



Clinical trial results:

Effects of discontinuing renin-angiotensin system inhibitors in patients with and without COVID-19

Summary

EudraCT number	2020-001544-26
Trial protocol	DK
Global end of trial date	22 December 2022

Results information

Result version number	v1 (current)
This version publication date	09 November 2025
First version publication date	09 November 2025

Trial information

Trial identification

Sponsor protocol code	RASCOVID-19
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Center for Clinical Metabolic Research, Gentofte Hospital
Sponsor organisation address	Gentofte Hospitalsvej 7, Hellerup, Denmark, 2900
Public contact	Filip Krag Knop, Center for Clinical Metabolic Research, Gentofte Hospital, 0045 38674266, filip.krag.knop.01@regionh.dk
Scientific contact	Filip Krag Knop, Center for Clinical Metabolic Research, Gentofte Hospital, 0045 38674266, filip.krag.knop.01@regionh.dk

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	22 December 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 December 2022
Global end of trial reached?	Yes
Global end of trial date	22 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This randomised clinical trial will compare the effects of continuing and discontinuing treatment with ACE inhibitors or ARBs in hospitalised patients with COVID-19 on the number of days alive and out of hospital within 14 days after randomisation (primary endpoint). Furthermore, in order to understand how continuing and discontinuing treatment with RAS inhibition affect RAS and its components, interferon signatures, T cell exhaustion markers and blood pressure, we will investigate how continuing and discontinuing RAS-inhibiting treatment affect these parameters in both hospitalised patients with COVID-19 and in non-hospitalised individuals treated with ACE inhibitors or ARBs without COVID-19.

Protection of trial subjects:

The protocol-related procedures are associated with minimal discomfort to the participants. The participants in group A and group B will either not receive their usual ACE inhibitor or ARB or continue their usual therapy during their admission, depending on assignment group. Discontinuation of the ACE/ARB therapy may result in a small temporary increase in blood pressure; however, blood pressure is routinely measured and, thus, closely monitored during their hospital admission. In case of admission period of less than 30 days, the participant will be instructed to contact his/her general practitioner at day 30 for blood pressure measurements and continuation of antihypertension therapy. At discharge, for all participants, the site investigator will also inform the general practitioner (an electronic discharge letter) and at day 30, site investigator will contact each participant to remind of contacting the general practitioner for blood pressure measurement and ensure continuation of antihypertensive therapy in both groups. ACE inhibitors and ARBs can be considered symptomatic treatment in heart failure, and thus, patients with systolic heart failure will not be included in the study. It is currently unclear whether or not discontinuation of RAS-inhibiting therapy will improve or worsen the prognosis of patients with COVID-19; therefore, neither the assignment to the continuation nor the discontinuation group can clearly be labelled disadvantageous for the participant. The total amount of blood loss will be less than 30 ml at each of the samples; this small amount is not expected to have a clinically relevant impact on the outcome for the participant. Participants will not receive any remuneration for participating in the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 May 2020
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	Denmark: 38
Worldwide total number of subjects	38
EEA total number of subjects	38

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)	18
From 65 to 84 years	16
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

Participants will be recruited amongst COVID-19 positive patients admitted in a COVID-19 clinic in the Capital Region of Copenhagen. Upon admission of patients treated with ACE inhibitors and ARBs, site investigators with an employment at the COVID-19 clinic in question will screen the admitted patients for eligibility.

Pre-assignment

Screening details:

A potential participant will be approached during the first days of hospital admission by the site investigator who will present the trial with verbal and written information regarding the project, and the patient will be invited to participate. The patient will be offered 24 hours for consideration of participation in the trial.

Pre-assignment period milestones

Number of subjects started	38
Number of subjects completed	38

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Continue RASi

Arm description:

Participants continuing RASi

Arm type	Active comparator
Investigational medicinal product name	RASi
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

RASi treatment with ACE and ARBs as prescribed prior to the inclusion in the trial.

