A pilot, open-label, multi-centre study to investigate the safety of Calf Intestinal Alkaline Phosphatase in patients with fulminant active ulcerative colitis refractory to steroid therapy.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON21005

Source
NTR

Brief title
AP IBD 02-01

Health condition

Fulminant ulcerative colitis

Sponsors and support

Primary sponsor: AM-Pharma B.V.
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Source(s) of monetary or material Support: -

Intervention

Outcome measures

Primary outcome

Safety and tollerability.

Secondary outcome

1. Rescue medication including ciclosporin,
experimental medication such as anti-CD-3 antibodies or colectomy rate at 9 weeks (63 days);

2. Clinical response based on change in the MTWI 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 evels and stool markers of disease activity (calprotectin).

Study description

Background summary

To study the safety and effect of Calf Intestinal Alkaline Phosphatase in patients with fulminant Ulcerative Colitis refractory to steroid therapy a simple open label design has been chosen to be conducted at three centers in the Netherlands. Subjects will receive 30.000 U CIAP/24 hrs for 7 consecutive days via a duodenal catheter. It is expected that administration of CIAP may attenuate or prevent the local and systemic inflammatory response in patients with fulminant ulcerative colitis. Patients will be followed for 9 weeks (63 days) after the start of study medication. Eligible patients will be hospitalized during the study period, and will be either dismissed upon partial recovery or after colectomy. The total study related follow up period is 9 weeks. A rescue procedure will be in place in case the clinical situation deteriorates.

Study objective

Ulcerative colitis 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 abnormal high expression of Toll-like receptors, including TLR-4, the major transducer of 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 and

2. prevent systemic inflammatory responses that result from transmigration of endotoxin though the leaky inflamed intestinal mucosa.

Therefore, it is expected that administration of CIAP may attenuate or prevent the local and systemic inflammatory response in patients with fulminant ulcerative colitis.

Study design

N/A

Intervention

Subjects will receive 30.000 U AP/24 hrs for 7 consecutive days via a duodenal catheter.

Contacts

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Eligibility criteria

Inclusion criteria

1. Patients between 18 and 70 years (inclusive) of age;

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 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 provided a signed and dated written informed consent.

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-ASA preparation within 2 weeks of screening;

b. Altered dose of azathioprine or mercaptopurine within 4 weeks of screening;

c. Patients who have started azathioprine in the last 3 months prior to baseline;

d. Received probiotic, antibiotics or cyclosporine within 1 month resp 2 months prior of screening;

e. Received any experimental treatment for this population e.g. infliximab, tacrolimus, FK506) within 2 months of screening.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-12-2006
Enrollment:	20
Type:	Actual

Ethics review

Positive opinion

Date:	21-04-2006
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL603
NTR-old	NTR659
Other	: N/A
ISRCTN	ISRCTN64619216

Study results

Summary results
N/A