Clinical trial results:
ASpirin as a Treatment for ARDS (STAR) trial: a randomised, double-blind, allocation concealed, placebo-controlled phase 2 trial.

Summary

EudraCT number	2014-002564-32
Trial protocol	GB
Global end of trial date	04 January 2019

Results information

Result version number	v1 (current)
This version publication date	04 February 2020
First version publication date	04 February 2020

Trial information

Trial identification

Sponsor protocol code	14043DMcA-AS

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02326350
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Belfast Health and Social Care Trust
Sponsor organisation address	Grosvenor road, Belfast, United Kingdom, BT179RN
Public contact	Danny McAuley, Queen's University Belfast, 0044 02890 976385, d.f.mcauley@qub.ac.uk
Scientific contact	Danny McAuley, Queen's University Belfast, 0044 02890 976385, d.f.mcauley@qub.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 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 May 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 November 2018
Global end of trial reached?	Yes
Global end of trial date	04 January 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The aim of this study was to test the hypothesis that aspirin was both safe and effective in the treatment of patients with acute respiratory distress syndrome (ARDS)

The trial objective was to undertaken a randomised double blind placebo controlled clinical trial to study whether aspirin improves important surrogate markers of clinical outcome and is safe in adult patients with ARDS.

Protection of trial subjects:

Patients were closely monitored for AEs.
A Clinical Trials Monitor monitored study site compliance with study and sponsor SOPs and provided feedback to the Trial Management Group on any actual or potential problems in relation to safeguarding patients safety and wellbeing.

The study protocol was published http://www.criticalcarehorizons.com/2018-star-protocol/.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 February 2015
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: 49
Worldwide total number of subjects	49
EEA total number of subjects	49

Notes:

Subjects enrolled per age group

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

Adolescents (12-17 years)	0
Adults (18-64 years)	38
From 65 to 84 years	9
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

The study was open to recruitment between Feb 9, 2015, and Nov 23, 2018. A total of 593 patients were screened and 49 were randomised to the study from 5 study sites in Northern Ireland.

Pre-assignment

Screening details:

Patients receiving invasive mechanical ventilation, ARDS as defined by the Berlin definition, Onset within 1 week of identified insult, Within the same 24 hour time period: Hypoxic respiratory failure, Bilateral infiltrates on chest X-ray consistent with pulmonary oedema not explained by another pulmonary pathology, No evidence of heart failure or

Pre-assignment period milestones

Number of subjects started	49
Number of subjects completed	49

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, Assessor

Blinding implementation details:

Identical placebo and central randomisation

Arms

Are arms mutually exclusive?	Yes
Arm title	Aspirin

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Aspirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

75mg

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

75gm

Number of subjects in period 1	Aspirin	Placebo
Started	24	25
Completed	24	25

Baseline characteristics

Reporting groups	
Reporting group title	Aspirin
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Aspirin	Placebo	Total
Number of subjects	24	25	49
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)	19	19	38
From 65-84 years	5	4	9
85 years and over	0	2	2
Age continuous Units: years			
arithmetic mean	55.4	56.4	
standard deviation	± 12.0	± 17.7	-
Gender categorical Units: Subjects			
Female	10	15	25
Male	14	10	24
Vasopressor Requirement Units: Subjects			
Yes	13	16	29
No	11	9	20
Mode of Ventilation Units: Subjects			
Controlled ventilation	7	13	20
PS	7	5	12
Other	10	7	17
Aetiology of ARDs- Smoke/Toxin inhalation Units: Subjects			
Yes	1	2	3
No	23	23	46
Aetiology of ARDS - Gastric Content Aspiration Units: Subjects			
Yes	6	6	12
No	18	19	37

