A Phase 3, Multicenter, Open-Label Extension Study of Oral Ozanimod for Moderately to Severely Active Crohn*s Disease

Published: 12-03-2018
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This study has been transitioned to CTIS with ID 2024-511553-22-00 check the CTIS register for the current data. The objective of this study is to demonstrate the long-term safety and explore tong-term efficacy of ozanimod for the treatment of...

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

Summary

ID

NL-OMON56255

Source
ToetsingOnline

Brief title
Open-Label Extension Study of Ozanimod in patients with Crohn*s Disease

Condition

- Gastrointestinal inflammatory conditions

Synonym
bowel disease, immune-mediated inflammatory disease of the gastrointestinal tract

Research involving
Human

Sponsors and support

Primary sponsor: Celgene International II Sàrl

Source(s) of monetary or material Support: Celgene International II Sàrl

Intervention

Keyword: Crohn's disease, Open-Label Extension

Outcome measures

Primary outcome

Key Efficacy Endpoints:

• Proportion of subjects with a CDAI score of < 150

• Proportion of subjects with a simple endoscopy score (SES-CD) decrease from baseline of >= 50%

• Proportion of subjects with average daily abdominal pain score <= 1 point, and average daily stool frequency <= 3 points with abdominal pain and stool frequency no worse than baseline

• Proportion of subjects with CDAI reduction from baseline of >= 100 points or CDAI score of < 150

• Proportion of subjects with absence of ulcers >= 0.5 cm with no segment with any ulcerated surface >= 10%

• Proportion of subjects with CDAI reduction from baseline of >= 70 points

• Change from baseline in CDAI

• Proportion of subjects with CDAI reduction from baseline of >= 100 points or CDAI score of < 150 and SES-CD decrease from baseline of >=50%

• Proportion of subjects with CDAI score of < 150 and SES-CD <= 4 points and a SES CD decrease >= 2 points

• Proportion of subjects with average daily abdominal pain score <= 1 point and average daily stool frequency <= 3 points and a stool frequency

no worse than baseline and SES-CD <= 4 points and a SES-CD decrease >=2 points

• Proportion of subjects with SES-CD <= 4 points and a SES-CD decrease>= 2 points

• Proportion of subjects with a CDAI score < 150 in subjects offcorticosteroids

• Proportion of subjects with a Crohn's Disease Endoscopic Index of Severity

(CDEIS) decrease from baseline of >= 50%

Secondary outcome

Exploratory Endpoints:

* Proportion of subjects with average daily abdominal pain score <= 1 point,

average daily stool frequency <= 3 points with abdominal pain and stool

frequency no worse than baseline, and SES-CD decrease from baseline >= 50%

* Efficacy in subjects (clinical response, clinical remission, and endoscopic

improvement) as a function of baseline and change from baseline in biomarkers

(eg, C-reactive protein, fecal calprotectin, high-density lipoprotein, IgA,

IL-7, collagen fragments)

• To assess impact of SARS-CoV-2 serologic status on subjects receiving

ozanimod and CD and to support health authority requests.

- Exploratory measurements of SARS-CoV-2 serology (anti-SARS-CoV-2 total or

IgG), from serum samples collected at W48 and annually thereafter.

Study description

Background summary

Crohn*s disease (CD) is an immune-mediated inflammatory disease of the gastrointestinal (GI) tract. Annual incidence varies geographically, with

estimates ranging from 3.1 to 14.6 per 100,000 people in the United States and from 0.1 to 16 per 100,000 worldwide (Lakatos, 2006). Subjects with CD suffer from diarrhea, rectal bleeding, weight loss, abdominal pain, and fever. Crohn*s disease is characterized by a lifelong chronic course of remissions and exacerbations. The pathology of this disease is characterized by transmural infiltration of lymphocytes and macrophages, granulomas, fissuring ulceration, and submucosal fibrosis. The transmural inflammatory process of CD predisposes subjects to the formation of fistulas and it has been estimated that approximately 35% of subjects will have at least 1 fistula during the course of their disease (Schwartz, 2002). In a recent study, within 10 years of diagnosis, 50% of adults with CD had undergone bowel surgery (Peyrin-Biroulet, 2010).
The current standard of medical care for patients with moderately to severely active CD consists of anti-inflammatory approaches, such as corticosteroids, azathioprine (AZA)/6-mercaptopurine (6-MP), methotrexate (MTX), and biologics such as anti-tumor necrosis factor (TNF)α, anti-IL-12/IL-23, or anti-integrins. Immunomodulators aid in corticosteroid withdrawal and in preventing relapse, but also are associated with considerable side effects. Infliximab, an anti-TNFα-therapy, is able to reduce signs and symptoms and induce and maintain remission in the majority of subjects for which it is indicated.
Therefore, there remains considerable unmet medical need for safe, effective, and oral treatments for adult subjects with CD, and the identification of biomarkers that predict response to therapy in a CD patient population with significant genotypic and phenotypic diversity.

