Multi-center, double-blind, randomized, placebo-controlled, phase IIa trial to evaluate spesolimab (BI 655130) efficacy in patients with fibrostenotic Crohn*s Disease

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To demonstrate that spesolimab is effective in maintaining Symptomatic Stenosis Responseand / or inducing Radiographic Stenosis Response (defined in Table 2.3: 1) in patients withsymptomatic CD-related small bowel stenosis, who have achieved...

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

Summary

ID

NL-OMON51041

Source
ToetsingOnline

Brief title
Study with spesolimab in people with CD with symptoms of bowel obstruction

Condition

- Gastrointestinal inflammatory conditions

Synonym
fibrostenotic Crohn□s Disease

Research involving
Human

Sponsors and support

Primary sponsor: Boehringer Ingelheim
Source(s) of monetary or material Support: Boehringer ingelheim;opdrachtgever

Intervention

Keyword: bowl obstruction, Crohn's disease, fibrosis, stenosis

Outcome measures

Primary outcome

Proportion of patients with maintained Symptomatic Stenosis Response (defined

in Table 2.3: 1) at Week 48

Proportion of patients with Radiographic Stenosis Response (defined in Table

2.3: 1) at Week 48

Secondary outcome

Proportion of patients with maintained Symptomatic Stenosis Response (defined

in Table 2.3: 1) at Week 24

Proportion of patients with Radiographic Stenosis Response (defined in Table

2.3: 1) at Week 24

Study description

Background summary

Crohn*s disease (CD) is a chronic condition that manifests clinically as recurrent gut
inflammatory episodes followed by periods of inflammatory remission and is one of the
recognized subtypes of Inflammatory Bowel Disease (IBD).

Under normal physiologic conditions acute gut inflammation, e.g. viral or bacterial
gastroenteritis, is followed by a complex tissue repairing or tissue remodelling response. This
response aims to repair the damage caused by inflammation and to recover normal structure
and function of the intestinal mucosa and rest of the layers of the gut wall. Tissue
remodelling response includes among others activation of mesenchymal cells, which produce
an extracellular matrix, mainly collagen and fibronectin, which leads to wound healing.
However, in IBD patients, the chronic or recurrent activation of tissue remodelling responses
leads to excessive accumulation of this extracellular matrix causing destruction of the
interstitium and increased apposition of collagen or fibronectins, which leads to fibrosis,
which manifest clinically as intestinal stenosis

Study objective

To demonstrate that spesolimab is effective in maintaining Symptomatic Stenosis Response
and / or inducing Radiographic Stenosis Response (defined in Table 2.3: 1) in patients with
symptomatic CD-related small bowel stenosis, who have achieved Symptomatic Stenosis
Response after standard medical therapy

Study design

The study has a screening period of up to 14 weeks until randomization.
In this lead-in period, the patient starts treatment for corticosteroids as described in section 4.2.1 in the protocol. As soon as the results of the therapeutic drug monitoring are known, the optimization of anti-inflammatory treatment with biologics will start.

After randomization, the treatment period with the study drug follows. The patient comes to the hospital every 4 weeks for an infusion of the study drug.
During the treatment period, the patient receives an MRE 3 times, an endoscopy 3 times, during which a biopsy is taken.
Questionnaires are taken every visit, blood taken for for example safety.
Stools are also collected 5 times for biomarker and pathogen analysis.

Intervention

IMP
Spesolimab is a humanized antagonistic monoclonal IgG1 antibody that blocks human IL36R signalling. Binding of spesolimab to IL36R is anticipated to prevent the subsequent activation of IL36R and downstream activation of pro-inflammatory and pro-fibrotic pathways in inflammatory skin and bowel diseases. Spesolimab may be unique in directly suppressing not only pro-inflammatory but also profibrotic mechanisms in these diseases.

Lead-in period
CORTICOSTEROIDS
Methylprednisolone 40 mg/d i.v. or 40 mg/d of oral prednisolone (or the equivalent dose of any systemic steroid formulation. Budesonide is not allowed)
Patients receiving i.v. steroids should be switched to oral prednisolone when clinically justified, to complete 2 weeks of steroid treatment followed by a defined tapering regime
Tapering Regime: Decrease by 5 mg/1wk until 10 mg and then decrease by 2.5 mg/1wk until 0 mg
OPTIMIZATION OF ANTI-INFLAMMATORY BIOLOGICAL TREATMENT
Anti-inflammatory biological treatment shall be individually optimized dependent on the prior (failed) treatment of each patient by introducing approved doses of TNF inhibitors (TNFi), vedolizumab, or ustekinumab following the algorithm below, optimization period of 8 weeks starts with the dose adaptation or treatment change as described in the protocol under section 4.2.1.1. This is restricted to locally approved dosing regimens of proposed agents.

Treatment period
After achievement of Symptomatic Stenosis Response patients need to maintain their optimized anti-inflammatory treatment initiated during the Lead-in Period after randomization and throughout the Blinded Randomized Treatment Period.
IMP
Intravenous administration of 1200 mg every 4 weeks (q4w) until Week 8 then 1200 mg every 8 weeks (q8w) until Week 40 (last trial drug administration)

Study burden and risks

- Patient may not experience results from study drug
- The patient may experience side effects from the study drug
- Patient must undergo examinations as part of the study that may be uncomfortable, such as an MRE or an endoscopy and a biopsy taken.

- Blood is taken regularly, which can be experienced as unpleasant.
- The patient is asked to fill in questionnaires, which may be perceived as burdensome.

Contacts

Public
Boehringer Ingelheim

Comeniusstraat 6
Alkmaar 1817MS
NL
Scientific
Boehringer Ingelheim

Comeniusstraat 6
Alkmaar 1817MS
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

-Male and female patients, 18 to 75 years when signing informed consent at screening
-Established diagnosis of clinical CD prior to screening
-Suspicion of symptomatic small bowel stenosis
-Presence of abdominal pain after eating or limitation in amount or types of food at screening
-1 or 2 naïve or anastomotic stenoses in the terminal ileum at screening, confirmed by MRE at randomization
-Have achieved Symptomatic Stenosis Response before randomization (i.e. 7 day average scores <2 for diary questions on the abdominal pain after eating AND on the limitation in amount or types of food)
-Endoscopic activity defined by Colonic Simple Endoscopic Score in CD (SES-CD)

*12 after Lead-in Period, at the time of randomization

Exclusion criteria

- Failure of > 2 different biological drug classes prior to screening (e.g. TNF inhibitors, Integrin Receptor antagonists and IL-12 / IL-23 antagonists)
- More than 2 small intestinal stenoses
- Systemic corticosteroid treatment of current obstructive symptoms for >1 week prior to screening
- Endoscopic balloon dilation or surgical treatment of the same small bowel stenosis within the last 6 months prior to screening Visit 1
- Patients who require immediate EBD or surgical intervention as per the investigator*s discretion
- Current complications of CD at screening Visit 1 and randomization (Day 1) that would possibly confound the evaluation of benefit from treatment with spesolimab
- Current stenosis in the colon
- Previous strictureplasty on current stricture, ileostomy, colostomy
- Any kind of bowel resection or diversion within 6 months or any other intra-abdominal surgery (except for abscess drainage) within 3 months prior to screening Visit 1
- Colorectal cancer present and past (<;5 years) history

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	12-11-2021
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Spesolimab
Generic name:	Spesolimab

Ethics review

Approved WMO Date:	05-08-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-11-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-12-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-12-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-06-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2020-005770-99-NL
CCMO	NL77271.056.21
Other	volgt nog