Effect of Telaprevir in triple therapy for chronic hepatitis C patients on Intrahepatic immunological Mechanisms

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To evaluate in detail the functionality of immune cells in the liver and blood in chronic HCV patients before, during and after treatment with telaprevir, pegylated-IFN-alfa and ribavirin.

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

Summary

ID

NL-OMON39260

Source
ToetsingOnline

Brief title
ETIM

Condition

- Hepatic and hepatobiliary disorders
- Viral infectious disorders

Synonym
Hepatitis C

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Hepatitis C, Immunology, Intrahepatic, Telaprevir

Outcome measures

Primary outcome

Difference in immunological parameters between patients with a high and a low viral load. (indirect to compare the patients who respond to the therapy and patients who stay infected)

Secondary outcome

Not applicable

Study description

Background summary

Chronic hepatitis C infection (HCV) is a disease that affects worldwide about 170 million people. The current standard of care therapy of chronic HCV patients consists of pegylated-IFN-α combined with ribavirin, and results in sustained clearance of HCV-RNA in only about 50% of the HCV genotype 1 infected patients. Telaprevir, a NS3A-4A inhibitor, has previously proven to offer therapeutic options to previous non-responders to the standard of care. Although, not all chronic HCV patients benefit from telaprevir and it is still not known why certain patients are also non-responsive to this triple therapy. In this study we try to understand why certain patients are also non-responsive to telaprevir, how triple therapy modulates the responsiveness to IFN-α and what the immunological consequences are of treatment with telaprevir, either directly or as a result of telaprevir-induced reduction of HCV-RNA levels.

Study objective

To evaluate in detail the functionality of immune cells in the liver and blood in chronic HCV patients before, during and after treatment with telaprevir, pegylated-IFN-alfa and ribavirin.

Study design

In this study, 25 chronic hepatitis C patients will be treated with telaprevir,

peginterferon-alfa and ribavirin in triple therapy. During this therapy, extra blood and fine needle aspiration biopsies (FNAB) will be taken.

Study burden and risks

For each patient, extra blood and four fine-needle aspiration biopsies (FNAB) will be collected for the assessment of intrahepatic immune responses and analyzed by either micro-array or flowcytometry.

Using this 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. The procedure is well tolerated by patients. A large series, in which thousands of FNABs were evaluated, describes an excellent safety profile with little discomfort reported by the patients. Furthermore, in our clinic, we are experienced with the collection of over hundreds of FNABs without any serious complications to the patient. Results from laboratory tests on these FNABs have been published in several papers. Finally, the FNAB can be performed on any patient without anaesthesia or other preparations.

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

• Patients between 18 and 70 years of age, with a chronic hepatitis C - genotype 1 infection.
• Patients are naive, non-responders or relapsers to previous treatment with peginterferon or conventional interferon plus ribavirin combination therapy.
• High viral load (>400,000 IU/ml)
• Indication for antiviral therapy of hepatitis C according to current clinical guidelines.
• Written informed consent.

Exclusion criteria

• Signs of progressive liver disease, beyond generally accepted criteria for HCV antiviral therapy
• 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
• Co-infections with human immunodeficiency virus (HIV) or Hepatitis B virus (HBV).
• Presence of contra-indications for antiviral therapy with telaprevir, peginterferon or ribavirin.
• Interfering substance abuse, such as alcohol (indicator: 28 drinks/ week).
• Earlier treatment with a protease/polymerase inhibitor or treatment with peginterferon/ ribavirin within 6 months before start of therapy
•Any other condition which in the opinion of the investigator would make the patient unsuitable for enrollment, or could interfere with the patient participating and completing in the study.

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):	31-05-2012
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Incivo
Generic name:	Telaprevir
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	23-12-2011
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	13-04-2012
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	19-10-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	02-11-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	04-04-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-04-2013
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
EudraCT	EUCTR2011-005636-26-NL
CCMO	NL38193.078.12