Biomarker-based Early Anti-inflammatory Therapy for severe COVID-19

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON23631

Source
Nationaal Trial Register

Brief title
BEAT-COVID1

Health condition

coronavirus; COVID-19

Sponsors and support

Primary sponsor: Prof. Dr. L.G. Visser
Source(s) of monetary or material Support: LUMC

Intervention

Outcome measures

Primary outcome

Biomarker profiles or signature which correlate with future clinical progression of patients infected with SARS-CoV-2 to multi-organ failure and acute severe lung injury requiring mechanical ventilation.

Secondary outcome

The kinetics of:
- Circulating soluble serum biomarkers of innate, adaptive and inflammatory immune responses, in order to decipher and validate biomarker signatures of disease severity and risk of acute disease progression.
- Circulating cellular immune responses, focusing on the distribution of various immune subsets (granulocytes, lymphocytes, monocytic and innate populations) and the innate responses to bacterial or viral motifs (LPS, CpG and PolyIC) and polyclonal and/or specific adaptive immune responses (PHA and SARS-CoV-2).
- Circulating cellular immune responses, focusing on the distribution and quantitation of >250 leukocyte subsets, including 20-25 different innate myeloid cells (granulocyte, monocyte, and dendritic cell subsets, etc.), >85 CD4 T-cell subsets, >45 CD8-NK cell subsets, and >115 B-cell & plasma cell subsets.
Special attention will be given to the B-cell system, particularly to minor clonal subsets and the kinetics of expanded plasma cell subsets, down to levels of 0.1 cell per µL.
- Nasal and lung (using cells from lung aspirates) cellular immune responses, focusing on the distribution of various immune subsets (granulocytes, lymphocytes, monocytic and innate populations) and their activation status based on surface markers by mass cytometry (>40 marker panel). Nasal metabolomics.
- Antibody glycosylation: Total IgG Fc glycosylation and SARS-CoV-19 specific IgG Fc glycosylation profiles (Fc glycosylation as general biomarker of immune activation, SARS-CoV-19 specific IgG Fc glycosylation as co-marker for development of immunity, see parameter “SARS-CoV2 specific serology
- Serum glycan profile, anti-glycan IgG/IgM profiles
- RNA expression profiles in whole blood to allow for pathway analysis and characterize different inflammatory responses. Particularly sepsis response phenotypes (e.g. glucosteroid receptor signaling pathway, T cell exhaustion) for the ICU patients.
- Viral load, focusing on measured cycle-threshold (Ct) value kinetics in consecutive (naso)pharynx swabs from SARS-CoV2 qPCR-positive individuals
- SARS-CoV2 whole genome sequencing (subset of patients)
- SARS-CoV2 specific serology, focusing on seroconversion and relative increase of SARS-CoV2-antigen specific seroreactivity, and neutralizing capacity
- Glycocalyx destruction and heparanase activity, functional glycocalyx assays
- Coagulation activation parameters
- Complement activation parameters
- Obesity-related pro(anti)-inflammatory markers
- Biomarker analysis by upconverting phosphor lateral flow assay (UCP-LFA)

Study description

Background summary

Rationale:
The clinical risk factors that predispose to the development of acute severe lung injury in COVID-19 are higher age, obesity, diabetes mellitus and a medical history of heart or lung

disease [1]. Besides these known factors, the underlying mechanisms that lead to increased inflammation that appears to be the mechanism of acute severe lung disease and multi-organ failure, remain largely unknown. The inflammatory cytokine IL-6 is increased in patients, and several clinical trials have now been registered which plan to investigate the effect of the anti-IL-6 monoclonal antibody tocilizumab, as an inhibitor of inflammation in COVID-19.
According to the observations of the Chinese patients in Wuhan and other epicentres of the pandemic, and confirmed by our own observations, progression towards severe lung injury and multi-organ failure occurs around one week after onset of symptoms. Beside the known risk factors that somewhat help clinicians predict which patients are vulnerable, in this study, pro-inflammatory biomarker profiles, including IL-6, will be used to stratify these patients in a more substantiated manner. The specific biomarker profiles which are associated with the development of acute severe lung disease, can be targeted in new and patient specific treatments for COVID-19, to prevent further deterioration.

Objectives:
- Identifying the pro-inflammatory biomarker profile in the pathophysiology of acute sever lung disease in SARS-CoV-2 infection, and using this profile to identify the patients who are at risk of developing acute severe lung disease and multi-organ failure.
- Identifying cellular immune biomarkers that predict higher chance to develop acute severe lung disease in SARS-CoV-2 infection, both at admission and during monitoring.

Study design:
Prospective Observational Cohort Study

Study population:
Patients with PCR confirmed COVID-19 admitted to the hospital, who are 18 years or older

Main study parameters/endpoints:
The main endpoint is the identification of pro-inflammatory biomarkers and cellular immune biomarkers in the development of acute severe lung injury and multi-organ failure in infection with SARS-CoV-2

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:
The burden of this study for the participants is related to extra blood samples and nasal swabs. Therefore, the risk is negligible and the burden minimal. The study is group related as we only plan to investigate the population with COVID-19 admitted to the hospital.

Study objective

N/A

Study design

During hospital admission: every Monday, Wednesday and Friday and 6 weeks after hospital stay.

Intervention

N/A

Contacts

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Eligibility criteria

Inclusion criteria

- Hospitalized patient with PCR confirmed COVID-19 infection
- Eighteen years or older

Exclusion criteria

- Not able to give consent by representative of the subject

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial

Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-04-2020
Enrollment:	250
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Plan description
N/A

Ethics review

Positive opinion

Date:	07-05-2020
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	NL8589

Register	ID
Other	METC Leiden-Den Haag-Delft : METC LDD P20.046

Study results

Summary results
N/A