Study objective

This study has been transitioned to CTIS with ID 2024-511553-22-00 check the CTIS register for the current data.

The objective of this study is to demonstrate the long-term safety and explore tong-term efficacy of ozanimod for the treatment of subjects with moderately to severely active CD.

Study design

This is a Phase 3, open-label, multicenter extension study to evaluate safety and efficacy of ozanimod in subjects with moderately to severely active CD. Approximately 1200 subjects who have previously participated in a study of ozanimod for CD will be eligible to participate in this study if they meet the eligibility criteria as outlined in the prior study (eg, RPC01-3201, RPC01-3202, RPC01-3203, or RPC01-2201).
Subjects entering the study from RPC01-2201 will continue to receive ozanimod 0.92 mg/day (equivalent to ozanimod
HCl 1 mg). Subjects entering the study from RPC01-3201, RPC01-3202, or RPC01-3203 will initiate ozanimod

treatment in accordance with a 7-day dose escalation regimen starting with ozanimod 0.23 mg (equivalent to ozanimod
HCl 0.25 mg) on Days 1 to 4, followed by ozanimod 0.46 mg (administered as two 0.23 mg capsules, equivalent to
ozanimod HCl 0.5 mg) on Days 5 to 7, and reaching the final dose level, 0.92 mg, on Day 8. Subjects will then receive
ozanimod at 0.92 mg/day for the duration of their participation in the study.

Subjects who are not in clinical response (CDAI [Crohn*s Disease Activity Index] reduction from baseline of >= 100 points or CDAI score of < 150) and/or clinical remission (CDAI score < 150 and/or average stool frequency score <= 3 with a stool frequency no worse than baseline and an average abdominal pain score <= 1) at study entry should be discontinued from investigational product (IP) if they do not show clinical improvement as determined by the investigator by Week 12 of this study. Subjects who discontinue from treatment due to lack of response, adverse events (AEs), or other reasons, even if alternative treatment is given, will be followed for 30 days (with a window up to 45 days) and 75 days (± 10 days)for collection of safety data, including lymphocyte recovery, and for assessment of their disease status.
This study will continue until the end of 2022, until marketing authorization is obtained in the subject*s country, or until the sponsor discontinues the development program, whichever comes first. The end of study is defined as either the date of the last visit of the last subject to complete the safety follow-up, or the date of receipt of the last datapoint from the last subject that is required for primary or secondary analysis, as pre-specified in the protocol, whichever is the later date.

Intervention

Subjects entering the study from RPC01-2201 will continue to receive ozanimod 0.92 mg/day (equivalent to ozanimod
HCl 1 mg). Subjects entering the study from RPC01-3201, RPC01-3202, or RPC01-3203 will initiate ozanimod
treatment in accordance with a 7-day dose escalation regimen starting with ozanimod 0.23 mg (equivalent to ozanimod
HCl 0.25 mg) on Days 1 to 4, followed by ozanimod 0.46 mg (administered as two 0.23 mg capsules, equivalent to
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ozanimod at 0.92 mg/day for the duration of their participation in the study.

Study burden and risks

Patients may experience drug-related side effects. For full list of side effects please refer to Appendix D of the main patient information sheet and infomed consent from. In addition to side effects patients may experience

discomforts and risks associated with the study procedures such as blood drawing, endoscopies.

Contacts

Public
Celgene International II Sàrl

Route de Perreux 1
Boudry 2017
CH
Scientific
Celgene International II Sàrl

Route de Perreux 1
Boudry 2017
CH

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Subjects must satisfy the following criteria to be enrolled in the study:
1. Subjects who are not in clinical response and/or clinical remission after completing 12 weeks in the Induction Studies RPC01-3201 or RPC01-3202, subjects who experience relapse in the Maintenance Study RPC01-3203, subjects who complete the Maintenance Study RPC01-3203, subjects who complete at least 1 year of RPC01 2201.
2. Subject should not have any constraints under local regulations, must provide written informed consent prior to any studyrelated procedures,

and must have the ability to comply with the Table of Events.
3. Female subjects of childbearing potential (FCBP):
Note: For the purposes of this study, a female subject is considered to be of childbearing potential if she 1) has not undergone a hysterectomy (the surgical removal of the uterus) or bilateral oophorectomy (the surgical removal of both ovaries) or 2) has not been postmenopausal for at least 24 consecutive months (that is, has had menses at any time during the preceding 24 consecutive months).
Must agree to practice a highly effective method of contraception throughout the study until completion of the 90-day Safety Follow-up Visit. Highly effective methods of contraception are those that alone or in combination result in a failure rate of a Pearl Index of less than 1% per year when used consistently and correctly. Examples of acceptable methods of birth control in the study are the following:
• combined hormonal (containing oestrogen and progestogen) contraception, which may be oral, intravaginal, or transdermal
• progestogen-only hormonal contraception associated with inhibition of ovulation, which may be oral, injectable, or implantable
• placement of an intrauterine device (IUD)
• placement of an intrauterine hormone-releasing system (IUS)
• bilateral tubal occlusion
• vasectomized partner
• complete sexual abstinence
Periodic abstinence (calendar, symptothermal, post-ovulation methods), withdrawal (coitus interruptus), spermicides only, and lactational amenorrhoea method are not acceptable methods of contraception.
Female condom and male condom should not be used together.
Counseling about pregnancy precautions and the potential risks of fetal exposure must be conducted for FCBP. The Investigator will educate all FCBP about the different options of contraceptive methods or abstinence at Day 1, as appropriate.
The subject will be re-educated every time her contraceptive measures/methods or ability to become pregnant changes. The female subject's chosen form of contraception must be effective by the time the female subject starts the study (for example, hormonal contraception should be initiated at least 28 days before Day 1).

Exclusion criteria

The presence of any of the following will exclude a subject from enrollment:
4.3.1. Exclusions Related to General Health:
1. Subject has any clinically relevant cardiovascular, hepatic, neurological, pulmonary [severe respiratory disease (pulmonary fibrosis or chronic obstructive pulmonary disease)], ophthalmological,

endocrine, psychiatric, or other major systemic disease making implementation of the protocol or interpretation of the study difficult or that would put the subject at risk by participating in the study.
2. Subject is pregnant, lactating, or has a positive urine beta human chorionic gonadotropin (β-hCG) test.
3. Subject has suspected or diagnosed intra-abdominal or perianal abscess that has not been appropriately treated.
4.3.2. Exclusions Related to Medications:
4. Hypersensitivity to active ingredients or excipients of ozanimod
5. Subject has received any of the following therapies since the first dose of IP in the prior ozanimod study:
• treatment with a biologic agent as well as other treatments for CD such as etrasimod, filgotinib, upadacitinib
• treatment with an investigational agent other than ozanimod
• treatment with D-penicillamine, leflunomide, thalidomide, natalizumab, fingolimod or other S1P modulators
• treatment with lymphocyte-depleting therapies (eg, Campath®, anti-CD4, cladribine, rituximab, ocrelizumab, cyclophosphamide, mitoxantrone, total body irradiation, bone marrow transplantation, alemtuzumab, daclizumab)
6. Subject is currently receiving or requires initiation of any of the following therapies:
• treatment with corticosteroids at a dose that exceeds the prednisone equivalent of >40 mg
• treatment with immunomodulatory agents (eg, AZA, 6-MP, or MTX)
• chronic non-steroidal anti-inflammatory drug (NSAID) use (note: occasional use of NSAIDs and acetaminophen [eg, headache, arthritis, myalgias, or menstrual cramps] and aspirin up to 325 mg/day is permitted)• treatment with Class Ia or Class III anti-arrhythmic drugs, treatment
with 2 or more agents in combination known to prolong PR interval, or treatment with additional prohibited systemic cardiac medication
• treatment with breast cancer resistance protein (BCRP) inhibitors (eg, cyclosporine, eltrombopag)
7. Subject is receiving treatment with any of the following drugs or interventions within the corresponding timeframe:
• CYP2C8 inhibitors (eg, gemfibrozil or clopidogrel) and inducers (eg, rifampicin)
• Monoamine oxidase inhibitors (eg, selegiline, phenelzine)
4.3.3. Exclusions Related to Laboratory Results and Other Assessments:
8. Subject has any clinically significant abnormal results (eg, labs or ECG) which, in the opinion of the Investigator, may put the subject at risk.
9. Subjects has a pre-dose resting HR < 55 bpm. One recheck is allowed at the Day 1 visit. If HR remains < 55 bpm at Day 1, one additional recheck is allowed at a later date within the available window for

rollover from the previous study.

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):	05-03-2020
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ozanimod
Generic name:	ozanimod

Ethics review

Approved WMO Date:	12-03-2018
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	22-10-2018
Application type:	First submission
Review commission:	METC Brabant (Tilburg)

Approved WMO Date:	04-02-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	20-02-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	05-03-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	11-03-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	25-07-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	01-08-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	11-09-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	01-10-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	17-12-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO	

Date:	16-03-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	21-07-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	22-07-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	05-01-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	22-02-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	24-03-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	26-03-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	26-06-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	12-07-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO	

Date:	26-07-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	17-10-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	01-11-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	18-01-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	07-02-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	06-04-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	11-04-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	21-04-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	10-05-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO	

Date:	27-07-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	17-08-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	26-10-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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
EU-CTR	CTIS2024-511553-22-00
EudraCT	EUCTR2017-004295-55-NL
CCMO	NL65022.028.18