Aetiology of ARDS- Near Drowning Units: Subjects			
Yes	0	0	0
No	24	25	49
Aetiology of ARDS- Thoracic trauma Units: Subjects			
Yes	2	2	4
No	22	23	45
Aetiology of ARDS-Sepsis Units: Subjects			
Yes	5	10	15
No	19	15	34
Aetiology of ARDs- Cardiopulmonary bypass Units: Subjects			
Yes	0	0	0
No	24	25	49
Aetiology of ARDS-Pancreatitis Units: Subjects			
Yes	1	0	1
No	23	25	48
Aetiology of ARDS- Non-thoracic trauma Units: Subjects			
Yes	0	1	1
No	24	24	48
Aetiology of ARDS- Other Units: Subjects			
Yes	1	3	4
No	23	22	45
Aetiology of ARDS- Pneumonia Units: Subjects			
Yes	14	13	27
No	10	12	22
Height Units: cm			
arithmetic mean	169.2	166.7	
standard deviation	± 13.3	± 11.8	-
Weight Units: kg			
arithmetic mean	78.1	76.8	
standard deviation	± 23.9	± 24.0	-
Worst PF Ratio (pre-randomisation) Units: kPa			
arithmetic mean	13.6	13.1	
standard deviation	± 6.4	± 6.1	-
PF Ratio			
This data was collected at baseline			
Units: kPa			
arithmetic mean	26.3	23.8	
standard deviation	± 7.7	± 6.7	-
Plateau Pressure			

Aspirin, n=12 Placebo, n=15			
Units: cm H2O			
arithmetic mean	23.5	24.1	
standard deviation	± 6	± 4.9	-
Lowest Platelets			
Units: 10^9 per litre			
arithmetic mean	229.5	168.4	
standard deviation	± 105.8	± 86.5	-
Tidal Volume per Predicted Body Weight (All patients)			
Units: ml per kg			
arithmetic mean	7.2	7.6	
standard deviation	± 2.3	± 2.4	-
Tidal Volume per Predicted Body Weight (Controlled ventilation)			
Aspirin, n=7 Placebo, n=13			
Units: ml per kg			
arithmetic mean	7.2	6.7	
standard deviation	± 2.3	± 2.1	-
SAPS			
Aspirin, n=23 Placebo, n=25			
Units: score			
arithmetic mean	48.4	50.8	
standard deviation	± 16.8	± 15.5	-
APACHE II			
Units: score			
arithmetic mean	24.4	22.0	
standard deviation	± 7.3	± 7.7	-
SOFA			
Aspirin, n=23 Placebo, n=24			
Units: score			
arithmetic mean	9.4	10.3	
standard deviation	± 3.3	± 4.0	-
Oxygenation Index			
Units: cmH2O/kPa			
arithmetic mean	59.3	66.3	
standard deviation	± 30.3	± 21.0	-
Lowest Mean Arterial Pressure			
Units: mmHg			
arithmetic mean	64.3	65.0	
standard deviation	± 7.2	± 5.3	-

End points

End points reporting groups	
Reporting group title	Aspirin
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Oxygenation Index - Day 7

End point title	Oxygenation Index - Day 7
End point description:	
End point type	Primary
End point timeframe: Day 7	

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	17		
Units: mmHg				
arithmetic mean (standard deviation)	54.4 (± 26.8)	42.4 (± 25.0)		

Statistical analyses

Statistical analysis title	Primary outcome: Oxygenation Index (Day 7)
Comparison groups	Aspirin v Placebo
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.19
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.1
upper limit	30.1

Primary: Oxygenation index - Day 7 (Imputed)

End point title	Oxygenation index - Day 7 (Imputed)

End point description:

End point type	Primary

End point timeframe:

Day 7

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: mmHg				
arithmetic mean (standard deviation)	45.7 (± 27.0)	46.8 (± 33.8)		

Statistical analyses

Statistical analysis title	Oxygenation Index - Day 7 (Imputed)
Comparison groups	Placebo v Aspirin
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.7
upper limit	16.6

Secondary: Oxygenation Index - Day 4

End point title	Oxygenation Index - Day 4

End point description:

End point type	Secondary

End point timeframe:

Day 4

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	23		
Units: mmHg				
arithmetic mean (standard deviation)	61.4 (± 36.9)	54.5 (± 28.8)		

Statistical analyses

Statistical analysis title	Oxygenation Index - Day 4
Comparison groups	Aspirin v Placebo
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.49
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	6.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13
upper limit	26.8

Secondary: Oxygenation index - Day 14

End point title	Oxygenation index - Day 14

End point description:

End point type	Secondary

End point timeframe:

Day 14

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	10		
Units: mmHg				
arithmetic mean (standard deviation)	52.3 (± 36.6)	37.4 (± 24.1)		

Statistical analyses

Statistical analysis title	Oxygenation Index - Day 14
Comparison groups	Aspirin v Placebo

Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.33
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	14.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.4
upper limit	46.1

Secondary: Respiratory Compliance - Day 4

End point title	Respiratory Compliance - Day 4
End point description:	

End point type	Secondary
End point timeframe:	
Day 4	

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: mL/cm H2O				
arithmetic mean (standard deviation)	31.5 (± 24.3)	24.6 (± 11.8)		

Statistical analyses

Statistical analysis title	Respiratory Compliance - Day 4
Comparison groups	Aspirin v Placebo
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.46
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	6.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.2
upper limit	25.9

Secondary: Respiratory Compliance - Day 7

End point title	Respiratory Compliance - Day 7

End point description:

End point type	Secondary

End point timeframe:

Day 7

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: mL/cm H2O				
arithmetic mean (standard deviation)	65.5 (± 81.2)	37.1 (± 25.4)		

Statistical analyses

Statistical analysis title	Respiratory Compliance - Day 7
Comparison groups	Aspirin v Placebo
Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.53
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	28.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-75.7
upper limit	132.4

Secondary: Respiratory Compliance - Day 14

End point title	Respiratory Compliance - Day 14

End point description:

End point type	Secondary

End point timeframe:

Day 14

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	1		
Units: mL/cm H2O				
arithmetic mean (standard deviation)	36.5 (± 0)	14.2 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Delta SOFA - Day 4

End point title	Delta SOFA - Day 4
End point description: Change from Day 0 to Day 4	
End point type	Secondary
End point timeframe: Day 4	

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	21		
Units: score				
arithmetic mean (standard deviation)	-1.3 (± 2.9)	-1.9 (± 2.9)		

Statistical analyses

Statistical analysis title	Delta SOFA - Day 4
Comparison groups	Aspirin v Placebo
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.85
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	2.3

Secondary: Delta SOFA - Day 7

End point title	Delta SOFA - Day 7
End point description: Change from Day 0 to Day 7	
End point type	Secondary
End point timeframe: Day 7	

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	21		
Units: score				
arithmetic mean (standard deviation)	-2.8 (± 3.8)	-4.4 (± 3.0)		

Statistical analyses

Statistical analysis title	Delta SOFA - Day 7
Comparison groups	Aspirin v Placebo
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.13
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	3.8

Secondary: Delta SOFA - Day 14

End point title	Delta SOFA - Day 14
End point description: Change from Day 0 to Day 14	

End point type	Secondary
End point timeframe:	
Day 14	

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: score				
arithmetic mean (standard deviation)	-2.7 (± 3.6)	-7.3 (± 4.0)		

Statistical analyses

Statistical analysis title	Delta SOFA - Day 14
Comparison groups	Aspirin v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	7.9

Secondary: PF ratio - Day 4

End point title	PF ratio - Day 4
End point description:	

End point type	Secondary
End point timeframe:	
Day 4	

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	23		
Units: kpa				
arithmetic mean (standard deviation)	26.1 (± 9.2)	25.6 (± 9.0)		

Statistical analyses

Statistical analysis title	PF ratio - Day 4
Comparison groups	Aspirin v Placebo
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.85
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.9
upper limit	5.9

Secondary: PF ratio - Day 7

End point title	PF ratio - Day 7
End point description:	
End point type	Secondary
End point timeframe:	
Day 7	

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	22		
Units: kPa				
arithmetic mean (standard deviation)	26.8 (± 9.9)	30.6 (± 12.2)		

Statistical analyses

Statistical analysis title	PF ratio - Day 7
Comparison groups	Aspirin v Placebo

Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.27
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.6
upper limit	3.1

Secondary: PF ratio - Day 14

End point title	PF ratio - Day 14
End point description:	
End point type	Secondary
End point timeframe:	
Day 14	

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	15		
Units: kPa				
arithmetic mean (standard deviation)	27.7 (± 9.9)	28.8 (± 8.8)		

Statistical analyses

Statistical analysis title	PF ratio - Day 14
Comparison groups	Aspirin v Placebo
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.76
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9
upper limit	6.6

Secondary: SUSAR	
End point title	SUSAR
End point description:	
Safety and tolerability was assessed by the occurrence of suspected unexpected serious adverse reactions (SUSAR).	
End point type	Secondary
End point timeframe:	
28 day	

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: events	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: SOFA - Day 4	
End point title	SOFA - Day 4
End point description:	
End point type	Secondary
End point timeframe:	
Day 4	

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	24		
Units: score				
arithmetic mean (standard deviation)	8.0 (± 4.01)	8.1 (± 4.17)		

Statistical analyses

Statistical analysis title	SOFA - Day 4
Comparison groups	Placebo v Aspirin

Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.88
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.64
upper limit	2.28

Secondary: SOFA - day7

End point title	SOFA - day7
End point description:	

End point type	Secondary
End point timeframe:	
Day 7	

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	22		
Units: score				
arithmetic mean (standard deviation)	6.5 (± 3.84)	6.2 (± 4.24)		

Statistical analyses

Statistical analysis title	SOFA - Day 7
Comparison groups	Aspirin v Placebo
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.81
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	2.79

Secondary: SOFA - day14

End point title	SOFA - day14
End point description:	

End point type	Secondary
End point timeframe:	
Day 14	

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	13		
Units: score				
arithmetic mean (standard deviation)	5.5 (± 4.22)	3.8 (± 2.35)		

Statistical analyses

Statistical analysis title	SOFA - Day 14
Comparison groups	Aspirin v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.22
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.14
upper limit	4.61

Other pre-specified: Ventilator Free Day Score

End point title	Ventilator Free Day Score
End point description:	

End point type	Other pre-specified
End point timeframe:	
28 day	

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: score				
median (inter-quartile range (Q1-Q3))	16 (0 to 21.5)	15 (0 to 21)		

Statistical analyses

Statistical analysis title	VFD Score
Comparison groups	Placebo v Aspirin
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.72
Method	Sign test

Other pre-specified: Duration of ventilation - All patients

End point title	Duration of ventilation - All patients

End point description:

End point type	Other pre-specified

End point timeframe:

Duration of ventilation

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: days				
median (inter-quartile range (Q1-Q3))	10 (5.5 to 15)	10 (6 to 19)		

Statistical analyses

Statistical analysis title	Duration of Ventilation - All patients
Comparison groups	Aspirin v Placebo

Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.43
Method	Sign test

Other pre-specified: Duration of ventilation - Achieved unassisted breathing

End point title	Duration of ventilation - Achieved unassisted breathing

End point description:

End point type	Other pre-specified

End point timeframe:
Duration of ventilation

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: days				
median (inter-quartile range (Q1-Q3))	8 (5 to 13)	9.5 (6 to 21)		

Statistical analyses

Statistical analysis title	Duration of ventilation - Achieved UB
Comparison groups	Aspirin v Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.37
Method	Sign test

Other pre-specified: Duration of ventilation - Died

End point title	Duration of ventilation - Died

End point description:

End point type	Other pre-specified

End point timeframe:
Duration of ventilation

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	5		
Units: days				
median (inter-quartile range (Q1-Q3))	13 (10 to 20)	15 (9 to 18)		

Statistical analyses

Statistical analysis title	Duration of ventilation - Died
Comparison groups	Aspirin v Placebo
Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.88
Method	Sign test

Other pre-specified: Duration of ICU stay - All patients

End point title	Duration of ICU stay - All patients

End point description:

End point type	Other pre-specified

End point timeframe:

ICU stay

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: days				
median (inter-quartile range (Q1-Q3))	12.5 (8 to 21.5)	15 (9 to 18)		

Statistical analyses

Statistical analysis title	Duration of ICU stay - All patients
Comparison groups	Aspirin v Placebo

Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.51
Method	Sign test

Other pre-specified: Duration of ICU stay - Alive at discharge

End point title	Duration of ICU stay - Alive at discharge

End point description:

End point type	Other pre-specified

End point timeframe:

ICU stay

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: days				
median (inter-quartile range (Q1-Q3))	12 (7 to 22)	14 (8 to 31.5)		

Statistical analyses

Statistical analysis title	Duration of ICU stay - Alive at discharge
Comparison groups	Aspirin v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.33
Method	Sign test

Other pre-specified: Duration of ICU stay - Died

End point title	Duration of ICU stay - Died

End point description:

End point type	Other pre-specified

End point timeframe:

Study period

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	5		
Units: days				
median (inter-quartile range (Q1-Q3))	16.5 (11.5 to 21.5)	15 (9 to 18)		

Statistical analyses

Statistical analysis title	Duration of ICU stay - Died
Comparison groups	Aspirin v Placebo
Number of subjects included in analysis	9
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.62
Method	Sign test

Other pre-specified: Duration of hospital stay - All patients	
End point title	Duration of hospital stay - All patients
End point description:	

End point type	Other pre-specified
End point timeframe:	
Hospital stay	

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: days				
median (inter-quartile range (Q1-Q3))	20.5 (15 to 29)	26 (15 to 67)		

Statistical analyses

Statistical analysis title	Duration of Hospital Stay - All patients
Comparison groups	Aspirin v Placebo

Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.51
Method	Sign test

Other pre-specified: Duration of hospital stay - Alive at discharge

End point title	Duration of hospital stay - Alive at discharge

End point description:

End point type	Other pre-specified

End point timeframe:

Hospital stay

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	20		
Units: days				
median (inter-quartile range (Q1-Q3))	22 (18 to 32)	29 (17 to 84)		

Statistical analyses

Statistical analysis title	Duration of Hospital stay - Alive at discharge
Comparison groups	Aspirin v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.31
Method	Sign test

Other pre-specified: Duration of hospital stay - Died

End point title	Duration of hospital stay - Died

End point description:

End point type	Other pre-specified

End point timeframe:

Hospital stay

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	5		
Units: days				
median (inter-quartile range (Q1-Q3))	17 (10 to 23)	15 (9 to 18)		

Statistical analyses

Statistical analysis title	Duration of hospital stay - Died
Comparison groups	Aspirin v Placebo
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.68
Method	Sign test

Other pre-specified: All cause mortality - 28 day

End point title	All cause mortality - 28 day

End point description:

End point type	Other pre-specified

End point timeframe:

28 days

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: subjects				
Alive	18	20		
Dead	6	5		

Statistical analyses

Statistical analysis title	Mortality rate- 28 days
Comparison groups	Aspirin v Placebo

Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.74
Method	Fisher exact

Other pre-specified: All cause mortality - 90 day

End point title	All cause mortality - 90 day

End point description:

End point type	Other pre-specified

End point timeframe:

90 days

End point values	Aspirin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: subjects				
Alive	17	20		
Dead	7	5		

Statistical analyses

Statistical analysis title	Mortality rate - 90 days
Comparison groups	Placebo v Aspirin
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.52
Method	Fisher exact

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs that occur between trial entry and up to 28 days after completion of the study drug was reported.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	1

Reporting groups

Reporting group title	Aspirin

Reporting group description:

Treatment arm

Reporting group title	Placebo

Reporting group description: -

Serious adverse events	Aspirin	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 24 (8.33%)	3 / 25 (12.00%)	
number of deaths (all causes)	7	5	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	1 / 24 (4.17%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
CVA infarct			
subjects affected / exposed	1 / 24 (4.17%)	2 / 25 (8.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid Haemorrhage			
subjects affected / exposed	0 / 24 (0.00%)	1 / 25 (4.00%)	
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: 0 %

Non-serious adverse events	Aspirin	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 24 (37.50%)	10 / 25 (40.00%)	
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications			
subjects affected / exposed	1 / 24 (4.17%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 24 (25.00%)	7 / 25 (28.00%)	
occurrences (all)	7	7	
Thrombocytosis			
subjects affected / exposed	1 / 24 (4.17%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Anaemia- Requiring transfusion			
subjects affected / exposed	0 / 24 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Eye disorders			
Bilateral sub-conjunctival Haemorrhage			
subjects affected / exposed	1 / 24 (4.17%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Gastrointestinal disorders			
subjects affected / exposed	0 / 24 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	1 / 24 (4.17%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Over-sedation			
subjects affected / exposed	0 / 24 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 July 2016	The exclusion criteria to allow recruitment of patients with a platelet count less than 100 x109/l was adjusted to less than 50 x109/ l.
09 August 2016	Extension of study form single site study to multi centre study.
23 August 2017	The exclusion of those with active or recurrent peptic ulcer disease was limited to active disease within the last 5 years.

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 DMC decided to stop the study prior to reaching the target population on the basis of slow recruitment. No safety concerns were highlighted by the DMC.
An SAE was identified post consent in a patient. Patient was not randomised to the study

Notes: