



Clinical trial results: Substitution of PERioperative Albumin Deficiency Disorders Summary

EudraCT number	2016-001313-24
Trial protocol	DE
Global end of trial date	21 April 2021

Results information

Result version number	v1 (current)
This version publication date	28 April 2023
First version publication date	28 April 2023
Summary attachment (see zip file)	Clinical Study Report SUPERADD (03.03 Endbericht SUPERADD EudraCT V2.0.pdf)

Trial information

Trial identification

Sponsor protocol code	SUPERADD
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03167645
WHO universal trial number (UTN)	U1111-1181-2625

Notes:

Sponsors

Sponsor organisation name	School of Medicine of the Technical University of Munich
Sponsor organisation address	Ismaningerstrasse 22, Munich, Germany, 81675
Public contact	Klinik für Anästhesiologie und Intensivmedizin, Technische Universität München, Fakultät für Medizin, 49 8941409635, s.schaller@tum.de
Scientific contact	Klinik für Anästhesiologie und Intensivmedizin, Technische Universität München, Fakultät für Medizin, 49 8941409635, s.schaller@tum.de

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	25 August 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 June 2020
Global end of trial reached?	Yes
Global end of trial date	21 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Reduction of postoperative complications of either high-risk surgical procedures or high-risk surgical patients through perioperative therapy of hypoalbuminemia (defined as <30g/l).

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance the ethical principles of Good Clinical Practice (GCP). Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. The study was regularly monitored by the Sponsor and all investigators connected to the study were GCP trained.

During the intervention period subjects were under supervision of an anesthesiologist either in the operation room or postoperative care unit (PACU).

Background therapy:

Standard of care, i.e., treatment of hypalbuminaemia only if serum albumin < 20 g/L and clinically necessary

Concomitant medication and supportive therapy were carried out according to standard clinical guidelines and at the judgement of the investigators

Evidence for comparator:

Human-Albumin 20 % Behring, salzarm Infusionslösung, solution for injection, CSL-Behring

Actual start date of recruitment	20 June 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research, Efficacy
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 600
Worldwide total number of subjects	600
EEA total number of subjects	600

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	204
From 65 to 84 years	372
85 years and over	24

Subject disposition

Recruitment

Recruitment details:

The study was conducted in Germany single-centre between June 20, 2017 (first Patient recruited) and June 3, 2020 (last patient completed).

After screening, checking for in- and exclusion criteria, and signing of the informed consent forms, the subjects will be randomized either in the intervention or observation group.

Pre-assignment

Screening details:

After giving their consent, the patient was included in the clinical study. Only patients who meet all inclusion criteria and who do not have any exclusion criteria were included in the clinical study (screening). As soon as hypoalbuminemia was found in the laboratory, randomization takes place.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind ^[1]
Roles blinded	Subject, Data analyst, Assessor

Blinding implementation details:

Patient and outcome-assessor were blinded.

The therapy takes place perioperatively and in the recovery room according to the mentioned guidelines without blinding. The doctors on the wards who diagnose and treat postoperative complications and the study doctors who record the postoperative complications until discharge are blinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	Intervention

Arm description:

goal-directed albumin therapy, i.e., treatment of hypalbuminaemia < 30 g/L with Human-Albumin 20 % Behring, salzarm Infusionslösung, solution for injection, CSL-Behring

Arm type	Experimental
Investigational medicinal product name	Human-Albumin 20% Behring
Investigational medicinal product code	ATC B05AA01
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

goal-directed albumin therapy, i.e., treatment of hypalbuminaemia < 30 g/L with Human-Albumin 20 % Behring, salzarm Infusionslösung, solution for injection, CSL-Behring

Arm title	Control-Group
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Arm description:

standard of care, i.e., treatment of hypalbuminaemia only if serum albumin < 20 g/L and clinically necessary

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Notes:

[1] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.

Justification: Patient and outcome-assessor blinded.

Number of subjects in period 1	Intervention	Control-Group
Started	300	300
Completed	264	240
Not completed	36	60
Lost to follow-up	31	57
Protocol deviation	5	3

Baseline characteristics

Reporting groups

Reporting group title	Intervention
Reporting group description: goal-directed albumin therapy, i.e., treatment of hypalbuminaemia < 30 g/L with Human-Albumin 20 % Behring, salzarm Infusionslösung, solution for injection, CSL-Behring	
Reporting group title	Control-Group
Reporting group description: standard of care, i.e., treatment of hypalbuminaemia only if serum albumin < 20 g/L and clinically necessary	

