Clinical trial results:
Infusion rate and volumekinetics for hyperoncotic albumin in healthy subjects (RAV),
- A phase IV, randomized, open-labeled, cross-over study

Summary

EudraCT number	2017-003687-12
Trial protocol	SE
Global end of trial date	31 January 2019

Results information

Result version number	v1 (current)
This version publication date	15 February 2025
First version publication date	15 February 2025
Summary attachment (see zip file)	Summery RAV (Summery RAV.docx)

Trial information

Trial identification

Sponsor protocol code	RAV1.2

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Region Ostergotland
Sponsor organisation address	University Hospital, Linkoeping, Sweden, 58185
Public contact	Burn Unit, Region Ostergotland, +46 101031154, joachim.zdolsek@regionostergotland.se
Scientific contact	Burn Unit, Region Ostergotland, +46 101031154, joachim.zdolsek@regionostergotland.se

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 December 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 January 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To study if infusion rate of intravenous administered hyperoncotic albumin is relavant for attraction of fluid from the interstitium and to compare this effect with isooncotic albumin.

Protection of trial subjects:

Infusions were performed adjacent to the Intensive Care Unit. Vital parameters were monitored.

Background therapy:

Healthy individuals

Evidence for comparator: -

Actual start date of recruitment	20 November 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	Sweden: 12
Worldwide total number of subjects	12
EEA total number of subjects	12

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)	12
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Healthy individuals

Pre-assignment

Screening details:

Healthy individuals

Period 1

Period 1 title	Study period up to 360 minutes (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Open label randomization

Arms

Arm title	Fast and slow infusions of albumin 20%

Arm description:

Volunteers receiving 3 mL/kg of 20% albumin over 30 min (fast) and slow 120 min

Arm type	Experimental
Investigational medicinal product name	Albumin 20%
Investigational medicinal product code	B05AA01
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

3 mL/kg of 20% albumin over 30 and 120 min in a cross over fashion.

Number of subjects in period 1	Fast and slow infusions of albumin 20%
Started	12
Completed	12

Baseline characteristics

Reporting groups	
Reporting group title	Study period up to 360 minutes
Reporting group description:	
Healthy individuals	

Reporting group values	Study period up to 360 minutes	Total	
Number of subjects	12	12	
Age categorical			
Age of subjects			
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)	12	12	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	28		
standard deviation	± 10	-	
Gender categorical			
Units: Subjects			
Female	6	6	
Male	6	6	

Subject analysis sets	
Subject analysis set title	Fast infusion plasma volume expansion 0-2h
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
AUC. plasma volume expansion 0-2 h after infusion start in L min/kg.	
Subject analysis set title	Slow infusion plasma volume expansion 0-2h
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
AUC. plasma volume expansion 0-2 h after infusion start in L min/kg.	
Subject analysis set title	Fast infusion plasma volume expansion 0-6h
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
AUC. plasma volume expansion 0-6 h after infusion start in L min/kg.	
Subject analysis set title	Slow infusion plasma volume expansion 0-6h
Subject analysis set type	Sub-group analysis

Subject analysis set description:

AUC. plasma volume expansion 0-6 h after infusion start in L min/kg.

Subject analysis set title	Intravascular half-life fast infusion
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Intravascular half-life for albumin after a fast infusion (30 minutes) of 3ml/kg Albumin 20%

Subject analysis set title	Intravascular half-life slow infusion
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Intravascular half-life for albumin after slow infusion (120 minutes) of 3ml/kg Albumin 20%

Reporting group values	Fast infusion plasma volume expansion 0-2h	Slow infusion plasma volume expansion 0-2h	Fast infusion plasma volume expansion 0-6h
Number of subjects	12	12	12
Age categorical			
Age of subjects			
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)	12	12	12
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	28	28	28
standard deviation	± 10	± 10	± 10
Gender categorical			
Units: Subjects			
Female	6	6	6
Male	6	6	6

Reporting group values	Slow infusion plasma volume expansion 0-6h	Intravascular half-life fast infusion	Intravascular half-life slow infusion
Number of subjects	12	12	12
Age categorical			
Age of subjects			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	12		
From 65-84 years	0		

85 years and over	0		

Age continuous Units: years			
arithmetic mean	28		
standard deviation	± 10	±	±
Gender categorical Units: Subjects			
Female	6		
Male	6		

