A trial to determine if vedolizumab (medication) can prevent Crohn's disease return better than a placebo after a surgical resection of the sick bowel.

Published: 24-04-2017
Last updated: 15-05-2024

Postoperative recurrence of CD (Crohn's disease) is very common in patients having undergone bowel resection, and often leads to further bowel resection. Postoperative recurrence is frustrating to both the physician and patient, and thus an...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON24487

Source
NTR

Brief title
Reprevio

Condition

- Gastrointestinal inflammatory conditions

Synonym
Inflammatory bowel disease

Health condition
Crohn's disease

Research involving
Human

Sponsors and support

Primary sponsor: Academic Medical Center, Amsterdam
Source(s) of monetary or material Support: Takeda

Intervention

Explanation

Outcome measures

Primary outcome

The proportion of patients with clinically significant endoscopic recurrence (Rutgeerts i2b, i3 or i4) at week 26.

Secondary outcome

- Proportion of patients without endoscopic recurrence (i0)

- Symptomatic recurrence (CDAI increase >70 points compared to baseline)

- Proportion of patients with normalized serum CRP at all time points and CRP at all visits

- Proportion of patients with normal fecal calprotectin (<50) at all visits

- Quality of life measured by IBDQ and SF-36

- Serum concentrations of vedolizumab and antibodies to vedolizumab before every infusion

Study description

Background summary

Study Design:

This multi-centre randomized placebo-controlled study will look into the effect of vedolizumab to prevent recurrence of CD after ileocolonic resection. All patients will undergo an ileocolonoscopy at week 26 following surgery (in line with current recommendations). The endpoint is the proportion of patients with clinically significant recurrence of CD (Modified Rutgeerts Grade 2b, 3 or 4) after 6 months after surgery.

In most centers across the world, patients in the postoperative phase are routinely undergoing ileocolonoscopy 6 months after surgery. To justify a 50% placebo-arm, we will

exclude patients with an unfavorable disease course or severe perianal fistulas.

Primary endpoint:

Proportion of patients with severe endoscopic postoperative recurrence of CD (Rutgeerts i2b, i3 or i4) 6 months after ileocolonic resection with anastomosis (stoma excluded).

It has been established that the endoscopic Rutgeerts' score is a strong surrogate marker for the further clinical course of the disease (see appendix for scoring system). All endoscopies will be video-recorded for later review and central re-reading.

ACCRUAL AND FEASIBILITY

This study will enroll 80 subjects at 13 sites in The Netherlands, Spain, France and Italy. The feasibility of enrollment in this study is highly plausible given the high rates of resections at these academic centres and lack of alternative treatments.

TREATMENT, DOSAGE AND ADMINISTRATION

Patients will be consented to participate with 2-3 weeks following ileocolonic resection. The first study-infusion will also be given within 2-3 weeks if all inclusion and exclusion criteria are met. Patients will receive intravenous infusions of 300 mg of VDZ or 250 ml or 0,9% sodium chloride only (placebo) at Week 0, Week 8, Week 16 and 24.

PERMITTED CONCOMITANT MEDICATIONS

Loperamide or cholestyramine for control of bile acid diarrhea Prednisone will be tapered over 4 weeks postoperatively All other medications will be discontinued postoperatively.

Study objective

Postoperative recurrence of CD (Crohn's disease) is very common in patients having undergone bowel resection, and often leads to further bowel resection. Postoperative recurrence is frustrating to both the physician and patient, and thus an effective strategy to prevent CD recurrence without unwanted side effects is warranted. The reduced incidence of CD recurrence with TNF (tumor neucrosis factor) inhibitor treatment is promising as a therapeutic option, however development of antibodies to anti-TNF biologics and the potential need for dose escalation suggests that an alternative therapeutic option with a different mode of action would be welcome. The efficacy of VDZ (vedolizumab) in the

induction and maintenance of remission in CD suggests that VDZ holds potential for preventing CD recurrence following bowel resection. This investigator-initiated study will assess this possibility.