Reporting group values	Intervention	Control-Group	Total
Number of subjects	300	300	600
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)	99	105	204
From 65-84 years	187	185	372
85 years and over	14	10	24
Age continuous			
Units: years			
median	70	69	
standard deviation	± 12	± 11	-
Gender categorical			
Units: Subjects			
Female	125	120	245
Male	175	180	355

End points

End points reporting groups

Reporting group title	Intervention
Reporting group description: goal-directed albumin therapy, i.e., treatment of hypalbuminaemia < 30 g/L with Human-Albumin 20 % Behring, salzarm Infusionslösung, solution for injection, CSL-Behring	
Reporting group title	Control-Group
Reporting group description: standard of care, i.e., treatment of hypalbuminaemia only if serum albumin < 20 g/L and clinically necessary	

Primary: Any complication CDC ≥ II within 15d

End point title	Any complication CDC ≥ II within 15d
End point description: Any complication CDC ≥ Grade II within 15 days	
End point type	Primary
End point timeframe: 15 days	

End point values	Intervention	Control-Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	295	297		
Units: Complications	250	259		

Attachments (see zip file)	Primary Endoint/Bildschirmfoto 2022-02-21 um 12.09.25.png
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Statistical analyses

Statistical analysis title	Risk difference
Comparison groups	Intervention v Control-Group
Number of subjects included in analysis	592
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.39
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	-2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.1
upper limit	3.2

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Safety assessment was done until hospital discharge.

Adverse event reporting additional description:

Safety assessment was done in 600 patients randomized according to POMS and Clavien-Dindo as for the primary and secondary outcomes.

Assessment type	Systematic
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Dictionary used

Dictionary name	POMS, Clavien-Dindo
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Dictionary version	999
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Reporting groups

Reporting group title	Intervention
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Reporting group description:

Interventionsgroup: HA Humanalbumin 20% Albumin > 30 g/l

Reporting group title	Control
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Reporting group description:

Control-Group: Standard of Care

Serious adverse events	Intervention	Control	
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 300 (5.00%)	6 / 300 (2.00%)	
number of deaths (all causes)	52	36	
number of deaths resulting from adverse events	14	6	
Injury, poisoning and procedural complications			
Hypovolaemic shock	Additional description: Recovered.		
subjects affected / exposed	4 / 300 (1.33%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 4	0 / 2	
Vascular disorders			
Pulmonary embolism	Additional description: Fatal		
subjects affected / exposed	1 / 300 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac disorders			
Cardiac arrest	Additional description: Fatal		

subjects affected / exposed	2 / 300 (0.67%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Gastrointestinal disorders			
Asphyxia	Additional description: Fatal		
subjects affected / exposed	1 / 300 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	1 / 300 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory failure	Additional description: Fatal. Palliative Care.		
subjects affected / exposed	2 / 300 (0.67%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 2	
Tracheal fistula			
subjects affected / exposed	1 / 300 (0.33%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infections and infestations			
Septic shock	Additional description: Fatal SAE.		
subjects affected / exposed	3 / 300 (1.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 3	0 / 1	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Intervention	Control	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	254 / 300 (84.67%)	262 / 300 (87.33%)	
Cardiac disorders			

Cardiovascular disorder subjects affected / exposed occurrences (all)	72 / 300 (24.00%) 72	78 / 300 (26.00%) 78	
Nervous system disorders Neurological symptom subjects affected / exposed occurrences (all)	52 / 300 (17.33%) 52	37 / 300 (12.33%) 37	
Blood and lymphatic system disorders Blood disorder subjects affected / exposed occurrences (all)	101 / 300 (33.67%) 101	99 / 300 (33.00%) 99	
General disorders and administration site conditions Pain subjects affected / exposed occurrences (all)	122 / 300 (40.67%) 122	110 / 300 (36.67%) 110	
Gastrointestinal disorders Gastrointestinal disorder subjects affected / exposed occurrences (all)	152 / 300 (50.67%) 152	143 / 300 (47.67%) 143	
Respiratory, thoracic and mediastinal disorders Respiratory disorder subjects affected / exposed occurrences (all)	153 / 300 (51.00%) 153	152 / 300 (50.67%) 152	
Skin and subcutaneous tissue disorders Wound complication subjects affected / exposed occurrences (all)	99 / 300 (33.00%) 99	93 / 300 (31.00%) 93	
Renal and urinary disorders Renal disorder subjects affected / exposed occurrences (all)	62 / 300 (20.67%) 62	60 / 300 (20.00%) 60	
Infections and infestations Infection subjects affected / exposed occurrences (all)	137 / 300 (45.67%) 137	139 / 300 (46.33%) 139	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 October 2018	The following major changes were included in the Amendment No. 1: 1. number of patients after interim analysis 2. Secondary endpoints (Clavien Dindo recording over the entire hospital stay)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported