COvid-19 vaccination and Biomarkers in cirrhosis And post-Liver Transplantation

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The primary objective of this observational study is:- to determine if patients with Chronic Liver Disease (CLD) mount comparable humoral immune responses to healthy controls at 8-months following SARS-CoV-2 vaccination.Secondary objectives of this...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatic and hepatobiliary disorders
Study type	Observational invasive

Summary

ID

NL-OMON51899

Source
ToetsingOnline

Brief title
COBALT

Condition

- Hepatic and hepatobiliary disorders
- Viral infectious disorders

Synonym
Coronavirus infection, Covid-19

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Cirrhosis, Covid-19, Liver Transplantation, Vaccination

Outcome measures

Primary outcome

To determine if patients with CLD mount comparable humoral immune responses to healthy controls at 8-months following SARS-CoV-2 vaccination.

Secondary outcome

- if there are differences in humoral immune response between subgroups with cirrhosis, autoimmune CLD or post-LT,

- the minimum effective level of humoral immunity in cirrhosis, autoimmune CLD or post-LT to provide protection against Covid-19,

- if there are adverse effects or toxicity from vaccination in the context of underlying cirrhosis, autoimmune CLD or post-LT,

- the degree of humoral response to booster doses of Covid-19 vaccination, if these are administered as part of routine clinical car

Study description

Background summary

The Covid-19 pandemic is the largest public health challenge in living memory. The illness due to Covid-19 has a variable presentation, ranging from asymptomatic to severe pneumonia with multiorgan failure. The efficacy of vaccinations for Covid-19 in patients with chronic liver disease (CLD) or post-liver transplantation (LT) is one of the most urgent public health questions in hepatology. Patients with chronic liver disease (CLD), including cirrhosis, have dysregulated innate and adaptive immunity, and therefore may be at higher risk of complications from Covid-19 or Covid-19 vaccination. Sub-optimal immune responses to vaccines are common in cirrhosis and post-LT, and thus additional protective strategies may be necessary for our patients.

Determination of the relative efficacy and toxicity of vaccines for Covid-19 in CLD and post-LT is an urgent, unmet clinical need.

Study objective

The primary objective of this observational study is:
- to determine if patients with Chronic Liver Disease (CLD) mount comparable humoral immune responses to healthy controls at 8-months following SARS-CoV-2 vaccination.

Secondary objectives of this observational study are to determine:
- if there are differences in humoral immune response between subgroups with cirrhosis, autoimmune CLD or post-LT,
- the minimum effective level of humoral immunity in cirrhosis, autoimmune CLD or post-LT to provide protection against Covid-19,
- if there are adverse effects or toxicity from vaccination in the context of underlying cirrhosis, autoimmune CLD or post-LT,
- the degree of humoral response to booster doses of Covid-19 vaccination, if these are administered as part of routine clinical care.

Study design

COBALT is a pan-European, large-scale, prospective observational cohort study in approximately 100 liver centres across Europe, sampling ~5,000 patients with cirrhosis, autoimmune CLD or post-LT for cirrhosis. Additionally, 500 healthy participants will be recruited.

-Biological sampling: The primary endpoint will be determined by sampling at 30 weeks (±6 weeks) following final vaccination dose (for either one-dose or two-dose regimens). For secondary endpoints, further optional sampling time points will be at baseline (within 4 weeks prior to initial vaccination dose), and at 7 weeks (±3 weeks) following final vaccination dose. Additionally, if patients undergo a booster Covid-19 vaccination dose, a further optional sampling point will be at 7 weeks (±4 weeks) following this booster dose.
-Data for secondary endpoints will be collected up to 12 months following inclusion, for all seven subgroups. Specific episodes to be collected are: diagnosis of Covid-19 (PCR positive), hospitalisation due to Covid-19, liver-related hospitalisation, liver-related mortality, all-cause hospitalisation, all-cause mortality and incident liver transplantation for patients with CLD.

Study burden and risks

All participants of the study will receive standard of care. The burden and risks associated with participation is very limited (1 physical examination and a maximum of 4 vena punctures-30 minutes in total), negligible risks,

resitricted to those associated with a peripheral venapuncture.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

i) Participant able to give written informed consent
ii) Diagnosis of:
a. Cirrhosis (on imaging or liver biopsy), or,
b. Autoimmune liver disease (PSC, PBC or AIH) without cirrhosis, or
c. Post-LT for cirrhosis >6 months, or
d. Healthy participant (absence of severe and uncontrolled cardiac, respiratory, liver,
renal or endocrine disease in opinion of PI or sub-I, see appendix 1).

iii) Age >18 years

Exclusion criteria

i) History of Covid-19 (PCR-positive episode)
ii) Participant unable to give written informed consent
iii) Uncontrolled HIV infection

Study design

Design

Study phase:	4
Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-07-2021
Enrollment:	120
Type:	Actual

Ethics review

Approved WMO

Date:	16-07-2021
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	19-04-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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
CCMO	NL77782.058.21