A phase II, multicenter, randomized, double-blind, multiple dose, placebo-controlled, parallel-group study to evaluate the efficacy, pharmacokinetics, and safety of BI 655066, an IL-23 p19 antagonist monoclonal antibody, in patients with moderately to severely active Crohn's disease, who are naïve to, or were previously treated with anti-TNF therapy.

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the main objectives of the study are to evaluate the efficacy of different doses of BI655066 + to evaluate the pharmacokinetics (how the body handles the study drug) and pharmacokinetics (interaction of the study drug with the body) for subjects...

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

Summary

ID

NL-OMON41584

Source
ToetsingOnline

Brief title
BI 655066 dosefinding for Crohn's disease

Condition

- Gastrointestinal inflammatory conditions

Synonym
Crohn's disease - inflammatory bowel disease

Research involving
Human

Sponsors and support

Primary sponsor: Boehringer Ingelheim
Source(s) of monetary or material Support: Boehringer Ingelheim b.v.

Intervention

Keyword: active Crohn's disease, anti-TNF therapy, dose finding, monoclonal antibody

Outcome measures

Primary outcome

to evaulate the efficacy of BI655066 in inducing clinical remission defined as

CDAI<150 after 12 weeks of treatment

Secondary outcome

- To evaluate efficacy of BI 655066 in inducing endoscopic response, clinical

response, mucosal healing and deep remission.

- To evaluate safety of BI 655066.

- To explore the pharmacokinetics and pharmacodynamics of BI 655066

therapy in Crohn*s disease

Study description

Background summary

Crohn*s disease is a chronic inflammatory bowel disease (IBD) that may affect

any part of the gastrointestinal tract from mouth to anus, causing a wide variety of symptoms.
The intensity of inflammation of the bowel can vary widely; people with Crohn's disease experience chronic recurring periods of *flare-ups* (fast progression of disease called acute phase) and remission (quiet periods which nearly do not require treatment called the chronic phase).
About 35.000 Dutch people and 15.000 Belgian people have IBD. 1000 subjects are newly diagnosed per year. The disease is mainly diagnosed between the age of 15-30 years.
After diagnosing the disease medicinal treatment will be started to compromise the inflammation, and to suppress the appearance of new inflammatory spots. In addition to that prescriptions to prevent anemia and diarrhea are also frequently prescribed.
Nearly 80% of Crohn*s disease patients require long medicinal treatment and guidance from a medical specialist. These drugs may work, but also have negative side effects; many patients show to be intolerant to anti-TNF, which is most frequently prescribed.

BI 655066 is an experimental drug, what will be used in patients with Crohn*s disease for the first time. It was studied in a clinical trial with 31 patients with psoriasis, a skin disease.
BI 655066 is a *humanized monoclonal antibody* specific to IL-23 p19; this means that BI655066 neutralizes a protein *IL-23 p19*, which is involved in the progression of Crohn*s disease. Neutralizing this protein will have effect in less decrease of the health condition of subjects with Crohn*s disease.
Research physicians will be allowed only to include subjects where the current therapy standard is ineffective or not effective enough as of effective date of local AM1 for the Netherlands.

Study objective

the main objectives of the study are to evaluate the efficacy of different doses of BI655066
+
to evaluate the pharmacokinetics (how the body handles the study drug) and pharmacokinetics (interaction of the study drug with the body) for subjects with Crohn's disease.

Study design

This study consists of 3 parts:

Period 1
The score of the Crohn's Disease Activity Index (CDAI) will be assessed by the research physician to determine a subjects eligibility for the trial.
In part 1 subjects will ave a chance of 1:1:1 of assignment to one of the

treatment arms of the study, on top of their use of standard of care medication.
(placebo : 200mg BI655066 : 600mg BI655066)
During the first 12 weeks (period 1) medication (or placebo) will be administered on the randomisation visit, after 2 weeks and after 12 weeks.

Period 2
After the first period the research physician will determine the Crohn's Disease Activity Index (CDAI) again at visit 6 of period 1, to assess eligibility for period 2.
a) Whenever a subject reached "deep remission" (definition, see study protocol), a period of 14 weeks "washout" (=no drug) will start. This is expected to be acceptable due to the long T1/2 time of BI655066. Subjects will be monitored during this period as well; in case of " flare-ups" of the disease, a change to active treatment is possible.
or
b) Whenever a subject did not reach "deep remission", active treatment with the highest dose of BI655066 will be started. this will be irrespective of the treatment a subject received during the first 12 weeks.

With this strategy any subject is guaranteed that, whenever recieving placebo, this will not take longer than 12 weeks & after that every subject (eligible to continue on period 2 and 3) can continue on active drug.

Period 3
When subjects return after 26 weeks for visit E1, the research physicians will assess a subject's clinical remission (definition, see study protocol).
a) Whenever there is clinical remission, the subject is allowed to continue in period 3 and will be treated with subcutaneous therapy untill the end of the study. (week 65)
or
b) whenever there is no clinical remission, this may suggest that a subject did not benefit from the past 26 weeks of treatment. These subjects will be asked to discontinue the trial, as it is considered unethical to let them continue beyond this point. the investigator will discuss the left options with the study subject.

Intervention

also see study protocol, flowchart + chapter 4.1.1:

perdiod 1:
BI655066 / placebo dosed 200 of 600 mg IV on visits 2,4,5

period 2:
if deep remission is seen on V6 (week 12) of period 1, a washoutperiod will start untill wk26. (based on T1/2 this is expected to be acceptable)

if there is NO deep remission seen on V6 (week 12) of period 1 / or there is a worsening of disease during the mentioned washout period (confirmed by colonoscopy) , 1 course (3x IV treatment, each 4 weeks apart) open label therapy 600 mg IV will be given.

period 3:
if a patient shows clinical remission on week 26, the 3rd period may start with 180 mg SC on visits E1, E2, E3 en E4.
if a patient does not show clinical remission on week 26, the study will end according to protocol.

Study burden and risks

The burden for subjects will mainly be based on the visits a subject is requested to bring to the hospital & the kind of examinations a subject is requested to undergo during the trial with trial purposes:
In respect to time investments subjects will be in close contacxt with their study physician for a period of 65 weeks. Depending of the specific visit, this visit will take 2 to 6 hours of the subject*s time per visit. In total every patient will be requested to spend an estimate of 48 hours (in this timeframe of 65 weeks total) at the hospital for interviews with the study staff and to undergo examinations.
During 3 to 4 visits the time spent onsite by the subject will take 4 to 6 hours per visit, due to the fact a colonoscopy needs to be performed. Only when there is a *flare* during period 2 of the study (week 12-26), an extra colonoscopy will be requested from the subject, which may maximize the total amount of examinations to 4 (instead of 3); this is only expected in rare cases.
The performer of the colonoscopy will most probably ask patients to bring some familiar person to the clinic with them, to stay with the subject during the examination and to bring them home after the clinic visit.
With respect to invasive procedures, subjects will be asked to undergo more frequent colonoscopies compared to the normal clinical standard. For this study colonoscopies are required to evaluate the effect of the investigational drug.

Description of risks a subject is exposed to when participating in this trial:
- there is a chance of 1:3 for a subject to be treated with placebo during the first 12 weeks. This may cause a (temporarily) deterioration in their state of health. After this 12 week period, all patients will be treated with BI655066.
- There is a chance that subjects (despite of their study treatment arm) experience side effects of the procedure of a colonoscopy. These side effects are in nature of the procedure not different from the normal clinical treatment. This colonoscopy is a common procedure to Crohn*s disease subjects and will be performed by experts to that procedure. The chance to experience side effects , is thus the same, but may only occur more frequent as the colonoscopies occur more frequent.

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

- Men or women 18-75 years at the time of consent.;- Diagnosis of Crohn's disease at least 3 months prior to screening.;- Moderate to severe active Crohn's disease, defined as CDAI > or<=220 and < or<=450.;- Presence of mucosal ulcers in at least one segment of the ileum or colon and a CDEIS
score * 7 (for patients with isolated ileitis *4), as assessed by ileocolonoscopy and confirmed by central independent reviewer(s) before randomization.;- Non-responsiveness or intolerance to previous standard treatment with at least 2 TNF antagonists (infliximab, adalimumab, or certolizumab pegol) at a dose approved for Crohn*s disease.

Exclusion criteria

- Complications of Crohn's disease such as strictures, stenoses, short gut syndrome, or any other manifestation that might require surgery.;- Presence of ileostomy or colostomy.;- Pregnant or nursing women.;- Signs or symptoms suggestive of active TB.;- History of malignancy.

Study design

Design

Study phase:	2
Study type:	Interventional
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):	07-04-2015
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	unknown
Generic name:	unknown

Ethics review

Approved WMO

Date:	25-02-2014
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	12-02-2015
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	26-06-2015
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	13-07-2015
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	11-09-2015
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	17-09-2015
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	11-12-2015
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	17-12-2015
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit

	Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	25-03-2016
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	17-05-2016
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	EUCTR2013-002902-29-NL
ClinicalTrials.gov	NCT02031276
CCMO	NL46413.068.13