Clinical trial results:
The efficacy and mechanism of surfactant therapy for critically ill infants with bronchiolitis: The Bronchiolitis Endotracheal Surfactant Study (BESS)

Summary

EudraCT number	2018-001169-18
Trial protocol	GB
Global end of trial date	03 April 2024
Results information	
Result version number	v1 (current)
This version publication date	13 November 2026
First version publication date	13 November 2026
Summary attachment (see zip file)	BESS Protocol_V7.0 19.03.2025 Signed.pdf (BESS Protocol_V7.0 19.03.2025 Signed.pdf) BESS - Final_Analysis_Report_v5.0_20260311.pdf (BESS - Final_Analysis_Report_v5.0_20260311.pdf)

Trial information

Trial identification	
Sponsor protocol code	UoL001360
Additional study identifiers	
ISRCTN number	ISRCTN11746266
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	IRAS Reference: 220853, REC Reference: 18/SC/0427

Notes:

Sponsors	
Sponsor organisation name	The University of Liverpool
Sponsor organisation address	Clinical Directorate, 4th Floor Thompson Yates Building, Faculty of Health and Life Sciences , Liverpool, United Kingdom, L3 5RB
Public contact	BESS Trial, Clinical Trials Research Centre (CTRC), 44 0151 795 8757, bess@liverpool.ac.uk
Scientific contact	BESS Trial, Clinical Trials Research Centre (CTRC), 44 0151 795 8757, bess@liverpool.ac.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	No

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 December 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 April 2024
Global end of trial reached?	Yes
Global end of trial date	03 April 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

BESS is a study that comprises three work packages. The Trial is Work Package A (WP-A), the parent and staff experience substudy is work package B (WP-B) and the mechanistic substudy is work package C (WP-C).

The hypothesis we are testing in The Trial (WP-A) is: Endotracheal surfactant reduces duration of mechanical ventilation by 18 hours.

This trial will test whether giving surfactant into the lungs of babies suffering from severe bronchiolitis reduces the time they spend on a mechanical ventilator to help them breathe.

We will do this by measuring the total time babies spend on a mechanical ventilator in hours and comparing the time required by babies given a surfactant (called poractant alfa) to babies given air (a dummy or placebo treatment). "18 hours" is included in the hypothesis as this is considered to be the smallest period of time that would be of benefit to a baby's wellbeing. The study will run over 3 winter seasons and involve about 284 babies.

Protection of trial subjects:

Administration of poractant alfa (porcine derived surfactant, Curosurf®) in infants with bronchiolitis is well tolerated and considered safe. Transient minor adverse reactions associated with administration of poractant alfa for the treatment of neonatal Respiratory Distress Syndrome (RDS) include bradycardia, hypotension, endotracheal tube blockage, and oxygen desaturation. The risk of such events is minimised by tracheal toilet prior to administration of poractant alfa, as recommended in the Summary of Product Characteristics.
Small volume (2x1mL/kg) non-bronchoscopic bronchoalveolar lavage (BAL) procedure on PICU is safe and well tolerated procedure. In a published audit of 27 children on PICU who underwent multiple small volume BAL installations (5x1mL/kg) as part of a single routine diagnostic procedure, 7 experienced transient oxygen desaturation requiring temporary increased FiO2. We will limit BAL sampling to a 2x1mL/kg instillation at each scheduled assessment. BAL sampling for this research study will cease on approval of v5 of this protocol.
Small volume (1.25mL (range 1.0 to 1.3mL)) blood sampling will be done on infants ventilated at Liverpool and Southampton PICUs and scheduled to coincide with routine blood sampling. Existing vascular access will be used when available. There is no risk of anaemia associated with this limited volume of blood sampling. The sample will be taken from an arterial line if present. If not by standard venesection. This additional blood sampling at Liverpool and Southampton PICUs will cease on approval of v5 of this protocol.
Capillary blood gas sampling or arterial blood gas sampling for subject monitoring (100microliters) will use data from routine blood gas sampling when either is collected within a 4-hour (+/-2hrs) window of a research-scheduled sample. As this is part of standard care no additional risks are expected.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 November 2018
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: 232
Worldwide total number of subjects	232
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	6
Newborns (0-27 days)	110
Infants and toddlers (28 days-23 months)	116
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

1009 patient were screened for eligibility. 391 of these were ineligible at screening, 618 were eligible. Of the 618 eligible at screening patients, 232 were randomised.

Pre-assignment period milestones

Number of subjects started	1009[1]
Number of subjects completed	232

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Ineligible at screening: 391
Reason: Number of subjects	Eligible but not approached: 264
Reason: Number of subjects	Declined to participate: 103
Reason: Number of subjects	Not randomised: 18
Reason: Number of subjects	Incomplete screening log: 1

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 1009 patient were screened for eligibility. 391 of these were ineligible at screening, 618 were eligible. Of the 618 eligible at screening patients, 232 were randomised i.e. the worldwide number enrolled in the trial.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Endotracheal poractant alfa

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Endotracheal poractant alfa
Investigational medicinal product code	
Other name	Curosurf®
Pharmaceutical forms	Endotracheopulmonary instillation
Routes of administration	Endotracheopulmonary use

Dosage and administration details:

Endotracheal poractant alfa (Curosurf®, porcine lung phospholipid fraction supplied at 80mg/mL), first dose 200mg/kg, repeated 12 hourly at 100mg/kg, up to a total of 3 doses according to the manufacturer's summary of product characteristics (SPC).

Arm title	Sham Intervention group

Arm description: -

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Endotracheopulmonary instillation
Routes of administration	Endotracheopulmonary use

Dosage and administration details:

An identical (to the experimental arm) series of up to three procedures (while intubated) using air as the placebo

Number of subjects in period 1	Endotracheal poractant alfa	Sham Intervention group
Started	115	117
Completed	113	116
Not completed	2	1
Withdrawn prior to experiencing primary outcome	2	1

Baseline characteristics

Reporting groups	
Reporting group title	Endotracheal poractant alfa
Reporting group description: -	
Reporting group title	Sham Intervention group
Reporting group description: -	

Reporting group values	Endotracheal poractant alfa	Sham Intervention group	Total
Number of subjects	115	117	232
Age categorical			
Age corrected for gestation			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	4	2	6
Newborns (0-27 days)	53	57	110
Infants and toddlers (28 days-23 months)	58	58	116
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Chronological age- not corrected for premature birth			
Units: weeks			
arithmetic mean	9.1	9.2	
standard deviation	± 7.5	± 7.0	-
Gender categorical			
Units: Subjects			
Female	52	50	102
Male	63	67	130
Premature (yes/ no)			
Units: Subjects			
Yes	66	61	127
No	49	56	105
Intubated on arrival to PICU (yes/ no)			
Units: Subjects			
Yes	90	97	187
No	25	20	45
O2 supplementation on arrival to PICU			
Units: Subjects			
Yes	113	115	228
No	1	2	3
Data unobtainable	1	0	1
Underlying viral infection identified:			
Units: Subjects			
Yes	101	111	212

No infection identified	8	5	13
No sample	4	0	4
Data unobtainable	2	1	3
Underlying bacterial infection identified: Units: Subjects			
Yes	29	31	60
No infection identified	79	82	161
No sample	4	2	6
Data unobtainable	3	2	5
Chronological age- not corrected for premature birth Units: weeks			
median	6.0	8.0	
inter-quartile range (Q1-Q3)	5.0 to 12.0	4.0 to 12.0	-
Chronological age- not corrected for premature birth Units: weeks			
median	6.0	8.0	
full range (min-max)	1.0 to 42.0	1.0 to 37.0	-
Age corrected for prematurity (weeks) Units: weeks			
arithmetic mean	5.0	4.8	
standard deviation	± 6.5	± 5.9	-
Age corrected for prematurity (weeks) Units: weeks			
median	4.0	3.0	
inter-quartile range (Q1-Q3)	0.0 to 8.0	1.0 to 7.0	-
Age corrected for prematurity (weeks) Units: weeks			
median	4.0	3.0	
full range (min-max)	-5.0 to 25.0	-4.0 to 23.0	-
Weight (Kg)			
Baseline weight in Kg: 115 of 115 Endotracheal poractant alfa participants had weight measured at baseline, data was unobtainable for 0 participants. 116 of 117 Sham Intervention group participants had weight measured at baseline, data was unobtainable for 1 participant.			
Units: Kg			
arithmetic mean	4.2	4.2	
standard deviation	± 1.5	± 1.5	-
Weight (Kg)			
Baseline weight in Kg: 115 of 115 Endotracheal poractant alfa participants had weight measured at baseline, data was unobtainable for 0 participants. 116 of 117 Sham Intervention group participants had weight measured at baseline, data was unobtainable for 1 participant.			
Units: Kg			
median	4.0	4.0	
inter-quartile range (Q1-Q3)	3.0 to 5.0	3.1 to 5.0	-
Weight (Kg)			
Baseline weight in Kg: 115 of 115 Endotracheal poractant alfa participants had weight measured at baseline, data was unobtainable for 0 participants. 116 of 117 Sham Intervention group participants had			

weight measured at baseline, data was unobtainable for 1 participant.			
Units: Kg			
median	4.0	4.0	
full range (min-max)	2.0 to 8.9	2.0 to 8.8	-
Time on mechanical ventilator prior to arrival at PICU (hours)			
Baseline time on mechanical ventilator prior to arrival at PICU (hours): 111 of 115 Endotracheal poractant alfa participants had time on mechanical ventilator prior to arrival at PICU (hours) measured at baseline, data was unobtainable for 4 participants. 116 of 117 Sham Intervention group participants had time on mechanical ventilator prior to arrival at PICU (hours) measured at baseline, data was unobtainable for 1 participant.			
Units: Hours			
arithmetic mean	29.4	29.4	
standard deviation	± 9.4	± 10.4	-
Time on mechanical ventilator prior to arrival at PICU (hours)			
Baseline time on mechanical ventilator prior to arrival at PICU (hours): 111 of 115 Endotracheal poractant alfa participants had time on mechanical ventilator prior to arrival at PICU (hours) measured at baseline, data was unobtainable for 4 participants. 116 of 117 Sham Intervention group participants had time on mechanical ventilator prior to arrival at PICU (hours) measured at baseline, data was unobtainable for 1 participant.			
Units: Hours			
median	30.1	29.9	
inter-quartile range (Q1-Q3)	22.7 to 37.0	21.3 to 37.1	-
Time on mechanical ventilator prior to arrival at PICU (hours)			
Baseline time on mechanical ventilator prior to arrival at PICU (hours): 111 of 115 Endotracheal poractant alfa participants had time on mechanical ventilator prior to arrival at PICU (hours) measured at baseline, data was unobtainable for 4 participants. 116 of 117 Sham Intervention group participants had time on mechanical ventilator prior to arrival at PICU (hours) measured at baseline, data was unobtainable for 1 participant.			
Units: Hours			
median	30.1	29.9	
full range (min-max)	9.1 to 47.5	4.1 to 47.6	-

End points

End points reporting groups

Reporting group title	Endotracheal poractant alfa
Reporting group description: -	
Reporting group title	Sham Intervention group
Reporting group description: -	
Subject analysis set title	Endotracheal poractant alfa (Safety set)
Subject analysis set type	Safety analysis
Subject analysis set description: Endotracheal poractant alfa (Safety set)	
Subject analysis set title	Sham Intervention group (Safety set)
Subject analysis set type	Safety analysis
Subject analysis set description: Sham Intervention group (Safety set)	
Subject analysis set title	Endotracheal poractant alfa (patient reported readmission)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Patients randomised to Endotracheal poractant alfa and completed the patient reported readmission to hospital.	
Subject analysis set title	Sham Intervention group (patient reported readmission)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Patients randomised to Sham Intervention group and completed the patient reported readmission to hospital.	
Subject analysis set title	Endotracheal poractant alfa (baseline weight)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Endotracheal poractant alfa (baseline weight) - 115 of 115 Endotracheal poractant alfa participants had weight measured at baseline, data was unobtainable for 0 participants	
Subject analysis set title	Sham Intervention group (baseline weight)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Sham Intervention group (baseline weight) - 116 of 117 Sham Intervention group participants had weight measured at baseline, data was unobtainable for 1 participant	
Subject analysis set title	Endotracheal poractant alfa (baseline time on ventilator)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Endotracheal poractant alfa (baseline time on mechanical ventilator prior to arrival at PICU (hours)) - 111 of 115 Endotracheal poractant alfa participants had time on mechanical ventilator prior to arrival at PICU (hours) measured at baseline, data was unobtainable for 4 participants.	
Subject analysis set title	Sham Intervention group (baseline time on ventilator)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Sham Intervention group (baseline time on mechanical ventilator prior to arrival at PICU (hours)) - 116 of 117 Sham Intervention group had time on mechanical ventilator prior to arrival at PICU (hours) measured at baseline, data was unobtainable for 1 participant.	

Primary: Primary outcome – Total duration of mechanical ventilation in hours - Time to successful extubation - Median (IQR)

End point title	Primary outcome – Total duration of mechanical ventilation in hours - Time to successful extubation - Median (IQR)

End point description:

A more extensive summary of results for this outcome can be found in the attached BESS - Final_Analysis_Report_v5.0_20260311.pdf.

End point type	Primary

End point timeframe:

Date/time of randomisation to date/time of successful extubation.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	116		
Units: hours				
median (inter-quartile range (Q1-Q3))	64.9 (43.2 to 92.1)	62.0 (39.3 to 95.1)		

Statistical analyses

Statistical analysis title	Two-sample t-test for log time on MV in hours
Comparison groups	Sham Intervention group v Endotracheal poractant alfa
Number of subjects included in analysis	229
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8625
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.18
upper limit	0.21

Primary: Primary outcome – Total duration of mechanical ventilation in hours - Time to successful extubation - Median (Range)

End point title	Primary outcome – Total duration of mechanical ventilation in hours - Time to successful extubation - Median (Range)

End point description:

End point type	Primary

End point timeframe:

Date/time of randomisation to date/time of successful extubation.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	116		
Units: hours				
median (full range (min-max))	64.9 (1.9 to 500.3)	62.0 (12.6 to 1631.6)		

Statistical analyses

Statistical analysis title	Two-sample t-test for log time on MV in hours
Comparison groups	Endotracheal poractant alfa v Sham Intervention group
Number of subjects included in analysis	229
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8625
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.18
upper limit	0.21

Primary: Primary outcome – Total duration of mechanical ventilation (MV) in hours

End point title	Primary outcome – Total duration of mechanical ventilation (MV) in hours

End point description:

End point type	Primary

End point timeframe:

Date/time of randomisation to date/time of successful extubation.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	116		
Units: log time on MV (hours)				
arithmetic mean (confidence interval 95%)	4.14 (4.01 to 4.28)	4.13 (3.99 to 4.27)		

Statistical analyses

Statistical analysis title	Two-sample t-test for log time on MV in hours
Comparison groups	Endotracheal poractant alfa v Sham Intervention group
Number of subjects included in analysis	229
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8625
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.18
upper limit	0.21

Statistical analysis title	Fixed Effects- log time on MV (hours) - Allocation
Comparison groups	Endotracheal poractant alfa v Sham Intervention group
Number of subjects included in analysis	229
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8806
Method	ANCOVA
Parameter estimate	Endotracheal poractant- Treatment effect
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.17
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.09

Secondary: Secondary outcome 1 – Readiness for SBT - Time to readiness for SBT in hours

End point title	Secondary outcome 1 – Readiness for SBT - Time to readiness for SBT in hours

End point description:

A more extensive summary of results for this outcome can be found in the attached BESS - Final_Analysis_Report_v5.0_20260311.pdf.

