EudraCT No.	**2020-002234-32**
Swissmedic No.	**2020DR3113**
Trial Name:	**CONVINCE**
Trial Title:	**Efficacy and Safety of Edoxaban and or Colchicine for patients with SARS-CoV-2 infection managed in the out of hospital setting (COVID 19): CorONa VIrus edoxabaN ColchicinE (CONVINCE)**

1. Title and Signature Page

FINAL REPORT

According to ICH Guideline E3

Investigational product:	Edoxaban and or Colchicin
Indication:	Patients with SARS-CoV-2 infection managed in the out of hospital setting
Trial description:	International, multicentre, open-label, randomised, study
Study period:	FPFV: 09/04/2021/ LPLV: 07/06/2022
Sponsor:	Insel Gruppe AG, Bern University Hospital, Inselspital Department of Cardiology, Freiburgstrasse, 3010 Bern, Switzerland Phone +41 31 632 50 00; Email: kardio.studien@insel.ch
Date of report:	23 March 2023
Identification Code:	CONVINCE
Phase:	Phase III
Coordinating Investigator & Sponsor-Investigator and Contact Person:	Prof. Dr. med. Stephan Windecker, Insel Gruppe AG, Bern University Hospital, Inselspital Department of Cardiology, Freiburgstrasse, 3010 Bern, Switzerland Phone +41 31 632 50 00; Email: kardio.studien@insel.ch and stephan.windecker@insel.ch

This study was performed in compliance with Good Clinical Practices (GCP), including the archiving of essential documents.

COORDINATING INVESTIGATOR SIGNATURE

Trial Title: Efficacy and Safety of Edoxaban and or Colchicine for patients with SARS-CoV-2 infection managed in the out of hospital setting (COVID 19): CorONa VIrus edoxabaN ColchicinE (CONVINCE)

I have read this report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study

Function	Name	Date	Signature
Final Report Author	Dr. Laura Morf, Head of Insel Cardiology Study Team, Department of Cardiology, Inselspital Bern	13.06.2023	
Reviewer	André Frenk, PhD, Clinic Manager, Department of Cardiology, Inselspital Bern	13.06.2023	
Coordinating Investigator & Sponsor	Prof. Dr. med. Stephan Windecker Chair, Department of Cardiology, Inselspital Bern	13.6.23	

2. Synoposis

Name of Sponsor: Insel Gruppe AG	*(For National Authority Use only)*
Name of Finished Product: Lixiana (Edoxaban) and/or Colchicin	
Name of active Ingredient: Edoxaban Tosilate Colchicin	

Title of Study:

Efficacy and Safety of Edoxaban and or Colchicine for patients with SARS-CoV-2 infection managed in the out of hospital setting (COVID 19): CorONa VIrus edoxabaN ColchicinE (CONVINCE)

Investigators:

See study center listing below

Activated study centre(s) and Investigators (local PI):

Switzerland:

- Insel Gruppe AG, University Hospital Bern, Inselspital Bern, Bern, Switzerland
  Prof. Dr. med. Stephan Windecker (Sponsor-Investigator and local PI Inselspital Bern)
- Cardiocentro Lugano, Ospedale Regionale di Lugano, Lugano
  Prof. Dr. Marco Valgimigli

Italy:

- ASST Grande Ospedale Metropolitano Niguarda, Milano
  Dott. Luca Bonacchini
- Ospedale A. Manzoni, ASST Lecco, Lecco
  Dott. Stefano Savonitto
- Presidio Ospedaliero di Rho, ASST Rhodense, Garbagnate Milanese
  Dott.ssa Barbara Federica Omazzi
- Fondazione IRCCS Policlinico San Matteo, Pavia
  Prof. Stefano Perlini
- Ospedale Papa Giovanni XXIII, Bergamo
  Prof.ssa Anna Falanga
- Ospedale “Infermi” di Rimini, AUSL della Romagna, Rimini
  Dott. Daniele Grosseto
- Ospedale di Jesolo, Azienda ULSS n. 4 Veneto Orientale, Jesolo
  Dott. Francesco Saverio Serino
- IRCCS MultiMedica, Sesto S. Giovanni (MI)
  Dott. Roberto Franco Enrico Pedretti
- Ospedale IRCCS San Raffaele, Milano
  Dott. Moreno Tresoldi

Belgium:

- Jessaziekenhuis Hasselt, Stadsomvaart 11, 3500-Hasselt
  Prof. Pascal Vranckx

Spain

- Hospital Clinic de Barcelona
  Dr. Marta Bodro Marimont

Main Publications:

Publication of Manuscript in process, see Appendix:

- 16.1.5 Statistical Analysis Report
- 16.1.6 Draft Rationale and Design and Manuscript

Studied period (years):	**Phase of development:**
FPFV: 09/04/2021 LPLV: 07/06/2022	Phase III

Objectives:

The aim of the CONVINCE study is 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, hospitalization, major vascular thrombotic events or the SARS-CoV-2 clearance rate under RT PCR.

Methodology:
An Investigator-initiated, multi-center, randomized 2X2 factorial design clinical trial in SARS-CoV-2 positive patients managed outside the hospital.

Number of patients:

Aim: 420

Reached: 60 Enrolled patients/ 1 Withdrawal /59 Completed Trial

Diagnosis and main criteria for inclusion:

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.

Test product, dose and mode of administration:

Randomization was performed within seven days from first SARS-CoV-2 positive diagnosis. Patients were randomized to first edoxaban or no edoxaban and second to colchicine or no colchicine.
Randomization was stratified per site and sex.

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).

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.

Duration of treatment: see section above

Reference therapy, dose and mode of administration: see description above

Criteria for evaluation:

This study has 2 primary endpoints, one for each randomization as follows:

Edoxaban vs. no active treatment
To assess the effect of edoxaban versus no active treatment on the composite endpoint 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 or death at day 25 (+/-3) after randomization.

Colchicine vs no active treatment
To assess the effect of colchicine versus no active treatment on the SARS-CoV-2 clearance rates under RT PCR or freedom from death or hospitalisation at day 14 (+/-3) after randomization.

Statistical analysis:

The study was designed to test the following hypotheses
1) The edoxaban regimen is superior to no edoxaban treatment for the composite of major vascular thrombotic events (MVTE) or death.
2) The colchicine regimen is superior to no colchicine treatment for the SARS-CoV-2 clearance rates under RT PCR or freedom from death or hospitalisation.

These hypotheses are tested independently.

Rates of primary endpoints are estimated as the cumulative incidence between randomization and end of study visit by Kaplan-Meier.

Summary – Conclusions

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.

Primary Endpoint Results summary:

Edoxaban vs. no active treatment
According to the statistical report, in the modified Intention-to-Treat (mITT) population for edoxaban comparison, 0 pre-specified events were observed (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 or death).

Colchicine vs no active treatment
In the mITT population for colchicine comparison, 27 events were observed (SARS-CoV-2 detection rate at day 14±3; hospitalization or death) were observed, 13 in the ‘Colchicine’ group and 14 in the ‘No colchicine’ group (p-value 0.919).

Conclusion:
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.

Date of report:

12 June 2023