Characterization of immune responses in Hepatitis B patients experiencing a flare after stopping nucleot(s)ide analogue therapy

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To characterize the immune response and gene expression profiles in blood of chronic HBV patients who present with a flare after treatment with antiviral therapy in order to be able to predict spontaneous resolution of flares in the future.

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

Summary

ID

NL-OMON50840

Source
ToetsingOnline

Brief title
HBV flare

Condition

- Hepatic and hepatobiliary disorders
- Viral infectious disorders

Synonym
cHBV, Chronic hepatitis B

Research involving
Human

Sponsors and support

Primary sponsor: Stichting Leveronderzoek
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: flare, HBV, immune responses

Outcome measures

Primary outcome

Determine the percentages of (NK cells, B cells, T cells, monocytes and MAIT cells) of the total lymphocyte population and the expression levels of the relevant activation and inhibitory markers as well as assessing their function and gene expression profile.

Secondary outcome

Not applicable.

Study description

Background summary

Long-term antiviral treatment for chronic hepatitis B with entecavir or tenofovir is effective but also associated with mounting costs and potential side effects. Discontinuation of treatment in patients who have undergone long-term viral suppression appears to be safe and has been associated with sustained response rates of 30 - 50% in several small series of patients treated with older agents. The spectrum of outcomes after nucleos(t)ide analogue cessation, ranging from functional cure to severe liver inflammation, links intimately to the immune system. Relapse occurs frequently off treatment and may lead to clinically significant flares. This risk should be as low as possible, and preferably also predictable and thus preventable. In other words, the ability to identify which patients should not stop or being able to predict an imminent relapse to re-initiate retreatment is of utmost importance. Immunologic biomarkers that discriminate between antiviral responses and pathologic inflammation after stopping therapy could facilitate clinical decisions, limit adverse outcomes, and identify mechanisms leading to

functional cure. However, specific mechanisms driving viral control and inflammation in the human liver have not been completely defined. Evaluating these mechanisms of intrahepatic immune responses in chronic hepatitis B patients experiencing a flare after stopping nucleot(s)ide analogue therapy requires longitudinal investigation of blood samples. This study will aim to characterize immune and virological parameters and gene expression profiles in blood of chronic HBV patients who present with a flare after stopping antiviral treatment in order to be able to predict spontaneous resolution of flares.

Study objective

To characterize the immune response and gene expression profiles in blood of chronic HBV patients who present with a flare after treatment with antiviral therapy in order to be able to predict spontaneous resolution of flares in the future.

Study design

Single centre prospective cohort study. Chronic hepatitis B patients who experience a flare after stopping nucleos(t)ide analogue therapy will undergo peripheral blood collections every 2-4 weeks for a maximum period of 6 months in order to characterize the intrahepatic immune response and gene expression profile.

Study burden and risks

Patients enrolled in this study and will not directly benefit from this study. During the course of the study peripheral blood collections will be performed every 2-4 weeks for each patient. Blood collections do 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)

Inclusion criteria

• Age between 18 and 65.
• Previously diagnosed with chronic HBV.
• Treated with entecavir or tenofovir.
• Flare defined as ALT>=2x upper limit of normal.
• Written informed consent.

Exclusion criteria

• Hepatic imaging (ultrasound, CT or MRI) with evidence of hepatocellular carcinoma.
• Females who are pregnant or breast-feeding.
• History or other evidence of severe illness, malignancy or any other condition which would make the patient, in the opinion of the investigators, unsuitable for the study.
• Received prolonged therapy with immunomodulatory agents (e.g. corticosteroids) or biologics (e.g. monoclonal antibody, interferon) within 6 months of screening.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2021
Enrollment:	50
Type:	Anticipated

Ethics review

Approved WMO

Date:	04-10-2021
Application type:	First submission
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	NL77987.078.21