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A phase III, randomised, multicentre, dose escalation, efficacy and safety study examining the effects of treatment with peginterferon alfa-2a with Child's A or B cirrhosis in Chronic Hepatitis C virus infection

Submission date 20/07/2005	**Recruitment status** No longer recruiting	[ ] Prospectively registered [ ] Protocol
Registration date 25/10/2005	**Overall study status** Completed	[ ] Statistical analysis plan [ ] Results
Last Edited 06/02/2014	**Condition category** Digestive System	[ ] Individual participant data [ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof William Rosenberg

Contact details
Professor of Hepatology
Level D MP811
Southampton General Hospital
Southampton
United Kingdom
SO16 6YD
+44 (0)23 80798945

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
RHM MED 0560/ML17066

Study information

Scientific Title

Acronym
PACIFIC

Study objectives
To investigate the incidence of mortality and morbidity amongst patients with cirrhosis (Child-Pugh Grade A and B) due to chronic hepatitis C treated with Pegylated Interferon (PEG-IFN).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Liver cirrhosis in Hepatitis C Virus infections.

Interventions
Intervention: PEG-IFN - 90 mg subcutaneously (sc) once weekly for one month, 135 mg sc once weekly for one month, rising to 180 mg thereafter as tolerated in 1 ml solution administered sc once weekly for a total of 48 weeks.
Control: conventional management.

Intervention Type

Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Peginterferon alfa-2a (PEG-IFN)

Primary outcome measure
1. Combined endpoint of non-detectable serum HCV-RNA (less than 100 copies/ml by the AMPLICORä Polymerase Chain Reaction [PCR] assay) at the end of the 24 week treatment-free follow-up period
2. Death
3. Liver transplantation (or need for)
4. Hepatocellular cancer

Secondary outcome measures
1. End-of-treatment virological and biochemical responses
2. Bleeding varices
3. Ascites
4. Spontaneous bacterial peritonitis and other infections
5. Encephalopathy
6. Quality of life as measured by the SF 36 and Fatigue Severity Scale

Overall study start date
01/04/2004

Completion date
01/04/2007

Eligibility

Key inclusion criteria
To be eligible for this trial, patients must have documentation of the following:
1. Aged over 18 years
2. Serologic evidence of Hepatitis C Virus (HCV) infection by an anti-HCV antibody test
3. Qualitative evidence of infection with HCV Ribonucleic Acid (RNA)
4. Chronic liver disease consistent with chronic hepatitis C infection on a biopsy as judged by a local pathologist
5. Patients must have had an abdominal ultrasound, Computed Tomography (CT) scan, or Magnetic Resonance Imaging (MRI) scan with evidence of cirrhosis, but without evidence of hepatocellular carcinoma (within two months of randomisation) and a serum alphafetoprotein (AFP) less than 100 ng/ml. Patients with elevated AFP should have evidence of no increase of more than 10 KIU/l for three months prior to entry
6. Negative urine pregnancy test (for women of childbearing potential) documented within the 24-hour period prior to the first dose of test drug. Additionally, all fertile male patients, male patients with female partners of childbearing age, and females must be using two reliable forms of effective contraception during the study

Participant type(s)

Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
100 total - 50 treatment arm, 50 conventional management arm

Key exclusion criteria
Patients with any of the following will not be eligible for participation:
1. Patients who are expected to need systemic antiviral therapy at any time during their participation in the study are excluded. Exception: patients who have had a limited (seven day) course of acyclovir or alcyclovir for herpetic lesions more than one month prior to the first administration of test drug are not excluded
2. Positive test at screening for anti-Hepatitis A Virus (anti-HAV) Immunoglobulin M (IgM) antibody (Ab), Hepatitis B surface Antigen (HBsAg), anti-Hepatitis B core (anti-HBc) IgM Ab, or anti-Human Immunodeficiency Virus (anti-HIV) Ab
3. Documented serum concentrations of ceruloplasmin or a1-antitrypsin consistent with an increased risk of metabolic liver disease
4. History or other evidence of a medical condition associated with chronic liver disease (e.g. hemochromatosis, autoimmune hepatitis, alcoholic liver disease, toxin exposures)
5. Women with ongoing pregnancy or breast feeding
6. Decompensated liver disease within the last three months
7. Neutrophil count less than 1500 cells/mm^3, Hgb less than 12 g/dl in women or 13 g/dl in men, or platelet count less than 60,000 cells/mm^3
8. Any patient with a baseline increased risk for anemia (e.g. thalassemia, spherocytosis, history of gastrointestinal [GI] bleeding etc.) or for whom anemia would be medically problematic
9. Serum creatinine level more than 1.5 times the upper limit of normal at screening
10. Patients unlikely to comply with the study schedule due to alcohol and/or drug abuse
11. History of severe psychiatric disease, especially depression. Severe psychiatric disease is defined as treatment with an antidepressant medication or a major tranquilizer at therapeutic doses for major depression or psychosis, respectively, for at least three months at any previous time or any history of the following: a suicidal attempt, hospitalisation for psychiatric disease, or a period of disability due to a psychiatric disease
12. History of immunologically mediated disease (e.g. inflammatory bowel disease, idiopathic thrombocytopenic purpura, lupus erythematosus, autoimmune hemolytic anemia, scleroderma, severe psoriasis, rheumatoid arthritis requiring more than intermittent nonsteroidal anti-inflammatory medications for management etc.)
13. History or other evidence of chronic pulmonary disease associated with functional limitation
14. History of a severe seizure disorder or current anticonvulsant use
15. Evidence of an active or suspected cancer or a history of malignancy where the risk of recurrence is more than 20% within two years. Patients with a lesion suspicious for hepatic malignancy on the screening imaging study will only be eligible if the likelihood of carcinoma is less than 10% following an appropriate evaluation
16. History of having received any systemic anti-neoplastic or immunomodulatory treatment

(including supraphysiologic doses of steroids and radiation) less than 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
17. History of major organ transplantation with an existing functional graft
18. History of thyroid disease poorly controlled on prescribed medications. Patients with elevated thyroid stimulating hormone concentrations with elevation of antibodies to thyroid peroxidase and any clinical manifestations of thyroid disease are excluded
19. History or other evidence of severe retinopathy
20. Inability or unwillingness to provide informed consent or abide by the requirements of the study
21. 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

Date of first enrolment
01/04/2004

Date of final enrolment
01/04/2007

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Professor of Hepatology
Southampton
United Kingdom
SO16 6YD

Sponsor information

Organisation
Southampton University Hospitals NHS Trust (UK)

Sponsor details
Southampton General Hospital
Tremona Road
Southampton
England
United Kingdom
SO16 6YD
+44 (0)23 80777222
wmr@soton.ac.uk

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/0485axj58

Funder(s)

Funder type
Industry

Funder Name
Peginterferon supplied free of charge from Roche Pharmaceuticals.

Funder Name
Investigator-led study, funded from Southampton NHS R&D Levy.

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration