



Clinical trial results:

A Phase Ib, single-arm, open-label study evaluating the pharmacokinetics, pharmacodynamics, and safety of tocilizumab in pediatric patients hospitalized with COVID-19

Summary

EudraCT number	2021-005332-27
Trial protocol	ES IT GR FR DE PL
Global end of trial date	27 March 2024

Results information

Result version number	v1 (current)
This version publication date	06 October 2024
First version publication date	06 October 2024

Trial information

Trial identification

Sponsor protocol code	WA43811
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05164133
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, 4058
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-000309-PIP07-21
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 May 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	27 March 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the pharmacokinetics, pharmacodynamics, safety, and exploratory efficacy of tocilizumab for the treatment of pediatric participants from birth to less than 18 years old hospitalized with COVID-19 and who received systemic corticosteroids and required supplemental oxygen or mechanical ventilation.

Protection of trial subjects:

All participants were required to sign an Informed Consent Form

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 February 2022
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 States: 2
Worldwide total number of subjects	2
EEA total number of subjects	0

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)	2
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants from birth to less than 18 years old, hospitalized with COVID-19 and receiving systemic corticosteroids and requiring supplemental oxygen or mechanical ventilation

Period 1

Period 1 title	Baseline (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Tocilizumab + SOC
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Arm description:

Participants received a single dose of tocilizumab (TCZ) with the option for a second dose after 8-24 hours if clinically indicated.

Arm type	Experimental
Investigational medicinal product name	Tocilizumab
Investigational medicinal product code	
Other name	TCZ
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received a single dose of intravenous TCZ.

Number of subjects in period 1	Tocilizumab + SOC
Started	2
Completed	1
Not completed	1
Consent withdrawn by subject	1

Baseline characteristics

Reporting groups

Reporting group title	Baseline
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Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	2	2	
Age Categorical			
Units: Subjects			
Children (2-11 years)	2	2	
Age Continuous			
Mean and SD were not summarized and are reported as 0.0.			
Units: years			
arithmetic mean	0.0		
standard deviation	± 0.0	-	
Gender Categorical			
Units: Subjects			
Female	1	1	
Male	1	1	
Race			
Units: Subjects			
Not reported or unknown	2	2	
Ethnicity			
Units: Subjects			
Hispanic or Latino	1	1	
Not stated	1	1	

End points

End points reporting groups

Reporting group title	Tocilizumab + SOC
Reporting group description: Participants received a single dose of tocilizumab (TCZ) with the option for a second dose after 8-24 hours if clinically indicated.	

Primary: Clearance (CL) of TCZ

End point title	Clearance (CL) of TCZ ^[1]
End point description: 999: Descriptive statistics were not calculated due to low sample size.	
End point type	Primary
End point timeframe: Through Day 28	
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: No formal statistical hypothesis testing was planned for this study. The trial was terminated early due to lack of recruitment, as only two participants were enrolled. For the primary endpoint of the characterization of the PK of TCZ through Day 28, individual PK parameters for each participant were produced and no descriptive statistics were calculated.

End point values	Tocilizumab + SOC			
Subject group type	Reporting group			
Number of subjects analysed	2 ^[2]			
Units: L/day				
number (not applicable)	999			

Notes:

[2] - Descriptive statistics were not calculated due to low sample size.

Statistical analyses

No statistical analyses for this end point

Primary: Volume of distribution of TCZ

End point title	Volume of distribution of TCZ ^[3]
End point description: 999: Descriptive statistics were not calculated due to low sample size.	
End point type	Primary
End point timeframe: Through Day 28	
Notes:	

[3] - 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: No formal statistical hypothesis testing was planned for this study. The trial was terminated early due to lack of recruitment, as only two participants were enrolled. For the primary endpoint of the characterization of the PK of TCZ through Day 28, individual PK parameters for each participant were produced and no descriptive statistics were calculated.

End point values	Tocilizumab + SOC			
Subject group type	Reporting group			
Number of subjects analysed	2 ^[4]			
Units: Liters				
number (not applicable)	999			

Notes:

[4] - Descriptive statistics were not calculated due to low sample size.

Statistical analyses

No statistical analyses for this end point

Primary: Maximum serum concentration (Cmax) of TCZ

End point title	Maximum serum concentration (Cmax) of TCZ ^[5]
End point description: 999: Descriptive statistics were not calculated due to low sample size.	
End point type	Primary
End point timeframe: Through Day 28	

Notes:

[5] - 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: No formal statistical hypothesis testing was planned for this study. The trial was terminated early due to lack of recruitment, as only two participants were enrolled. For the primary endpoint of the characterization of the PK of TCZ through Day 28, individual PK parameters for each participant were produced and no descriptive statistics were calculated.

