ISRCTN79659320 https://doi.org/10.1186/ISRCTN79659320

Efficacy and safety of peginterferon alpha-2a (40KD) (PEGASYS®) or adefovir dipivoxil in positive chronic hepatitis B patients

Submission date 10/11/2009	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 07/12/2009	**Overall study status** Completed	
Last Edited 27/10/2022	**Condition category** Digestive System	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof Jinlin Hou

Contact details
Nanfang Hospital
Guangzhou
China
510515

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
NCT00962533

Secondary identifying numbers
ML18376

Study information

Scientific Title
A randomised open label study evaluating the efficacy and safety of peginterferon alpha-2a (40KD) (PEGASYS®) or adefovir dipivoxil in patients with lamivudine-resistant HBeAg positive chronic hepatitis B

Study objectives
To compare the efficacy and safety of peginterferon alpha-2a with adefovir dipivoxil in patients with lamivudine-resistant HBeAg positive chronic hepatitis B.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Prospective randomised open-label study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Chronic hepatitis B

Interventions
Eligible patients were randomised to treatment with one of the following:
1. Peginterferon alpha-2a 180 µg subcutaneously (sc) once weekly for 48 weeks, in combination with continued lamivudine 100 mg orally (po) daily for the first 12 weeks
2. Adefovir dipivoxil 10 mg daily for 72 weeks, in combination with continued lamivudine 100 mg po daily for the first 12 weeks

At the end of treatment, patients were followed up for an additional 24 weeks.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Peginterferon alpha-2a (PEGASYS®), adefovir dipivoxil

Primary outcome measure
Rate of HBeAg seroconversion rate defined as loss of HBeAg and presence of anti-HBe antibodies at Week 72.

Secondary outcome measures
1. Loss of HBeAg at weeks 48 and 72
2. HBV DNA reduction (HBV DNA less than 100,000 copies/mL) at weeks 48 and 72
3. HBV DNA at least 1 log reduction from baseline at weeks 48 and 72
4. HBV DNA undetectable (less than 400 copies/mL by Cobas Amplicor HBV Monitor) at weeks 48 and 72
5. ALT normalisation at weeks 48 and 72
6. HBsAg seroconversion (loss of HBsAg and presence of anti-HBs antibodies) at weeks 48 and 72
7. Quantitative changes from baseline in HBeAg and HBsAg
8. The proportion of patients with YMDD mutant HBV DNA (INNO-LiPA)
9. Frequency and severity of on-treatment adverse events and changes from baseline in vital signs and laboratory parameters

Overall study start date
01/10/2005

Completion date
01/06/2008

Eligibility

Key inclusion criteria
1. Male and female patients aged greater than or equal to 18 years and less than or equal to 65 years
2. Hepatitis B surface antigen (HBsAg) positive, hepatitis B 'e' antigen (HBeAg) positive for at least 6 months, and anti-HBs negative
3. Treatment with lamivudine for at least 6 months and ongoing
4. Laboratory or clinical signs of lamivudine resistance (for example hepatitis B virus deoxyribonucleic acid [HBV DNA] rebound greater than 100,000 copies/mL and/or alanine aminotransferase [ALT] flares)
5. Lamivudine resistant in terms of YMDD mutant HBV detection (INNO-LiPA method)
6. ALT greater than upper limit of normal (ULN) but less than or equal to 10 x ULN, on at least two occasions taken greater than or equal to 14 days apart in the previous 6 months. At least one test should be performed after signing the consent form.
7. Negative urine or serum pregnancy test (for women of childbearing potential) documented within the 24-hour period prior to the first dose of test drug. Additionally, all females must be using reliable contraception during the study and for 3 months after treatment completion.
8. No evidence of cirrhosis as confirmed by liver biopsy taken in the previous 6 months

Participant type(s)

Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
A total of 231 patients

Key exclusion criteria
1. Patients who had previously received treatment with adefovir dipivoxil or other drugs with activity against HBV within the prior 6 months, except for lamivudine
2. Antiviral, anti-neoplastic or immuno-modulatory treatment (including supraphysiologic doses of steroids and radiation) 6 months prior to the first dose of randomised treatment (except for less than or equal to 7 days of acyclovir for herpetic lesions more than 1 month prior to first administration of randomised treatment). Patients who are expected to need systemic antiviral therapy other than that provided by the study at any time during their participation are also excluded.
3. Women with ongoing pregnancy or breast feeding
4. Co-infection with active hepatitis A, hepatitis C, hepatitis D and/or human immunodeficiency virus (HIV)
5. Evidence of decompensated liver disease (Child-Pugh score greater than 5). Child-Pugh greater than 5 means, if one of the following five conditions are met, the patient has to be excluded:
5.1. Serum albumin less than 35 g/L
5.2. Prothrombin time greater than or equal to 4 seconds prolonged
5.3. Serum bilirubin greater than 34 µmol/L
5.4. History of encephalopathy
5.5. History of variceal bleeding
5.6. Ascites
6. History or other evidence of a medical condition associated with chronic liver disease other than viral hepatitis (e.g., haemochromatosis, autoimmune hepatitis, metabolic liver disease, alcoholic liver disease, toxin exposures, thalassaemia)
7. Signs or symptoms of hepatocellular carcinoma. Patients with a value of alpha-fetoprotein greater than 100 ng/mL are excluded, unless stability (less than 10% increase) has been documented over at least the previous 3 months. Patients with values greater than 20 ng/mL but less than or equal to 100 ng/mL may be enrolled, if hepatic neoplasia has been excluded by liver imaging
8. Neutrophil count less than 1500 cells/mm^3 or platelet count less than 90,000 cells/mm^3 at screening
9. Haemoglobin less than 11.5 g/dL for females and less than 12.5 g/dL for men at screening
10. Serum creatinine level greater than 1.5 x ULN at screening
11. Phosphorus less than 0.65 mmol/L
12. History of severe psychiatric disease, especially depression. Severe psychiatric disease is defined as treatment with an antidepressant medication or a major tranquiliser at therapeutic doses for major depression or psychosis, respectively, for at least 3 months at any previous time

or any history of the following: a suicide attempt, hospitalisation for psychiatric disease, or a period of disability due to a psychiatric disease.
13. History of a severe seizure disorder or current anticonvulsant use
14. History of immunologically mediated disease (e.g. inflammatory bowel disease, idiopathic thrombocytopenic purpura, lupus erythematosus, autoimmune haemolytic anaemia, scleroderma, psoriasis, rheumatoid arthritis etc.)
15. History of chronic pulmonary disease associated with functional limitation
16. History of severe cardiac disease (e.g. New York Heart Association [NYHA] Functional Class III or IV, myocardial infarction within 6 months, ventricular tachyarrhythmias requiring ongoing treatment, unstable angina or other significant cardiovascular diseases)
17. Major organ transplantation or other evidence of severe illness, malignancy, or any other conditions which would make the patient, in the opinion of the investigator, unsuitable for the study
18. History of thyroid disease poorly controlled on prescribed medications, elevated thyroid stimulating hormone (TSH) concentrations with elevation of antibodies to thyroid peroxidase and any clinical manifestations of thyroid disease
19. Evidence of severe retinopathy or clinically relevant ophthalmologic disorder (e.g. due to hypertension or diabetes mellitus cytomegalovirus [CMV] retinitis, macula degeneration)
20. Patients consuming alcohol in excess of 20 g/day for women and 30 g/day for men in the 6 months preceding enrolment
21. Evidence of drug abuse or treatment with methadone within one year of study entry
22. Patients included in another trial or having been given investigational drugs within 12 weeks prior to screening
23. Inability or unwillingness to provide informed consent or abide by the requirements of the study

Date of first enrolment
01/10/2005

Date of final enrolment
01/06/2008

Locations

Countries of recruitment
China

Hong Kong

Study participating centre
Nanfang Hospital
Guangzhou
China
510515

Sponsor information

Organisation
Shanghai Roche Pharmaceuticals Ltd (China)

Sponsor details
1100 Longdong Avenue
Shanghai
China
201203

Sponsor type
Industry

Website
http://www.roche.com.cn

ROR
https://ror.org/02hv5e369

Funder(s)

Funder type
Industry

Funder Name
Shanghai Roche Pharmaceuticals Ltd (China)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan
Not provided at time of registration

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		01/01/2021	27/10/2022	Yes	No