EU Clinical Trials Register

Clinical trial results:
Placebo-controlled, double-blind, randomized trial to assess the efficacy and safety of Adrecizumab against placebo in subjects with cardiogenic shock

Summary

EudraCT number	2018-002824-17
Trial protocol	DE
Global end of trial date	24 April 2021

Results information

Result version number	v1 (current)
This version publication date	22 October 2022
First version publication date	22 October 2022
Summary attachment (see zip file)	Synopsis Clinical Study Report (CTC181431 Final CSR Synopsis_2022_01_18 Version 1.0.pdf)

Trial information

Trial identification

Sponsor protocol code	ACCOST-HH

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03989531
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Medical Center Hamburg-Eppendorf
Sponsor organisation address	Martinistrasse 52, Hamburg, Germany, 20246
Public contact	Mahir Karakas, University Medical Centre Hamburg-Eppendorf, 0049 40741057975, m.karakas@uke.de
Scientific contact	Mahir Karakas, University Medical Centre Hamburg-Eppendorf, 0049 40741057975, m.karakas@uke.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	18 January 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 April 2021
Global end of trial reached?	Yes
Global end of trial date	24 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1) To assess safety and tolerability of Adrecizumab in patients with cardiogenic shock
2) To evaluate if improvement of vascular integrity with Adrecizumab is superior to placebo in reduction of morbidity endpoints in patients with cardiogenic shock

Protection of trial subjects:

There is substantial need to improve therapeutic options in cardiogenic shock, and i.v. Adrecizumab appears a safe and promising approach for this condition. All necessary measures were taken to assure safety of the patients, e.g., by individualized treatment regime, application of investigational medicinal product (IMP) only on top of SOC, supervision, and timely study visits.
Adrecizumab emerged as a safe intervention with large impact on disease burden in cardiogenic shock. The risk for the participants in this trial was not beyond the usual risks associated with the natural course of the disease and were even lower, since a proven intervention scheme was used.
An emergency un-blinding procedure as well as a data monitoring and safety board (DSMB) was established to minimise the risk for the patients.
Patient insurance covered any damage resulting from patients' participation in the trial.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	28 March 2019
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	Germany: 150
Worldwide total number of subjects	150
EEA total number of subjects	150

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)	62
From 65 to 84 years	84
85 years and over	4

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Adolescents (12-17 years)	0
Adults (18-64 years)	62
From 65 to 84 years	84
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

First patient first visit (FPFV) was performed on 05-APR-2019. In total, 150 patients have been enrolled at four study sites. Site 01: Universitätsklinikum Hamburg-Eppendorf: 108 patients, Site 02: Charité – Universitätsmedizin Berlin: 13 patients, Site 03: Universitätsklinikum Ulm: 23 patients, Site 04: Universitätsklinikum Mannheim: 6 patients

Pre-assignment

Screening details:

• Hospitalization for cardiogenic shock
Cardiogenic shock is usually defined as:
 - Systolic blood pressure < 90 mmHg > 30 min or inotropes required to maintain pressure > 90 mmHg during systole
- Signs of left heart insufficiency and/or pulmonary congestion
- Signs of impaired organ perfusion

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

Blinding implementation details:

Study sites had blinded staff members. All study related patient contact was through blinded staff members at the respective study sites.

Arms

Are arms mutually exclusive?	Yes
Arm title	Experimental intervention

Arm description:

Adrecizumab on top of standard of care

Arm type	Experimental
Investigational medicinal product name	Adrecizumab
Investigational medicinal product code	HAM8101
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion , Intravenous use

Dosage and administration details:

Patients randomized to Adrecizumab received a single dose of 8 mg/kg body weight on top of SOC. For drip infusion, it was diluted in 100 mL sterile 0.9% sodium chloride solution. Single infusion over 60 min.

Arm title	Control intervention

Arm description:

Placebo/ control substance (NaCl 0.9%) on top of standard of care

Arm type	Placebo
Investigational medicinal product name	Physiological saline (NaCl 0.9%)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion , Intravenous use

Dosage and administration details:

Administration of i.v. Placebo/ control substance (NaCl 0.9%) according to the dosing rules for

Adrecizumab.

Number of subjects in period 1	Experimental intervention	Control intervention
Started	77	73
Completed	77	73

Baseline characteristics

Reporting groups

Reporting group title	Experimental intervention
Reporting group description:	
Adrecizumab on top of standard of care	
Reporting group title	Control intervention
Reporting group description:	
Placebo/ control substance (NaCl 0.9%) on top of standard of care	

Reporting group values	Experimental intervention	Control intervention	Total
Number of subjects	77	73	150
Age categorical			
Units: Subjects			
Adults ≤ 65 years	31	31	62
Adults > 65 years	46	42	88
Gender categorical			
Units: Subjects			
Female	17	14	31
Male	60	59	119
Type of un-derlying cardio-genic shock			
Units: Subjects			
Acute Myocardial Infarction	37	36	73
other entities	40	37	77

End points

End points reporting groups

Reporting group title	Experimental intervention
Reporting group description:	
Adrecizumab on top of standard of care	
Reporting group title	Control intervention
Reporting group description:	
Placebo/ control substance (NaCl 0.9%) on top of standard of care	

Primary: Number of days through day 30 without need for cardiovascular organ support, including vasopressors, or mechanical support (VA-ECMO, Impella)

End point title	Number of days through day 30 without need for cardiovascular organ support, including vasopressors, or mechanical support (VA-ECMO, Impella)
End point description:	
End point type	Primary
End point timeframe:	
30 days	

End point values	Experimental intervention	Control intervention		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	73		
Units: Days				
number (not applicable)	12.37	14.05		

Statistical analyses

Statistical analysis title	Efficacy Data - Primary Endpoint

Statistical analysis description:

The primary endpoint, i.e. number of days within 30 days without need for ventilation, was analysed using an ANCOVA model with random group as factor and all stratification variables in the randomisation as covariates, namely age, sex, and type of underlying cardiogenic shock (acute myocardial infarction versus other entities). The treatment effect with corresponding 95% confidence interval and p-value will be presented.

Comparison groups	Experimental intervention v Control intervention
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.367
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.69

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.37
upper limit	2

Secondary: Ventilation requirement

End point title	Ventilation requirement
End point description:	
Requirement and length of mechanical ventilation	
End point type	Secondary
End point timeframe:	
90 days	

End point values	Experimental intervention	Control intervention		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	73		
Units: Number of subjects	62	61		

Statistical analyses

No statistical analyses for this end point

Secondary: All-cause death within 30 days

End point title	All-cause death within 30 days
End point description:	
End point type	Secondary
End point timeframe:	
30 days	

End point values	Experimental intervention	Control intervention		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	73		
Units: patients	31	29		

Statistical analyses

No statistical analyses for this end point

Secondary: Cardiovascular death within 30 days

End point title	Cardiovascular death within 30 days
End point description:	
End point type	Secondary
End point timeframe:	
30 days	

End point values	Experimental intervention	Control intervention		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	73		
Units: patients	25	25		

Statistical analyses

No statistical analyses for this end point

Secondary: Length of stay at Intensive Care Unit/ Intermediate Care Unit/ Heart Failure Unit

End point title	Length of stay at Intensive Care Unit/ Intermediate Care Unit/ Heart Failure Unit
End point description:	
Length of stay at Intensive Care Unit/ Intermediate Care Unit/ Heart Failure Unit in hours after application of IMP up to a total of 30 days	
End point type	Secondary
End point timeframe:	
30 days	

End point values	Experimental intervention	Control intervention		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	73		
Units: Hours				
arithmetic mean (full range (min-max))	14.79 (12.3 to 17.27)	15.36 (12.83 to 17.90)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events: 90 days	
Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27

Reporting groups

Reporting group title	Experimental intervention
Reporting group description: Adrecizumab on top of standard of care	
Reporting group title	Control intervention
Reporting group description: Placebo/ control substance (NaCl 0.9%) on top of standard of care	

Serious adverse events	Experimental intervention	Control intervention	
Total subjects affected by serious adverse events			
subjects affected / exposed	59 / 77 (76.62%)	57 / 73 (78.08%)	
number of deaths (all causes)	37	31	
number of deaths resulting from adverse events			
Cardiac disorders			
Cardiogenic shock			
subjects affected / exposed	53 / 77 (68.83%)	47 / 73 (64.38%)	
occurrences causally related to treatment / all	0 / 20	0 / 21	
deaths causally related to treatment / all	0 / 20	0 / 21	

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

Non-serious adverse events	Experimental intervention	Control intervention	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	72 / 77 (93.51%)	71 / 73 (97.26%)	
Investigations			
decreased glomerular filtration rate (GFR)			
subjects affected / exposed	72 / 77 (93.51%)	71 / 73 (97.26%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 April 2021	The protocol was updated (Version 7.0, 22. JAN 2021): • Synopsis The information on the study duration has been adapted. • Synopsis, 8.3 Secondary Endpoints Four of the secondary endpoints are now defined as optional endpoints. • Synopsis, 8.3 Secondary Endpoints The synopsis was reconciled with the contents of the section Statistical Methods Planned in the Protocol and Determination of Sample Size. • Synopsis Three notes have been added that describe in more detail the statistical analysis as defined in the Statistical Analysis Plan. • Synopsis, 9.7.2.1 Proposed Sample Size The number of patients to be statistically evaluated was clarified.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

 None reported