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A pilot study of Combivir® therapy for patients with primary biliary cirrhosis

Submission date 12/09/2003	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 12/09/2003	**Overall study status** Completed	
Last Edited 15/11/2011	**Condition category** Digestive System	

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
N0265092544

Study information

Scientific Title

Study objectives

This study will further test the hypothesis that there is an infectious aetiology involved in the development of primary biliary cirrhosis (PBC) by undertaking a randomised, controlled, phase II pilot study of Combivir® therapy in patients with PBC.

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

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Primary biliary cirrhosis (PBC)

Interventions
This investigation is designed as a randomised, controlled, phase II pilot study of Combivir® in approximately 60 patients with PBC. It is expected that the majority of PBC patients will already be taking ursodeoxycholic acid and patients enrolled in the study will have been on this treatment for at least 6 months.

Patients will be randomised to continue with ursodeoxycholic acid alone or in combination with Combivir®. The clinical, virological, histological and immune effects of the study drug will be examined. The clinical end point of the study will be 1 year of therapy or evidence for developing end stage liver disease. All PBC patients except for those with decompensated liver disease will be enrolled in the study after obtaining an informed written consent.

The PBC patients will already be on ursodeoxycholic acid at an adjusted dose of 13 - 15 mg/kg of body weight/day in 2 - 3 divided doses. Patients treated with Combivir® will receive one tablet twice a day: Lamivudine 150 mg and Zidovudine 300 mg twice a day. Those patients not on ursodeoxycholic acid at the start of the study will be treated with ursodeoxycholic acid at the dose indicated for a period of 6 months prior to randomisation to ursodeoxycholic acid alone or in combination with Combivir® twice a day.

At enrolment, each patient with PBC will be assessed for the inclusion criteria. Prior to therapy, patients will have a thorough history taken to assess symptoms. An objective graded clinical parameter scale will include the development, presence or worsening of pruritus, fatigue, sicca syndrome or right upper quadrant pain. At the same time patients will be examined for the presence or development of overt clinical signs such as jaundice, splenomegaly or hepatomegaly. At this point, the baseline blood tests will include: full blood count (FBC), reticulocyte count, prothrombin time (PT), erythrocyte sedimentation rate (ESR), blood urea nitrogen (BUN), creatinine, sodium, potassium, calcium, phosphate, albumin, total protein, bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline

phosphatase, cholesterol, creatine kinase (CK), amylase, immunoglobulins, antinuclear antibodies (ANA), and quantitated AMA. All of these are laboratory assessments that are clinically useful in following patients with PBC.

Unless problems develop in the interim, patients will be seen at months 1, 3, 6, 9 and 12 after initiation of therapy. At the initial clinic visit, blood will be drawn for BUN, creatinine, electrolytes, amylase, bilirubin, AST, ALT, alkaline phosphatase, albumin, PT, serum lactate and FBC. Subsequently, samples will be drawn for hepatic biochemistry, as well as virological and immunological studies. Patients will undergo a physical exam at each visit and also be questioned about changes in symptoms. Liver biopsies will be performed as clinically indicated.

Response to therapy will be based on changes in symptomatology, development of overt clinical signs, immunological parameters, improvement of liver function and biochemistry. Immunological studies include quantitative AMA levels. Reverse transcription polymerase chain reaction (RT-PCR) and Western blot virological studies will be performed on serum samples before and after therapy in the Hepatitis Research Laboratory, Alton Ochsner Medical Foundation, USA.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Ursodeoxycholic acid, Combivir® (lamivudine and zidovudine)

Primary outcome(s)
Not provided at time of registration

Key secondary outcome(s))
Not provided at time of registration

Completion date
01/05/2005

Eligibility

Key inclusion criteria
Patients will be recruited from the Liver Out-Patients Department at the Queen Elizabeth Hospital:
1. Patients greater than 20 years old of either sex
2. Elevated alkaline phosphatase or alanine aminotransferase (ALT) within 3 months prior to the start of therapy
3. Positive serum anti-mitochondrial antibodies (AMA) (titre greater than 1:20)
4. Liver biopsy histology compatible with PBC

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Adult

Sex
All

Key exclusion criteria
1. Patients treated with immunosuppressive or anti-inflammatory agents
2. Advance liver disease: Child's class B or C
3. Patients with secondary hepatological diagnosis
4. Alcohol abuse (greater than 50 g of alcohol per day)
5. Other significant co-morbidity (e.g. cardiac or renal failure)
6. Pregnancy or breast feeding
7. Sexually active female of child bearing age not using effective contraception

Date of first enrolment
01/10/2001

Date of final enrolment
01/05/2005

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Liver Medicine
Birmingham
United Kingdom
B15 2TH

Sponsor information

Organisation
Department of Health (UK)

Funder(s)

Funder type
Industry

Funder Name
University Hospital Birmingham NHS Trust (UK)

Funder Name
NHS R&D Support Funding

Funder Name
GlaxoSmithKline (GSK) (UK)

Alternative Name(s)
GlaxoSmithKline plc., GSK plc., GlaxoSmithKline plc, GSK

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/12/2004		Yes	No