A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study To Investigate The Efficacy And Safety Of Mongersen (GED-0301) For The Treatment Of Adult and Adolescent Subjects With Active Crohn*s Disease

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To evaluate the efficacy of GED-0301 at Week 12, administered as either a single 160 mg tablet or as four 40 mg tablets, compared with placebo on clinical activity in subjects with active CD

Ethical review	Approved WMO
Status	Will not start
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON45444

Source
ToetsingOnline

Brief title
DEFINE - GED-0301-CD-003

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

The proportion of subjects achieving clinical remission, defined as a CDAI score < 150, at Week 12

Secondary outcome

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

The proportion of subjects with endoscopic response-25 (ER-25), defined as a reduction of at least 25% from baseline in 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

The proportion of subjects achieving clinical remission, defined as a CDAI score < 150, at Week 4

The proportion of subjects with endoscopic response-50 (ER-50), defined as a reduction of at least 50% in SES-CD compared with baseline, at Week 12

The proportion of subjects achieving clinical remission, defined as a PCDAI score <= 10 at Week 12 (adolescent subjects only)

The plasma concentration of GED-0301 at Week 4 and Week 8

Type, frequency, severity, seriousness, and relationship of AEs to IP

Number of subjects who discontinue IP due to any AE

Clinically significant changes in vital signs, ECG, and/or laboratory findings

Type, frequency, severity, seriousness, and relationship of AEs to IP

Number of subjects who discontinue IP due to any AE through Week 12

Clinically significant changes in vital signs, ECG, and/or laboratory findings

through Week 12 and 4-week Follow-up

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 at Week 12, administered as either a single 160 mg tablet or as four 40 mg tablets, compared with placebo on clinical activity in subjects with active CD

Study design

This is a Phase 3, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy and safety of oral GED-0301, administered as either a single 160 mg tablet or as four 40 mg tablets, versus placebo in

subjects with active CD.

Intervention

Subjects will receive double-blind treatment with oral GED-0301 160 mg or placebo QD for 12 weeks as follows:
• GED-0301 (1 x 160 mg gastro-resistant, delayed release, pH-dependent tablet) and 4 placebo tablets (identical in appearance to GED-0301 40 mg tablet);
• GED-0301 (4 x 40 mg gastro-resistant, delayed release, pH-dependent tablets) and 1 placebo tablet (identical in appearance to GED-0301 160 mg tablet);
• Placebo (4 placebo tablets identical in appearance to GED-0301 40 mg tablet and 1 placebo tablet identical in appearance to GED-0301 160 mg tablet).

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
Adolescents (12-15 years)
Adolescents (16-17 years)
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
• Presence of ileitis, ileocolitis, or colitis, as determined by ileocolonoscopy at screening
• Active disease, defined as a CDAI score >= 220 and <= 450 at screening
• Must have a 7-day average daily liquid or soft stool frequency >= 3.5 or abdominal pain >= 1.5 at screening
• 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, AZA, 6-MP, or MTX); or biologics for the treatment of CD (ie, infliximab, adalimumab, certolizumab, or vedolizumab)

Exclusion criteria

1. diagnosis of UC, indeterminate colitis, ischemic colitis, microscopic colitis, radiation colitis, diverticular disease-associated colitis, or colitis due to immunodeficiency.
2. local manifestations of CD such as abscesses, short bowel syndrome, or other disease complications for which surgery might be indicated or which could confound the evaluation of efficacy.
3. strictures with prestenotic dilatation, requiring procedural intervention, or with obstructive symptoms. In addition, subjects with colonic strictures that are not passable with an age-appropriate colonoscope, or strictures in the ileum or ileocecal valve that are fibrotic in nature, will be excluded.

4. intestinal resection within 6 months or any intra-abdominal surgery within 3 months prior to the Screening Visit.
5. ileostomy or a colostomy.
6. prior treatment with mycophenolic acid, tacrolimus, sirolimus, cyclosporine, thalidomide or apheresis (eg, Adacolumn®) within 8 weeks prior to the Screening Visit.
7. intravenous (IV) corticosteroids within 2 weeks prior to the Screening Visit.
8. changed or discontinued the dose of oral aminosalicylates within 2 weeks prior to the Screening Visit.
9. changed or discontinued the dose of oral corticosteroids (prednisone <= 20 mg/day or equivalent, budesonide <= 9 mg/day) within 3 weeks prior to the Screening Visit.
10. Adolescents with delayed growth or pubertal development who are on corticosteroids at baseline and who should not continue treatment with the same dose of corticosteroids until Week 12 visit.
11. immunosuppressants (eg, AZA, 6-MP, or MTX) within 12 weeks prior to the Screening Visit and has changed or discontinued the dose of immunosuppressants within 8 weeks prior to the Screening Visit.
12. topical GI treatments, such as, 5-aminosalicylic acid (5-ASA) or corticosteroid enemas or suppositories within 2 weeks prior to the Screening Visit.

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:	Will not start
Enrollment:	42
Type:	Anticipated

Ethics review

Approved WMO Date:	31-01-2017
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	24-04-2017
Application type:	First submission
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:	16-08-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	13-09-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-09-2017
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	EUCTR2015-001924-40-NL
CCMO	NL60150.000.17