End points

End points reporting groups

Reporting group title	Fast and slow infusions of albumin 20%
Reporting group description: Volunteers receiving 3 mL/kg of 20% albumin over 30 min (fast) and slow 120 min	
Subject analysis set title	Fast infusion plasma volume expansion 0-2h
Subject analysis set type	Sub-group analysis
Subject analysis set description: AUC. plasma volume expansion 0-2 h after infusion start in L min/kg.	
Subject analysis set title	Slow infusion plasma volume expansion 0-2h
Subject analysis set type	Sub-group analysis
Subject analysis set description: AUC. plasma volume expansion 0-2 h after infusion start in L min/kg.	
Subject analysis set title	Fast infusion plasma volume expansion 0-6h
Subject analysis set type	Sub-group analysis
Subject analysis set description: AUC. plasma volume expansion 0-6 h after infusion start in L min/kg.	
Subject analysis set title	Slow infusion plasma volume expansion 0-6h
Subject analysis set type	Sub-group analysis
Subject analysis set description: AUC. plasma volume expansion 0-6 h after infusion start in L min/kg.	
Subject analysis set title	Intravascular half-life fast infusion
Subject analysis set type	Sub-group analysis
Subject analysis set description: Intravascular half-life for albumin after a fast infusion (30 minutes) of 3ml/kg Albumin 20%	
Subject analysis set title	Intravascular half-life slow infusion
Subject analysis set type	Sub-group analysis
Subject analysis set description: Intravascular half-life for albumin after slow infusion (120 minutes) of 3ml/kg Albumin 20%	

Primary: Plasmavolume expansion 120 minutes

End point title	Plasmavolume expansion 120 minutes
End point description: Difference in AUC for volume expansion for the 30 and the 120 minute infusions.	
End point type	Primary
End point timeframe: 120 minutes after start of infusions.	

End point values	Fast infusion plasma volume expansion 0-2h	Slow infusion plasma volume expansion 0-2h		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	12		
Units: L min/kg				
median (inter-quartile range (Q1-Q3))	0.44 (0.40 to 0.65)	0.26 (0.19 to 0.42)		

Statistical analyses

Statistical analysis title	Difference in volume expansion during the first 2
Comparison groups	Fast infusion plasma volume expansion 0-2h v Slow infusion plasma volume expansion 0-2h
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.15
upper limit	0.8
Variability estimate	Standard deviation

Primary: Plasma volume expansion 360 minutes	
End point title	Plasma volume expansion 360 minutes
End point description:	
Comparison plasma volume expansion during 360 minute for a fast infusion (30 minutes) an a slow infusion (120 minutes)	
End point type	Primary
End point timeframe:	
From start of infusions to the end of the study 360 minutes later	

End point values	Fast infusion plasma volume expansion 0-6h	Slow infusion plasma volume expansion 0-6h		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	12		
Units: L min/kg				
median (inter-quartile range (Q1-Q3))	1.08 (0.73 to 1.90)	0.97 (0.67 to 1.68)		

Statistical analyses

Statistical analysis title	Volume expansion from start to end of the study.

Statistical analysis description:

Volume expansion during the entire study 0 to 360 minutes for both infusions. Fast (30 minutes) and slow (120 minutes)

Comparison groups	Slow infusion plasma volume expansion 0-6h v Fast infusion plasma volume expansion 0-6h
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.31 [1]
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.8

Notes:

[1] - Difference between the infusion not significant.

Secondary: Intravascular half life for slow and fast infusions of hyperoncotic albumin

End point title	Intravascular half life for slow and fast infusions of hyperoncotic albumin

End point description:

End point type	Secondary

End point timeframe:

Calculations from measurements during observation from start of infusion up to 360 minutes later.

End point values	Intravascular half-life fast infusion	Intravascular half-life slow infusion		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	12		
Units: h				
median (inter-quartile range (Q1-Q3))	8.0 (5.4 to 11.6)	6.3 (4.4 to 8.4)		

Statistical analyses

Statistical analysis title	Difference in half life depending on infusion rate
Comparison groups	Intravascular half-life fast infusion v Intravascular half-life slow infusion

Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.028
Method	t-test, 2-sided

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
From start of infusion to end of study 260 minutes later	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups	
Reporting group title	None

Reporting group description: -

Serious adverse events	None		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	None		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)		

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: There were no adverse events.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

No limitations associated with the performance of the study.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/92941