Impact of Immune Responses in Chronic Hepatitis C Genotype 1 Virus Infected Patients during Treatment with Peg-Interferon-alpha-2b and Ribavirin.

Published: 12-09-2006
Last updated: 20-05-2024

Primary aimTo evaluate the effects of peginterferon and ribavirin therapy on the immune response in chronic HCV genotype 1 patients before, during and after treatment.Secondary aims1. To determine if differential modulation of Treg activity or DC...

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

Summary

ID

NL-OMON30088

Source
ToetsingOnline

Brief title
CIRES = hCv Immune RESponses

Condition

- Hepatic and hepatobiliary disorders
- Immune disorders NEC
- Viral infectious disorders

Synonym
HCV, hepatitis C

Research involving
Human

Sponsors and support

Primary sponsor: Foundation for Liver Research (SLO)
Source(s) of monetary or material Support: Foundation for Liver Research (SLO)

Intervention

Keyword: Hepatitis C, Immunology, Treatment

Outcome measures

Primary outcome

Outcome measurements

Peripheral blood

-Frequency, phenotype and function of HCV specific T cells.

-Frequency, phenotype and function of Treg and DCs.

-Determination of immunoregulatory cytokines in blood (Elispot or ELISA).

Intrahepatic

-Frequency, phenotype and function of intrahepatic Treg.

-Determination of immuneregulatory cytokines in the liver (Elispot or ELISA).

Secondary outcome

No extra secundary outcome variables

Study description

Background summary

Background
Treatment of chronic hepatitis C (HCV) has shown a remarkable success. However, genotype 1 patients have reduced response rates (1-4). A better understanding

and improvement of these results can now be considered the greatest challenge.

In chronically infected patients, HCV-specific T-cell responses are generally weak, narrowly focused, and often dysfunctional. The presence of HCV-specific regulatory CD4+ T-lymphocytes (Treg) that are able to suppress the activity of HCV-specific CD4+ helper and CD8+ cytotoxic T cells (5, 6) and dysfunction of DC (dendritic cells) are possible mechanisms responsible for this impaired immune response.

Another recent study by our group (9) showed an increased expression of FoxP3 in the liver of HCV-positive liver transplantation recipients as compared to non-HCV recipients. FoxP3 is a key transcription factor expressed in Treg. Furthermore, we found that the expression of the immunosuppressive cytokine IL-10, was enhanced in the liver but not in peripheral blood of HCV-positive patients. These results indicate increased Treg frequency and immunoregulatory activity, locally in the liver, as a result of HCV re-infection. Hence, these Data highlight the importance of monitoring intrahepatic immune responses in addition to peripheral immune responses. Using the minimally-invasive technique of fine-needle aspiration biopsy (FNAB), it is now possible to obtain safe and frequent liver samples to monitor local antiviral immune responses in chronic HCV patients during antiviral therapy (10)

Rationale of the study
Our previous studies and current literature support the concept that Treg may contribute to HCV persistence by suppressing HCV-spec immune responses. The current study is designed to examine if peginterferon and ribavirin therapy affects the activity of Treg and DC, and if this results in enhanced HCV-specific immune responses.

Study objective

Primary aim
To evaluate the effects of peginterferon and ribavirin therapy on the immune response in chronic HCV genotype 1 patients before, during and after treatment.

Secondary aims
1. To determine if differential modulation of Treg activity or DC function during treatment may contribute to response to treatment of chronic HCV patients.
2. To determine if, and to what extent, HCV-specific immune responses in blood reflect the intrahepatic immune response.

Study design

Design (type of trial)
Monocenter, translational open label study with one arm of 20 patients.

Study burden and risks

Possible risks and discomforts

Since extra blood is drawn at the same time as the collection blood for regular bloodtesting, there is no additive risk involved in the retrieval of extra blood.
Normally, a venapunture can give the patient the sensation of minor pain and cause a small swelling, bruise and/or infection. Furthermore, a FNAB can also give the patient the sensation of minor pain and cause a small swelling, bruise and/or infection. Other burdens or risks have not occured in our clinic, nor have they been described in the international literature.

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

-Male and female patients between 18-70 years of age, with evidence of a chronic hepatitis C Genotype 1 infection.
-No previous treatment with, peginterferon or conventional interferon plus ribavirin combination therapy.
-Indication for antiviral therapy of hepatitis C according to current clinical guidelines.
-Written informed consent.

Exclusion criteria

•History or other evidence of severe illness, malignancy or any other condition which would make the patient, in the opinion of the investigator, unsuitable for the study.
•Presence of contra-indications for antiviral therapy with interferon or antiviral therapy.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-02-2007
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	12-09-2006
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	NL13410.078.06