



## Clinical trial results:

**A randomized, controlled, multicenter, open label phase II clinical study to evaluate infliximab in the treatment of patients with severe COVID-19 disease (INFLIXCOVID)**

### Summary

EudraCT number	2021-002098-25
Trial protocol	DE
Global end of trial date	31 March 2023

### Results information

Result version number	v1 (current)
This version publication date	06 December 2023
First version publication date	06 December 2023

### Trial information

#### Trial identification

Sponsor protocol code	ZKSJ0137_INFLIXCOVID
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04922827
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Friedrich Schiller University Jena
Sponsor organisation address	Fürstengraben 1, Jena, Germany, 07737
Public contact	Center for Clinical Studies, University Hospital Jena, 0049 36419396648, ZKS-Projektmanagement@med.uni-jena.de
Scientific contact	Clinic for Internal Medicine IV , University Hospital Jena, 0049 36419324401 , Andreas.Stallmach@med.uni-jena.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	20 June 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 March 2023
Global end of trial reached?	Yes
Global end of trial date	31 March 2023
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

Evaluation of the efficacy of the TNF- $\alpha$  antibody infliximab in the treatment of patients with severe COVID-19 compared with the standard of care (SOC).

Protection of trial subjects:

Subjects allocated to the interventional group received investigational medicinal product (IMP) once, according to the Summary of Product Characteristics (SmPC) with respect to the type and duration of application. The dosage of 5mg/kg bodyweight was equivalent to patients with chronic inflammatory bowel disease, ankylosing spondylitis or psoriasis. Study-specific treatment risks were reduced to a minimum, namely, blood sampling was linked to routine sampling as far as possible, and transthoracic echocardiography is a non-invasive procedure bearing no patient-relevant risks.

Background therapy:

Both treatment groups received standard of care treatment according to the current guidelines.

Evidence for comparator: -

Actual start date of recruitment	29 September 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: 9
Worldwide total number of subjects	9
EEA total number of subjects	9

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)	2
From 65 to 84 years	6

85 years and over	1
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## Subject disposition

### Recruitment

Recruitment details:

9 patients were recruited and randomized within a time period from 29th of September 2021 until 31st of March 2023.

### Pre-assignment

Screening details:

All 9 randomized patients were treated according to their allocation. One screening failure.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Infliximab + Standard of Care

Arm description:

Infliximab and Standard of Care.

Within 3 h after randomization i. v. administration of 5 mg/kg body weight infliximab is applied. The infusion duration is two hours. The further treatment of COVID-19 is carried out according to the current treatment recommendations.

The following additional treatments for COVID-19 are allowed within the study:

- dexamethasone 1x 6 mg
- remdesivir

The following additional treatments for COVID-19 are not allowed within the study up to and including day 28 after randomization:

- treatment with TNF- $\alpha$  antibodies outside of study medication
- treatment with other experimental procedures

Arm type	Experimental
Investigational medicinal product name	Remsima 100 mg powder for concentrate for solution for infusion
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

single dosage 5 mg/kg i. v., infusion duration of 2 h

<b>Arm title</b>	Standard of Care
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Arm description:

Standard of Care.

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- treatment with TNF- $\alpha$  antibodies outside of study medication
- treatment with other experimental procedures

Arm type	No intervention
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<b>Number of subjects in period 1</b>	Infliximab + Standard of Care	Standard of Care
Started	4	5
Completed	4	5

## Baseline characteristics

### Reporting groups

Reporting group title	Infliximab + Standard of Care
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Reporting group description:

Infliximab and Standard of Care.

Within 3 h after randomization i. v. administration of 5 mg/kg body weight infliximab is applied. The infusion duration is two hours. The further treatment of COVID-19 is carried out according to the current treatment recommendations.

The following additional treatments for COVID-19 are allowed within the study:

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- treatment with TNF- $\alpha$  antibodies outside of study medication
- treatment with other experimental procedures

Reporting group title	Standard of Care
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Reporting group description:

Standard of Care.

The treatment of COVID-19 is carried out according to the current treatment recommendations.

The following additional treatments for COVID-19 are allowed within the study:

- dexamethasone 1x 6 mg
- remdesivir

The following additional treatments for COVID-19 are not allowed within the study up to and including day 28 after randomization:

- treatment with TNF- $\alpha$  antibodies outside of study medication
- treatment with other experimental procedures

Reporting group values	Infliximab + Standard of Care	Standard of Care	Total
Number of subjects	4	5	9
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			
median	70.5	79	
full range (min-max)	42 to 86	53 to 81	-
Gender categorical			
Units: Subjects			
Female	1	1	2

Male	3	4	7
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### Subject analysis sets

Subject analysis set title	FAS
Subject analysis set type	Full analysis

Subject analysis set description:

Full analysis set according intention-to-treat principle

Reporting group values	FAS		
Number of subjects	9		
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
median	75		
full range (min-max)	42 to 86		
Gender categorical Units: Subjects			
Female	2		
Male	7		

## End points

### End points reporting groups

Reporting group title	Infliximab + Standard of Care
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Reporting group description:

Infliximab and Standard of Care.

Within 3 h after randomization i. v. administration of 5 mg/kg body weight infliximab is applied. The infusion duration is two hours. The further treatment of COVID-19 is carried out according to the current treatment recommendations.

The following additional treatments for COVID-19 are allowed within the study:

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- treatment with TNF- $\alpha$  antibodies outside of study medication
- treatment with other experimental procedures

Reporting group title	Standard of Care
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Reporting group description:

Standard of Care.

The treatment of COVID-19 is carried out according to the current treatment recommendations.

The following additional treatments for COVID-19 are allowed within the study:

- dexamethasone 1x 6 mg
- remdesivir

The following additional treatments for COVID-19 are not allowed within the study up to and including day 28 after randomization:

- treatment with TNF- $\alpha$  antibodies outside of study medication
- treatment with other experimental procedures

Subject analysis set title	FAS
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Subject analysis set type	Full analysis
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Subject analysis set description:

Full analysis set according intention-to-treat principle

### Primary: 28-day survival

End point title	28-day survival <sup>[1]</sup>
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End point description:

28 day survival

End point type	Primary
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End point timeframe:

28 days

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: Due to slow recruitment, the planned patient numbers could not be reached by far. Reached patient numbers do not allow for well founded statistical analysis.

End point values	Infliximab + Standard of Care	Standard of Care	FAS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	4	5	9	
Units: Subjects	4	4	8	



## **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From randomization (V0) to Follow-Up day 90 after randomization (V5).

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.1
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### Reporting groups

Reporting group title	Infliximab + Standard of Care
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Reporting group description:

Infliximab and Standard of care

Reporting group title	Standard of Care
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Reporting group description:

Standard of care

Serious adverse events	Infliximab + Standard of Care	Standard of Care	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	2 / 5 (40.00%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	1	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Frequency threshold for reporting non-serious adverse events: 0 %

<b>Non-serious adverse events</b>	<b>Infliximab + Standard of Care</b>	<b>Standard of Care</b>	
Total subjects affected by non-serious adverse events subjects affected / exposed	4 / 4 (100.00%)	4 / 5 (80.00%)	
Vascular disorders Deep vein thrombosis subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 5 (0.00%) 0	
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)  Inflammation subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 2  0 / 4 (0.00%) 0	0 / 5 (0.00%) 0  1 / 5 (20.00%) 1	
Respiratory, thoracic and mediastinal disorders Hypercapnia subjects affected / exposed occurrences (all)  Pneumothorax subjects affected / exposed occurrences (all)  Respiratory failure subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0  0 / 4 (0.00%) 0  1 / 4 (25.00%) 1	1 / 5 (20.00%) 1  1 / 5 (20.00%) 1  1 / 5 (20.00%) 2	
Investigations Fibrin D dimer increased subjects affected / exposed occurrences (all)  Full blood count decreased subjects affected / exposed occurrences (all)  Hyperkalaemia subjects affected / exposed occurrences (all)  Hypernatraemia	0 / 4 (0.00%) 0  0 / 4 (0.00%) 0  0 / 4 (0.00%) 0	1 / 5 (20.00%) 1  1 / 5 (20.00%) 1  1 / 5 (20.00%) 1	

subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 5 (20.00%) 1	
Hyponatraemia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 5 (20.00%) 1	
Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	2 / 5 (40.00%) 3	
Cardiac failure subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 5 (20.00%) 1	
Nervous system disorders Hypertonia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 5 (20.00%) 1	
Speech disorder subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 5 (0.00%) 0	
Syncope subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 5 (20.00%) 1	
Blood and lymphatic system disorders Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 5 (20.00%) 1	
Gastrointestinal disorders Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 5 (20.00%) 1	
Vomiting subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 5 (0.00%) 0	
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 5 (0.00%) 0	

Renal and urinary disorders			
Polyuria			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Spinal pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Infections and infestations			
Infection			
subjects affected / exposed	1 / 4 (25.00%)	4 / 5 (80.00%)	
occurrences (all)	1	2	
Lung abscess			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Opportunistic infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Viral infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Candida infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
COVID-19			
subjects affected / exposed	0 / 4 (0.00%)	2 / 5 (40.00%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Hyperglycaemia			

subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 April 2022	Extension of recruitment period.

Notes:

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### 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.

Low recruitment numbers due to strongly decreasing incidence of patients with severe COVID-19 infection. Therefore, no statements about positive effects on effectiveness of the IMP possible. Nevertheless, no negative safety signal from the IMP.

Notes:

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/36056419>