



Clinical trial results:

A randomized, double-blind, placebo-controlled trial to evaluate the efficacy and safety of AIC649 in the treatment of otherwise healthy subjects with asymptomatic or mildly symptomatic SARS-CoV-2 infection

Summary

EudraCT number	2021-000167-69
Trial protocol	DE
Global end of trial date	06 May 2022

Results information

Result version number	v1 (current)
This version publication date	22 May 2023
First version publication date	22 May 2023
Summary attachment (see zip file)	AIC649-02-II-01_Clinical trial report Synopsis (AIC649-02-II-01_CTR Synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	AIC649-02-II-01
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AiCuris Anti-infective Cures AG
Sponsor organisation address	Friedrich-Ebert-Straße 475, Wuppertal, Germany, 42117
Public contact	Company Itself, AiCuris Anti-Infective Cures AG, +49 202317630, info@aicuris.com
Scientific contact	Company Itself, AiCuris Anti-Infective Cures AG, +49 202317630, info@aicuris.com

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	29 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 May 2022
Global end of trial reached?	Yes
Global end of trial date	06 May 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the safety and tolerability of multiple dosing of AIC649

Protection of trial subjects:

The trial has been conducted in compliance with GCP standards which provides public assurance that safety and well-being of trial subjects as well as the rights, integrity, and confidentiality of trial subjects are protected.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 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	Germany: 8
Worldwide total number of subjects	8
EEA total number of subjects	8

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)	8
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Adults m/f subjects, 18-55 years age inclusive for SARS-CoV-2 nonvaccinated- or not fully vaccinated subjects and 18-65 years-of-age inclusive for SARS-CoV-2 fully vaccinated subjects, of any ethnic origin, with RT-PCR/qRT-PCR positive, asymptomatic or with at most mild COVID-19 symptoms (Exclude: Fever defined as $\geq 38.5^{\circ}\text{C}$ / Moderate or severe cough)

Pre-assignment

Screening details:

In total, 18 subjects were screened for eligibility, of these 10 subjects (55.6%) were screen failures and 8 (44.4%) were considered eligible and were enrolled and randomized to a treatment group.

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, Data analyst, Carer, Assessor

Blinding implementation details:

Treatment administration was double-blind. As, in contrast to the saline solution (placebo), the AIC649 solution had a slightly yellow color, the blind was maintained by means of colored syringes.

All involved medical, administrative, and operational staff of the clinical trial sites, of CRO and of AiCuris Anti-infective Cures AG remained blinded during the course of the trial until Database Lock and finalization of the Statistical Analysis Plan (SAP).

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo group

Arm description:

0.9% w/v saline solution as Placebo (1 mL) administered as intravenous bolus injection on Days 1, 3 and 5

Arm type	Placebo
Investigational medicinal product name	0.9% w/v saline solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Administered Placebo 0.9% w/v saline solution, 1 mL, as bolus intravenous injection on Days 1, 3, and 5 (3 administrations).

Arm title	Verum Group
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Arm description:

AIC649 (1000000000 viral particles in 1 mL) administered as intravenous bolus injection on Days 1, 3, and 5

Arm type	Experimental
Investigational medicinal product name	AIC649
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Administered AIC649 lyophilizate (1 vial containing 1×1000000000 viral particles) to be reconstituted with 1.1 mL water for injection (WFI) and given as 1 mL bolus intravenous injection on Days 1, 3, and 5

(3 administrations).

Number of subjects in period 1	Placebo group	Verum Group
Started	4	4
Completed	4	4

Baseline characteristics

Reporting groups

Reporting group title

Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	8	8	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	8	8	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	32.8		
standard deviation	± 10.74	-	
Gender categorical			
Units: Subjects			
Female	1	1	
Male	7	7	

End points

End points reporting groups

Reporting group title	Placebo group
Reporting group description: 0.9% w/v saline solution as Placebo (1 mL) administered as intravenous bolus injection on Days 1, 3 and 5	
Reporting group title	Verum Group
Reporting group description: AIC649 (1000000000 viral particles in 1 mL) administered as intravenous bolus injection on Days 1, 3, and 5	

Primary: Adverse events

End point title	Adverse events ^[1]
End point description:	
End point type	Primary
End point timeframe: Data was collected for upto 27 days after first dosing.	
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: Descriptive statistics were performed	

End point values	Placebo group	Verum Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: number	11	14		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First Subject First Visit: 06Feb2022 Signing date of ICF until Last Subject Last Visit: 06May2022

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.1
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Reporting groups

Reporting group title	Placebo group
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Reporting group description:

0.9% w/v saline solution as Placebo (1 mL) administered as bolus on Days 1, 3 and 5.

Reporting group title	Verum group
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Reporting group description:

AIC649 (109 viral particles in 1 mL) as bolus on Days 1, 3, and 5,

Serious adverse events	Placebo group	Verum group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Placebo group	Verum group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	4 / 4 (100.00%)	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 4 (50.00%)	1 / 4 (25.00%)	
occurrences (all)	3	1	
Syncope			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Infusion site phlebitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Injection site pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Vessel puncture site haematoma			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	2	
Vessel puncture site thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Eye disorders			
Conjunctival irritation			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Dry eye			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Swelling of eyelid			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			

subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Increased upper airway secretion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Nasal congestion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Paranasal sinus discomfort			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Throat irritation			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Tonsillar hypertrophy			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Rash macular			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 March 2021	Amendment 1 (Version 2) The Protocol Version 1 was amended to: • reflect inclusion of South Africa as a participating country, which also resulted in: - o adjustment of sample volumes for cell subpopulations and cytokines, - o removal of the Coordinating Investigator role, • provide clarification of: - o inclusion of mildly symptomatic SARS-CoV-2 subjects, - o inclusion, exclusion and discharge criteria, - o procedures in the event of moderate or severe COVID-19 symptoms, - o subject numbering procedures, - o trial medication packaging, preparation and dosing, - o cytokines / chemokines to be analyzed • use throat swabbing rather than throat wash for SARS-CoV-2 sampling at Screening, • add ECG and vital sign assessments on Day 1, 3, and 5 at 1h, 2h, and 4h post-dosing • address minor typos in the text.
01 June 2021	Amendment 2 (Version 3) The Protocol Version 2 was amended to reflect the requests of the Paul-Ehrlich-Institut. These primarily required: • Description or clarification of: - o Exclusion criteria (#11) - o Stopping criteria - o Withdrawal criteria - o Endpoint descriptions - o Eligibility of subjects with mild COVID-19 disease - o Start of COVID-19 symptoms - o Documentation of local tolerability AEs - o Follow-up of unblinded subjects • Removal of: - o Provision to replace early termination subjects • Addition of: - o Further sentinel subjects - o Extended follow-up of subjects with moderate/severe COVID-19

10 June 2021	Amendment 3 (Version 4) The Protocol Version 3 was amended to reflect the requests of the Ethics Committee in addition to some administrative changes. These primarily required: • addition and clarification of timing and documentation of body temperature, respiratory rate, pulse rate, and SpO2 measures after subject discharge from the unit, • description of measures to be taken in the event of worsening COVID-19 symptoms after discharge from the unit, • clarification of the selection criteria relating to: - o documentation of informed consent, - o the use of oral contraceptives as a highly effective methods of contraception, - o the exclusion of vulnerable subjects, • inclusion of FSH determination for potentially post-menopausal women, • clarification that IL-6 and IL-10 will be determined in both the general cytokine panel in the immediate safety analysis, • addition of subject training for taking readings, documentation of results and provision of equipment for use during out-patient follow up period (and subsequent collection at the End-of-Trial examination), • inclusion of a subject diary and diary review at appropriate timepoints, • clarification of withdrawal criteria, • use of PBMCs instead of monocytes for ex-vivo stimulation experiments.
11 November 2021	Amendment 4 (Version 5) The Protocol Version 4 was amended to remove the exclusion of SARS-CoV-2 vaccinated subjects and to exclude the subjects with any vaccination in the 14-day period prior to the trial or planned for any time during the trial period. The sentinel treatment approach was extended to distinguish between vaccinated and non-vaccinated subjects. Subgroup analyses of efficacy and safety, based on vaccination status at Baseline, were therefore also included.
18 February 2022	Amendment 5 (Version 6) The Protocol Version 5 was amended primarily to adjust the population selection criteria for: • All subjects by: - o increasing the threshold for fever from $\geq 38^{\circ}\text{C}$ to moderate or severe ($\geq 38.5^{\circ}\text{C}$) - o permitting mild cough, - o fully SARS-CoV-2 vaccinated status is defined according to local requirements, - o reduced minimum time since last smoking from 1 year to 3 months prior to enrollment, - o Adjustment of exclusion criterion #11 for laboratory parameters. • Fully vaccinated subjects only by: - o extending the permitted age range from 18 to 55 years up to 18 to 65 years, - o removing the minimum viral genome copy number, - o remove the maximum time period between first positive SARS-CoV-2 test by RT-PCR, qRT-PCR, or antigen test and enrollment (Day -1). In addition, stratification by SARS by qRT-PCR viral load titer was removed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

