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A phase I/II, partially randomised, open-labelled study of visilizumab in patients with severe ulcerative colitis refractory to intravenous corticosteroids

Submission date
08/09/2005

Recruitment status
No longer recruiting

Registration date
20/02/2006

Overall study status
Completed

Last Edited
09/09/2008

Condition category
Digestive System

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

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
291-408

Study information

Scientific Title

Study objectives
To evaluate the safety and tolerability of visilizumab when administered to patients with severe ulcerative colitis (UC) that is refractory to intravenous steroids.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the local Medical Ethics Committee on 15th October 2003 (ref: 03 /220).

Primary study design
Interventional

Study design
Partially randomised, open labelled study, phase I/II

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Ulcerative colitis

Interventions
In stage 1, patients were randomised to receive one of the following doses: 5.0 or 7.5 or 10.0 or 12.5 µg/kg. Due to amendment C (dated 06/05/2005) it was decided that in stage 2 all patients would receive 5.0 µg/kg. Visilizumab was administered intravenously on two consecutive daily doses.

Intervention Type
Drug

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
Visilizumab

Primary outcome(s)
To evaluate the safety of tolerability of visilizumab when administered to patients with severe UC that is refractory to IV steroids.

Key secondary outcome(s)
1. To obtain preliminary evidence of biological activity in this indication. This will be assessed by quantifying the number of patients who experience an improvement in disease symptoms (as indicated by a decrease in scores on Modified Truelove and Witts Severity Index [MTWSI] and a Mayo-Clinic system for assessing UC activities), and to avoid surgical intervention

2. To compare patients with and without detectable whole blood Epstein-Barr Virus (EBV) for the safety profiles of visilizumab
3. To determine the optimal clinical dose (OCD) of visilizumab in the study patient population
4. To determine relationships between pharmacokinetics and pharmacodynamics of visilizumab, laboratory immunologic parameters, clinical response and toxicity
5. To evaluate the safety and tolerability of a second course of treatment with visilizumab when administered to patients who responded to a first course, but subsequently relapsed

Completion date
31/01/2006

Eligibility

Key inclusion criteria
1. 18 to 70 years of age
2. A diagnosis of UC verified by colonoscopy or barium enema performed within 36 months prior to study entry
3. For first time therapy with visilizumab, active disease documented by a Modified Truelove and Witts Severity Index (MTWSI) score of 11 to 21 despite a course of intravenous (IV) steroids that occurred within 60 days prior to study day one and lasted at least five days. Patients who undergo re-treatment with visilizumab must meet the same MTWSI score requirement but need not to have failed IV steroids before re-treatment
4. If patient is a male or female of reproductive potential, he or she must agree to use adequate contraception during the study and for three months after receiving visilizumab
5. For women of childbearing potential, a negative serum pregnancy test at baseline screening
6. Patients must have been tested negative for Clostridium difficile within 10 days prior to treatment with visilizumab
7. Patients who are capable of understanding the purpose and risks of the study and who provide a signed and dated informed consent. For US sites only, patients must also provide an authorisation to use protected health information.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Ulcerative colitis (UC) requiring immediate surgical, endoscopic, or radiologic interventions, including massive haemorrhage, perforation and sepsis, suppurative complications (intra-abdominal or perianal abscesses) or toxic megacolon

2. History of total proctocolectomy, or subtotal colectomy with ileorectal anastomosis
3. Presence of ileostomy
4. White blood cell count less than 2.5 x 10^3/µl, platelet count less than 150 x 10^3µl, or haemoglobin less than 8 g/dl
5. Patients with serious infections, particularly those of viral etiology, e.g. active cytomegalovirus (CMV) colitis. This includes any incidence of opportunistic infections within the past year.
6. Patients who have received a live vaccine within six weeks prior to study entry (patients may not receive a live vaccine during treatment or for six weeks after treatment with visilizumab)
7. Patients with a history of thrombophlebitis or pulmonary embolus
8. Significant organ dysfunction including: cardiac, renal, liver, central nervous system, pulmonary, vascular, gastrointestinal endocrine or metabolic dysfunction (e.g. creatinine greater than 1.6 mg/dl, or alanine aminotransferase (ALT), aspartate aminotransferase (AST) or alkaline phosphatase greater than 1.5 x upper limit of normal) or history of coronary artery disease within six months prior to study entry
9. Patients with a history of lymphoproliferative disorder (LPD) or malignancy other than non-melanoma skin cancer or carcinoma in situ of the cervix that has been adequately treated
10. Pregnant women or nursing mothers
11. Seropositive for infection with human immunodeficiency virus-1 (HIV-1), hepatitis B virus (HBV) surface antigen, or hepatitis C virus (HBC) antibody
12. An Epstein-Barr virus (EBV) deoxyribonucleic acid (DNA) load greater than 5000 copies/ml in stage 1 and greater than 30,000 copies/ml in stage 2
13. Treatment with any investigational drugs or therapies within 60 days prior to study entry
14. Treatment with an antibody therapy within 60 days prior to study entry
15. Treatment with cyclosporine or tacrolimus (FK506) within three months prior to study entry
16. All of the following: a history of seizures, a history of both chronic and current treatment with anticonvulsant medication, and no documentation of therapeutic blood levels of anticonvulsant medication within seven days before study enrolment

Date of first enrolment
01/07/2003

Date of final enrolment
31/01/2006

Locations

Countries of recruitment
Austria

Belgium

Bulgaria

Canada

Germany

Netherlands

United States of America

Study participating centre
Academic Medical Center
Amsterdam
Netherlands
1105AZ

Sponsor information

Organisation
PDL BioPharma Inc. (USA)

ROR
https://ror.org/03ya6pd97

Funder(s)

Funder type
Industry

Funder Name
PDL BioPharma Inc. (USA)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration