.0	332.0

Platelet function, Thrombin generation time to peak

Research Assay	Treatment Arm	Testing Period	N	Q1	Median	Q3	Min	Max
Thrombin generation time to peak with 1 pM TF (minutes)	Placebo	Pre-treatment	9	9.8	**11.2**	15.2	6.5	19.4
		30 min Post-treatment	8	9.2	**11.4**	12.6	7.4	13.8
		120 min Post-treatment	3	8.9	**9.9**	9.9	8.9	9.9
	Desmopressin	Pre-treatment	6	7.7	**13.6**	19.9	5.7	35.0
		30 min Post-treatment	5	6.0	**12.7**	18.8	5.2	27.7
		120 min Post-treatment	3	5.4	**6.7**	9.9	5.4	9.9
Thrombin generation time to peak with 5 pM TF (minutes)	Placebo	Pre-treatment	9	5.1	**6.4**	6.8	4.7	10.5
		30 min Post-treatment	8	5.5	**6.2**	7.9	4.8	10.5
		120 min Post-treatment	3	5.0	**5.7**	6.0	5.0	6.0
	Desmopressin	Pre-treatment	6	4.7	**6.3**	9.8	4.2	28.0
		30 min Post-treatment	5	4.3	**7.6**	9.7	4.2	20.0
		120 min Post-treatment	3	4.3	**4.7**	10.0	4.3	10.0

Platelet function, thrombin generation ETP

Research Assay	Treatment Arm	Testing Period	N	Q1	Median	Q3	Min	Max
Thrombin generation ETP (nM-min) with 1 pM TF	Placebo	Pre-treatment	9	1488.0	**1594.0**	1675.0	629.0	1986.0
		30 min Post-treatment	8	1221.5	**1595.0**	1670.0	697.0	1942.0
		120 min Post-treatment	3	1428.0	**1575.0**	1867.0	1428.0	1867.0
	Desmopressin	Pre-treatment	6	814.0	**1434.5**	1998.0	378.0	3221.0
		30 min Post-treatment	5	915.0	**1303.0**	1883.0	697.0	3962.0
		120 min Post-treatment	3	1270.0	**1757.0**	3970.0	1270.0	3970.0
Thrombin generation ETP (nM-min) with 5 pM TF	Placebo	Pre-treatment	9	1282.0	**1513.0**	1832.0	967.0	2448.0
		30 min Post-treatment	8	1351.5	**1792.0**	2089.0	991.0	2387.0
		120 min Post-treatment	3	1325.0	**1500.0**	2212.0	1325.0	2212.0
	Desmopressin	Pre-treatment	6	1094.0	**1535.0**	2164.0	790.0	2939.0
		30 min Post-treatment	5	1418.0	**1461.0**	1692.0	1314.0	3169.0
		120 min Post-treatment	3	1166.0	**1682.0**	2845.0	1166.0	2845.0

Platelet function, thrombin generation lag-time

Research Assay	Treatment Arm	Testing Period	N	Q1	Median	Q3	Min	Max
Thrombin generation lag time with 1 pM TF (minutes)	Placebo	Pre-treatment	9	6.8	**8.7**	11.5	4.5	14.9
		30 min Post-treatment	8	7.7	**8.4**	9.5	5.4	11.0
		120 min Post-treatment	3	6.2	**7.0**	7.5	6.2	7.5
	Desmopressin	Pre-treatment	6	5.0	**9.9**	16.1	3.9	19.7
		30 min Post-treatment	5	4.0	**10.0**	14.7	3.4	15.8
		120 min Post-treatment	3	3.4	**4.4**	7.4	3.4	7.4
Thrombin generation lag time with 5 pM TF (minutes)	Placebo	Pre-treatment	9	2.9	**3.4**	3.9	2.7	7.5
		30 min Post-treatment	8	3.0	**3.4**	4.9	2.5	6.8
		120 min Post-treatment	3	3.0	**3.3**	3.5	3.0	3.5
	Desmopressin	Pre-treatment	6	2.7	**3.5**	6.8	2.0	12.5
		30 min Post-treatment	5	2.2	**4.3**	6.3	2.0	10.5
		120 min Post-treatment	3	2.3	**2.3**	6.7	2.3	6.7

Platelet function, VWF antigen and activity level

Research Assay	Treatment Arm	Testing Period	N	Q1	Median	Q3	Min	Max
VWF antigen level (IU/mL)	Placebo	Pre-treatment	22	3.8	**4.5**	7.4	1.9	11.3
		30 min Post-treatment	21	4.2	**4.7**	7.3	2.0	11.8
		120 min Post-treatment	16	4.2	**5.1**	8.4	1.9	12.0
	Desmopressin	Pre-treatment	19	4.2	**4.8**	7.5	2.7	10.5
		30 min Post-treatment	18	4.2	**4.6**	7.7	3.0	11.4
		120 min Post-treatment	16	4.2	**4.7**	6.9	2.9	10.6
VWF activity level (IU/mL)	Placebo	Pre-treatment	21	3.7	**4.8**	5.6	1.6	13.1
		30 min Post-treatment	20	3.9	**4.8**	6.0	1.8	12.6
		120 min Post-treatment	15	4.2	**4.8**	6.9	1.7	11.1
	Desmopressin	Pre-treatment	18	3.8	**4.9**	7.4	2.8	11.8
		30 min Post-treatment	17	4.1	**4.8**	6.1	3.3	12.6
		120 min Post-treatment	14	3.9	**4.9**	7.1	2.9	11.2

Platelet function, VWF collagen binding

Research Assay	Treatment Arm	Testing Period	N	Q1	Median	Q3	Min	Max
VWF collagen binding (IU/mL)	Placebo	Pre-treatment	17	3.1	**4.4**	8.2	1.6	14.1
		30 min Post-treatment	16	3.1	**4.7**	8.9	1.4	13.2
		120 min Post-treatment	12	4.4	**6.6**	9.4	1.7	13.2
	Desmopressin	Pre-treatment	16	4.1	**6.0**	8.7	2.0	14.0
		30 min Post-treatment	14	4.0	**6.3**	7.9	2.5	15.3
		120 min Post-treatment	13	3.7	**6.2**	7.1	2.0	14.9

Change from baseline in PFA-closure and difference in the change between the two arms

Change from pre-treatment levels	Arm	N	Q1	Median	Q3	Min	Max
PFA-200 closure time with ADP/collagen cartridge: pre-treatment - 30 minutes post-treatment (seconds)	Placebo	2	-47.0	**-38.0**	-29.0	-47.0	-29.0
	Desmopressin	2	-46.0	**-27.0**	-8.0	-46.0	-8.0
PFA-200 closure time with ADP/collagen cartridge: pre-treatment - 120 minutes post-treatment (seconds)	Placebo	0	.	**.**	.	.	.
	Desmopressin	0	.	**.**	.	.	.
PFA-200 closure time with P2Y cartridge: pre-treatment - 30 minutes post-treatment (seconds)	Placebo	4	-158.0	**-82.5**	-6.5	-158.0	-6.0
	Desmopressin	2	-17.0	**-2.5**	12.0	-17.0	12.0
PFA-200 closure time with P2Y cartridge: pre-treatment - 120 minutes post-treatment (seconds)	Placebo	2	-39.0	**-21.0**	-3.0	-39.0	-3.0
	Desmopressin	1	-10.0	**-10.0**	-10.0	-10.0	-10.0

Change from pre-treatment levels	Arm	N	Q1	Median	Q3	Min	Max
Difference **Between arms**	**A:Placebo** **B:Desmopressin**	**Mean 95% CI**					
PFA-200 closure time with ADP/collagen cartridge: pre-treatment - 30 minutes post-treatment (seconds)	A - B	-11.0 (-101.5 -79.5)					
PFA-200 closure time with P2Y cartridge: pre-treatment - 30 minutes post-treatment (seconds)	A - B	-79.8 (-263.6 -104.1)					
PFA-200 closure time with P2Y cartridge: pre-treatment - 120 minutes post-treatment (seconds)	A - B	-11.0 (-407.1 -385.1)					

Change from baseline in thrombin generation peak and difference in the change between the two arms

Change from pre-treatment levels	Arm	N	Q1	Median	Q3	Min	Max
Thrombin generation peak (nM) with 1 pM TF: pre-treatment - 30 minutes post-treatment	Placebo	8	-5.5	**12.5**	25.0	-31.0	63.0
	Desmopressin	5	-12.0	**25.0**	29.0	-48.0	112.0
Thrombin generation peak (nM) with 1 pM TF: pre-treatment - 120 minutes post-treatment	Placebo	3	-26.0	**23.0**	72.0	-26.0	72.0
	Desmopressin	3	-74.0	**21.0**	123.0	-74.0	123.0
Thrombin generation peak (nM) with 5 pM TF: pre-treatment - 30 minutes post-treatment	Placebo	8	-4.5	**2.0**	11.0	-22.0	52.0
	Desmopressin	5	8.0	**18.0**	27.0	-6.0	37.0
Thrombin generation peak (nM) with 5 pM TF: pre-treatment - 120 minutes post-treatment	Placebo	3	-35.0	**16.0**	91.0	-35.0	91.0
	Desmopressin	3	-24.0	**-3.0**	7.0	-24.0	7.0

Difference Between arms	**A:Placebo B:Desmopressin**	**Mean 95% CI**
Thrombin generation peak (nM) with 1 pM TF: pre-treatment - 30 minutes post-treatment	A - B	-9.2 (-62.5 -44.1)
Thrombin generation peak (nM) with 1 pM TF: pre-treatment - 120 minutes post-treatment	A - B	-0.3 (-176.7 -176.0)

Change from pre-treatment levels	Arm	N	Q1	Median	Q3	Min	Max
Thrombin generation peak (nM) with 5 pM TF: pre-treatment - 30 minutes post-treatment	A - B	-10.9 (-35.8 -14.0)					
Thrombin generation peak (nM) with 5 pM TF: pre-treatment - 120 minutes post-treatment	A - B	30.7 (-74.0 -135.4)					

Change from baseline in thrombin generation time to peak and difference in the change between the two arms

Change from pre-treatment levels	Arm	N	Q1	Median	Q3	Min	Max
Thrombin generation time to peak (minutes) with 1 pM TF :pre-treatment - 30 minutes post-treatment	Placebo	8	-2.3	**-1.7**	-0.3	-7.7	1.2
	Desmopressin	5	-7.2	**-1.7**	-0.5	-7.3	1.5
Thrombin generation time to peak (minutes) with 1 pM TF :pre-treatment - 120 minutes post-treatment	Placebo	3	-10.5	**-1.3**	1.2	-10.5	1.2
	Desmopressin	3	-10.0	**-1.0**	-0.3	-10.0	-0.3
Thrombin generation time to peak (minutes) with 5 pM TF: pre-treatment - 30 minutes post-treatment	Placebo	8	-0.3	**-0.2**	0.0	-0.7	1.2
	Desmopressin	5	-0.5	**-0.2**	-0.2	-8.0	0.2
Thrombin generation time to peak (minutes) with 5 pM TF: pre-treatment - 120 minutes post-treatment	Placebo	3	-4.5	**-0.5**	1.0	-4.5	1.0
	Desmopressin	3	-0.3	**0.2**	0.5	-0.3	0.5
Difference Between arms	**A:Placebo B:Desmopressin**	**Mean 95% CI**					
Thrombin generation time to peak (minutes) with 1							

pM TF : pre-treatment - 30 minutes post-treatment	A - B	1.2 (-2.9 -5.2)
Thrombin generation time to peak (minutes) with 1 pM TF : pre-treatment - 120 minutes post-treatment	A - B	0.2 (-12.9 -13.4)
Thrombin generation time to peak (minutes) with 5 pM TF: pre-treatment - 30 minutes post-treatment	A - B	1.7 (-1.0 -4.4)
Thrombin generation time to peak (minutes) with 5 pM TF: pre-treatment - 120 minutes post-treatment	A - B	-1.4 (-6.1 -3.2)

Change from baseline in thrombin generation ETP and difference in the change between the two arms

Change from pre-treatment levels	Arm	N	Q1	Median	Q3	Min	Max
Thrombin generation ETP (nM-min) with 1 pM TF: pre-treatment - 30 minutes post-treatment	Placebo	8	-30.5	**0.5**	43.5	-98.0	227.0
	Desmopressin	5	-115.0	**80.0**	537.0	-117.0	741.0
Thrombin generation ETP (nM-min) with 1 pM TF: pre-treatment - 120 minutes post-treatment	Placebo	3	-95.0	**87.0**	246.0	-95.0	246.0
	Desmopressin	3	-241.0	**47.0**	749.0	-241.0	749.0
Thrombin generation ETP (nM-min) with 5 pM TF: pre-treatment - 30 minutes post-treatment	Placebo	8	-51.0	**18.0**	332.5	-61.0	665.0
	Desmopressin	5	145.0	**230.0**	324.0	-62.0	524.0
Thrombin generation ETP (nM-min) with 5 pM TF: pre-treatment - 120 minutes post-treatment	Placebo	3	43.0	**78.0**	699.0	43.0	699.0
	Desmopressin	3	-94.0	**-72.0**	72.0	-94.0	72.0

Difference Between arms	**A:Placebo B:Desmopressin**	**Mean 95% CI**
Thrombin generation ETP (nM-min) with 1 pM TF: pre-treatment - 30 minutes post-treatment	A - B	-205.7 (-518.2 -106.8)
Thrombin generation ETP (nM-min) with 1 pM TF: pre-treatment - 120 minutes post-treatment	A - B	-105.7 (-966.5 -755.2)
Thrombin generation ETP (nM-min) with 5 pM TF: pre-treatment - 30 minutes post-treatment	A - B	-81.8 (-405.9 -242.3)
Thrombin generation ETP (nM-min) with 5 pM TF: pre-treatment - 120 minutes post-treatment	A - B	304.7 (-304.3 -913.7)

Change from baseline in thrombin generation lag-time and difference in the change between the two arms

Change from pre-treatment levels	Arm	N	Q1	Median	Q3	Min	Max
Thrombin generation lag time (minutes) with 1 pM TF: pre-treatment - 30 minutes post-treatment	Placebo	8	-1.7	**-0.8**	0.6	-5.9	0.8
	Desmopressin	5	-3.8	**-1.0**	-0.5	-6.0	1.7
Thrombin generation lag time (minutes) with 1 pM TF: pre-treatment - 120 minutes post-treatment	Placebo	3	-8.7	**-1.2**	0.8	-8.7	0.8
	Desmopressin	3	-8.7	**-0.7**	-0.5	-8.7	-0.5
Thrombin generation lag time (minutes) with 5 pM TF: pre-treatment - 30 minutes post-treatment	Placebo	8	-0.5	**-0.2**	0.0	-0.8	0.7
	Desmopressin	5	-0.5	**-0.5**	0.0	-2.0	0.0
Thrombin generation lag time (minutes) with 5 pM TF: pre-treatment - 120 minutes post-treatment	Placebo	3	-4.0	**-0.3**	0.7	-4.0	0.7
	Desmopressin	3	-0.3	**-0.2**	0.3	-0.3	0.3
Difference Between arms	**A:Placebo B:Desmopressin**	**Mean 95% CI**					
Thrombin generation lag time (minutes) with 1 pM TF: pre-treatment - 30 minutes post-treatment	A - B	0.8 (-2.3 -4.0)					
Thrombin generation lag time (minutes) with 1 pM TF: pre-treatment - 120 minutes post-treatment	A - B	0.3 (-10.7 -11.3)					
Thrombin generation lag time (minutes) with 5 pM TF: pre-treatment - 30 minutes post-treatment	A - B	0.4 (-0.4 -1.2)					
Thrombin generation lag time (minutes) with 5 pM TF: pre-treatment - 120 minutes post-treatment	A - B	-1.2 (-5.1 -2.8)					

Change from baseline in VWF antigen levels and activity and difference in the change between the two arms

Change from pre-treatment levels	Arm	N	Q1	Median	Q3	Min	Max
VWF antigen level (IU/mL): pre-treatment - 30 minutes post-treatment	Placebo	21	-0.1	**0.0**	0.2	-2.6	1.6
	Desmopressin	18	0.0	**0.0**	0.8	-0.8	1.5
VWF antigen level (IU/mL): pre-treatment - 120 minutes post-treatment	Placebo	16	-0.1	**0.0**	0.4	-4.5	1.0
	Desmopressin	16	-0.2	**0.0**	0.2	-0.7	1.6
VWF activity level (IU/mL): pre-treatment - 30 minutes post-treatment	Placebo	20	-0.2	**0.1**	0.4	-3.5	1.2
	Desmopressin	17	0.0	**0.4**	0.7	-1.4	1.4
VWF activity level (IU/mL): pre-treatment - 120 minutes post-treatment	Placebo	15	-0.8	**-0.1**	0.5	-1.9	1.4
	Desmopressin	14	-0.2	**0.0**	0.2	-0.5	1.4
Difference Between arms	**A:Placebo B:Desmopressin**	**Mean 95% CI**					
VWF antigen level (IU/mL): pre-treatment - 30 minutes post-treatment	A - B	-0.4 (-0.8 -0.1)					
VWF antigen level (IU/mL): pre-treatment - 120 minutes post-treatment	A - B	-0.2 (-0.9 -0.5)					
VWF activity level (IU/mL): pre-treatment - 30 minutes post-treatment	A - B	-0.4 (-1.1 -0.2)					
VWF activity level (IU/mL): pre-treatment - 120 minutes post-treatment	A - B	-0.3 (-0.9 -0.2)					

Change from baseline in VWF collagen binding and difference in the change between the two arms

Change from pre-treatment levels	Arm	N	Q1	Median	Q3	Min	Max
VWF collagen binding (IU/mL): pre-treatment - 30 minutes post-treatment	Placebo	16	-0.3	**-0.1**	0.3	-2.4	2.8
	Desmopressin	14	-0.5	**0.4**	1.3	-2.2	3.3
VWF collagen binding (IU/mL): pre-treatment - 120 minutes post-treatment	Placebo	11	-0.9	**0.0**	1.0	-1.6	3.6
	Desmopressin	13	0.0	**0.3**	0.9	-2.4	2.8
Difference Between arms	**A:Placebo B:Desmopressin**	**Mean 95% CI**					
pre-treatment - 30 minutes post-treatment	A - B	-0.4 (-1.4 -0.6)					
pre-treatment - 120 minutes post-treatment	A - B	-0.1 (-1.3 -1.1)					

Post-treatment bleeding and thromboembolic events - n (%)

	Placebo (N=22)	Desmopressin (N=19)	Overall (N=41)
Participants experiencing onset of new active bleeding up to 24 hours after administration of IMP	1 (4.5)	0 (0.0)	1 (2.4)
Participants experiencing one or more thromboembolic events within 1 day after administration of IMP	0 (0.0)	0 (0.0)	0 (0.0)
Participants experiencing one or more thromboembolic events within 7 days after administration of IMP	1 (4.5)	1 (5.3)	2 (4.9)
Participants experiencing one or more thromboembolic events within 28 days after administration of IMP	4 (18.2)	1 (5.3)	5 (12.2)

Statistics for blood products received post-treatment

			Placebo (N=20)		Desmopressin (N=18)		Overall (N=38)
Count of participants (%) who received at least one of red blood/ cells or platelet or FFP or cryoprecipitate units in the 24 hours following the start of the IMP infusion			5 (25.0)		5 (27.8)		10 (26.3)
	Treatment Arm	**N**	**Q1**	**Median**	**Q3**	**Min**	**Max**
Number of red cell units received within 24 hours after IMP administration	Placebo	4	1.0	**1.0**	1.0	1.0	1.0
	Desmopressin	3	1.0	**1.0**	2.0	1.0	2.0
Number of platelet units received within 24 hours after IMP administration	Placebo	4	1.0	**1.5**	2.0	1.0	2.0
	Desmopressin	3	1.0	**1.0**	3.0	1.0	3.0
Number of FFP units received by these participants within 24 hours after IMP administration	Placebo	0	0.0	**0.0**	0.0	0.0	0.0
	Desmopressin	0	0.0	**0.0**	0.0	0.0	0.0
Number of cryoprecipitate units received by these participants within 24 hours after IMP administration	Placebo	0	0.0	**0.0**	0.0	0.0	0.0
	Desmopressin	0	0.0	**0.0**	0.0	0.0	0.0

- **Adverse Events:**

	Placebo (N=22)	Desmopressin (N=21)	Overall (N=43)
Total serious adverse events (SAEs) up to day 28	34	23	57
Number of participants experiencing at least one SAE- N (%)	13 (59.1)	11 (52.4)	24 (55.8)
Total suspected unexpected serious adverse reactions (SUSARs) up to day 28- N(%)	0 (0.0)	0 (0.0)	0 (0.0)
Deaths up to day 28- N (%)	6 (27.3)	8 (38.1)	14 (32.6)

Trial ID	Trial arm	SAE description	Causal relationship to IMP?	Expected?	Serious criteria
R002	Placebo	Pneumonia	Unrelated	NA	Other Medically Significant Event
R002	Placebo	Abdominal compartment syndrome	Unrelated	NA	Other Medically Significant Event
R002	Placebo	Acute kidney injury	Unrelated	NA	Other Medically Significant Event
R008	Placebo	Atrial fibrillation	Unlikely	NA	Other Medically Significant Event
R010	Placebo	Posterior reversible encephalopathy syndrome	Unrelated	NA	Likelihood of Persistent or Significant Disability or Incapacity
R010	Placebo	Febrile neutropenia	Unrelated	NA	Other Medically Significant Event
R010	Placebo	Axillary vein thrombosis	Unlikely	NA	Other Medically Significant Event
R013	Placebo	Acute myocardial infarction	Unrelated	NA	Life-Threatening
R013	Placebo	Septic shock	Unrelated	NA	Life-Threatening
R016	Placebo	Pneumonia	Unrelated	NA	Other Medically Significant Event
R016	Placebo	Medical device site thrombosis	Unrelated	NA	Other Medically Significant Event
R016	Placebo	Intra-abdominal fluid collection	Unrelated	NA	Other Medically Significant Event
R016	Placebo	Delirium	Unrelated	NA	Other Medically Significant Event
R016	Placebo	Pulmonary oedema	Unrelated	NA	Life-Threatening
R017	Placebo	Sepsis	Unrelated	NA	Other Medically Significant Event

