Clinical trial results:
A placebo-controlled double blind, randomised feasibility trial of Desmopressin (DDAVP) in critical illness prior to procedures.

Summary

EudraCT number	2016-001126-33
Trial protocol	GB
Global end of trial date	22 October 2019

Results information

Result version number	v1 (current)
This version publication date	13 October 2021
First version publication date	13 October 2021
Summary attachment (see zip file)	Addendum - Study Continuous Characteristics (Study Continuous Characteristics.pdf)

Trial information

Trial identification

Sponsor protocol code	15/87

Additional study identifiers

ISRCTN number	ISRCTN12845429
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	NHS Blood and Transplant
Sponsor organisation address	Oak House, Reeds Crescent, Watford, United Kingdom, WD24 4QN
Public contact	Miss Emma Laing, NHS Blood and Transplant Clinical Trials Unit, +44 01223588091, emma.laing@nhsbt.nhs.uk
Scientific contact	Miss Emma Laing, NHS Blood and Transplant Clinical Trials Unit, +44 01223588091, emma.laing@nhsbt.nhs.uk

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	09 June 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 June 2019
Global end of trial reached?	Yes
Global end of trial date	22 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a feasibility trial, to evaluate whether it is feasible to administer desmopressin (or placebo) prior to an interventional procedure, in order to reduce the patient's risk of bleeding. The primary outcome will measure the proportion of eligible patients who are randomised into trial and receive the IMP.

Protection of trial subjects:

The majority of participants screened and enrolled into the study were incapacitated at the point of study entry due to the severity of their condition. The protocol therefore allowed for patients to be consented into the study via a Personal or Professional Legal Representative, or via the waiver of consent (if the procedure was an emergency). If the emergency waiver was used, full informed consent was then sought later. Patients were also approached for consent if/when capacity was regained. The process for consent was approved by an approved Research Ethics Committee in the UK.

Background therapy:

Approximately one third of patients in intensive care have a low platelet count and the majority undergo at least one invasive procedure during their time in intensive care, putting them at an increased risk of bleeding. This trial assessed the feasibility of administering desmopressin to thrombocytopenic patients in Intensive Care prior to a procedure or radiological intervention, for prophylaxis against bleeding. There were no restrictions on concomitant care for participants in this trial.

Evidence for comparator:

Not applicable - this was a trial comparing desmopressin (intervention) to placebo (saline).

Actual start date of recruitment	01 February 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 214
Worldwide total number of subjects	214
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	199
From 65 to 84 years	14
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Recruitment start date: 13/03/2017
Recruitment end date: 06/06/2019

UK only (three participating hospitals).

Pre-assignment

Screening details:

A total of 384 screenings were undertaken across three centres at Oxford University Hospitals (Oxford), Royal Berkshire Hospital (Reading) and University Hospital of Wales (Cardiff). These screenings resulted in 213 patients fulfilling the study's eligibility criteria.

Pre-assignment period milestones

Number of subjects started	214
Number of subjects completed	43[1]

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Not approached: 5
Reason: Number of subjects	Declined: 15
Reason: Number of subjects	Patient missed: 134
Reason: Number of subjects	Clinical decision: 8
Reason: Number of subjects	Other: 9

Notes:

[1] - The number of subjects reported to be in the pre-assignment period is not consistent with the number starting period 1. It is expected that the number completing the pre-assignment period are also present in the arms in period 1.
Justification: In total, 214 participants were screened resulting in 43 participants that were randomised (171 not randomised).

Period 1

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

Blinding implementation details:

In this trial the participants, the PI, Research Nurse(s), other local Investigators, Trial Statistician and all members of the Clinical Trials Unit were blinded to the treatment allocation. An Independent Statistician produced the allocation sequence.

There were members of the site team who were unblinded - these staff performed randomisation and preparation of the IMP infusion, but were not involved in follow-up assessments after that point.

Arms

Are arms mutually exclusive?	No
Arm title	Desmopressin

Arm description:

A single intravenous infusion of desmopressin (0.3µg/kg in 50mL 0.9% sodium chloride), slowly infused over 20 minutes.

Arm type	Experimental

Investigational medicinal product name	Desmopressin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

A single infusion of 0.3µg/kg desmopressin acetate in 50mL 0.9% saline given over 20 minutes.

Arm title	Placebo

Arm description:

A placebo control of a single intravenous infusion of 50mL 0.9% sodium chloride, also infused intravenously over 20 minutes.

Arm type	Placebo
Investigational medicinal product name	Sodium Chloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

A single intravenous infusion of 50mL 0.9% sodium chloride, infused over 20 minutes.

Arm title	Eligible not randomised

Arm description:

The number of patients who were found to be eligible for the trial but were not consented/randomised for the reasons shown below:

- Not approached (n=5)
- Declined to participate (n=15)
- Clinical decision (n=8)
- Patient missed (n=134)
- Other (n=9)

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Eligible and randomised

Arm description:

The number of patients who were found to be eligible for the trial and were consented/randomised into one of the two arms (desmopressin or placebo).

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

Dosage and administration details:

A single infusion of 0.3µg/kg desmopressin acetate in 50mL 0.9% saline given over 20 minutes.

Investigational medicinal product name	Sodium Chloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

A single intravenous infusion of 50mL 0.9% sodium chloride, infused over 20 minutes.

Number of subjects in period 1	Desmopressin	Placebo	Eligible not randomised
Started	21	22	171
Completed	19	21	171
Not completed	2	1	0
Physician decision	1	-	-
Consent withdrawn by subject	1	-	-
Protocol deviation	-	1	-

Number of subjects in period 1	Eligible and randomised
Started	43
Completed	40
Not completed	3
Physician decision	-
Consent withdrawn by subject	2
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Desmopressin
Reporting group description:	
A single intravenous infusion of desmopressin (0.3µg/kg in 50mL 0.9% sodium chloride), slowly infused over 20 minutes.	
Reporting group title	Placebo
Reporting group description:	
A placebo control of a single intravenous infusion of 50mL 0.9% sodium chloride, also infused intravenously over 20 minutes.	
Reporting group title	Eligible not randomised
Reporting group description:	
The number of patients who were found to be eligible for the trial but were not consented/randomised for the reasons shown below: • Not approached (n=5) • Declined to participate (n=15) • Clinical decision (n=8) • Patient missed (n=134) • Other (n=9)	
Reporting group title	Eligible and randomised
Reporting group description:	
The number of patients who were found to be eligible for the trial and were consented/randomised into one of the two arms (desmopressin or placebo).	

Reporting group values	Desmopressin	Placebo	Eligible not randomised
Number of subjects	21	22	171
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	13	14	0
From 65-84 years	7	7	0
85 years and over	0	1	0
Not recorded	1	0	171
Age continuous Units: years			
median	58	60	59
full range (min-max)	22 to 78	28 to 87	22 to 87
Gender categorical Units: Subjects			
Female	9	9	0
Male	12	13	0
Not recorded	0	0	171

ICU Admission Reason (National Audit and Research Centre Codes – ICNARC) Units: Subjects			
Bowel obstruction	1	1	0
Haemorrhage	2	0	0
Infection	11	15	0
Liver cirrhosis	1	2	0
Malignancy	3	0	0
Trauma	0	2	0
Other	1	2	0
Not recorded	2	0	171
Procedure Type Units: Subjects			
Arterial line insertion	2	1	0
Central venous catheter insertion	3	6	0
Vascath insertion	2	2	0
Drain insertion	1	1	0
Lumbar puncture	0	1	0
Pulmonary artery catheter insertion	1	0	0
Arterial Line Removal	3	2	0
Central venous catheter removal	4	5	0
Vascath removal	3	3	0
Arterial line & Central venous catheter insertion	1	0	0
Drain removal	0	1	0
Not recorded	1	0	171
Initial consent given by: Units: Subjects			
Patient	2	3	0
Patient's representative – personal	5	7	0
Patient's representative – professional	1	0	0
Emergency waiver	12	12	0
Not recorded	1	0	171
ICU admission route: Units: Subjects			
Emergency Department	8	6	0
Ward	5	7	0
Hospital Transfer	0	1	0
Theatre	6	7	0
Other	1	1	0
Not recorded	1	0	171
Renal Failure Units: Subjects			
None	7	10	0
Acute	10	12	0
Chronic	2	0	0
Not recorded	2	0	171
Antiplatelet drugs given within 7 days of randomisation Units: Subjects			
Yes	0	1	0
No	19	21	0

Not recorded	2	0	171
Anticoagulant drugs given within 7 days of randomisation Units: Subjects			
Yes	6	9	0
No	13	13	0
Not recorded	2	0	171
Procoagulant drugs given within 7 days of randomisation Units: Subjects			
Yes	6	6	0
No	13	16	0
Not recorded	2	0	171

Reporting group values	Eligible and randomised	Total	
Number of subjects	43	214	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	27	27	
From 65-84 years	14	14	
85 years and over	1	1	
Not recorded	1	172	
Age continuous Units: years			
median	58		
full range (min-max)	22 to 87	-	
Gender categorical Units: Subjects			
Female	18	18	
Male	25	25	
Not recorded	0	171	
ICU Admission Reason (National Audit and Research Centre Codes – ICNARC) Units: Subjects			
Bowel obstruction	2	2	
Haemorrhage	2	2	
Infection	26	26	
Liver cirrhosis	3	3	
Malignancy	3	3	
Trauma	2	2	
Other	3	3	
Not recorded	2	173	
Procedure Type Units: Subjects			

Arterial line insertion	3	3	
Central venous catheter insertion	9	9	
Vascath insertion	4	4	
Drain insertion	2	2	
Lumbar puncture	1	1	
Pulmonary artery catheter insertion	1	1	
Arterial Line Removal	5	5	
Central venous catheter removal	9	9	
Vascath removal	6	6	
Arterial line & Central venous catheter insertion	1	1	
Drain removal	1	1	
Not recorded	1	172	
Initial consent given by: Units: Subjects			
Patient	5	5	
Patient's representative – personal	12	12	
Patient's representative – professional	1	1	
Emergency waiver	24	24	
Not recorded	1	172	
ICU admission route: Units: Subjects			
Emergency Department	14	14	
Ward	12	12	
Hospital Transfer	1	1	
Theatre	13	13	
Other	2	2	
Not recorded	1	172	
Renal Failure Units: Subjects			
None	17	17	
Acute	22	22	
Chronic	2	2	
Not recorded	2	173	
Antiplatelet drugs given within 7 days of randomisation Units: Subjects			
Yes	1	1	
No	40	40	
Not recorded	2	173	
Anticoagulant drugs given within 7 days of randomisation Units: Subjects			
Yes	15	15	
No	26	26	
Not recorded	2	173	
Procoagulant drugs given within 7 days of randomisation Units: Subjects			
Yes	12	12	
No	29	29	
Not recorded	2	173	

End points

End points reporting groups

Reporting group title	Desmopressin

Reporting group description:

A single intravenous infusion of desmopressin (0.3µg/kg in 50mL 0.9% sodium chloride), slowly infused over 20 minutes.

Reporting group title	Placebo

Reporting group description:

A placebo control of a single intravenous infusion of 50mL 0.9% sodium chloride, also infused intravenously over 20 minutes.

Reporting group title	Eligible not randomised

Reporting group description:

The number of patients who were found to be eligible for the trial but were not consented/randomised for the reasons shown below:

- Not approached (n=5)
- Declined to participate (n=15)
- Clinical decision (n=8)
- Patient missed (n=134)
- Other (n=9)

Reporting group title	Eligible and randomised

Reporting group description:

The number of patients who were found to be eligible for the trial and were consented/randomised into one of the two arms (desmopressin or placebo).

Primary: Proportion of eligible patients who are randomised into trial and receive the IMP.

End point title	Proportion of eligible patients who are randomised into trial and receive the IMP.[1]

End point description:

Primary outcome (feasibility). This is not a comparison between those randomised and not randomised. Therefore the header 'comparison groups' does not apply - we were unable to edit.

End point type	Primary

End point timeframe:

All data between 1 February 2017 and 7 June 2019 was used to calculate the primary outcome.

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This was a feasibility trial and the primary outcome was the 'proportion of eligible patients who are randomised into trial and receive the IMP'.

End point values	Eligible not randomised	Eligible and randomised		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	171	40		
Units: Subjects	171	40		

Statistical analyses

Statistical analysis title	Primary outcome
Statistical analysis description: Proportion of eligible patients who are randomised into trial and receive the IMP.	
Comparison groups	Eligible not randomised v Eligible and randomised
Number of subjects included in analysis	211
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage
Point estimate	18.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.8
upper limit	24.7

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

The timeframe for safety reporting in this trial was from the start of trial treatment until 28 days post-trial treatment.

Adverse event reporting additional description:

All serious adverse events had to be reported in an expedited fashion. All non-serious adverse events did not require reporting.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Desmopressin

Reporting group description:

A single intravenous infusion of desmopressin (0.3µg/kg in 50mL 0.9% sodium chloride), slowly infused over 20 minutes.

Reporting group title	Placebo

Reporting group description:

A placebo control of a single intravenous infusion of 50mL 0.9% sodium chloride, also infused intravenously over 20 minutes.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Non-serious adverse events were not collected during this trial.

Serious adverse events	Desmopressin	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 19 (57.89%)	13 / 21 (61.90%)	
number of deaths (all causes)	8	6	
number of deaths resulting from adverse events			
Vascular disorders			
Axillary vein thrombosis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Endotracheal intubation			

subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheostomy			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Medical device site thrombosis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	4 / 19 (21.05%)	2 / 21 (9.52%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 4	0 / 1	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumomediastinum			

subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary oedema			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Endotracheal intubation complication			
subjects affected / exposed	0 / 19 (0.00%)	2 / 21 (9.52%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 19 (5.26%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	2 / 19 (10.53%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block first degree			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bradycardia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulseless electrical activity			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Intracranial mass			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osmotic demyelination syndrome			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic infarction			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Gastrointestinal disorders			
Abdominal compartment syndrome			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intra-abdominal fluid collection			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Alcoholic liver disease			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatic failure			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal and urinary disorders			
Acute kidney injury			

subjects affected / exposed	1 / 19 (5.26%)	2 / 21 (9.52%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Infections and infestations			
Candida infection			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes simplex			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung abscess			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 19 (5.26%)	3 / 21 (14.29%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia fungal			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			

subjects affected / exposed	1 / 19 (5.26%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Metabolism and nutrition disorders			
Hypernatraemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Desmopressin	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 October 2017	CHANGES TO INCLUSION / EXCLUSION CRITERIA: - addition of inclusion of patients who are in the process of being admitted to ICU, in addition to those already on ICU. - re-defined exclusion of 'active bleeding' to 'haemorrhagic shock'. - re-defined hyponatraemia as serum sodium <=129mmol/l. CLARIFICATION ON DOSING IMP FOR PATIENTS WITH BMI > 30kg/m2 OR FLUID OVERLOAD. ADDITION OF TWO NEW SITES.
08 February 2019	ADDITION OF TTP (Thrombotic Thrombocytopenic Purpura) AS AN EXCLUSION CRITERION CORRECTION OF ERROR IN SAFETY REPORTING SECTION DATA SHARING POLICY (ADDED DETAILS)
12 July 2019	ADDITION OF SECONDARY OUTCOME MEASURE RELATING TO RESEARCH ASSAY TESTS

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study continuous characteristics (e.g. platelet count, APACHEII, GCS score) could not be submitted as part of this dataset for technical reasons. The results for these characteristics (by desmopressin and placebo groups) are available on request.

Notes: