Clinical trial results:
Prospective open-label randomized controlled phase 2b clinical study in parallel groups for the assessment of efficacy and safety of immune therapy with COVID-19 convalescent plasma plus standard treatment vs. standard treatment alone of subjects with severe COVID-19

Summary

EudraCT number	2020-002122-82
Trial protocol	DE
Global end of trial date	18 April 2023

Results information

Result version number	v1 (current)
This version publication date	26 June 2024
First version publication date	26 June 2024

Trial information

Trial identification

Sponsor protocol code	UKER-COV2-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04712344
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Universitätsklinikum Erlangen
Sponsor organisation address	Maximiliansplatz 2, Erlangen, Germany, 91054
Public contact	Transfusionsmedizinische Abteilung, Universitätsklinikum Erlangen, 0049 91318536346, holger.hackstein@uk-erlangen.de
Scientific contact	Transfusionsmedizinische Abteilung, Universitätsklinikum Erlangen, 0049 91318536346, holger.hackstein@uk-erlangen.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	06 November 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 April 2023
Global end of trial reached?	Yes
Global end of trial date	18 April 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Assessment of impact of immune therapy with COVID-19 convalescent plasma on severity of COVID-19

Protection of trial subjects:

Vigorous inclusion and exclusion criteria; close monitoring visits

Background therapy:

standard of care

Evidence for comparator: -

Actual start date of recruitment	18 January 2021
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: 53
Worldwide total number of subjects	53
EEA total number of subjects	53

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)	29
From 65 to 84 years	24
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patient recruitment was performed on 4 ICUs at the University Hospital Erlangen and the Hospital Nürnberg Süd

Pre-assignment

Screening details:

florid SARS-CoV-2 infection confirmed by PCR, ARDS with Horovitz index <300mmHg, necessity of invasive mechanical ventilation

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:

n.a.

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment

Arm description:

COVID-19 convalescent plasma + best medical care

Arm type	Experimental
Investigational medicinal product name	COVID-19 Immunplasma FAU
Investigational medicinal product code	
Other name	COVID-19 convalescent plasma
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

single dose: strength 0,89 (0,87-0,91) ml/ml; quantity 200-300ml; solution for infusion after thawing, i.v. drip within approx. 60minutes;
total dose: three units during day1 and day2

Arm title	Control

Arm description:

best medical care

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Treatment	Control
Started	26	27
Completed	26	27

Baseline characteristics

Reporting groups	
Reporting group title	Treatment
Reporting group description: COVID-19 convalescent plasma + best medical care	
Reporting group title	Control
Reporting group description: best medical care	

Reporting group values	Treatment	Control	Total
Number of subjects	26	27	53
Age categorical 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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	64.12	62.04	
standard deviation	± 11.96	± 9.30	-
Gender categorical Units: Subjects			
Female	6	5	11
Male	20	22	42
Smoker Units: Subjects			
Smoker	2	3	5
Non-smoker	18	15	33
Unknown	6	9	15
BMI Units: kilogram(s)/square metre			
arithmetic mean	29.35	29.68	
standard deviation	± 5.65	± 5.40	-

End points

End points reporting groups	
Reporting group title	Treatment
Reporting group description: COVID-19 convalescent plasma + best medical care	
Reporting group title	Control
Reporting group description: best medical care	

Primary: Change in SOFA score until day 8	
End point title	Change in SOFA score until day 8
End point description: Missing values, ECMO, death or rescue therapy before day 8 triggered LOCF	
End point type	Primary
End point timeframe: From baseline visit (day 1, visit 2) to day 8 (visit 9)	

End point values	Treatment	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	27		
Units: none				
arithmetic mean (standard deviation)	-1.58 (± 3.07)	-1.04 (± 2.99)		

Statistical analyses

Statistical analysis title	Analysis of primary endpoint
Comparison groups	Treatment v Control
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.26
Method	t-test, 1-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.54
Confidence interval	
level	95 %
sides	1-sided
upper limit	0.86

Secondary: Rescue therapy

End point title	Rescue therapy
End point description: all available values (no LOCF)	
End point type	Secondary
End point timeframe: day 8 (visit 9)	

End point values	Treatment	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	27		
Units: subject	4	9		

Statistical analyses

No statistical analyses for this end point

Secondary: ECMO until day 8

End point title	ECMO until day 8
End point description: all available values (no LOCF)	
End point type	Secondary
End point timeframe: From baseline visit (day 1) until and including day 8 (visit 9)	

End point values	Treatment	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	27		
Units: day				
arithmetic mean (standard deviation)	0.35 (± 1.13)	0.74 (± 1.77)		

Statistical analyses

No statistical analyses for this end point

Secondary: ECMO until day 15

End point title	ECMO until day 15
End point description: all available values (no LOCF)	
End point type	Secondary

End point timeframe:
From baseline visit (day 1) until and including day 15 (visit 13)

End point values	Treatment	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	27		
Units: day				
arithmetic mean (standard deviation)	0.92 (± 2.35)	1.67 (± 3.83)		

Statistical analyses

No statistical analyses for this end point

Secondary: ECMO until day 29

End point title	ECMO until day 29
End point description: all available values (no LOCF)	
End point type	Secondary
End point timeframe: From baseline visit (day 1) until and including day 29 (visit 15)	

End point values	Treatment	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	27		
Units: day				
arithmetic mean (standard deviation)	2.08 (± 5.43)	2.81 (± 5.88)		

Statistical analyses

No statistical analyses for this end point

Secondary: Invasive mechanical ventilation until day 8

End point title	Invasive mechanical ventilation until day 8
End point description: all available values (no LOCF)	
End point type	Secondary
End point timeframe: From baseline visit (day 1) until and including day 8 (visit 9)	

End point values	Treatment	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	27		
Units: day				
arithmetic mean (standard deviation)	7.81 (± 0.49)	7.85 (± 0.46)		

Statistical analyses

No statistical analyses for this end point

Secondary: Invasive mechanical ventilation until day 15

End point title	Invasive mechanical ventilation until day 15
End point description: all available values (no LOCF)	
End point type	Secondary
End point timeframe: From baseline visit (day 1) until and including day 15 (visit 13)	

End point values	Treatment	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	27		
Units: day				
arithmetic mean (standard deviation)	11.77 (± 2.27)	12.33 (± 2.37)		

Statistical analyses

No statistical analyses for this end point

Secondary: Invasive mechanical ventilation until day 29

End point title	Invasive mechanical ventilation until day 29
End point description: all available values (no LOCF)	
End point type	Secondary
End point timeframe: From baseline visit (day 1) until and including day 29 (visit 15)	

End point values	Treatment	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	27		
Units: day				
arithmetic mean (standard deviation)	16.88 (± 8.35)	17.59 (± 7.81)		

Statistical analyses

No statistical analyses for this end point

Secondary: Survival until day 29

End point title	Survival until day 29

End point description:

subjects alive at day 29; all available values (no LOCF)

End point type	Secondary

End point timeframe:

Until day 29 (visit 15)

End point values	Treatment	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	27		
Units: subject	19	19		

Statistical analyses

No statistical analyses for this end point

Secondary: Survival until EoS (day 61, visit 16)

End point title	Survival until EoS (day 61, visit 16)

End point description:

subjects alive at day 61; all available values (no LOCF)

End point type	Secondary

End point timeframe:

Until EoS (day 61, visit 16)

End point values	Treatment	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	27		
Units: subject	19	16		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in SOFA score to all subsequent visits

End point title	Change in SOFA score to all subsequent visits

End point description:

all available values (no LOCF)

End point type	Secondary

End point timeframe:

from baseline until visit 3 (day 2), visit 4 (day 3), visit 5 (day 4), visit 6 (day 5), visit 7 (day 6), visit 8 (day 9), visit 9 (day 8), visit 10 (day 9), visit 11 (day 10), visit 12 (day 11), visit 13 (day 15), visit 14 (day 22), visit 15 (day 29)

End point values	Treatment	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7[1]	7[2]		
Units: none				
arithmetic mean (standard deviation)	-3.43 (± 3.46)	-2.71 (± 5.06)		

Notes:

[1] - see table, N

[2] - see table, N

Attachments (see zip file)	Change in SOFA score baseline subsequent visits/Change in

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From Baseline Visit (Visit 2, day 1) until day 11 (Visit 12)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups	
Reporting group title	Safety Evaluation Set
Reporting group description: all randomized subjects	

Serious adverse events	Safety Evaluation Set		
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 53 (33.96%)		
number of deaths (all causes)	11		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Endotracheal intubation complication			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Traumatic haemothorax			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Embolism arterial			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac arrest			

subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	7 / 53 (13.21%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 7		
Pneumothorax			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory disorder			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Lung assist device therapy			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	4 / 53 (7.55%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Infections and infestations			
Infection			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Safety Evaluation Set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	53 / 53 (100.00%)		
Vascular disorders			
Haemodynamic instability			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences (all)	2		
Shock			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences (all)	2		
Thrombosis			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Surgical and medical procedures			
Antibiotic therapy			
subjects affected / exposed	5 / 53 (9.43%)		
occurrences (all)	6		
Haemodialysis			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
General disorders and administration site conditions			
Hyperthermia			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Hypothermia			
subjects affected / exposed	7 / 53 (13.21%)		
occurrences (all)	7		
Pyrexia			
subjects affected / exposed	16 / 53 (30.19%)		
occurrences (all)	17		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	5 / 53 (9.43%)		
occurrences (all)	5		
Respiratory failure			

subjects affected / exposed	4 / 53 (7.55%)		
occurrences (all)	4		
Psychiatric disorders			
Delirium			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Blood bilirubin increased			
subjects affected / exposed	22 / 53 (41.51%)		
occurrences (all)	2		
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Blood creatinine increased			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Blood lactic acid increased			
subjects affected / exposed	12 / 53 (22.64%)		
occurrences (all)	15		
Blood triglycerides increased			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Blood urea increased			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
C-reactive protein increased			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Haemoglobin decreased			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	2		
Transaminases			

subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Transaminases increased			
subjects affected / exposed	4 / 53 (7.55%)		
occurrences (all)	4		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Cardiovascular insufficiency			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences (all)	2		
Coagulopathy			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Heparin-induced thrombocytopenia			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Gastrointestinal disorders			
Anal haemorrhage			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences (all)	2		
Ileus			

subjects affected / exposed	2 / 53 (3.77%)		
occurrences (all)	2		
Ileus paralytic			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Subileus			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences (all)	2		
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	10 / 53 (18.87%)		
occurrences (all)	10		
Hepatic failure			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Hepatic function abnormal			
subjects affected / exposed	5 / 53 (9.43%)		
occurrences (all)	6		
Liver disorder			
subjects affected / exposed	5 / 53 (9.43%)		
occurrences (all)	5		
Liver injury			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Subcutaneous emphysema			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	13 / 53 (24.53%)		
occurrences (all)	13		
Musculoskeletal and connective tissue disorders			
Muscle haemorrhage			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		

Infections and infestations			
Aspergillus infection			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Herpes simplex			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Herpes simplex reactivation			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Infection			
subjects affected / exposed	14 / 53 (26.42%)		
occurrences (all)	15		
Pneumonia			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Proteus infection			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Sepsis			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Staphylococcal infection			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences (all)	2		
Superinfection			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Superinfection bacterial			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Catabolic state			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Hyperchloraemia			

subjects affected / exposed	18 / 53 (33.96%)		
occurrences (all)	19		
Hyperglycaemia			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Hyperkalaemia			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Hyperlactacidaemia			
subjects affected / exposed	8 / 53 (15.09%)		
occurrences (all)	8		
Hypernatraemia			
subjects affected / exposed	14 / 53 (26.42%)		
occurrences (all)	15		
Hypervolaemia			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Hypoglycaemia			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Hyponatraemia			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 October 2020	Extension of IMP shelf life (6 -> 12 months); extension of manufacturing authorization
08 December 2020	Addition of new tertiary endpoints
16 June 2021	Rescue medication allowed after day 8 (primary endpoint); virus mutation analysis added; long term follow-up for Post-COVID syndrome added; AE-recording adapted
15 March 2022	variables for statistical analysis added
31 May 2022	Recruitment prematurely terminated (as only very few patients still required intensive medical care for COVID-19)

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.

recruitment prematurely terminated (53 instead of 58 subjects)

Notes: