Clinical trial results:
A Pilot, Randomised, Unblinded, Feasibility, Safety, Biochemical and Physiological Efficacy Study of 20% vs 5% Human Albumin Solution for Fluid Bolus Therapy in Critically Ill Adults

Summary

EudraCT number	2016-001940-20
Trial protocol	GB
Global end of trial date	30 June 2017

Results information

Result version number	v1 (current)
This version publication date	14 May 2020
First version publication date	14 May 2020
Summary attachment (see zip file)	Published trial manuscript (SWIPE ICM Oct 2018.pdf) SWIPE Trial supplementary appendix (SWIPE Trial Supplement 2 ICM 20 Mar 2018.pdf)

Trial information

Trial identification

Sponsor protocol code	R04336

Additional study identifiers

ISRCTN number	ISRCTN15839026
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Australian & New Zealand Clinical Trials Registry: ACTRN12615000349549

Notes:

Sponsors

Sponsor organisation name	Manchester University NHS Foundation Trust
Sponsor organisation address	Oxford Road, Manchester, United Kingdom, M13 9WL
Public contact	Lynne Webster, Manchester University NHS Foundation Trust, +44 01612764125, lynne.webster@mft.nhs.uk
Scientific contact	Lynne Webster, Manchester University NHS Foundation Trust, +44 01612764125, lynne.webster@mft.nhs.uk

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 June 2017
Global end of trial reached?	Yes
Global end of trial date	30 June 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Our principle aim is to compare the effects of 5% versus 20% albumin solution when given as fluid resuscitation in critically ill adults. As this is a pilot study, the main objective is to test whether the study processes and procedures are both feasible and safe.

The sorts of effects we will compare include routine observations such as heart rate, blood pressure and the amount of urine a patient produces every hour. We will also compare the biochemical levels of sodium and chloride in patient's blood. The most important comparison we will make is the total amount of fluid (in ml) that patients receive during the study period.

Protection of trial subjects:

There is the possibility that patients may not have the capacity to consent so the study would allow their personal or professional legal representative to provide valid consent on their behalf. This process is in keeping with standard and established approach to consent in critically ill incapacitated adults. Retrospective consent would then be sought once the patient was able.
Additional blood samples will be taken in addition to standard care at 1, 2 and 4 hours post infusion when the patient will still be present in Intensive Care Unit.
The study was run in the UK and also in Australia and care was taken when sending UK data over to Australia, that no identifying information was included. It was sent via an encrypted database.

Background therapy:

There are no mandated background therapy's however nor does the protocol restrict any other treatment a patient may be given such as oxygen therapy, antibiotics, radiological interventions, blood products or surgical intervention.

Evidence for comparator:

Both 5% and 20% albumin solutions are legally licenced for use as fluid resuscitation. Both solutions are in widespread use for this purpose around the world but have never been compared before. It is hypothesized that those patients receiving 20% solution, which is more concentrated, will receive less fluid, sodium and chloride and thus potentially be at a reduced risk of organ failure and death.

Actual start date of recruitment	01 April 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 20
Country: Number of subjects enrolled	Australia: 307
Worldwide total number of subjects	327
EEA total number of subjects	20

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)	164
From 65 to 84 years	148
85 years and over	15

Subject disposition

Recruitment

Recruitment details:

The trial opened to recruitment in Australia on 01/07/2015. The UK site began recruiting on 30/11/2016 and closed on 26/03/2017 at Manchester Royal Infirmary. Patients recruited from Intensive Care Unit who had been there for less than 24 hours.

Pre-assignment

Screening details:

Patients admitted to intensive care unit less than 24 hours prior to approach with a requirement to receive fluid bolus as determined by treating clinician

Pre-assignment period milestones

Number of subjects started	327
Number of subjects completed	321

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 6

Period 1

Period 1 title	Treatment period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Blinding in this trial was not possible as the two infusions come in different sized bottles - 20% in 100mL glass bottles and 5% in 500mL bottles.

Arms

Are arms mutually exclusive?	Yes
Arm title	5% Albumin group

Arm description:

This group is classed as the control group and will be given 5% Albumin each time the treating physician decides that a fluid bolus needs to be given during the first 48 hours in ICU.

Arm type	Active comparator
Investigational medicinal product name	Alburex 5
Investigational medicinal product code	B05AA01
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The maximum dose administered will be at the discretion of the treating clinician and within the maximum dosing recommended by the IMPs manufacturer. We expect this to be no more than 4 doses during the 48 hour study period.

Arm title	20% Albumin

Arm description:

This group is classed as the treatment group and will be given each time the treating physician decides that a fluid bolus is required during the first 48 hours in the Intensive Care Unit.

Arm type	Experimental

Investigational medicinal product name	Alburex 20
Investigational medicinal product code	PL 15036/0032 ATC B05AA01
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The maximum dose will be prescribed and administered at the discretion of the treating clinician, within the recommendations provided by the IMPs manufacturer. We do not expect the patient to receive more than 4 doses within the 48 hour study period.

Number of subjects in period 1[1]	5% Albumin group	20% Albumin
Started	168	153
Completed	168	153

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Six participants withdrew consent prior to beginning treatment.

Baseline characteristics

Reporting groups	
Reporting group title	5% Albumin group
Reporting group description:	
This group is classed as the control group and will be given 5% Albumin each time the treating physician decides that a fluid bolus needs to be given during the first 48 hours in ICU.	
Reporting group title	20% Albumin
Reporting group description:	
This group is classed as the treatment group and will be given each time the treating physician decides that a fluid bolus is required during the first 48 hours in the Intensive Care Unit.	

Reporting group values	5% Albumin group	20% Albumin	Total
Number of subjects	168	153	321
Age categorical			
321 Adult patients were enrolled.			
Units: Subjects			
Adults (18-64 years)	82	76	158
From 65-84 years	82	66	148
85 years and over	4	11	15
Age continuous			
Units: years			
median	65.4	65.4	
inter-quartile range (Q1-Q3)	55.5 to 72.2	58.4 to 74	-
Gender categorical			
Units: Subjects			
Female	67	58	125
Male	101	95	196
Source of ICU admission			
Location patient was admitted to ICU from.			
Units: Subjects			
Operating theatre	114	107	221
Emergency Department	22	16	38
Ward	24	17	41
Other hospital	8	13	21

End points

End points reporting groups

Reporting group title	5% Albumin group

Reporting group description:

This group is classed as the control group and will be given 5% Albumin each time the treating physician decides that a fluid bolus needs to be given during the first 48 hours in ICU.

Reporting group title	20% Albumin

Reporting group description:

This group is classed as the treatment group and will be given each time the treating physician decides that a fluid bolus is required during the first 48 hours in the Intensive Care Unit.

Primary: Volume of resuscitation fluid

End point title	Volume of resuscitation fluid[1]

End point description:

End point type	Primary

End point timeframe:

Up to 48 hours after randomisation

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: All data for the primary outcome were visually assessed for normality. In view of its non-parametric distribution we used a Mann-Whitney U test to analyse the difference in the primary outcome measure of median volume of resuscitation fluid.

End point values	5% Albumin group	20% Albumin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168	153		
Units: millilitre(s)				
median (inter-quartile range (Q1-Q3))	900 (500 to 1250)	300 (200 to 500)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative fluid balance

End point title	Cumulative fluid balance

End point description:

Total fluid in minus total fluid out, cumulatively up to 48 hours.

End point type	Secondary

End point timeframe:

48 hours after randomisation

End point values	5% Albumin group	20% Albumin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168	153		
Units: millilitre(s)				
arithmetic mean (standard deviation)	930 (± 2038)	354 (± 2124)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 90 days following randomisation or hospital discharge (whichever sooner)	
Adverse event reporting additional description:	
Hyperalbuminaemia (serum albumin >45 g/L)	
Assessment type	Systematic

Dictionary used	
Dictionary name	N/A
Dictionary version	1

Reporting groups	
Reporting group title	20% Albumin
Reporting group description:	
Hyperalbuminaemia (>45 g/L) as an adverse event	
Reporting group title	4% Albumin
Reporting group description:	
Hyperalbuminaemia (>45 g/L) as an adverse event	

Serious adverse events	20% Albumin	4% Albumin	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 153 (0.00%)	0 / 168 (0.00%)	
number of deaths (all causes)	10	19	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	20% Albumin	4% Albumin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 153 (1.96%)	3 / 168 (1.79%)	
Blood and lymphatic system disorders			
Hyperalbuminaemia	Additional description: Hyperalbuminaemia defined as a serum measurement >45 g/L within the first 72 hours after randomisation.		
subjects affected / exposed	3 / 153 (1.96%)	3 / 168 (1.79%)	
occurrences (all)	3	3	

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

None reported