A Phase 3, long-term active treatment extension study of mongersen (GED-0301) in subjects with Crohn*s disease

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To evaluate the long-term safety of oral GED-0301 in subjects with Crohn*s disease

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

Summary

ID

NL-OMON46186

Source
ToetsingOnline

Brief title
GED-0301-CD-004

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

Safety of GED-0301, assessed by type, frequency and severity of adverse events, and its relationship to investigational product, discontinuation due to adverse events, and clinically significant changes in electrocardiograms (ECGs), vital signs, and/or laboratory findings Through Week 208 and 4 weeks postdose.

Secondary outcome

Secondary endpoints are not included for adult subjects in this study.

Secondary endpoints for Adolescents subjects from GED-0301-CD-003:

- The proportion of subjects with clinical remissiona at Week 40.

- The proportion of subjects with endoscopic remission defined as SESCD <= 2 at Week 40

- The proportion of subjects who have clinical remissiona, defined as a PCDAI <= 10 points at Week 40.

- The change from baseline (GED-0301-CD-003) in weight, height, body mass index (BMI), and height velocity z-scores (adjusted for chronological age) at Week 40

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 long-term safety of oral GED-0301 in subjects with Crohn*s disease

Study design

This is a Phase 3, double-blind, long-term active treatment extension study to evaluate the long-term safety and exploratory efficacy of GED-0301 for 208 weeks in subjects with CD who previously participated in either of the following two Phase 3 GED-0301 studies:
• Study GED-0301-CD-002
• Study GED-0301-CD-003

Intervention

Subjects will receive blinded-active GED-0301 treatment during the 208-week Long-term Active Treatment Period. GED-0301 will be provided as 40-mg film-coated tablets or matching placebo tablets in blister cards.

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

1. Subject is a male or female >= 18 years of age at the time of signing the informed consent form (ICF).;2. Subject must understand and voluntarily sign an ICF prior to any study-related assessments/procedures being conducted.;3. Subject is willing and able to adhere to the study visit schedule and other protocol requirements.;4. Subject must have completed through Week 12 in the previous GED-0301 study AND either:;Completed participation through the last study treatment visit;at Week 52 in Study GED-0301-CD-002 or at Week 12

in Study GED-0301-CD-003 OR Met the *early escape criteria* and were discontinued after Week 12 in Study GED-0301-CD-002.;5. Females of childbearing potential (FCBP) must have a negative pregnancy test at screening and enrollment (Visits 1 and 2). While on IP and for at least 28 days after taking the last dose of IP, FCBP who engage in activity in which conception is possible must use one of the approved contraceptive options ;6. Male subjects when engaging in sexual activity with females who are able to become pregnant must use barrier contraception while on IP and for at least 28 days after the last dose.;Inclusion Criteria for Adolscent Subjects: 1. male or female, 12 to 17
years of age at the time of assent/informed
consent in core GED-0301-CD-003 study and must affirmatively
agree to participate in this study by signing an assent with a
parent/legal guardian who can understand and voluntarily sign an ICF.
Adolescent subjects who turn 18 by the screening visit for GED-0301-CD-004 study must also understand and voluntarily sign an ICF prior to any study-related assessments/procedures being conducted.
2. able to swallow the IP tablets.
3. willing and able to adhere to study visit schedule and protocol requirements, and a parent or legal guardian willing to supervise adherence to protocol requirements.
4. must have completed through the Week 12 Visit in Study GED-0301-CD-003.
5. Females of childbearing potential (FCBP)5 must have a negative pregnancy test at screening and enrollment (Visits 1 and 2). FCBP must either practice true abstinence from heterosexual contact or use one of the approved contraceptive options while on IP and for at least 28 days after taking the last dose of IP.

Exclusion criteria

1. Subject had experienced a serious adverse event related to the IP while participating in the core Phase 3 GED-0301 study.
2. Subject has any continuing serious medical condition, laboratory abnormality, or psychiatric illness that occurred while participating in the core Phase 3 GED-0301 study.
3. Subject has or had a flare or worsening of CD that, in the opinion of the Investigator, would not be in the best interest for the subject to participate in this long-term active treatment study.
4. Subject has initiated biologic agents, such as TNF-α blockers or integrin antagonists while, or after participating in the core Phase 3 GED-0301 study.
5. Subject diagnosed with colorectal cancer or confirmed diagnosis of colorectal dysplasia (with the exception of adenomatous colonic polyps that have been completely resected) while participating in the core Phase 3 GED-0301 study.
6. newly diagnosed malignancy while participating in the previous Phase

3 GED-0301 study.
7. pregnant or breastfeeding.
8. Subject has been newly diagnosed with substance abuse.
9. New condition that may put subject at risk or confound the ability to interpret data from the study.
9. known hypersensitivity to oligonucleotides, GED-0301 or any ingredient in the IP.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-02-2017
Enrollment:	42
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:	11-10-2016
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den

	Haag)
Approved WMO Date:	18-10-2016
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:	30-03-2017
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:	10-05-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-06-2017
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	EUCTR2015-001963-37-NL
CCMO	NL55745.000.16