ISRCTN96199656 https://doi.org/10.1186/ISRCTN96199656

A double blind, placebo controlled study to evaluate the safety and immunogenicity of escalating doses of 10^8 colony forming units (CFU), 10^9 CFU and 10^10 CFU of M04NM11 in patients who have chronic hepatitis B infection

Submission date 02/06/2008	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 26/06/2008	**Overall study status** Completed	
Last Edited 06/05/2016	**Condition category** 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
MS04.03

Study information

Scientific Title
A double blind, placebo controlled study to evaluate the safety and immunogenicity of escalating doses of 10^8 colony forming units (CFU), 10^9 CFU and 10^10 CFU of M04NM11 in patients who have chronic hepatitis B infection

Study objectives
To show that M04NM11 is safe, compared to placebo, when given in escalating doses to patients with chronic hepatitis B virus.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval has been obtained from the following Ethics Committees:
1. Multicentre Research Ethics Committee for Scotland on the 15/11/2006, ref: 06/MRE10/37
2. Clinical Centre Kragujevac Ethics Committee on the 18/01/2007, ref: 01-460/22.01
3. Clinical Centre of Serbia Ethics Committee on the 25/01/2007, ref: 39/10
4. Clinical Centre Novi Sud Ethics Committee on the 31/01/2007, ref: 00-01/13

Study design
Multicentre double-blind randomised dose escalation study

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
Patients will visit the clinic a total of 20 times over the one year treatment period.

M04NM11 or placebo will be administered orally in escalating doses of 10^8 CFU, 10^9 CFU and 10^10 CFU within each patient if well tolerated. Patients will receive up to six doses at 28 day intervals over a five month period, with a six month follow-up period.

During this time, they will be required to provide blood and urine samples for assessment of safety and efficacy. A stool sample will be taken at the end of the trial.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)

M04NM11

Primary outcome(s)
1. The incidence of clinically significant changes in serum biochemistry and haematology tests, particularly elevations of ALT or bilirubin, or prolongation of PT
2. The incidence of adverse events, including flu-like symptoms, attributable to the investigational product
3. The incidence of serious adverse events attributable to the investigational product

The primary outcome measures will be at screening; on days 3, 7, 14 and 28 after the first dose; days 7, 14 and 28 after the second dose and days 14 and 28 after subsequent doses. Following receipt of the final dose, patients will be followed up for a further 20 weeks up to day 308.

Key secondary outcome(s))
1. The proportion of patients in each group who experience a decrease in HBV DNA load of greater than or equal to 2 log10, or a reduction to less than 10 x 4 copies/mL, maintained until day 168 (28 days after the final dose)
2. The proportion of patients in groups 1 and 2 who become HBeAg negative at any study visit before day 168 (28 days after the final dose)
3. The proportion of patients in each group who were negative for anti-HBe at baseline, who have anti-HBe at day 168 (28 days after the final dose), or if patients were anti-HBe positive at baseline the proportion who have a four-fold increase in anti-HBe titre at day 168
4. The proportion of patients in each group with normal ALT levels by day 168
5. The proportion of patients in each group who demonstrate a significant change in the frequency of HBV specific interferon gamma producing T cells determined by enzyme-linked immunosorbent spot (ELISPOT) assay or by intracellular cytokine staining
6. The proportion of patients who maintain a treatment effect in the follow up period as demonstrated by maintenance of the reduction in HBV DNA load achieved during the treatment period, maintenance of HBeAg negative status or conversion to HBeAg negative status between days 196 and 308 (two to six months after the last dose)

Completion date
30/06/2009

Eligibility

Key inclusion criteria
1. Participating patients must be over 18 years of age, either sex
2. Have been hepatitis B surface antigen (HBsAg) positive for at least six months
3. A detailed medical history demonstrating stable alanine aminotransferase (ALT), prothrombin time (PT) and serum bilirubin and a liver biopsy in the previous 24 months
4. Patients will be stratified and recruited according to hepatitis B 'e' antigen (HBeAg) status and viral deoxyribonucleic acid (DNA) load

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Have any hypersensitivity to the investigational medicinal product (IMP)
2. Are hepatitis C virus (HCV) or hepatitis D virus (HDV) positive
3. Are receiving or have received medication for their hepatitis B in the previous 12 months
4. Have evidence of hepatic decompensation, cirrhosis or ALT greater than 5.1 x upper limit of normal (ULN), PT greater than 1.25 x ULN or total bilirubin greater than 1.5 x ULN
5. Immuno-suppression or close contact with immuno-suppressed people

Date of first enrolment
01/12/2006

Date of final enrolment
30/06/2009

Locations

Countries of recruitment
United Kingdom

England

Serbia

Study participating centre
Clinical Research Centre
London
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Sponsor information

Organisation
Emergent Product Development UK Ltd (UK)

ROR
https://ror.org/007nce146

Funder(s)

Funder type
Industry

Funder Name
Emergent Product Development UK Ltd (UK) - commercially funded

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration