

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

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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.

<b>Ethical review</b>	Approved WMO
<b>Status</b>	Pending
<b>Health condition type</b>	Hepatic and hepatobiliary disorders
<b>Study type</b>	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 regimen<sup>4</sup>.

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**

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's Gravendijkwal 230

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## 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