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

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

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON24114

Bron
Nationaal Trial Register

Verkorte titel
N/A

Aandoening

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

Ondersteuning

Primaire sponsor: Roche Pahrmaceuticals
Giliad UCB
Overige ondersteuning: Roche Pharmaceuticals
Giliad UCB

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

To establish the rate of response (HBV-DNA levels < 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.

Toelichting onderzoek

Achtergrond van het onderzoek

Treatment of chronic hepatitis B is still suboptimal. Only 30- 40 percent of the patients treated with pegineteferon alfa or in combination with lamivudine wil reach a sustained viral response.

The goal of this study will be to establish the rate of response and to determine if markers can predict response. All patients will receive Peginterferon alfa 180 micrograms once per week and Adefovir Dipivoxil 10 mg daily for 48 weeks. Follow-up will be continued untill 72 weeks.

Doel van het onderzoek

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

Onderzoeksproduct en/of interventie

During prescreening and at the end of treatment at 48 weeks each patient will undergo a liverbiopsy.

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

During treatment the patient has to visit the outpatientclinic 22 times for check up, to draw blood and collect urine. These latter for analysis.

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Male and female patients > 18 years of age;

2. Positive HBsAg for more than 6 months;

3. a) For HBeAg positive patients: HBeAg positive, anti-HBe negative and HBV DNA > 100,000 cop/mL (> 17,000 IU/mL) as measured by PCR.

b)For HBeAg negative patients: HBeAg negative for more than 6 months, and anti-HBeAg positive, HBV DNA (>100,000 cop/mL (> 17,000 IU/mL)) as measured by PCR;

4. Patients with 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 6 months;

6. Elevated serum ALAT > ULN but □ 10X ULN as determined by two abnormal values taken >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 > 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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Patients co-infected with HCV, HDV, 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 6 weeks before enrollment or any other antiviral therapy for their chronic hepatitis B within 6 months before enrollment (e.g. INF);

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-HAV IgM, anti-HIV, anti-HCV, HCV 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 (□7 day) course of acyclovir for herpetic lesions more than 1 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 > 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 Wilson’s disease and alfa1-antitrypsin deficiency, alcoholic liver disease, toxin exposures, thalassemia);

10. Women with ongoing pregnancy or who are breast feeding;

11. Neutrophil count <1500 cells/mm3 or platelet count <90,000 cells/mm3 at screening;

12. Hemoglobin < 7.1 mmol/L (< 11.5 g/dL) for females and < 7.8 mmol/L (< 12.5 g/dL) for men at screening;

13. Serum creatinine level >1.5 times the upper limit of normal 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 tranquilizer at therapeutic doses for depression or psychosis for at least 3 months, a suicidal attempt, hospitalization 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., NYHA Functional Class III or IV, myocardial infarction within 6 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 □20% within 2 years. Patients with a lesion suspicious of hepatic malignancy on a screening imaging study will only be eligible if the likelihood of carcinoma is □10% following an appropriate evaluation;

19. History of having received any systemic anti-neoplastic (including radiation) or immunomodulatory treatment (including systemic corticosteroids) □6 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. 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 >100 ng/mL are excluded, unless stability (less than 10% increase) has been documented over at least the previous 3 months;

26. Evidence of current hard drug(s) and/or alcohol abuse (20g/day for women and 30g/day for men);

27. Patients included in another trial or having been given investigational drugs within 12 weeks prior to screening.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Anders
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-10-2005
Aantal proefpersonen:	100
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	02-11-2005
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL468
NTR-old	NTR509
Ander register	: MEC 05/148
ISRCTN	ISRCTN77073364

Resultaten

Samenvatting resultaten
N/A