Arm title	Discontinue RASi
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Arm description:

Participants discontinuing RASi

Arm type	discontinuing RASi treatment
Investigational medicinal product name	N/A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Not mentioned

Dosage and administration details:

N/A

Number of subjects in period 1	Continue RASi	Discontinue RASi
Started	17	21
Completed	17	21

Baseline characteristics

Reporting groups

Reporting group title	Continue RASi
Reporting group description:	
Participants continuing RASi	
Reporting group title	Discontinue RASi
Reporting group description:	
Participants discontinuing RASi	

Reporting group values	Continue RASi	Discontinue RASi	Total
Number of subjects	17	21	38
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	8	10	18
From 65-84 years	7	9	16
85 years and over	2	2	4
Age continuous			
Units: years			
arithmetic mean	69.4	68.8	
standard deviation	± 13.0	± 10.5	-
Gender categorical			
Units: Subjects			
Female	6	10	16
Male	11	11	22
Smoker			
Units: Subjects			
Smoker	17	21	38
COPD			
Units: Subjects			
COPD	17	21	38
Astma			
Units: Subjects			
Astma	17	21	38
BMI			
Units: kg/m ²			
arithmetic mean	25.17	24.68	
full range (min-max)	18.43 to 31.91	19.28 to 30.09	-
Systolic blood pressure			
Units: mm Hg			
arithmetic mean	146	143	

inter-quartile range (Q1-Q3)	130 to 159	125 to 154	-
diastolic blood pressure			
Units: mm Hg			
arithmetic mean	80	81	
inter-quartile range (Q1-Q3)	74 to 84	72 to 96	-

Subject analysis sets

Subject analysis set title	Covid patients
Subject analysis set type	Per protocol

Subject analysis set description:

Patients with positive PCR for SARS-CoV-2 RNA

Reporting group values	Covid patients		
Number of subjects	38		
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)	18		
From 65-84 years	16		
85 years and over	4		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	±		
Gender categorical			
Units: Subjects			
Female			
Male			
Smoker			
Units: Subjects			
Smoker	38		
COPD			
Units: Subjects			
COPD	38		
Astma			
Units: Subjects			
Astma	38		
BMI			
Units: kg/m ²			
arithmetic mean			
full range (min-max)			
Systolic blood pressure			
Units: mm Hg			
arithmetic mean			

inter-quartile range (Q1-Q3)			
diastolic blood pressure			
Units: mm Hg			
arithmetic mean			
inter-quartile range (Q1-Q3)			

End points

End points reporting groups

Reporting group title	Continue RASi
Reporting group description:	
Participants continuing RASi	
Reporting group title	Discontinue RASi
Reporting group description:	
Participants discontinuing RASi	
Subject analysis set title	Covid patients
Subject analysis set type	Per protocol
Subject analysis set description:	
Patients with positive PCR for SARS-CoV-2 RNA	

Primary: The primary endpoint is days alive and out of hospital within 14 days after recruitment

End point title	The primary endpoint is days alive and out of hospital within 14 days after recruitment
End point description:	
End point type	Primary
End point timeframe:	
Number of days alive and out of hospital within 14 days after recruitment	

End point values	Continue RASi	Discontinue RASi		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	21		
Units: days				
arithmetic mean (inter-quartile range (Q1-Q3))				
Days alive and out of hospital within 14 days	8.94 (6.46 to 11.42)	9.76 (8.07 to 11.45)		

Statistical analyses

Statistical analysis title	Welch Two Sample t-test
Comparison groups	Continue RASi v Discontinue RASi
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Welch Two Sample t-test

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From inclusion to 14 days after recruitment

Assessment type	Systematic
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Dictionary used

Dictionary name	GCP units SOP
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Dictionary version	F5
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Reporting groups

Reporting group title	Continue RASi
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Reporting group description:

Participants continuing RASi

Reporting group title	Discontinue RASi
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Reporting group description:

Participants discontinuing RASi

Serious adverse events	Continue RASi	Discontinue RASi	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 17 (23.53%)	3 / 21 (14.29%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Investigations			
Death			
subjects affected / exposed	0 / 17 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Reduced strength and difficulty of finding words	Additional description: Reduced strength and difficulty of finding words		
subjects affected / exposed	1 / 17 (5.88%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 17 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			

subjects affected / exposed	1 / 17 (5.88%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Fracture	Additional description: Collum femoris fracture		
subjects affected / exposed	1 / 17 (5.88%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Continue RASi	Discontinue RASi	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 17 (11.76%)	1 / 21 (4.76%)	
Cardiac disorders			
Hypertension			
subjects affected / exposed	0 / 17 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Epistaxis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 17 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
increased ALAT			
subjects affected / exposed	1 / 17 (5.88%)	0 / 21 (0.00%)	
occurrences (all)	1	0	
Increased liverenzymes	Additional description: LDH and ALAT		
subjects affected / exposed	1 / 17 (5.88%)	0 / 21 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			

Hypophosphataemia subjects affected / exposed occurrences (all)	Additional description: and hyposodiumaemia		
	1 / 17 (5.88%)	0 / 21 (0.00%)	
	1	0	

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

None reported