A Phase 3, randomized, double-blind, placebo-controlled, multicenter study to investigate the efficacy and safety of mongersen (GED-0301) for the treatment of subjects with active Crohn's disease.

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To evaluate the efficacy of GED-0301 compared with placebo on clinical activity at Week 12, as measured by the Crohn's Disease Activity Index (CDAI) in subjects with active Crohn's disease (CD).

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

Summary

ID

NL-OMON45908

Source
ToetsingOnline

Brief title
GED-0301-CD-002

Condition

- Gastrointestinal inflammatory conditions

Synonym
chronic bowel inflammation, inflammatory bowel disease

Research involving

Human

Sponsors and support

Primary sponsor: Celgene Corporation
Source(s) of monetary or material Support: Celgene

Intervention

Keyword: Crohn's disease, Inflammatory bowel disease, Mongersen

Outcome measures

Primary outcome

Efficacy as clinical remision: the proportion of subjects achieving clinical remission defined as a Crohn's Disease Activity Index (CDAI) score < 150 at Week 12.

Secondary outcome

* The proportion of subjects with endoscopic remission, defined as Simple Endoscopic Score for Crohn's Disease (SES-CD) * 2 at Week 52.

* The proportion of subjects achieving clinical remission, defined as a CDAI score < 150 at Week 52 .

* The proportion of subjects who have a clinical response, defined as a decrease from baseline in CDAI * 100 points at Week 12.

* The proportion of subjects with endoscopic response -50 (ER-50), defined as a reduction of at least 50% in the SES-CD compared with baseline, at Week 52.

* The proportion of subjects achieving sustained clinical remission, defined as a CDAI score < 150, at both Week 12 and Week 52.

* The proportion of subjects who achieve corticosteroid-free clinical remission (CADI <150) at Week 52 among subjects receiving oral

corticosteroids at baseline.

* The proportion of subjects with endoscopic response -25 (ER-25), defined as a

reduction of at least 25% from baseline in the SES-CD, at Week 12.

* The proportion of subjects who have a clinical response, defined as a

decrease from baseline in CDAI * 100 points at Week 4.

Study description

Background summary

Mongersen (GED-0301) is being studied for the treatment of subjects with active Crohn*s disease (CD). Although the etiology of CD has not been completely elucidated, there has been significant advancement in the understanding of the disease pathogenesis. There is evidence that the chronic intestinal inflammation is caused by an excessive immune response to mucosal antigens that is not appropriately controlled by the normal counter-regulatory mechanisms. GED-0301 is an antisense oligodeoxynucleotide that is complementary to the sequence of the messenger ribonucleic acid (mRNA) transcript of Smad7, and consequently inhibits Smad7 mRNA. GED-0301 is formulated as a gastro-resistant delayed release pH-dependent tablet designed to deliver the active substance in the distal gastrointestinal (GI) tract. This formulation is not intended to achieve systemic absorption, but rather to obtain a local release and therapeutic benefit directly on the intestinal inflammatory lesions. This information supports the potential efficacy of GED-0301 in the treatment of CD.

Study objective

To evaluate the efficacy of GED-0301 compared with placebo on clinical activity at Week 12, as measured by the Crohn's Disease Activity Index (CDAI) in subjects with active Crohn's disease (CD).

Study design

This is a Phase 3, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy and safety of 3 treatment regimens of oral GED-0301 versus placebo in subjects with active CD.
Subjects will participate for a maximum of 60 weeks in this study: up to 4 weeks in the
Screening Period; 52 weeks in the Double-blind Treatment Period; and 4 weeks in

the Follow-up Period.

Intervention

Subjects will receive double-blind, oral GED-0301 or identically appearing placebo (QD) as follows:
* GED-0301 160 mg QD for 12 weeks; followed by placebo QD for 4 weeks; followed by alternating GED-0301 160 mg QD for 4 weeks and placebo QD for 4 weeks, until the the Week 52 Visit;
* GED-0301 160 mg QD for 12 weeks; followed by placebo QD for 4 weeks; followed by alternating GED-0301 40 mg QD for 4 weeks and placebo QD for 4 weeks, until the Week 52 Visit;
* GED-0301 160 mg QD for 12 weeks; followed by continuous GED-0301 40 mg QD, until the Week 52 Visit;
* Placebo QD until the Week 52 Visit.

Study burden and risks

Treatment of patients with CD represents a difficult challenge. The natural history of CD is characterized by a remitting and relapsing course that progresses to complications and surgery in the majority of patients. A stepwise approach according to disease location and severity at presentation has been advocated, with the primary aim of inducing and maintaining clinical remission, improving quality of life (QoL), and minimizing short- and long-term toxicity and complications. Treatment of CD currently involves pharmacological treatment and surgery, the latter of which is indicated for medically refractory disease, strictures, abscesses and neoplastic lesions.
Based on current data available, potential therapeutic benefit, and the safety monitoring specified in the protocol, it is appropriate to proceed with the proposed study in the patient population at the dose regimen specified in the protocol.

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

Diagnosis of CD with a duration of at least 3 months prior to the Screening Visit
Diagnosis of ileitis, ileocolitis or colitis, as determined by ileocolonoscopy at screening
Active disease, defined as a CDAI score * 220 and * 450 at screening
Subject must have a 7-day average stool frequency * 3.5 or abdominal pain * 1.5 at screening
Subject must have a total SES-CD * 6 at screening, or the ileum segmental SES-CD * 4 at screening
Must have failed or experienced intolerance to at least one of the following: budesonide; systemic corticosteroids; immunosuppressants (ie, azathioprine [AZA], 6-mercaptopurine [6-MP], or methotrexate [MTX]); or biologics for the treatment of CD (ie, infliximab, adalimimumab, certolizumab, vedolizumab)

Exclusion criteria

Diagnosis of ulcerative colitis (UC), indeterminate colitis, ischemic colitis, microscopic colitis, radiation colitis or diverticular disease-associated colitis
Subject has local manifestations of CD such as strictures, abscesses, short bowel syndrome; or other disease complications for which surgery might be indicated or could confound the evaluation of efficacy
Strictures with prestenotic dilatation, requiring procedural intervention, or with obstructive symptoms. In addition, colonic strictures that are not

passable with an adult colonoscope, or strictures in the ileum or ileocecal valve that are fibrotic in nature, will be excluded.
Subject had any intestinal resection within 6 months or any intraabdominal surgery within 3 months prior to the Screening Visit.
Subject had prior treatment with mycophenolic acid, tacrolimus, sirolimus, cyclosporine, thalidomide or apheresis (eg, Adacolumn®) within 8 weeks prior to the Screening Visit.
Use of intravenous (IV) corticosteroids within 2 weeks prior to the Screening Visit.
Use of topical GI treatment such as 5-aminosalicylic acid (5-ASA) or corticosteroid enemas or suppositories within 2 weeks prior to the Screening Visit.
Use of bile acid sequestrants, (eg, cholestyramine) within 3 weeks prior to the Screening Visit.
Prior treatment with biologics for the treatment of CD (approved or investigational), other than infliximab, adalimimumab, certolizumab or vedolizumab.
Prior treatment with more than 3 biologics for the treatment of CD (ie, infliximab, adalimimumab, certolizumab, vedolizumab).
Treatment with a biologic within 8 weeks prior to the Screening Visit, or 5 elimination half lives, whichever is longer.

Study design

Design

Study phase:	3
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):	04-11-2016
Enrollment:	33

Type:	Actual

Ethics review

Approved WMO Date:	05-02-2016
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	29-09-2016
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-10-2016
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-10-2016
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	05-12-2016
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	17-01-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	06-03-2017
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-04-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-05-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-08-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	11-09-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	23-10-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2015-001925-18-NL
ClinicalTrials.gov	NCT02596893
CCMO	NL55490.000.16