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Response and markers of response in chronic hepatitis B patients treated with peg-interferon alfa-2a and adefovir

Submission date	Recruitment status	[_] Prospectively registered
15/09/2006	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
15/09/2006	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
29/09/2021	Infections and Infestations	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
MEC 05/148

Study information

Scientific Title

Response and markers of response in chronic hepatitis B patients treated with peg-interferon alfa-2a and adefovir

Study objectives
There are predictive markers of treatment response (or non-response) at baseline or during early beginning of treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the local medical ethics committee

Study design
Non-randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chronic Hepatitis B Virus (HBV)

Interventions
During pre-screening and at the end of treatment at 48 weeks each patient will undergo a liver biopsy.

All patients will receive PEGASYS® 180 microgram, administered subcutaneously once per week for 48 weeks and stopped thereafter. The dose of Adefovir (ADF) and dipivoxil (HEPSERA®) will be 10 mg daily for 48 weeks and stopped thereafter.

During treatment the patient has to visit the outpatient clinic 22 times for check up, to draw blood and collect urine. The latter were taken for analysis.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Peg-interferon alfa-2a, adefovir

Primary outcome(s)
To establish the rate of response (HBV-DNA levels less than 100,000 cop/mL [17,000 IU/mL]) at end of follow-up and to determine if markers at base line and early during treatment can predict response.

Key secondary outcome(s))
1. To establish rate of response at levels HBV-DNA less than 10,000 cop/mL (1,700 IU/mL), less than 400 cop/mL (72 IU/mL) and at limit of detection (less than 300 cop/mL [54 IU/mL]) at end of follow-up.
2. To establish predictive markers for response of primary and secondary end points.
3. To establish the rate of HBeAg seroconversion at end of follow-up in HBeAg positive patients only.

Completion date
01/10/2008

Eligibility

Key inclusion criteria
1. Male and female patients over 18 years of age
2. Positive Hepatitis B surface Antigens (HBsAg) for more than six months
3. a. for Hepatitis B 'e' Antigen (HBeAg) positive patients: HBeAg positive, anti-HBe negative and Hepatitis B Virus Deoxyribonucleic Acid (HBV DNA) more than 100,000 cop/mL (more than 17,000 IU/mL) as measured by Polymerase Chain Reaction (PCR)
b. for HBeAg negative patients: HBeAg negative for more than six months, and anti-HBeAg positive, HBV DNA (more than 100,000 cop/mL [more than 17,000 IU/mL]) as measured by PCR
4. Patients with Chronic Hepatitis B (CHB) who are either naïve to HBV treatment, or have received and have not responded/relapsed to either conventional Interferon (IFN) or Lamivudine (LAM) in the past
5. If the patient has used LAM, the patient must have been on LAM for a period of at least six months
6. Elevated serum Alanine Aminotransferase (ALAT) more than Upper Limit of Normal (ULN) but less than or equal to 10 x ULN as determined by two abnormal values taken more than 14 days apart during the six months before the first dose of study drug with at least one of the determinations obtained during the screening period
7. A liver biopsy obtained at a maximum of one year prior to study enrollment, demonstrating liver disease consistent with chronic hepatitis B and/or more than fibrosis stage 2 (Ishak classification). Patients with cirrhosis or marked fibrosis on liver biopsy must also have a liver imaging study to rule out hepatic carcinoma.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
92

Key exclusion criteria
1. Patients co-infected with Hepatitis C Virus (HCV), Hepatitis D Virus (HDV), Human Immunodeficiency Virus (HIV) or who have decompensated liver disease, hepato-cellular carcinoma, pre-existing severe depression or other psychiatric disease, significant cardiac disease, significant renal disease, seizure disorders or severe retinopathy will be excluded
2. Patients who have received LAM therapy for their chronic hepatitis B within six weeks before enrolment or any other antiviral therapy for their chronic hepatitis B within six months before enrolment (e.g. IFN)
3. Patients must not have received any other systemic anti-viral, anti-neoplastic or immuno-modulatory treatment (including supraphysiologic doses of steroids or radiation)
4. Positive test at screening for anti-Hepatitis A Virus Immunoglobulin M (HAV IgM), anti-HIV, anti-HCV, HCV Ribonucleic Acid (RNA) or anti-HDV
5. Patients who are expected to need systemic antiviral therapy other than that provided by the study at any time during their participation in the study are also excluded.
Exception: patients who have had a limited (less than or equal to seven day) course of acyclovir for herpetic lesions more than one month prior to the first administration of test drug are not excluded
6. Evidence of decompensated liver disease (Child B-C)
7. Serum total bilirubin more than twice the upper limit of normal at screening
8. History or other evidence of bleeding from esophageal varices or other conditions consistent with decompensated liver disease
9. History or other evidence of a medical condition associated with chronic liver disease other than HBV (e.g., hemochromatosis, autoimmune hepatitis, metabolic liver diseases including Wilsons disease and alfa1-antitrypsin deficiency, alcoholic liver disease, toxin exposures, thalassemia)
10. Women with ongoing pregnancy or who are breast feeding
11. Neutrophil count less than 1500 cells/mm^3 or platelet count less than 90,000 cells/mm^3 at screening
12. Hemoglobin less than 7.1 mmol/L (less than 11.5 g/dL) for females and less than 7.8 mmol/L (less than 12.5 g/dL) for men at screening
13. Serum creatinine level more than 1.5 times the ULN at screening
14. History of severe psychiatric disease, especially depression. Severe psychiatric disease is defined as major depression or psychosis, a period of treatment with an antidepressant medication or major tranquiliser at therapeutic doses for depression or psychosis for at least three months, a suicidal attempt, hospitalisation for psychiatric disease, or a period of disability due to a psychiatric disease
15. History of immunologically mediated disease (e.g., inflammatory bowel disease, idiopathic thrombocytopenic purpura, lupus erythematosus, autoimmune hemolytic anemia, scleroderma, severe psoriasis, rheumatoid arthritis)
16. History or other evidence of chronic pulmonary disease associated with functional limitation. Severe cardiac disease (e.g., New York Heart Association [NYHA] Functional Class III or IV, myocardial infarction within six months, ventricular tachyarrhythmias requiring ongoing treatment, unstable angina or other significant cardiovascular diseases)
17. History of a severe seizure disorder or current anticonvulsant use
18. Evidence of an active or suspected cancer or a history of malignancy where the risk of recurrence is more than or equal to 20% within two years. Patients with a lesion suspicious of hepatic malignancy on a screening imaging study will only be eligible if the likelihood of carcinoma is less than or equal to 10% following an appropriate evaluation

19. History of having received any systemic anti-neoplastic (including radiation) or immunomodulatory treatment (including systemic corticosteroids) more than or equal to six months prior to the first dose of study drug or the expectation that such treatment will be needed at any time during the study
20. Major organ transplantation
21. Thyroid disease with thyroid function poorly controlled on prescribed medications. Patients with elevated thyroid stimulating hormone or T4 concentrations, with elevation of antibodies to thyroid peroxidase and any clinical manifestations of thyroid disease are excluded
22. History or other evidence of severe retinopathy (e.g. CytoMegaloVirus [CMV] retinitis, macula degeneration) or clinically relevant ophthalmological disorder due to diabetes mellitus or hypertension
23. Inability or unwillingness to provide informed consent or abide by the requirements of the study
24. History or other evidence of severe illness or any other conditions which would make the patient, in the opinion of the investigator, unsuitable for the study
25. Patients with a value of alfa-fetoprotein more than 100 ng/mL are excluded, unless stability (less than 10% increase) has been documented over at least the previous three months
26. Evidence of current hard drug(s) and/or alcohol abuse (20 g/day for women and 30 g/day for men)
27. Patients included in another trial or having been given investigational drugs within 12 weeks prior to screening

Date of first enrolment
01/10/2005

Date of final enrolment
01/10/2008

Locations

Countries of recruitment
Netherlands

Study participating centre
Academic Medical Center (AMC)
Amsterdam
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1100 DD

Sponsor information

Organisation
Academic Medical Center (AMC) (The Netherlands)

ROR
https://ror.org/03t4gr691

Funder(s)

Funder type
Industry

Funder Name
UCB (International)

Funder Name
Roche Nederland BV (The Netherlands)

Funder Name
Giliad Sciences (International)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/10/2011		Yes	No
Results article	results	01/12/2017		Yes	No
Results article	results	25/09/2021	29/09/2021	Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes