Cross-sectional study on peripheral and intrahepatic immune cells derived from chronic hepatitis B patients not on treatment

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The focus of the research is a cross-sectional comparison between the samples of fine needle liver aspirates of patients at different chronic HBV infection phases with the aim to identify correlates between intrahepatic immune changes at the...

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

Summary

ID

NL-OMON50279

Source
ToetsingOnline

Brief title
HBV-FNAB study

Condition

- Hepatic and hepatobiliary disorders
- Viral infectious disorders

Synonym
chronic hepatitis B

Research involving
Human

Sponsors and support

Primary sponsor: Stichting Leveronderzoek
Source(s) of monetary or material Support: Janssen-Cilag,Stichting Leveronderzoek

Intervention

Keyword: - chronic HBV infection phases, - fine needle liver aspirate biopsy, - intrahepatic immune change

Outcome measures

Primary outcome

Per visit max.175 ml of peripheral blood and fine needle aspirate biopsies

(FNAB) will be collected. Multiple assessments are scheduled for the same time

point: vital signs, physical examination, blood collection for safety,

biochemical and serological parameters, blood collection for PBMC isolation,

blood collection for serum and whole blood parameters and liver FNABs. Cells

from blood and liver will be evaluated for their phenotype by flow cytometry,

and for their gene expression by RNA sequencing.

Secondary outcome

not applicable

Study description

Background summary

Globally 360 million people are chronically infected with hepatitis B virus (HBV). In these patients the immune system is incapable of clearing the virus. The levels of HBV DNA, ALT and hepatitis B envelope antigen (HBeAg) vary greatly between patients, and may fluctuate in the same patient. The long-term consequences of chronic HBV infection can be severe, since patients are at increased risk for developing liver fibrosis, cirrhosis and/or hepatocellular carcinoma. To better describe the disease state of the patient and to guide treatment strategies, a clinical distinction into four phases was made based on

variations in serum HBV DNA, ALT and HBeAg levels. These four clinical HBV phases are known as the immune tolerant (IT), immune active (IA), inactive carrier (IC) and HBeAg-negative hepatitis (ENEG) phase. The molecular events characterizing each phase and determining the transition between clinical phases are still poorly understood.
The goal of this study is to understand the mechanism of immune control in chronic HBV infection through detailed analysis of intrahepatic and peripheral immune cell populations comparing the settings of immune control in the different phases. Comparisons will be made between IT and IC, both of which have minimal or no hepatic inflammation but very different levels of HBV replication. Also comparison with IA and ENEG patients will be done, recognizing that inflammation may confound results.

Study objective

The focus of the research is a cross-sectional comparison between the samples of fine needle liver aspirates of patients at different chronic HBV infection phases with the aim to identify correlates between intrahepatic immune changes at the cellular or molecular level and viral control.

Study design

Cross-sectional, prospective multi-center study in about 125 CHB patients at 3 sites (Erasmus MC Rotterdam, University Hospital Toronto and Massachusetts General Hospital).

Study burden and risks

Patients enrolled in this study will not directly benefit from this study as this is an exploratory study to identify correlates between intrahepatic immune changes at the cellular or molecular level and viral control.
Per patient 1 or 2 FNABs will be collected. This is a minimally invasive technique to obtain safe and repeated liver samples. The procedure is well tolerated by patients and has been performed for many years by our team without any complications related to the procedure. Moreover, it can be performed on any patient without anaesthesia or other preparations. Furthermore, blood collections will be performed for each patient at each visit. Three is the maximal number of blood collections in this study and blood collection does not pose an extra risk for the patient.

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

- man or woman, age of ><=18 and <<= 70 years
- chronic Hepatitis B (HBsAg positive for minimum 6 months)
- no evidence of cirrhosis
- HBV Genotype A, B, C, D or E
- otherwise healthy and medically stable
- written informed consent
- not on treatment for CHB
- disease stage specific ALT, HBeAg and HBV DNA (according to protocol)

Exclusion criteria

- positive HIV test
- hepatitis A, C, D or E co-infection
- decompensated cirrhosis or hepatocellular carcinoma (documented medical history)
- participation in another translational research study or clinical study
- use of any investigational drug or use of an invasive investigational medical

device within 90 days before screening
- any condition for which, in the opinion of the investigator, participation would not be in the best interest of the subject
- major surgery (e.g. requiring general anaesthesia) within 12 weeks before screening
- history of drug or alcohol abuse within 1 year before screening

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-03-2019
Enrollment:	45
Type:	Actual

Ethics review

Approved WMO

Date:	28-07-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	30-07-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	02-05-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-08-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-03-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-01-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL61959.078.17