Clinical trial results:
Efficacy and Safety of Edoxaban and or Colchicine for patients with SARS-CoV-2 infection managed in the out of hospital setting (COVID 19)

Summary

EudraCT number	2020-002234-32
Trial protocol	BE IT
Global end of trial date	31 August 2022

Results information

Result version number	v1 (current)
This version publication date	10 September 2023
First version publication date	10 September 2023
Summary attachment (see zip file)	CONVINCE-CIP (CONVINCE_Protocol_V2.pdf) CONVINCE SAP (CONVINCE-SAP.pdf) CONVINCE Synopsis Final Report (CONVINCE-FINALReportSynopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	CONVINCE

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04516941
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Insel Gruppe AG
Sponsor organisation address	Fraiburgstrase 18, Bern, Switzerland,
Public contact	Prof.Stephan Windecker, Insel Gruppe AG - Inselspital Universitätsklinik für Kardiologie, +41 316325000, kardio.studien@insel.ch
Scientific contact	Prof.Stephan Windecker, Insel Gruppe AG - Inselspital Universitätsklinik für Kardiologie, +41 316325000, kardio.studien@insel.ch

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	12 June 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 August 2022
Global end of trial reached?	Yes
Global end of trial date	31 August 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The aim of the CONVINCE study is therefore to assess the safety and efficacy of edoxaban and/or colchicine administration in SARS-CoV-2 infected patients who are managed outside the hospital with respect to the occurrence of fatalities, hospitalisation, major vascular thrombotic events or the SARS-CoV-2 clearance rate under RT PCR

Protection of trial subjects:

- Regular patient follow-up with adverse event collection

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 April 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	Belgium: 26
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Switzerland: 29
Worldwide total number of subjects	60
EEA total number of subjects	31

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)	58
From 65 to 84 years	2

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients ≥ 18 years old with symptoms compatible with active Coronavirus infection and laboratory confirmed SARS-CoV-2 infection (under RT PCR) who are managed at home or in another out-of-hospital setting

Pre-assignment

Screening details:

Eligible patients can be consented and randomised at any within 7 days from first SARS- CoV-2 positive diagnosis

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Edoxaban only

Arm description:

SARS-CoV-2 positive patients managed outside the hospital.
Edoxaban 60 mg q.d., or 30 mg q.d. in patients with CrCl = or <50 ml/min or body weight equal, less than 60 kg and concomitant prescription of ciclosporin, dronedarone, erythromycin, ketoconazole, from randomization to end of study visit at day 25 (+/-3).

Arm type	Experimental
Investigational medicinal product name	Lixiana (Edoxaban)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Edoxaban 60 mg q.d., or 30 mg q.d. in patients with CrCl = or <50 ml/min or body weight equal, less than 60 kg and concomitant prescription of ciclosporin, dronedarone, erythromycin, ketoconazole, from randomization to end of study visit at day 25 (+/-3).

Arm title	No Edoxaban

Arm description: -

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Colchicine only

Arm description:

Colchicine at 0.5 mg per os (PO) twice daily for the first 3 days and then once daily from randomization to study visit FU at day 14 (+/-3) days. Treatment could be continued to the day 25 (+3/-3 days). If the creatinine clearance (CrCl) was between 15-30 ml/min the loading dosage was 0.5 mg once daily while the maintenance dosage remained unchanged.

Arm type	Experimental
Investigational medicinal product name	Colchicine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Colchicine at 0.5 mg per os (PO) twice daily for the first 3 days and then once daily from randomization to study visit FU at day 14 (+/-3) days. Treatment could be continued to the day 25 (+3/-3 days). If the creatinine clearance (CrCl) was between 15-30 ml/min the loading dosage was 0.5 mg once daily while the maintenance dosage remained unchanged.

Arm title	No Colchicine
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Edoxaban only	No Edoxaban	Colchicine only
Started	29	30	30
Completed	29	30	30

Number of subjects in period 1	No Colchicine
Started	29
Completed	29

Baseline characteristics

Reporting groups[1]	
Reporting group title	Edoxaban only
Reporting group description:	
SARS-CoV-2 positive patients managed outside the hospital. Edoxaban 60 mg q.d., or 30 mg q.d. in patients with CrCl = or <50 ml/min or body weight equal, less than 60 kg and concomitant prescription of ciclosporin, dronedarone, erythromycin, ketoconazole, from randomization to end of study visit at day 25 (+/-3).	
Reporting group title	No Edoxaban
Reporting group description: -	
Reporting group title	Colchicine only
Reporting group description:	
Colchicine at 0.5 mg per os (PO) twice daily for the first 3 days and then once daily from randomization to study visit FU at day 14 (+/-3) days. Treatment could be continued to the day 25 (+3/-3 days). If the creatinine clearance (CrCl) was between 15-30 ml/min the loading dosage was 0.5 mg once daily while the maintenance dosage remained unchanged.	
Reporting group title	No Colchicine
Reporting group description: -	

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.
Justification: 60 patients were consented; 1 of those refused further participation in the study, 59 of those were randomized: 16 in Edoxaban + Colchicine group, 13 in Edoxaban group, 14 in Colchicine group, 16 in standard of care (this means 29 in Edoxaban group, 30 in No Edoxaban group, 30 in Colchicine group, 29 in No Colchicine group). All 59 patients completed the study.

Reporting group values	Edoxaban only	No Edoxaban	Colchicine only
Number of subjects	29	30	30
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			
Adults			
Age continuous			
Baseline Characteristics Age			
Units: years			
median	51	48	47.5
full range (min-max)	24 to 73	25 to 65	25 to 66
Gender categorical Units: Subjects			
Female	16	16	16
Male	13	14	14

Reporting group values	No Colchicine	Total	

Number of subjects	29	59	
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 Adults			
Age continuous			
Baseline Characteristics Age			
Units: years			
median	49		
full range (min-max)	24 to 73	-	
Gender categorical Units: Subjects			
Female	16	32	
Male	13	27	

End points

End points reporting groups

Reporting group title	Edoxaban only

Reporting group description:

SARS-CoV-2 positive patients managed outside the hospital.
Edoxaban 60 mg q.d., or 30 mg q.d. in patients with CrCl = or <50 ml/min or body weight equal, less than 60 kg and concomitant prescription of ciclosporin, dronedarone, erythromycin, ketoconazole, from randomization to end of study visit at day 25 (+/-3).

Reporting group title	No Edoxaban

Reporting group description: -

Reporting group title	Colchicine only

Reporting group description:

Colchicine at 0.5 mg per os (PO) twice daily for the first 3 days and then once daily from randomization to study visit FU at day 14 (+/-3) days. Treatment could be continued to the day 25 (+3/-3 days). If the creatinine clearance (CrCl) was between 15-30 ml/min the loading dosage was 0.5 mg once daily while the maintenance dosage remained unchanged.

Reporting group title	No Colchicine

Reporting group description: -

Primary: Edoxaban vs. no active treatment

End point title	Edoxaban vs. no active treatment[1]

End point description:

This study has 2 co-primary endpoint
Edoxaban vs. no active treatment
Major vascular thrombotic events (MVTE) at 25 (+/-3) days defined as a composite of:
• Asymptomatic proximal deep-vein thrombosis
• Symptomatic proximal or distal deep-vein thrombosis
• Symptomatic pulmonary embolism or thrombosis
• Myocardial infarction
• Ischemic stroke
• non-CNS systemic embolism
• Death

End point type	Primary

End point timeframe:

Major vascular thrombotic events (MVTE) at 25 (+/-3) 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: Among COVID-19 patients managed in the out-of-hospital setting, this study showed no difference in the two co-primary endpoints with edoxaban and/or colchicine versus standard of care. In consideration of the premature trial discontinuation and the consequent insufficient study power, the current study does not allow to draw definitive conclusions on the safety and the efficacy of edoxaban and/or colchicine administration in SARS-CoV-2 infected patients managed outside the hospital.

End point values	Edoxaban only	No Edoxaban	Colchicine only	No Colchicine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	30	30	29
Units: Major vascular thrombotic events (MVTE)	29	30	30	29

Statistical analyses

No statistical analyses for this end point

Primary: Colchicine vs no active treatment

End point title	Colchicine vs no active treatment[2]

End point description:

This study has 2 co-primary endpoints, one each randomization as follows
Colchicine vs no active treatment
The SARS-CoV-2 detection rates at day 14 (+/-3) under RT PCR or freedom from death or hospitalisation

End point type	Primary

End point timeframe:

The SARS-CoV-2 detection rates at day 14 (+/-3) under RT PCR or freedom from death or hospitalisation

Notes:

[2] - 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: Among COVID-19 patients managed in the out-of-hospital setting, this study showed no difference in the two co-primary endpoints with edoxaban and/or colchicine versus standard of care. In consideration of the premature trial discontinuation and the consequent insufficient study power, the current study does not allow to draw definitive conclusions on the safety and the efficacy of edoxaban and/or colchicine administration in SARS-CoV-2 infected patients managed outside the hospital.

End point values	Edoxaban only	No Edoxaban	Colchicine only	No Colchicine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	30	30	29
Units: The SARS-CoV-2 detection rates at day 14	29	30	30	29

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: Enrolment to End of Study (25 days +/-3 days post randomization)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25

Frequency threshold for reporting non-serious adverse events: 0.1 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Among COVID-19 patients managed in the out-of-hospital setting, this study showed no difference in the two co-primary endpoints with edoxaban and/or colchicine versus standard of care. In consideration of the premature trial discontinuation and the consequent insufficient study power, the current study does not allow to draw definitive conclusions on the safety and the efficacy of edoxaban and/or colchicine administration in SARS-CoV-2 infected patients managed outside the hospital.

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? Yes

Date	Interruption	Restart date
31 August 2022	The Sponsor has terminated trial per 31. August 2022, as a result of the insufficient rate of patient accrual and in view of the newly available scientific evidence. 60 patients were consented; 1 of those refused further participation in the study, 59 of those were randomized: 16 in Edoxaban + Colchicine group, 13 in Edoxaban group, 14 in Colchicine group, 16 in standard of care (this means 29 in Edoxaban group, 30 in No Edoxaban group, 30 in Colchicine group, 29 in No Colchicine group). All 59 patients completed the study.	-

Notes:

Limitations and caveats

None reported