End point type	Secondary

End point timeframe:

Date/time of randomisation to the date/time of the observation at which readiness for SBT is first reported.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	104		
Units: hours				
median (inter-quartile range (Q1-Q3))	57.3 (32.4 to 75.6)	37.2 (25.6 to 81.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary outcome 1 – Readiness for SBT - Frequency of the SBT criteria being met per participant

End point title	Secondary outcome 1 – Readiness for SBT - Frequency of the SBT criteria being met per participant

End point description:

End point type	Secondary

End point timeframe:

Date/time of randomisation to the date/time of the observation at which readiness for SBT is first reported.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	117		
Units: Total occurrences of SBT readiness				
0 occurences of SBT readiness	17	13		
1 occurence of SBT readiness	71	63		
2 occurences of SBT readiness	20	25		
3 occurences of SBT readiness	4	8		
4 occurences of SBT readiness	1	5		
5 occurences of SBT readiness	2	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary outcome 1 – Readiness for SBT - Two-sample t-test for log time to SBT in hours

End point title	Secondary outcome 1 – Readiness for SBT - Two-sample t-test for log time to SBT in hours

End point description:

End point type	Secondary

End point timeframe:

Date/time of randomisation to the date/time of the observation at which readiness for SBT is first reported.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	104		
Units: log hours				
arithmetic mean (confidence interval 95%)	3.78 (3.55 to 4.00)	3.79 (3.61 to 3.97)		

Statistical analyses

Statistical analysis title	Endotracheal poractant alfa- Sham Intervention

Statistical analysis description:

Result for two-sample t-test for log time to SBT in hours
Difference (Endotracheal poractant alfa- Sham Intervention group)

Comparison groups	Endotracheal poractant alfa v Sham Intervention group
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9373
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	0.27

Secondary: Secondary outcome 1 – sensitivity analysis: First SBT criteria - two-

sample t-test for time to SBT: sensitivity analysis

End point title	Secondary outcome 1 – sensitivity analysis: First SBT criteria - two-sample t-test for time to SBT: sensitivity analysis

End point description:

End point type	Secondary

End point timeframe:

Date/time of randomisation to the date/time of the observation at which readiness for SBT is first reported.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	104		
Units: log hours				
arithmetic mean (confidence interval 95%)	3.78 (3.55 to 4.00)	3.80 (3.61 to 3.98)		

Statistical analyses

Statistical analysis title	Endotracheal poractant alfa- Sham Intervention

Statistical analysis description:

Result for two-sample t-test for time to SBT: sensitivity analysis
Difference (Endotracheal poractant alfa- Sham Intervention group)

Comparison groups	Sham Intervention group v Endotracheal poractant alfa
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8994
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.27

Secondary: Secondary outcome 2 – Number of trial interventions - Frequency of trial interventions

End point title	Secondary outcome 2 – Number of trial interventions - Frequency of trial interventions

End point description:

A more extensive summary of results for this outcome can be found in the attached BESS -

Final_Analysis_Report_v5.0_20260311.pdf.

End point type	Secondary

End point timeframe:

add

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	117		
Units: Total trial interventions				
0 trial interventions	6	3		
1 trial intervention	17	10		
2 trial interventions	17	21		
3 trial interventions	75	83		

Statistical analyses

Statistical analysis title	Fishers exact
Comparison groups	Endotracheal poractant alfa v Sham Intervention group
Number of subjects included in analysis	232
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3166
Method	Fisher exact

Secondary: Secondary outcome 4 – Duration of oxygen supplementation - Time on oxygen supplementation (of any kind) - Mean (S.D.)

End point title	Secondary outcome 4 – Duration of oxygen supplementation - Time on oxygen supplementation (of any kind) - Mean (S.D.)

End point description:

A more extensive summary of results for this outcome can be found in the attached BESS - Final_Analysis_Report_v5.0_20260311.pdf.

End point type	Secondary

End point timeframe:

Date and time of final successful extubation (if this has been observed) to final date and time that any type of oxygen supplementation is ended.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	117		
Units: Time on oxygen supplementation (hours)				
arithmetic mean (standard deviation)	280.9 (± 2455.2)	58.4 (± 74.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary outcome 4 – Duration of oxygen supplementation - Time on oxygen supplementation (of any kind) - Median (IQR)

End point title	Secondary outcome 4 – Duration of oxygen supplementation - Time on oxygen supplementation (of any kind) - Median (IQR)

End point description:

End point type	Secondary

End point timeframe:

Date and time of final successful extubation (if this has been observed) to final date and time that any type of oxygen supplementation is ended.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	117		
Units: Time on oxygen supplementation (hours)				
median (inter-quartile range (Q1-Q3))	40.9 (17.0 to 90.0)	34.0 (16.0 to 81.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary outcome 4 – Duration of oxygen supplementation - Time on oxygen supplementation (of any kind) - Median (Range)

End point title	Secondary outcome 4 – Duration of oxygen supplementation - Time on oxygen supplementation (of any kind) - Median (Range)

End point description:

End point type	Secondary

End point timeframe:

Date and time of final successful extubation (if this has been observed) to final date and time that any type of oxygen supplementation is ended.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	117		
Units: Time on oxygen supplementation (hours)				
median (full range (min-max))	40.9 (0.0 to 26376.3)	34.0 (0.0 to 536.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary outcome 4 – Duration of oxygen supplementation - Results of two-sample t-test for duration of oxygen supplementation

End point title	Secondary outcome 4 – Duration of oxygen supplementation - Results of two-sample t-test for duration of oxygen supplementation

End point description:

End point type	Secondary

End point timeframe:

Date and time of final successful extubation (if this has been observed) to final date and time that any type of oxygen supplementation is ended.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	117		
Units: log hours				
arithmetic mean (confidence interval 95%)	3.07 (2.58 to 3.56)	2.18 (1.48 to 2.89)		

Statistical analyses

Statistical analysis title	Endotracheal poractant alfa- Sham Intervention

Statistical analysis description:

Results of two-sample t-test for duration of oxygen supplementation:
Difference (Endotracheal poractant alfa- Sham Intervention group)

Comparison groups	Endotracheal poractant alfa v Sham Intervention group
Number of subjects included in analysis	232
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0428
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	1.74

Secondary: Secondary outcome 5 – Use of steroids to assist extubation - Frequency of steroid use

End point title	Secondary outcome 5 – Use of steroids to assist extubation - Frequency of steroid use
End point description:	

End point type	Secondary
End point timeframe:	
add	

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	117		
Units: No. participants				
Yes	51	49		
No	64	68		

Statistical analyses

Statistical analysis title	Pearson's Chi-Square test
Comparison groups	Endotracheal poractant alfa v Sham Intervention group
Number of subjects included in analysis	232
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7044
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	1.06

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.42

Secondary: Secondary outcome 6 - Time on post-extubation respiratory support (non-invasive) - Mean (S.D.)

End point title	Secondary outcome 6 - Time on post-extubation respiratory support (non-invasive) - Mean (S.D.)

End point description:

A more extensive summary of results for this outcome can be found in the attached BESS - Final_Analysis_Report_v5.0_20260311.pdf.

End point type	Secondary

End point timeframe:

Date and time of final successful extubation (if this has been observed) to final date and time that NIV is ended.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	117		
Units: Hours				
arithmetic mean (standard deviation)	17.1 (± 34.1)	19.5 (± 48.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary outcome 6 - Time on post-extubation respiratory support (non-invasive) - Median (IQR)

End point title	Secondary outcome 6 - Time on post-extubation respiratory support (non-invasive) - Median (IQR)

End point description:

End point type	Secondary

End point timeframe:

Date and time of final successful extubation (if this has been observed) to final date and time that NIV is ended.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	117		
Units: Hours				
median (inter-quartile range (Q1-Q3))	0.0 (0.0 to 15.7)	0.0 (0.0 to 0.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary outcome 6 - Time on post-extubation respiratory support (non-invasive) - Median (Range)

End point title	Secondary outcome 6 - Time on post-extubation respiratory support (non-invasive) - Median (Range)

End point description:

End point type	Secondary

End point timeframe:

Date and time of final successful extubation (if this has been observed) to final date and time that NIV is ended.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	117		
Units: Hours				
median (full range (min-max))	0.0 (0.0 to 146.0)	0.0 (0.0 to 285.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary outcome 6 - Results of two-sample t-test for duration of post-extubation respiratory support

End point title	Secondary outcome 6 - Results of two-sample t-test for duration of post-extubation respiratory support

End point description:

End point type	Secondary

End point timeframe:

Date and time of final successful extubation (if this has been observed) to final date and time that NIV is ended.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	117		
Units: log hours				
arithmetic mean (confidence interval 95%)	-3.73 (-4.63 to -2.82)	-4.24 (-5.11 to -3.38)		

Statistical analyses

Statistical analysis title	Endotracheal poractant alfa- Sham Intervention

Statistical analysis description:

Results of two-sample t-test for duration of post-extubation respiratory support:
Difference (Endotracheal poractant alfa- Sham Intervention group)

Comparison groups	Endotracheal poractant alfa v Sham Intervention group
Number of subjects included in analysis	232
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4125
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.72
upper limit	1.76

Secondary: Secondary outcome 7 - Time in PICU - Mean (S.D.)

End point title	Secondary outcome 7 - Time in PICU - Mean (S.D.)

End point description:

A more extensive summary of results for this outcome can be found in the attached BESS - Final_Analysis_Report_v5.0_20260311.pdf.

End point type	Secondary

End point timeframe:

Date/time of randomisation to the date/ time of discharge from PICU or the date of death if the death occurred before PICU discharge.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	116		
Units: Hours				
arithmetic mean (standard deviation)	121.6 (± 80.9)	134.8 (± 198.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary outcome 7 - Time in PICU - Median (IQR)

End point title	Secondary outcome 7 - Time in PICU - Median (IQR)

End point description:

End point type	Secondary

End point timeframe:

Date/time of randomisation to the date/ time of discharge from PICU or the date of death if the death occurred before PICU discharge.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	116		
Units: Hours				
median (inter-quartile range (Q1-Q3))	104.4 (67.9 to 153.1)	93.4 (66.6 to 144.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary outcome 7 - Time in PICU - Median (Range)

End point title	Secondary outcome 7 - Time in PICU - Median (Range)

End point description:

End point type	Secondary

End point timeframe:

Date/time of randomisation to the date/ time of discharge from PICU or the date of death if the death occurred before PICU discharge.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	116		
Units: Hours				
median (full range (min-max))	104.4 (17.9 to 571.7)	93.4 (24.4 to 2095.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary outcome 7 - Time in hospital (including both time in PICU and time in hospital) - Mean (S.D.)

End point title	Secondary outcome 7 - Time in hospital (including both time in PICU and time in hospital) - Mean (S.D.)

End point description:

End point type	Secondary

End point timeframe:

Date/time of randomisation to the date/time of hospital discharge or the date of death if death occurred before hospital discharge.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	114		
Units: Hours				
arithmetic mean (standard deviation)	200.8 (± 174.3)	171.2 (± 100.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary outcome 7 - Time in hospital (including both time in PICU and time in hospital) - Median (IQR)

End point title	Secondary outcome 7 - Time in hospital (including both time in PICU and time in hospital) - Median (IQR)

End point description:

End point type	Secondary

End point timeframe:

Date/time of randomisation to the date/time of hospital discharge or the date of death if death occurred before hospital discharge.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	114		
Units: Hours				
median (inter-quartile range (Q1-Q3))	165.3 (111.3 to 231.2)	142.2 (96.6 to 221.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary outcome 7 - Time in hospital (including both time in PICU and time in hospital) - Median (Range)

End point title	Secondary outcome 7 - Time in hospital (including both time in PICU and time in hospital) - Median (Range)

End point description:

End point type	Secondary

End point timeframe:

Date/time of randomisation to the date/time of hospital discharge or the date of death if death occurred before hospital discharge.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	114		
Units: Hours				
median (full range (min-max))	165.3 (17.9 to 1616.2)	142.2 (34.3 to 430.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary outcome 7 - Results of two-sample t-test for duration of stay in PICU in hours

End point title	Secondary outcome 7 - Results of two-sample t-test for duration of stay in PICU in hours

End point description:

End point type	Secondary

End point timeframe:

Date/time of randomisation to the date/ time of discharge from PICU or the date of death if the death occurred before PICU discharge.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	116		
Units: log hours				
log mean (confidence interval 95%)	4.62 (4.51 to 4.73)	4.62 (4.50 to 4.74)		

Statistical analyses

Statistical analysis title	Endotracheal poractant alfa- Sham Intervention

Statistical analysis description:

Results of two-sample t-test for duration of stay in PICU in hours
Difference (Endotracheal poractant alfa- Sham Intervention group)

Comparison groups	Endotracheal poractant alfa v Sham Intervention group
Number of subjects included in analysis	230
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9453
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.17

Secondary: Secondary outcome 7 - Results of two-sample t-test for duration of stay in hospital (post PICU stay)

End point title	Secondary outcome 7 - Results of two-sample t-test for duration of stay in hospital (post PICU stay)

End point description:

End point type	Secondary

End point timeframe:

Date/time of discharge from PICU to Date/time of hospital discharge.

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	114		
Units: log hours				
log mean (confidence interval 95%)	5.09 (4.98 to 5.21)	4.97 (4.86 to 5.08)		

Statistical analyses

Statistical analysis title	Endotracheal poractant alfa- Sham Intervention

Statistical analysis description:

Results of two-sample t-test for duration of stay in hospital (post PICU stay)
Difference (Endotracheal poractant alfa- Sham Intervention group)

Comparison groups	Endotracheal poractant alfa v Sham Intervention group
Number of subjects included in analysis	227
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1331
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0.28

Secondary: Secondary outcome 8 – Liverpool Respiratory Symptom Questionnaire - Summary of LRSQ data at 6 months - Mean (S.D.)

End point title	Secondary outcome 8 – Liverpool Respiratory Symptom Questionnaire - Summary of LRSQ data at 6 months - Mean (S.D.)

End point description:

A more extensive summary of results for this outcome can be found in the attached BESS - Final_Analysis_Report_v5.0_20260311.pdf.

End point type	Secondary

End point timeframe:

At 6 months

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	14		
Units: LRSQ Score				
arithmetic mean (standard deviation)	22.1 (± 25.9)	26.4 (± 27.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary outcome 8 – Liverpool Respiratory Symptom Questionnaire - Summary of LRSQ data at 6 months - Median (IQR)

End point title	Secondary outcome 8 – Liverpool Respiratory Symptom Questionnaire - Summary of LRSQ data at 6 months - Median (IQR)

End point description:

End point type	Secondary

End point timeframe:

At 6 months

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	14		
Units: LRSQ Score				
median (inter-quartile range (Q1-Q3))	12.0 (11.0 to 18.0)	14.5 (4.0 to 60.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary outcome 8 – Liverpool Respiratory Symptom Questionnaire - Summary of LRSQ data at 6 months - Median (Range)

End point title	Secondary outcome 8 – Liverpool Respiratory Symptom Questionnaire - Summary of LRSQ data at 6 months - Median (Range)

End point description:

End point type	Secondary
End point timeframe: At 6 months	

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	14		
Units: LRSQ Score				
median (full range (min-max))	12.0 (0.0 to 80.0)	14.5 (0.0 to 74.0)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Safety outcome 1 – Failure to administer intervention due to AE - Frequency of trial interventions not delivered due to AE

End point title	Safety outcome 1 – Failure to administer intervention due to AE - Frequency of trial interventions not delivered due to AE
End point description:	

End point type	Other pre-specified
End point timeframe: add	

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	117		
Units: Participants				
0 trial interventions not delivered	112	117		
1 trial intervention not delivered	3	0		

Statistical analyses

Statistical analysis title	Fisher's Exact Test
Comparison groups	Endotracheal poractant alfa v Sham Intervention group

Number of subjects included in analysis	232
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1202
Method	Fisher exact

Other pre-specified: Safety outcome 2 – Incidence of air leak - Frequency of the total incidences or air leak per participant

End point title	Safety outcome 2 – Incidence of air leak - Frequency of the total incidences or air leak per participant

End point description:

End point type	Other pre-specified

End point timeframe:

add

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	117		
Units: Participants				
0 incidences of air leaks	114	116		
1 incidence of air leak	1	1		

Statistical analyses

Statistical analysis title	Fisher's Exact Test
Comparison groups	Endotracheal poractant alfa v Sham Intervention group
Number of subjects included in analysis	232
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Fisher exact

Other pre-specified: Safety outcome 3 – Parent reported readmission to hospital - Frequency of the total reported readmissions to hospital

End point title	Safety outcome 3 – Parent reported readmission to hospital - Frequency of the total reported readmissions to hospital

End point description:

End point type	Other pre-specified

End point timeframe: add

End point values	Endotracheal poractant alfa (patient reported readmission)	Sham Intervention group (patient reported readmission)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	28		
Units: Participants				
0 readmissions	15	23		
1 readmission	6	5		
2 readmissions	1	0		
3 readmissions	4	0		
4 readmissions	0	0		
5 readmissions	0	0		
>=6 readmissions	0	0		

Statistical analyses

Statistical analysis title	Fisher's Exact Test
Comparison groups	Endotracheal poractant alfa (patient reported readmission) v Sham Intervention group (patient reported readmission)
Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0561
Method	Fisher exact

Other pre-specified: Safety outcome 4 – Any need to replace the endotracheal tube - Frequency of endotracheal tubes replacements

End point title	Safety outcome 4 – Any need to replace the endotracheal tube - Frequency of endotracheal tubes replacements
End point description:	
End point type	Other pre-specified
End point timeframe: add	

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	117		
Units: Participants				
Endotracheal tube replaced: Yes	18	21		
Endotracheal tube replaced: No	97	96		

Statistical analyses

Statistical analysis title	Pearson's Chi-Square test
Comparison groups	Endotracheal poractant alfa v Sham Intervention group
Number of subjects included in analysis	232
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.64
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	1.55

Post-hoc: Virology – post-hoc request - Virology reported on the discharge CRF

End point title	Virology – post-hoc request - Virology reported on the discharge CRF

End point description:

End point type	Post-hoc

End point timeframe:

Virology reported on the discharge CRF

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	117		
Units: Participants				
Adenovirus	3	6		
Coronavirus OC43	0	1		
Enterovirus	5	8		
Influenza A	0	2		

Influenza A/H1	0	1		
Influenza B	0	1		
Metapneumovirus	2	5		
No Infection Identified	8	5		
No Sample	4	0		
No form returned	2	1		
Parainfluenza 1	1	0		
Parainfluenza 3	1	1		
Parainfluenza 4	1	0		
Respiratory Syncytial virus	87	88		
Rhinovirus	21	29		
SARS-CoV-2 (COVID-19)	1	1		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Bacteriology – post-hoc request - Bacteriology reported on the discharge CRF

End point title	Bacteriology – post-hoc request - Bacteriology reported on the discharge CRF

End point description:

End point type	Post-hoc

End point timeframe:

Bacteriology reported on the discharge CRF

End point values	Endotracheal poractant alfa	Sham Intervention group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	117		
Units: Participants				
Haemophilus influenzae	18	17		
No Infection Identified	79	82		
No Sample	4	2		
No form returned	4	4		
Normal flora	3	0		
Staphylococcus aureus	5	12		
Strep. Pneumonia (group B strep.)	4	3		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Safety outcome data by safety set – Post hoc - Safety outcome 1 - Frequency of trial interventions not delivered due to AE

End point title	Safety outcome data by safety set – Post hoc - Safety outcome 1 - Frequency of trial interventions not delivered due to AE

End point description:

End point type	Post-hoc

End point timeframe:

add

End point values	Endotracheal poractant alfa (Safety set)	Sham Intervention group (Safety set)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	109	114		
Units: Participants				
0 trial interventions not delivered:	107	114		
1 trial intervention not delivered:	2	0		

Statistical analyses

Statistical analysis title	Fisher's Exact Test
Comparison groups	Endotracheal poractant alfa (Safety set) v Sham Intervention group (Safety set)
Number of subjects included in analysis	223
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.2378
Method	Fisher exact

Post-hoc: Safety outcome data by safety set – Post hoc - Safety outcome 2 - Frequency of the total incidences or air leak per participant

End point title	Safety outcome data by safety set – Post hoc - Safety outcome 2 - Frequency of the total incidences or air leak per participant

End point description:

End point type	Post-hoc

End point timeframe:

add

End point values	Endotracheal poractant alfa (Safety set)	Sham Intervention group (Safety set)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	109	114		
Units: Participants				
0 incidences of air leaks:	108	113		
1 incidence of air leaks:	1	1		

Statistical analyses

Statistical analysis title	Fisher's Exact Test
Comparison groups	Endotracheal poractant alfa (Safety set) v Sham Intervention group (Safety set)
Number of subjects included in analysis	223
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 1
Method	Fisher exact

Post-hoc: Safety outcome data by safety set – Post hoc - Safety outcome 3 - Frequency of the total reported readmissions to hospital

End point title	Safety outcome data by safety set – Post hoc - Safety outcome 3 - Frequency of the total reported readmissions to hospital

End point description:

End point type	Post-hoc

End point timeframe:

add

End point values	Endotracheal poractant alfa (Safety set)	Sham Intervention group (Safety set)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	28		
Units: Participants				
0 readmissions:	15	23		
1 readmission:	6	5		
2 readmissions:	1	0		
3 readmissions:	4	0		
4 readmissions:	0	0		
5 readmissions:	0	0		
>=6 readmissions:	0	0		

Statistical analyses

Statistical analysis title	Fisher's Exact Test
Comparison groups	Endotracheal poractant alfa (Safety set) v Sham Intervention group (Safety set)
Number of subjects included in analysis	54
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.0561
Method	Fisher exact

Post-hoc: Safety outcome data by safety set – Post hoc - Safety outcome 4 – Any need to replace the endotracheal tube

End point title	Safety outcome data by safety set – Post hoc - Safety outcome 4 – Any need to replace the endotracheal tube
End point description:	
End point type	Post-hoc
End point timeframe: add	

End point values	Endotracheal poractant alfa (Safety set)	Sham Intervention group (Safety set)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	109	114		
Units: Participants				
Endotracheal tube replaced: Yes	18	20		
Endotracheal tube replaced: No	91	94		

Statistical analyses

Statistical analysis title	Pearson's Chi-Square test
Comparison groups	Endotracheal poractant alfa (Safety set) v Sham Intervention group (Safety set)

Number of subjects included in analysis	223
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.838
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.68

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs from randomisation until 24 hrs after last administration of poractant alfa are reported. Related AEs occurring after this time point until 90 days post randomisation / discharge / death are reported. SAEs/SARs are reported regardless of timeframe

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Endotracheal poractant alfa (Safety set)
Reporting group description: -	
Reporting group title	Sham Intervention group (Safety set)

Reporting group description: -

Serious adverse events	Endotracheal poractant alfa (Safety set)	Sham Intervention group (Safety set)	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 109 (5.50%)	6 / 114 (5.26%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Endotracheal intubation complication			
subjects affected / exposed	0 / 109 (0.00%)	1 / 114 (0.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 109 (0.00%)	1 / 114 (0.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 109 (0.92%)	0 / 114 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			

Hypoxia			
subjects affected / exposed	1 / 109 (0.92%)	0 / 114 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obliterative bronchiolitis			
subjects affected / exposed	0 / 109 (0.00%)	1 / 114 (0.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 109 (0.92%)	1 / 114 (0.88%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary haemorrhage			
subjects affected / exposed	1 / 109 (0.92%)	0 / 114 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Adenovirus infection			
subjects affected / exposed	0 / 109 (0.00%)	1 / 114 (0.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	2 / 109 (1.83%)	0 / 114 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parainfluenzae virus infection			
subjects affected / exposed	1 / 109 (0.92%)	0 / 114 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 109 (0.00%)	1 / 114 (0.88%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Endotracheal poractant alfa (Safety set)	Sham Intervention group (Safety set)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 109 (12.84%)	8 / 114 (7.02%)	
Investigations			
Oxygen saturation decreased			
subjects affected / exposed	4 / 109 (3.67%)	0 / 114 (0.00%)	
occurrences (all)	5	0	
Injury, poisoning and procedural complications			
Endotracheal intubation complication			
subjects affected / exposed	1 / 109 (0.92%)	1 / 114 (0.88%)	
occurrences (all)	1	1	
Sedation complication			
subjects affected / exposed	1 / 109 (0.92%)	0 / 114 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	4 / 109 (3.67%)	0 / 114 (0.00%)	
occurrences (all)	4	0	
Surgical and medical procedures			
Extubation			
subjects affected / exposed	2 / 109 (1.83%)	1 / 114 (0.88%)	
occurrences (all)	2	1	
Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 109 (0.00%)	1 / 114 (0.88%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Perforation			
subjects affected / exposed	0 / 109 (0.00%)	1 / 114 (0.88%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	0 / 109 (0.00%)	1 / 114 (0.88%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			

Otorrhoea			
subjects affected / exposed	0 / 109 (0.00%)	1 / 114 (0.88%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Genital discharge			
subjects affected / exposed	1 / 109 (0.92%)	0 / 114 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 109 (0.00%)	1 / 114 (0.88%)	
occurrences (all)	0	1	
Hypoxia			
subjects affected / exposed	0 / 109 (0.00%)	1 / 114 (0.88%)	
occurrences (all)	0	1	
Respiratory depth decreased			
subjects affected / exposed	1 / 109 (0.92%)	0 / 114 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	0 / 109 (0.00%)	1 / 114 (0.88%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	1 / 109 (0.92%)	0 / 114 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 109 (0.92%)	0 / 114 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 July 2019	Amendment from Protocol V2.0 to V3.0 - See section 18.3 of attached BESS Protocol V7.0 for a summary of amendments.
24 November 2022	Amendment from Protocol V3.0 to V4.0 - See section 18.4 of attached BESS Protocol V7.0 for a summary of amendments.
07 February 2023	Amendment from Protocol V4.0 to V5.0 - See section 18.5 of attached BESS Protocol V7.0 for a summary of amendments.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
20 March 2020	There was a temporary halt to recruitment from 20/03/2020 until 01/10/2020 due to COVID-19.	01 October 2020

Notes:

Limitations and caveats

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

Results for a primary outcome sensitivity analysis and for Secondary outcome 3 - Change over time in blood/ gas measurements are not included in this summary but results are provided in the attached "BESS - Final_Analysis_Report_v5.0_20260311.pdf"

Notes: