SIMILAR Trial: Santeon InflixMab biosimILAr Research
A randomized, controlled, double blind, phase 4 noninferiority trial to assess efficacy of Infliximab-biosimilar (Inflectra) compared to Infliximab-innovator (Remicade) in patients with inflammatory bowel disease in remission

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The objective of this study is to compare the efficacy of Infliximab-biosimilar to Infliximab-innovator and to demonstrate its noninferiority up to 30 weeks, in patients with ulcerative colitis or Crohn*s disease in remission under treatment with...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal conditions NEC
Study type	Observational invasive

Summary

ID

NL-OMON43635

Source
ToetsingOnline

Brief title
SIMILAR Trial: Santeon InflixMab biosimILAr Research

Condition

- Gastrointestinal conditions NEC
- Autoimmune disorders

Synonym
Inflammatory Bowel disease: ulcerative colitis and Crohn's disease

Research involving
Human

Sponsors and support

Primary sponsor: Santeon
Source(s) of monetary or material Support: Financiering door Santeon dmv de besparing door het gebruik van Inflectra. De middelen worden niet gratis verstrekt door de farmacie of door de ziekenhuizen. Alle medicatie wordt gedeclareerd bij de verzekeraar.

Intervention

Keyword: Biosimilar, IBD, Inflectra, Infliximab

Outcome measures

Primary outcome

Efficacy of Infliximab-Biosimilar and Infliximab will be assessed by evaluation

of the duration of clinical remission and the relapse rate for each diagnosis

seperately.

Secondary outcome

- Evaluation of adverse effects and overall safety of Infliximab-biosimilar in

comparison with Infliximab-innovator up to 30 weeks.

- Evaluation of pharmacokinetics of Infliximab-biosimilar in comparison with

Infliximab-innovator up to 30 weeks.

This will be done by evaluating the following secondary endpoints;

• SIBDQ scores

• Pharmacokinetic evaluation (trough levels)

and

• Adverse and serious adverse events

• Assessment and monitoring of TB signs and symptoms.

• Physical Examination findings

• Clinical laboratory analyses, including calprotectin.

Study description

Background summary

In this study patients with an established diagnosis of UC or CD, in clinical and endoscopic remission and medically treated with Infliximab, will be randomized to switch to the biosimilar Infliximab-biosimilar or to continue with Infliximab-innovator. The study will be a randomized, controlled, double blind, multicenter phase IV study and designed to assess the non-inferiority in safety and efficacy of infliximab-biosimilar to infliximab-innovator. A biosimilar is a copy of an original biopharmaceutical and has similar biologic activity, physicochemical characteristics, efficacy and safety. Manufacturing of biosimilars is complex: due to changes in cell lines or in the production process post-translational modification may occur resulting in highly similar but not identical products. These changes may influence biological and/or immunogenic characteristics. Earlier phase I and phase III studies comparing Infliximab-biosimilar with Infliximab-innovator show no difference between in both efficacy and safety in the treatment of ankylosing spondylitis and rheumatoid arthritis. No results from studies with IBD patients have been published. If IBD patients currently treated with Infliximab can be treated with the lower-cost biosimilar, substantial cost-reduction can be achieved making biologicals available to a wider patient group.

Study objective

The objective of this study is to compare the efficacy of Infliximab-biosimilar to Infliximab-innovator and to demonstrate its noninferiority up to 30 weeks, in patients with ulcerative colitis or Crohn*s disease in remission under treatment with infliximab for at least 12 weeks

Study design

This will be a randomized, double-blind, multicentre, prospective study to assess the non-inferiority in efficacy of Infliximab-Biosimilar (5mg/kg or 10mg/kg) compared to Infliximab (5mg/kg to10mg/kg) up to 30 weeks, in patients with CD or UC in remission under treatment with Infliximab for at least 12 weeks.

Study burden and risks

The burden of participation is the risk of a relapse. Patients need to visit the hospital at maximum 2 extra times; during the screening period and if the interim control does not coincide with the study drug infusion. An endoscopy will be performed in case of worsening of symptoms in combination with a calprotectin >250 mg/g. Furthermore patients need to fill in stool diaries. Furthermore patients need to fill in stool diaries. In the control group patients receive standard of care. Both groups will probably not benefit from this trial.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
1. Patient, male or female, is aged above 18 years.
2. Patient has an established diagnosis of ulcerative colitis or Crohn*s disease.
3. Patient has ulcerative colitis or Crohn*s disease in clinical remission defined as:
a. Crohn*s disease: HBI score <5 and a fecal calprotectin <250 mg/g.
b. Ulcerative colitis: total Mayo score of <=2 and a fecal calprotectin <250 mg/g.
4. Patient is being treated with Infliximab 5mg/kg to 10mg/kg with stable dosing intervals between 6 to 10 weeks for at least 12 weeks.
5. Patient may receive one of the following treatments:
a. 5-aminosalicylates (no dosage changes for at least 8 weeks for inclusion)
b. Antibiotics
c. Azathioprine, 6-mercaptopurine (6-MP) or tioguanine (6-TG) (no dosage changes for at least 8 weeks for inclusion)
d. Methotrexate (MTX) (no dosage changes for at least 8 weeks for inclusion)
6. Patient has stable renal and hepatic function at time of screening, defined as:
a. Serum creatinine <1.5 x upper limit of normal (ULN) or an estimated creatinine clearance level >50mL/min
b. Serum alanine aminotransferase <2.5 x ULN
c. Serum aspartate aminotransferase <2.5 x ULN
d. Serum total bilirubin <2 x ULN
7. Patient has the following hematology laboratory test results at time of screening:
a. Hemoglobin >=5.5mmol/l
b. White blood cell count: >=3.5 x 109 cells/l
c. Neutrophil count: >=1.5 x 109 cells/l
d. Platelet count: >=100 x 109 cells/l
8. Patient is able to understand the intention, the nature and the possible risks of the study, to cooperate with the investigator and to understand given instructions.
9. Patient is informed about the intention and nature of the study including all possible risks and has given his written consent before inclusion.
10.
a. Female patients of child of childbearing potential agree to use 1 of the following medically acceptable methods of contraception during the course of the study and for 12 weeks following discontinuation of study drug (excluding women who are not of childbearing potential or who have been sterilized):Barrier contraceptives (male condom, female condom, or diaphragm with a spermicidal gel)
b. Hormonal contraceptives (implants, injectables, combination oral contraceptives, transdermal patches, or contraceptive rings)
c. Intrauterine device.
Female patients who have been surgically sterilized for less than 6 months prior to the date of informed consent must agree to use 1 medically acceptable methods of contraception. Menopausal females must have experienced their last period more than 12 months prior to the date of informed consent to be classified as not of childbearing potential.

Exclusion criteria

1. Patient has an allergy or hypersensitivity to one of the components of infliximab and/or immunoglobulin products, except hypersensitivity reactions which have a positive response to hydrocortisone and thereby are under control.
2. Patient has a history of tuberculosis (TB) or a current diagnosis of TB or other severe or chronic infection such as abscess, opportunistic infection or invasive fungal infection. Patients with a past history of a severe or chronic infection will not be excluded.
3. Patient has had recent exposure to persons with active TB. In that case screening for latent TB (defined as a positive result for interferon-γ release assay (IGRA) with a negative examination of chest X-ray) will be performed. If there is sufficient documentation of prophylaxis or complete resolution following TB-treatment based on hospital-specific guidelines the patient can be enrolled. If the result of the IGRA is indeterminate at screening, 1 retest will be done. If the repeated IGRA result is indeterminate again, the patient will be excluded. Patients with a positive IGRA result and a negative examination of chest X-ray who has received at least the first 30 days of TB-therapy can be enrolled.
4. Patient who is taking any of the following concomitant medications or treatment:
a. Current use of corticosteroids (prednisone, prednisolone or budesonide).
b. Alkylating agents: current use or within 12 months to randomization
c. Live or live-attenuated vaccine within 8 weeks of randomization.
d. Any other biological treatments than infliximab.
f. Any planned abdominal surgery for IBD at the time of randomization and/or during the study period.
5. Patient has one or more of the following medical conditions:
a. Active entero-vesical, entero-retroperitoneal, entero-cutaneous and entero-vaginal fistula for within 6 months prior to screening. Entero-enteral fistulae without clinical significant symptoms upon investigator*s opinion and anal fistulae without draining problems are allowed.
b. Current short bowel syndrome.
c. History of any malignancy within the 5 years prior to randomization except cutaneous basal cell carcinoma, cutaneous squamous cell carcinoma or completely excised and cured squamous carcinoma of the uterine cervix.
d. History of lymphoma or lymphoproliferative disease or bone marrow hyperplasia.
e. New York Heart Association (NYHA) class III or IV heart failure.
f. History of organ transplantation, including corneal graft/transplantation.
g. Ileostomy of colostomy.
6. Patient has had treatment with any other investigational device or medical product within 4 weeks of randomization or 5 half-lives, whichever is longer.
7. Female patient who is currently pregnant, breastfeeding, or planning to become pregnant or breastfeed within 12 weeks of the last dose of study drug.

Study design

Design

Study phase:	4
Study type:	Observational invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-01-2016
Enrollment:	182
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Inflectra
Generic name:	Infliximab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Remicade
Generic name:	Infliximab
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	14-08-2015
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	14-09-2015
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-12-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-07-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-08-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-08-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
EudraCT	EUCTR2015-001954-14-NL
ClinicalTrials.gov	NCT02452151.
CCMO	NL53452.100.15