A Multi-center, Randomized, Open-label study for Induction of HBsAg decline using an add-on treatment of peginterferon alfa-2a in HBeAg-negative chronic hepatitis B patients treated with nucleos(t)ide analogues

Published: 03-11-2011
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To investigate whether addition of PEG-IFN alfa-2a in HBeAg-negative chronic hepatitis B patients who are pretreated with NA enhances the degree of HBsAg decline

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

Summary

ID

NL-OMON45209

Source
ToetsingOnline

Brief title
Addition of PEG-IFN to NA therapy in HBeAg-negative 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: Hoffmann-La Roche,stichting Leveronderzoek

Intervention

Keyword: HBeAg negative chronic hepatitis B, HBsAg decline, nucleoside analogues, peginterferon alfa-2a

Outcome measures

Primary outcome

Primary outcome

• HBsAg decline > 1 log from baseline at week 48

Secondary outcome

Secondary outcomes

• HBsAg decline > 1 log at weeks 24 and 72

• HBsAg decline > 0.5 log at weeks 24 and 48

• HBsAg loss at weeks 48 and 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 whether addition of PEG-IFN alfa-2a in HBeAg-negative chronic hepatitis B patients who are pretreated with NA enhances the degree of HBsAg decline

Study design

Multicenter, international, randomized, open-label study with two treatment arms

Patients will be randomized in a 2:1 ratio to start add-on treatment with PEG-IFN alfa-2a or continue NA monotherapy

Intervention

Addition of peginterferon alfa-2a for 48 weeks in chronich hepatitis B patients treated with nucleos(t)ide analogues.

Study burden and risks

Patients will be treated with peginterferon alfa-2a, 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 > six months)
• HBeAg negative within six months prior to initiation of peginterferon alfa-2a
• (Peg)interferon naïve or experienced patients may both participate
• Treatment with nucleos(t)ide analogues for at least 1 year at screening
• HBV DNA < 200 IU/ml during nucleos(t)ide analogue treatment (except Telbivudine) within one month prior to initiation of peginterferon alfa-2a
• Compensated liver disease
• Age > 18 years
• Adequate contraception
• Written informed consent

Exclusion criteria

• Treatment with any investigational drug within 30 days of entry to this protocol
• Current treatment with Telbivudine
• Severe hepatitis activity as documented by ALT>10 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, hepatitis D 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. Current methadone usage is allowed.
• 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 phase:	4
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):	10-04-2012
Enrollment:	50
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Pegasys
Generic name:	peginterferon alfa-2a
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	03-11-2011
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	17-02-2012
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	25-10-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	29-01-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	11-02-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-07-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-04-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-05-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-12-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-01-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-04-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-04-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	16-03-2017
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	EUCTR2011-002010-37-NL
ClinicalTrials.gov	NCT01373684
CCMO	NL36655.078.11