Trial ID	Trial arm	SAE description	Causal relationship to IMP?	Expected?	Serious criteria
R017	Placebo	Acute pulmonary oedema	Unrelated	NA	Other Medically Significant Event
R105	Placebo	Alcoholic liver disease	Unrelated	NA	Death
R108	Placebo	Hepatic failure	Unrelated	NA	Death
R112	Placebo	Multiple organ dysfunction syndrome	Unrelated	NA	Death
R204	Placebo	Pneumonia	Unrelated	NA	Death
R205	Placebo	Multiple organ dysfunction syndrome	Unlikely	NA	Other Medically Significant Event
R205	Placebo	Osmotic demyelination syndrome	Unlikely	NA	Required Hospitalisation or Prolongation of Existing Hospital Stay
R210	Placebo	Subarachnoid haemorrhage	Unrelated	NA	Other Medically Significant Event
R210	Placebo	Endotracheal intubation	Unrelated	NA	Required Hospitalisation or Prolongation of Existing Hospital Stay
R210	Placebo	Acute kidney injury	Unrelated	NA	Required Hospitalisation or Prolongation of Existing Hospital Stay
R210	Placebo	Atrioventricular block first degree	Unrelated	NA	Other Medically Significant Event
R210	Placebo	Epididymitis	Unrelated	NA	Required Hospitalisation or Prolongation of Existing Hospital Stay
R210	Placebo	Herpes simplex	Unrelated	NA	Other Medically Significant Event
R210	Placebo	Drug hypersensitivity	Unrelated	NA	Other Medically Significant Event
R210	Placebo	Endotracheal intubation complication	Unrelated	NA	Life-Threatening
R210	Placebo	Endotracheal intubation complication	Unrelated	NA	Life-Threatening
R210	Placebo	Candida infection	Unrelated	NA	Life-Threatening
R210	Placebo	Tracheostomy	Unrelated	NA	Other Medically Significant Event
R212	Placebo	Intracranial mass	Unrelated	NA	Required Hospitalisation or Prolongation of Existing Hospital Stay
R001	Desmopressin	Acute respiratory distress syndrome	Unrelated	NA	Death
R001	Desmopressin	Gastrointestinal haemorrhage	Unrelated	NA	Other Medically Significant Event

Trial ID	Trial arm	SAE description	Causal relationship to IMP?	Expected?	Serious criteria
R001	Desmopressin	Pneumomediastinum	Unrelated	NA	Other Medically Significant Event
R001	Desmopressin	Acute kidney injury	Unrelated	NA	Other Medically Significant Event
R003	**Desmopressin**	**Hypotension**	**Probably**	**Yes**	**Other Medically Significant Event**
R003	Desmopressin	Acute myocardial infarction	Unlikely	NA	Other Medically Significant Event
R003	Desmopressin	Atrial fibrillation	Unrelated	NA	Other Medically Significant Event
R003	Desmopressin	Multiple organ dysfunction syndrome	Unrelated	NA	Death
R006	Desmopressin	Supraventricular tachycardia	Unrelated	NA	Other Medically Significant Event
R006	Desmopressin	Lung abscess	Unrelated	NA	Required Hospitalisation or Prolongation of Existing Hospital Stay
R006	Desmopressin	Atrial fibrillation	Unrelated	NA	Other Medically Significant Event
R006	Desmopressin	Bradycardia	Unrelated	NA	Other Medically Significant Event
R007	Desmopressin	Pneumonia	Unrelated	NA	Other Medically Significant Event
R007	Desmopressin	Hypernatraemia	Unlikely	NA	Other Medically Significant Event
R007	Desmopressin	Lower gastrointestinal haemorrhage	Unrelated	NA	Death
R014	Desmopressin	Septic shock	Unrelated	NA	Death
R106	Desmopressin	Pulseless electrical activity	Unlikely	NA	Life-Threatening
R111	Desmopressin	Multiple organ dysfunction syndrome	Unrelated	NA	Death
R203	Desmopressin	Pneumonia fungal	Unrelated	NA	Death
R206	Desmopressin	Rectal haemorrhage	Unlikely	NA	Required Hospitalisation or Prolongation of Existing Hospital Stay
R207	Desmopressin	Multiple organ dysfunction syndrome	Unrelated	NA	Death
R214	Desmopressin	Multiple organ dysfunction syndrome	Unrelated	NA	Life-Threatening
R214	Desmopressin	Splenic infarction	Unrelated	NA	Death