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A pilot, open-label, multicentre study to investigate the safety of calf intestine alkaline phosphatase in patients with fulminant active ulcerative colitis refractory to steroid therapy

Submission date
07/06/2006

Recruitment status
No longer recruiting

Registration date
07/06/2006

Overall study status
Completed

Last Edited
07/09/2011

Condition category
Digestive System

[X] 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
N/A

Study information

Scientific Title

Acronym
AP IBD 02-01

Study objectives
Ulcerative colitis (UC) is characterized by abnormal activation of the colon epithelium, which is considered to be a central pathogenic mechanism. Activation of colon epithelium cells in UC is associated with an abnormally high expression of Toll-like receptors (TLR), including TLR-4, the major transducer of lipopolysaccharide (LPS), binding specifically the lipid A portion of LPS. Alkaline phosphatase binds and subsequently dephosphorylates LPS, thereby eliminating the ability of LPS to activate TLR-4. This is expected to:
1. Prevent activation of the intestinal epithelium
2. Prevent systemic inflammatory responses that result from transmigration of endotoxin though the leaky inflamed intestinal mucosa.
Therefore, it is expected that administration of calf intestine alkaline phosphatase (CIAP) may attenuate or prevent the local and systemic inflammatory response in patients with fulminant ulcerative colitis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
A pilot, open-label, non-randomized, multicentre study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Fulminant ulcerative colitis

Interventions
Subjects will receive 30,000 U alkaline phosphatase per 24 hr for 7 consecutive days via a duodenal catheter.

Intervention Type
Other

Phase
Not Specified

Primary outcome(s)
Safety and tolerability

Key secondary outcome(s))
1. Rescue medication including cyclosporin,
experimental medication such as anti-CD-3 antibodies or colectomy rate at 9 weeks (63 days)
2. Clinical response based on change in the MTWSI for disease activity between baseline - day 15 - clinical, endoscopical and serological activity scores at baseline and after 1 week of treatment, including the Modified Truelove and Witts Severity Index, the Mayo score, colon biopsy samples
3. CRP plasma levels and stool markers of disease activity (calprotectin)

Completion date
31/12/2007

Eligibility

Key inclusion criteria
1. Patients between 18 and 70 years (inclusive)
2. A diagnosis of UC verified by colonoscopy and confirmed by histology
3. Active disease documented by a Modified True Love and Witts Severity Index (MTWSI) score of 11-21, despite an ongoing treatment course of intravenous steroids for a minimum of 3 days prior to the study; a stool frequency >8 stools or a stool frequency between 3 and 8 and a C-reactive protein (CRP) >45 mg/l (Travis criteria)
4. Women of childbearing potential who have a negative serum pregnancy test at baseline screening
5. Patients must have tested negative for stool cultures including Clostridium difficile
6. Patients who are capable of understanding the purpose and risks of the study and who provide a signed and dated written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. UC requiring immediate surgical, endoscopic, or radiological interventions, including massive hemorrhage, perforation and sepsis, suppurative complications (intra-abdominal or peri-anal abscesses) or toxic colon
2. History of large bowel surgery
3. Patients with serious infections
4. Significant organ dysfunction
5. Pregnant women or nursing mothers
6. Concomitant medications:

a.. Altered dose of any 5-aminosalicylates (5-ASA) preparation within two weeks of screening
b. Altered dose of azathioprine or mercaptopurine within four weeks of screening
c. Patients who have started azathioprine in the last three months prior to baseline
d. Received probiotic, antibiotics or cyclosporine within 1 month or 2 months respectively prior of screening
e. Received any experimental treatment for this population e.g. infliximab, tacrolimus, (FK506) within two months of screening

Date of first enrolment
06/12/2006

Date of final enrolment
31/12/2007

Locations

Countries of recruitment
Netherlands

Study participating centre
AM-Pharma B.V.
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Sponsor information

Organisation
AM-Pharma B.V. (The Netherlands)

ROR
https://ror.org/02bpbnv34

Funder(s)

Funder type
Industry

Funder Name
AM-Pharma B.V.

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration