**Dept. of Intensive Care**



**The COVID STEROID 2 trial is approved by the relevant authorities in the participating countries**

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# Questions? Contact:

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**Higher vs. Lower Doses of Dexamethasone in Patients with COVID-19 and Severe Hypoxia:**

**the COVID STEROID 2 trial**

Information to clinical staff

Your department participates in

**the** **COVID STEROID 2 trial**

**The COVID STEROID 2 trial compares higher vs. lower doses of dexamethasone for patients with COVID-19 and severe hypoxia**

**The COVID STEROID 2 trial will include 1,000 patients from hospitals in Denmark, Sweden, Switzerland and India**

**General information**

# Background

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may cause severe airway infection (COVID-19) and hypoxic respiratory failure.

Low-dose dexamethasone improves survival in hospitalised patients with COVID-19. Higher doses of corticosteroids may be beneficial in acute respiratory distress syndrome (ARDS) caused by bacteria because they reduce the duration of mechanical ventilation and potentially also mortality. It is unclear if higher doses of dexamethasone are also beneficial in patients with severe COVID-19; on the other hand, higher doses of dexamethasone may cause serious adverse events. At present, it is unclear what dose of dexamethasone is most beneficial in patients with COVID-19 and severe hypoxia, and clinical equipoise exists.

# Methods

1,000 patients with COVID-19 and severe hypoxia will be randomised to:

**dexamethasone 12 mg**

**OR**

**dexamethasone 6 mg**

The trial intervention will be given once daily for up to 10 days as bolus injection in addition to standard care, i.e. days with use of steroids for COVID-19 prior to enrolment will be subtracted so that no patients will get steroids for more than 10 consecutive days.

If the patient is readmitted or transferred to another COVID STEROID 2 site, the trial medication will continue for a maximum of 10 days from randomisation. If the participant is transferred to a non-trial site, the intervention will be stopped.

We recommend against co-administration of open-label corticosteroids and other anti-inflammatory agents after randomisation.

All other co-interventions are given at the discretion of the clinicians.

**The full protocol can be accessed at**

[www.cric.nu/covid-steroid-2/](http://www.cric.nu/covid-steroid-2/)

# Outcomes

* Days alive without life support at day 28 and 90 after randomisation (the primary outcome)
* Mortality at day 28, 90 and 180 after randomisation
* Serious adverse reactions at day 28
* Days alive and out of hospital at day 90 after randomisation
* Health-related quality of life (HRQoL) at day 180 after randomisation

**Financial affairs**

The trial budget is 7.000.000 DKK. The trial is primarily funded by the Novo Nordic Foundation and Rigshospitalet.

# Ethics

The trial is approved by the relevant Committee on Health Research Ethics. We will obtain informed consent according to the local regulations.

**Eligibility**

Please note any patient fulfilling the inclusion criteria:

* ≥ 18 years **AND**
* Confirmed SARS-CoV-2 **AND**
* One of the following:
* Invasive mechanical ventilation **OR**
* Non-invasive ventilation or continuous use of CPAP for hypoxia **OR**
* Oxygen supplementation with an oxygen flow ≥10 L/min irrespective of system used

Please advise the local COVID STEROID 2 team, if you have a patient who fulfill all 3 inclusion criteria.

As the clinical staff must be blinded to the allocation, the trial allocation and medication is performed by unblinded staff not involved in the care of the patient.

**Serious adverse events/reactions**

Please note any serious adverse event in patients enrolled in the COVID STEROID 2 trial and report these to the local COVID STEROID 2 investigator.

We kindly ask you to pay special attention to the occurrence of the following serious adverse reactions:

* New episodes of septic shock
* Invasive fungal infections
* Clinically important gastrointestinal bleeding requiring ≥ 2 units of RBCs
* Anaphylaxis

Please contact the coordinating investigator Marie Warrer Petersen without undue delay, if you suspect a suspected unexpected adverse reaction (SUSAR) to the trial medication (tel. +4535457237 or covid-steroid@cric.nu). Please also contact this number in case of need for emergency unblinding.

**Trial medications**

# The trial medication is prepared once daily by unblinded staff not involved in the care of these patients and is given once daily as bolus injection for up to 10 days. The intervention period ranges from 6-10 days and depends on the number of days with corticosteroid use before randomisation. All patients who have received 5 consecutive days of steroids before randomisation will be excluded from the trial.

# The interventions look identical and are both given in a volume of 5 ml to maintain blinding. We have adjusted the dose according to the generic of dexamethasone used (e.g. dexamethasone phosphate). Please remember to document in the patient files (paper or electronic) that the trial medication has been administered on each day.

**Instructions or questions?**

All trial-related documents can be found at our webpage [www.cric.nu/covid-steroid-2](http://www.cric.nu/covid-steroid-2).

If you have questions for the trial, you may also contact the coordinating investigator Marie Warrer Petersen via the phone number or e-mail presented below.

**COVID STEROID hotline**

**+45 3545 7237**

**Available 24/7**

**or**

**covid-steroid@cric.nu**