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.

Gepubliceerd: 21-04-2006 Laatst bijgewerkt: 13-12-2022

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...

Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON21005

Bron
NTR

Verkorte titel
AP IBD 02-01

Aandoening

Fulminant ulcerative colitis

Ondersteuning

Primaire sponsor: AM-Pharma B.V.
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Overige ondersteuning: -

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Safety and tollerability.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

N/A

Onderzoeksproduct en/of interventie

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

Contactpersonen

Publiek

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	06-12-2006
Aantal proefpersonen:	20
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	21-04-2006
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL603

Register	ID
NTR-old	NTR659
Ander register	: N/A
ISRCTN	ISRCTN64619216

Resultaten

Samenvatting resultaten
N/A