End point values	Tocilizumab + SOC			
Subject group type	Reporting group			
Number of subjects analysed	2 ^[6]			
Units: ug/mL				
number (not applicable)	999			

Notes:

[6] - Descriptive statistics were not calculated due to low sample size.

Statistical analyses

No statistical analyses for this end point

Primary: Area under the curve from Days 0-28 (AUC Days 0-28) of TCZ

End point title	Area under the curve from Days 0-28 (AUC Days 0-28) of
End point description: 999: Descriptive statistics were not calculated due to low sample size.	
End point type	Primary
End point timeframe: Days 0-28	

Notes:

[7] - 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: No formal statistical hypothesis testing was planned for this study. The trial was terminated early due to lack of recruitment, as only two participants were enrolled. For the primary

endpoint of the characterization of the PK of TCZ through Day 28, individual PK parameters for each participant were produced and no descriptive statistics were calculated.

End point values	Tocilizumab + SOC			
Subject group type	Reporting group			
Number of subjects analysed	2 ^[8]			
Units: ug.Day/mL				
number (not applicable)	999			

Notes:

[8] - Descriptive statistics were not calculated due to low sample size.

Statistical analyses

No statistical analyses for this end point

Primary: Serum concentration on Day 28 of TCZ

End point title	Serum concentration on Day 28 of TCZ ^[9]
End point description: 999: Descriptive statistics were not calculated due to low sample size.	
End point type	Primary
End point timeframe: Day 28	

Notes:

[9] - 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: No formal statistical hypothesis testing was planned for this study. The trial was terminated early due to lack of recruitment, as only two participants were enrolled. For the primary endpoint of the characterization of the PK of TCZ through Day 28, individual PK parameters for each participant were produced and no descriptive statistics were calculated.

End point values	Tocilizumab + SOC			
Subject group type	Reporting group			
Number of subjects analysed	2 ^[10]			
Units: ug/mL				
number (not applicable)	999			

Notes:

[10] - Descriptive statistics were not calculated due to low sample size.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of 90% saturation of sIL-6R

End point title	Duration of 90% saturation of sIL-6R
End point description: 999: Descriptive statistics were not calculated due to low sample size.	
End point type	Secondary
End point timeframe: Through Day 28	

End point values	Tocilizumab + SOC			
Subject group type	Reporting group			
Number of subjects analysed	2 ^[11]			
Units: Day				
number (not applicable)	999			

Notes:

[11] - Descriptive statistics were not calculated due to low sample size.

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of IL-6

End point title	Concentration of IL-6
End point description:	
999: Descriptive statistics were not calculated due to low sample size.	
End point type	Secondary
End point timeframe:	
Day 1 - Day 21	

End point values	Tocilizumab + SOC			
Subject group type	Reporting group			
Number of subjects analysed	2 ^[12]			
Units: ng/L				
number (not applicable)	999			

Notes:

[12] - Descriptive statistics were not calculated due to low sample size.

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of sIL-6R

End point title	Concentration of sIL-6R
End point description:	
999: Descriptive statistics were not calculated due to low sample size.	
End point type	Secondary
End point timeframe:	
Day 1 - Day 21	

End point values	Tocilizumab + SOC			
Subject group type	Reporting group			
Number of subjects analysed	2 ^[13]			
Units: ng/mL				
number (not applicable)	999			

Notes:

[13] - Descriptive statistics were not calculated due to low sample size.

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of C-reactive protein (CRP)

End point title	Concentration of C-reactive protein (CRP)
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End point description:

999: Descriptive statistics were not calculated due to low sample size.

End point type	Secondary
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End point timeframe:

Through Day 60

End point values	Tocilizumab + SOC			
Subject group type	Reporting group			
Number of subjects analysed	2 ^[14]			
Units: mg/mL				
number (not applicable)	999			

Notes:

[14] - Descriptive statistics were not calculated due to low sample size.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 60 days

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.0
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Reporting groups

Reporting group title	Tocilizumab + SOC
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Reporting group description:

Participants received a single dose of tocilizumab (TCZ) with the option for a second dose after 8-24 hours if clinically indicated.

Serious adverse events	Tocilizumab + SOC		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Product issues			
Device dislocation			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Tocilizumab + SOC		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Descriptive statistics were not calculated due to low sample size and early study termination.
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Notes: