Longitudinal Characterization of Intrahepatic Immune Responses and Gene Expression Profiles in Patients with Viral Hepatitis. An investigator initiated single centre study.

Published: 26-01-2017
Last updated: 11-04-2024

To characterize the phenotype, function and gene expression profiles of immune cells and hepatocytes in blood and liver of patients with viral hepatitis before, during and after treatment with antivirals.

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

Summary

ID

NL-OMON45711

Source
ToetsingOnline

Brief title
Longitudinal characterization of viral hepatitis patients.

Condition

- Hepatic and hepatobiliary disorders
- Viral infectious disorders

Synonym
chronic hepatitis B. chronic hepatitis C

Research involving
Human

Sponsors and support

Primary sponsor: Stichting Leveronderzoek
Source(s) of monetary or material Support: Stichting Leveronderzoek

Intervention

Keyword: antiviral therapy, gene expression profiling, immune response, viral hepatitis

Outcome measures

Primary outcome

To evaluate the functionality of immune cells in the liver and blood in chronic

HCV and chronic HBV patients before, and during or after treatment with

antiviral treatment, as well as their gene expression profiles.

Secondary outcome

not applicable

Study description

Background summary

Viral hepatitis, caused by the hepatitis B virus (HBV) or the hepatitis C virus (HCV), affects approximately 350 million people worldwide, resulting in a significant disease burden worldwide. Chronic hepatitis B and C infection are responsible for the majority of cases of fibrosis/cirrhosis and hepatocellular carcinoma. The treatment for both chronic HBV and HCV has improved greatly. The standard of care for chronic HBV patients eligible for treatment is currently either entecavir or tenofovir (both nucleos(t)ide analogues), which are tolerated extremely well, but have to be taken life-long. Also, the development of direct acting antiviral drugs (DAA) to treat HCV is a major improvement, and have entered clinical practice in the last 2 years. DAA have a favorable tolerability profile, high barrier to resistance and a short treatment duration using an all oral regimen4.
For both chronic HBV as for chronic HCV, there is limited information on putative restoration of the impaired peripheral and intrahepatic immune system during or after successful treatment with antivirals. This is important for the evaluation of strategies to further improve therapy in patients with viral breakthroughs for HCV, but also to better understand the processes of

regression of fibrosis as has been observed to occur upon elimination of HBV or HCV. In addition, a better understanding of the immune status of chronic HBV patients on therapy may provide important information that may help in decision-making on the design and selection of novel antivirals that are in the pipeline and that are aimed at complete eradication of HBV from infected hepatocytes, instead of suppression of viral replication as is currently achieved by tenofovir and entecavir. The aim of this study is to perform longitudinal sampling of chronically infected patients who are being treated for HBV or HCV to describe the intrahepatic effects on both the immunological and transcriptomic level.

Study objective

To characterize the phenotype, function and gene expression profiles of immune cells and hepatocytes in blood and liver of patients with viral hepatitis before, during and after treatment with antivirals.

Study design

Investigator-initiated prospective single centre study

Intervention

Per time point max. 50 ml of peripheral blood and fine needle aspirate biopsies will be collected.

Study burden and risks

Patients enrolled in this study will be treated for their chronic hepatitis C or B and will not directly benefit from this study. Per patient 3 fine-needle aspiration biopsies 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, 3 blood collections will be performed for each patient. Blood collections do not pose an extra risk for the patient.

Contacts

Public
Stichting Leveronderzoek

's Gravendijkwal 230

Rotterdam 3015 CE
NL
Scientific
Stichting Leveronderzoek

's Gravendijkwal 230
Rotterdam 3015 CE
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Diagnosed with chronic HCV or chronic HBV
* Hepatitis C viral RNA detectable in case of chronic HCV infection or HBsAg positive for over 6 months in case of chronic HBV infection.
* Non-cirrhotic compensated liver disease.
* Age * 18 years and * 70 years.
* Written informed consent.

Exclusion criteria

* Extensive bridging fibrosis indicated by histology (gold standard), imaging, transient elastography or clinical decompensated cirrhosis (Child-Pugh Grade B or C).
* 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):	02-01-2017
Enrollment:	50
Type:	Anticipated

Ethics review

Approved WMO

Date:	26-01-2017
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	NL60125.078.16