Pre-emptive tocilizumab in hypoxic COVID-19 patients, a prospective randomized trial

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON20031

Source
NTR

Brief title
PreToVid

Health condition

COVID-19 with Hypoxia

Sponsors and support

Primary sponsor: UMCG, Roche
Source(s) of monetary or material Support: UMCG

Intervention

Outcome measures

Primary outcome

30-day mortality (from randomization)

Secondary outcome

- To asses in a randomized comparison days in hospital (calculated from randomisation).
- To asses in a randomized comparison the percentage of patients who need ICU care.
- To asses in a randomized comparison the percentage of patients who develop respiratory failure and need mechanical ventilation.
- To asses in a randomized comparison the days on a ventilator.
- To asses in a randomized comparison normalisation of HRCT after resolution of disease.
- To asses in a randomized comparison seroconversion 14 days after randomisation
- To identify potential biomarkers predictive of response (blood: cytokines (including Il-6 and IL-18), lymphopenia, CRP, ferritin, LDH, sCD25; nasal epithelial brushes: epithelial transcriptome immune response by bulk and single-cell RNA seq; faeces: microbiome, viral load), gender, age, co-morbidity and plasma levels tocilizumab by exploratory analysis.
- To assess safety and feasibility of pre-emptive use of tocilizumab (AE grade ≥4).
- To assess in a randomized comparison OS after 3 months (after randomization).

Study description

Background summary

This trial aims to develop an effective treatment strategy for COVID-19 patients with hypoxia OR other signs of hyperinflammation (ferritin >2000 µg/L or doubling of serum ferritin in 20-48 hours). The rationale for tocilizumab is: 1) Patients with respiratory failure caused by COVID-19 have a dismal prognosis; 2) The hyper inflammatory state in COVID-19 patients is a main reason for respiratory insufficiency and dead; 3) Tocilizumab is an effective drug to control cytokine storms without hampering the functional immune response; 4) Extensive experience is present with tocilizumab in the clinical setting with cytokine release syndromes (e.g. after CAR-T cell therapy).
The rationale to apply tocilizumab in the pre-emptive phase i.e. at the moment of hypoxia (defined according to cytokine release syndrome (CRS) grade II), or other signs of hyperinflammation (ferritin >2000 µg/L or doubling of serum ferritin in 20-48 hours), is to modulate the cytokine storm at an early phase before the phase of respiratory failure is reached. This is in line with the early application of tocilizumab in the clinical setting to modulate cytokine storms after CAR-T cell therapy.

Study objective

Based on literature we assume a 20% day 30 mortality of patients admitted to the hospital ward with COVID-19. We aim to lower this day 30 mortality to 10%.

Study design

at entry, prior to first infusion, and 24h, 72h, 1 week, 2 weeks, 3 months after first infusion

Intervention

Patients in this study are treated with intravenous tociluzumab: 8 mg/kg (maximum dose 800 mg), which can be repeated at the same dose after 8 hours if the hypoxia has not improved. This is the approved dose for cytokine release syndrome.

Contacts

Public
UMCG
Margriet Dijkstra

+31 50 3610468
Scientific
UMCG
Margriet Dijkstra

+31 50 3610468

Eligibility criteria

Inclusion criteria

♦ Patients 18 years and older
♦ Patients with a diagnosis of COVID-19 based on a compatible clinical presentation AND a positive SARS-CoV-2 PCR on a respiratory sample such as a nasopharyngeal swab, sputum, or BAL fluid
♦ Clinical features compatible with hyperinflammation:
- Hypoxia, without other explanation for hypoxia than COVID-19 OR
- ferritin >2000 µg/L or doubling of serum ferritin in 20-48 hours
Hypoxia is defined according to ASTCT CRS Consensus grading: grade II. [Lee DW, et al. BBMT 2019;25(4):625-638] Inclusion of patients already requiring oxygen administration prior to COVID-19 should be discussed with the study team.
♦ Written informed consent.
♦ Patient is capable of giving informed consent.

Exclusion criteria

♦ Pregnancy
♦ allergy to tocilizumab

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-04-2020
Enrollment:	354
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	03-04-2020
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL8504
Other	METc UMCG : METc 2020/172

Study results