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Using the blood pressure medication losartan to improve outcomes for patients with SARS CoV-2

Submission date
22/06/2020

Recruitment status
Stopped

Registration date
10/07/2020

Overall study status
Stopped

Last Edited
13/12/2021

Condition category
Infections and Infestations

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
There is an ongoing pandemic of severe respiratory disease (Covid-19) caused by a novel Coronavirus (SARS-CoV-2) that was first detected in China in December, 2019. The first cases were observed in Sweden in January, 2020, and there is currently ongoing spread in all Swedish regions. Unfortunately, there is currently no available specific treatment for Covid-19. Several investigators have suggested that treatment with angiotensin-converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARB) might lead to an improvement in disease outcomes for Covid-19 patients.

Who can participate?
Patients treated in a hospital in Sweden for confirmed Covid-19

What does the study involve?
Participating patients will be randomized to either receive a blood pressure-lowering drug (losartan) in addition to standard treatment, or standard treatment alone. Patients will be followed up for 28 days

What are the possible benefits and risks of participating?
The risks with losartan treatment are well-known and involve having too-low blood pressure, kidney problems and salt balance problems. All participating patients will be monitored for these problems and they will be dealt with if they occur. Possible benefits may involve a less severe course of the Covid-19 disease.

Where is the study run from?
The hospital Södersjukhuset in Stockholm, Sweden

When is the study starting and how long is it expected to run for?
April 2020 to January 2022

Who is funding the study?
Swedish Research Council

Who is the main contact?
Dr Anders Hedman (scientific), anders.hedman@sll.se
Dr Gustaf Edgran (public), gustaf.edgren@ki.se

Contact information

Type(s)
Public

Contact name
Dr Gustaf Edgren

ORCID ID
https://orcid.org/0000-0002-2198-4745

Contact details
Sjukhusbacken 10
Stockholm
Sweden
11867
+46 86164782
gustaf.edgren@ki.se

Type(s)
Scientific

Contact name
Dr Anders Hedman

Contact details
VO Kardiologi
Södersjukhuset AB
Stockholm
Sweden
118 83
+46-8-616 100 00
anders.hedman@sll.se

Additional identifiers

Clinical Trials Information System (CTIS)
2020-002040-22

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number

Nil known

Study information

Scientific Title
RAAS blockagE in SARS COV-2 Critically ill patiEnts– a Randomized controlled trial

Acronym
RECOVER

Study objectives
The study will test the hypothesis that addition of losartan to standard treatment will decrease risk of the occurrence of the composite endpoint of admission to intensive care unit, or death

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 18/05/2020, Swedish Ethical Review Authority (Etikprövningsmyndigheten, Box 2110, 750 02, Uppsala, Sweden; +46 10-475 08 00; registrator@etikprovning.se), ref: 2020-02185

Study design
Open-label pragmatic phase IV randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
COVID-19 (SARS-CoV-2 infection)

Interventions
Patients in the active arm of the trial will be receiving open-label Losartan in a dosage titrated with regards to blood pressure and renal function up to a maximum of 100 mg once daily. Active treatment with Losartan will continue until death or discharge from hospital, or for a maximum of 28 days post-randomization.

The starting dose will be 25 mg for patients with a systolic blood pressure of 120 - 130 mmHg at randomization and 50 mg for patients with a systolic blood pressure of > 140 mmHg.

Patients randomized to the control group will receive standard treatment. There will be no placebo intervention. If blood pressure medication is warranted according to existing guidelines a non-ACEi or ARB medication should be chosen.

The randomization will be performed using an online randomization system, in a 1:1 ratio, with a pre-generated random sequence in blocks of random size from 2 to 6.

Intervention Type

Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Losartan

Primary outcome(s)
Time to first occurrence of a composite endpoint (admission to intensive care unit, or death), within 28 days of randomization

Key secondary outcome(s))
Measured using case report form:
1. All-cause mortality at day 28 from randomization
2. Occurrence of ICU admission during hospital stay
3. Need for and duration of invasive mechanical ventilation
4. Peak level and area under the curve during hospitalization for National Early Warning score 2 (NEWS2) score
5. Peak level and area under the curve during hospitalization for CRP score

Completion date
31/01/2022

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria
1. Positive PCR laboratory test for SARS-CoV-2
2. Age > 18 years
3. Admitted for in-hospital care no more than 48 hours earlier
4. GCS ≥ 14

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
302

Key exclusion criteria
1. Admitted to ICU prior to randomization.
2. Current treatment with blood pressure lowering agent, affecting the RAAS system (i.e. Angiotensin Converting Enzyme inhibitor (ACEi), Angiotensin Receptor Blocker (ARB), Aldosteron antagonist or Renin inhibitor)
3. Patients with heart condition eg. heart failure with reduced ejection fraction, EF < 40%, who has an evidence based indication for ACE inhibitors or Angiotensin receptor blockers
4. Prior serious adverse reaction to an ARB or ACEi
5. Systolic blood pressure below 120 mmHg or symptomatic hypotension. Blood pressure will be taken in supine position after 5 minutes rest with manual or automatic blood pressure manometers
6. Estimated Glomerular Filtration Rate (eGFR) of < 50ml/min/1.73 m^2
7. Potassium > 5 mEq/l
8. Women of childbearing age. Pregnant or breastfeeding. Women that are postmenopausal can be included. Women and childbearing age can be included after a negative pregnancy test
9. Known renal artery stenosis
10. Severe hepatic failure (i.e. ALAT/ASAT > 5x normal upper limit)
11. Volume depletion, chock or new onset of acute kidney injury that, in the opinion of the investigator, would preclude administration of ARB/ACE-inhibitors
12. Any condition or therapy which would make the participant unsuitable for the study, according to the investigators opinion
13. Inability to provide informed consent
14. Moribund or palliative patients deemed unlike to survive hospital stay or who cannot make an informed decision for participations (e.g. non-adults or patients with dementia)

Date of first enrolment
03/08/2020

Date of final enrolment
31/12/2021

Locations

Countries of recruitment
Sweden

Study participating centre
Södersjukhuset
Sjukhusbacken 10
Stockholm
Sweden
11867

Sponsor information

Organisation
Stockholm South General Hospital

ROR
https://ror.org/00ncfk576

Funder(s)

Funder type
Government

Funder Name
Vetenskapsrådet

Alternative Name(s)
Swedish Research Council, VR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Sweden

Results and Publications

Individual participant data (IPD) sharing plan
Data will likely not be made publicly available due to data privacy issues

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet version v5	11/11/2025	11/11/2025	No	Yes
Protocol file		22/06/2020	07/08/2020	No	No