

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

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<b>Registration date</b> 10/07/2020	<b>Overall study status</b> Stopped	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 13/12/2021	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Individual participant data <input type="checkbox"/> 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  
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## Contact information

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Public

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## Additional identifiers

**EudraCT/CTIS number**  
2020-002040-22

**IRAS number**

**ClinicalTrials.gov number**  
Nil known

## Secondary identifying numbers

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](mailto:registrator@etikprovning.se)), ref: 2020-02185

## Study design

Open-label pragmatic phase IV randomized controlled trial

## Primary study design

Interventional

## Secondary study design

Randomised controlled trial

## Study setting(s)

Hospital

## Study type(s)

Treatment

## Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

## 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 measure**

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

### **Secondary outcome measures**

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

### **Overall study start date**

21/04/2020

### **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  $\geq$  14

### **Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

750

**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), Aldosterone 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<sup>2</sup>
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, shock 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 unlikely 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

**Sponsor details**

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**Sponsor type**

Hospital/treatment centre

**Website**

<https://www.sodersjukhuset.se/>

**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

**Publication and dissemination plan**

Planned publication in peer-reviewed journal.

**Intention to publish date**

01/05/2022

**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?
<a href="#">Protocol file</a>	version v5	22/06/2020	07/08/2020	No	No