LOWERING VIRAL LOAD WITH NUCLEOS(T)IDE ANALOGUES PRIOR TO PEGINTERFERON ALFA-2B TREATMENT TO INCREASE SUSTAINED RESPONSE IN HBEAG-POSITIVE CHRONIC HEPATITIS B (PEGON-STUDY)

Published: 16-12-2011
Last updated: 30-04-2024

To investigate sustained HBeAg response to peg-interferon alfa-2b in chronic HBeAg-positive hepatitis Bpatients who are pretreated with nucleos(t)ide analogues, thereby lowering viral load

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

Summary

ID

NL-OMON37588

Source
ToetsingOnline

Brief title
Peginterferon Add-on study in Chronich hepatitis B patients

Condition

- Hepatic and hepatobiliary disorders
- Viral infectious disorders

Synonym
chronic hepatitis B virus infection

Research involving
Human

Sponsors and support

Primary sponsor: Stichting Leveronderzoek
Source(s) of monetary or material Support: Merck Sharp & Dohme (MSD),Stichting Lever Onderzoek (SLO)

Intervention

Keyword: chronic hepatitis B, nucleos(t)ide analogues, peginterferon alfa-2b, sustained response

Outcome measures

Primary outcome

Sustained response defined as HBV DNA level < 200 IU/ml and HBeAg

seroconversion at week 96

Secondary outcome

• Undetectable HBV-DNA (<20 IU/ml)

• HBsAg loss from serum

• HBsAg decline

• HBeAg loss from serum

• Combined response defined as the combined presence of HBV DNA

level < 200 IU/mL and HBeAg seroconversion at week 72

Study description

Background summary

The introduction of nucleos(t)ide analogues heralded a new era in the treatment of chronic hepatitis B, and
provided a safe, effective, and well-tolerated alternative for interferon.
Although treatment with nucleos(t)

ide analogues profoundly suppresses serum HBV DNA levels and response can be maintained over
prolonged periods with ongoing therapy, response to treatment may not be durable in a large proportion
of patients after discontinuation of therapy, indicating the necessity of long-term, and maybe indefinite,
treatment. In contrast, antiviral potency of peginterferon (PEG-IFN) is inferior to nucleoside analogues,
but response to PEG-IFN probably is more durable in the majority of patients due to its
immunomodulatory effects. However, sustained response can only be achieved in about 30% of PEG-IFN
treated patients.
HBV specific T cell responses are ususally weak or absent in chronic HBV patients. Treatment with a
nucleoside analogue and subsequent viral decline has shown to restore immune responsiveness in chronic
HBV infected patients. Add-on treatment with PEG-IFN can be expected to further stimulate adaptive
immune reactivity and may therefore result in higher rates of response.

Study objective

To investigate sustained HBeAg response to peg-interferon alfa-2b in chronic HBeAg-positive hepatitis B
patients who are pretreated with nucleos(t)ide analogues, thereby lowering viral load

Study design

Multicenter randomized open-label study with two treatment arms

Intervention

Addition of peginterferon alfa-2b therapy for 48 weeks in chronic hepatitis B patients treated with nucleos
(t)ide analogues

Study burden and risks

Patients will be treated with peginterferon alfa-2b, an antiviral agent with many side effects. As a
consequence, blood will be drawn more frequently (every 4 weeks during peginterferon treatment vs.
every twelve weeks during nucleos(t)ide analogue monotherapy) to monitor for side effects during

peginterferon treatment. Normally, a venapuncture can give the patient a sensation of minor pain and
cause a small swelling, bruise, and/or infection.

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

• Chronic hepatitis B (HBsAg positive > 6 months);
• HBeAg positive, anti-HBe negative within 4 weeks prior to initiation of peginterferon alfa-2b;
• HBV DNA < 2000 IU/ml within one month prior to initiation of peginterferon alfa-2b after a minimum of 12 months nucleos(t)ide analogue treatment, except Telbivudine;
• Compensated liver disease;
• Age >= 18 years and <= 70 years;
• Written informed consent;

Exclusion criteria

•Treatment with any investigational drug within 30 days of entry to this protocol;
•Treatment with Telbivudine;
•Severe hepatitis activity as documented by ALT >5 x ULN;
•History of decompensated cirrhosis (defined as jaundice in the presence of cirrhosis, ascites, bleeding gastric or esophageal varices or encephalopathy);
•Pre-existent neutropenia (neutrophils <1,500/mm3) or thrombocytopenia (platelets <90,000/mm3);
•Co-infection with hepatitis C virus or human immunodeficiency virus (HIV);
•Other acquired or inherited causes of liver disease: alcoholic liver disease, obesity induced liver disease, drug related liver disease, auto-immune hepatitis, hemochromatosis, Wilson*s disease or alpha-1 antitrypsin deficiency;
•Alpha fetoprotein > 50 ng/ml;
•Hyper- or hypothyroidism (subjects requiring medication to maintain TSH levels in the normal range are eligible if all other inclusion/exclusion criteria are met);
•Immune suppressive treatment within the previous 6 months;
•Contra-indications for alfa-interferon therapy like suspected hypersensitivity to interferon or Peginterferon or any known pre-existing medical condition that could interfere with the patient's participation in and completion of the study;
•Pregnancy, breast-feeding;
•Other significant medical illness that might interfere with this study: significant pulmonary dysfunction in the previous 6 months, malignancy other than skin basocellular carcinoma in previous 5 years, immunodeficiency syndromes (e.g. HIV positivity, auto-immune diseases, organ transplants other than cornea and hair transplant);
•Any medical condition requiring, or likely to require chronic systemic administration of steroids, during the course of the study;
•Substance abuse, such as alcohol (>80 g/day), I.V. drugs and inhaled drugs in the past 2 years;
•Any other condition which in the opinion of the investigator would make the patient unsuitable for enrollment, or could interfere with the patient participating in and completing the study;

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-06-2012
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	PegIntron
Generic name:	peginterferon alfa-2b
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	16-12-2011
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-02-2012
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-12-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-12-2012
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	EUCTR2011-005607-32-NL
CCMO	NL39035.078.11