Study design

Primary outcome : week 26-28

Proportion of patients without endoscopic recurrence (i0) : week 26-28

Symptomatic recurrence (CDAI increase >70 points compared to baseline) : at baseline and every 8 weeks before infusion

Proportion of patients with normalized serum CRP at all time points and CRP at all visits : at baseline and every 8 weeks before infusion

Proportion of patients with normal fecal calprotectin (<50) : at all visits

- Quality of life measured by IBDQ and SF-36 : at baseline and every 8 weeks before infusion

- Serum concentrations of vedolizumab and antibodies to vedolizumab before every infusion : at all infusion visits before infusion.

Intervention

Vedolizumab 300 milligram 8 weekly (4 doses) or placebo 8 wekkly (4 doses)

Contacts

Public
G. D'Haens
Amsterdam
The Netherlands
Scientific
G. D'Haens
Amsterdam
The Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Adults (18-64 years)
Elderly (65 years and older)
Elderly (65 years and older)

Inclusion criteria

1. In the opinion of the investigator, the subject is capable of understanding and complying with protocol requirements.

2. The subject signs and dates a written, informed consent form and any required privacy authorization prior to the initiation of any study procedures.

3. Established Crohn’s disease as the indication for ileocolonic resection

4. Age > 18

5. Ileocolonic resection with ileocolonic anastomosis and removal of all tissue macroscopically affected by CD according to the surgeon

6. Presence of at least 1 risk factor for recurrence:

• Active smoking > 10 cigarettes/day

• 2nd, 3rd or later resection

• Surgery for perforating complication (abscess, fistula)

• Previous exposure to anti-TNF antibodies

7. Male or non-pregnant, non-lactating females. Females of child bearing potential must have a negative serum pregnancy test prior to randomization, and must use a hormonal (oral, implantable or injectable) or barrier method of birth control throughout the study. Females unable to bear children must have documentation of such in the source records (i.e., tubal ligation, hysterectomy, or post-menopausal [defined as a minimum of one year since the last menstrual period]).

8. Anti-TNF discontinued for at least 6 weeks before screening.

9. Written informed consent must be obtained and documented

Exclusion criteria

1. Patients that need to continue postoperative medication for their CD as per investigator's discretion, eg for fistulizing perianal CD.

2. Previous treatment with VDZ

3. Clinically significant CD elsewhere in the gastrointestinal tract not removed with surgery

4. Patients with clinically documented short bowel syndrome.

5. Patients with a history of cancer (other than resected cutaneous basal or squamous cell carcinoma or in situ cervical cancer) with less than 2 disease-free documented years.

6. Patients with the following laboratory abnormalities at screening:

White blood count < 3 x 109/L

Lymphocyte count < 0.5 x 109/L

Hemoglobin < 8 g/dL

Platelet count < 125 x 109/L or > 800 x 109/L

ALT or AST > 3.0 times the upper limit of normal (ULN)

Alkaline Phosphatase > 2.0 times the ULN

Serum Creatinine > 2 times the ULN

Prothrombin time (INR) > 1.5 times normal

7. Active participation in another trial.

8. Patients with abdominal abscess, active or latent tuberculosis or cancer.

9. A history of alcohol or illicit drug use that in the opinion of the principal investigator (PI) would interfere with study procedures.

10. Patients with psychiatric problems that in the opinion of the PI would interfere with study procedures.

11. Patients unable to attend all study visits.

12. Patients with a history of non-compliance with clinical study protocols.

13. Contraindication for endoscopy.

14. History of cancer or colonic dysplasia

15. Received other biologics within the last 6 weeks of screening

16. Known HIV, hepatitis B or C infection

17. Evidence of or treatment for C. difficile infection or other intestinal pathogen within 4 weeks prior to enrollment or at screening

18. Received any investigational drug in the past 30 days or 5 half-lives, whichever is longer.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-05-2017
Enrollment:	40
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Approved WMO

Date:	16-06-2016
Application type:	First submission

Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

Study registrations

Followed up by the following (possibly more current) registration

ID: 55604
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL6213
NTR-old	NTR6385
EudraCT	2015-000555-24
CCMO	NL52520.018.15
OMON	NL-OMON55604

Study results