An Open Label Extension Study of Etrasimod in Subjects with Moderately to Severely Active Ulcerative Colitis

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

Summary

ID

NL-OMON54866

Source
ToetsingOnline

Brief title
ELEVATE UC OLE (APD334-303)

Condition

- Gastrointestinal inflammatory conditions

Synonym
Ulcerative colitis

Research involving
Human

Sponsors and support

Primary sponsor: Arena Pharmaceuticals, Inc.
Source(s) of monetary or material Support: Industry

Intervention

Keyword: Ulcerative Colitis

Outcome measures

Primary outcome

The long-term safety profile of etrasimod will be assessed through the following:

* Incidence of treatment emergent adverse events (TEAEs) and serious adverse events (SAEs)

* Incidence and severity of laboratory abnormalities, and change from baseline in laboratory values (hematology, serum chemistry, coagulation, and urinalysis)

* Incidence of vital sign abnormalities and changes from baseline

Secondary outcome

* The proportion of subjects achieving clinical remission at each of the following weeks: Weeks 52, 104, 156, 208, and 260, among subject achieving clinical remission at study entry

* The proportion of subjects achieving clinical response at each of the following weeks: Weeks 52, 104, 156, 208, and 260

* The proportion of subjects achieving symptomatic remission at Weeks 52, 104, 156, 208, and 260

* The proportion of subjects achieving non invasive clinical response at each of the following weeks: Weeks 12, 24, 36, 52, 104, 156, 208, and 260

* The proportion of subjects achieving in clinical remission at the following weeks: Weeks 12, 52, 104, 156, 208, and 260, among subject achieving clinical remission at study entry

* The proportion of subjects achieving symptomatic response at Weeks 12, 24,

36, 52, 104, 156, 208, and 260

* Longitudinal change from both OLE and parent study baseline in SF, RB, and SF

+ RB at each of the following weeks: Weeks 12, 24, 36, 52, 104, 156, 208, and

260

* The proportion of subjects achieving endoscopic improvement at each of the

following weeks: Weeks 52, 104, 156, 208, and 260

Study description

Background summary

Crohn*s disease (CD) and ulcerative colitis (UC) are chronic recurrent, remittent, or progressive inflammatory conditions that may affect the entire gastrointestinal tract (CD) and the colonic mucosa (UC), and are associated with an increased risk for colon cancer. Treatment for subjects with UC is generally for symptomatic care (relief of symptoms) and mucosal healing and includes 5 major classes of medications: 5 aminosalicylic acid (5 ASA), antibiotics, corticosteroids, immunomodulators, biologic therapies (eg, tumor necrosis factor [TNF] inhibitors and anti integrins) and most recently Janus kinase (JAK) inhibitor therapy.
An unmet medical need exists for the development of targeted therapies for the treatment of UC with easily administered and stable oral drugs, particularly as most patients treated with biologics experience inadequate responses or lose responsiveness over time, even though their initial response may have been positive.
Etrasimod (APD334) is an orally administered, selective, synthetic sphingosine 1 phosphate (S1P) receptor 1, 4, 5 modulator that is being developed to treat immune-mediated inflammatory disorders, including UC. A Phase 2 study with etrasimod in subjects with moderately to severely active UC demonstrated consistent and clinically meaningful improvements in endpoint measures reflecting cardinal symptoms of UC and objective findings of endoscopic improvement.

Study objective

The primary objective is to the safety of long term administration of etrasimod in subjects with moderately to severely active UC. The secondary objective is

to assess the the long-term efficacy of etrasimod in subjects with moderately to severely active UC.

Study design

This is a multicenter, open label extension (OLE) study to evaluate the safety and efficacy of etrasimod in subjects with moderately to severely active UC who previously received double blinded treatment (either etrasimod 2 mg/day or placebo) during participation in one of two Phase 3 double blinded, placebo controlled studies (either Study APD334 301, APD334 302 and/or any other qualified region-specific studies).
Subjects are eligible for enrollment into the OLE study only if they completed Study APD334 301 (ie, through Week 52) or they met any of the criteria related to disease worsening as detailed in the inclusion criteria or completed Study APD334 302 (through Week 12).
The OLE study consists of:
1. An Open Label Treatment Period (up to 260 weeks [up to 5 years]) and
2. A 2 Week and 4-Week Follow Up visit (2 weeks and 4 weeks, respectively, after Week 260/End of Treatment [EoT] visit).
All subjects will receive etrasimod 2 mg once daily for up to 260 weeks (up to 5 years) or until marketing authorization is obtained in their country.

Intervention

Etrasimod, 2 mg tablets, by mouth, once daily.

Study burden and risks

Common adverse events that have been reported with S1P receptor modulators include bradycardia at the first dose or atrioventricular (AV) block, macular edema, hypertension, headache, cough, dyspnea, back pain, influenza, and diarrhea.
Safety and tolerability of etrasimod has been evaluated in Phase 1 studies with healthy adult subjects at single doses up to 5 mg and repeat doses up to 3 mg once daily and in Phase 2 studies in subjects with UC (refer to the latest IB). Etrasimod was found to be safe and well tolerated in these studies, with no clinically significant safety concerns with respect to vital signs, electrocardiograms (ECGs), pulmonary function tests (PFTs), ophthalmoscopy, or clinical laboratory tests. Etrasimod produced a dose dependent sustained decrease in total lymphocyte count, which is expected given etrasimod*s mechanism of action. Lymphocyte counts returned to approximately baseline levels within 7 days after the last dose.
25 visits will take place in 5 years. If the subject completes all visites, a total amount of 572 ml of blood will be drawn. Participant will have at least one proctosigmoidoscopy/colonoscopy, biopsy, eye examination (ophthalmoscopy)

and optical coherence tomography (OCT) performed throughout the study.

Contacts

Public
Arena Pharmaceuticals, Inc.

Nancy Ridge Drive 6154
San Diego CA 92121
US
Scientific
Arena Pharmaceuticals, Inc.

Nancy Ridge Drive 6154
San Diego CA 92121
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Must have met the eligibility criteria and have been enrolled in one of the two Phase 3 studies (APD334-301 or APD334-302) or other qualified region-specific studies and also meet the following additional criteria:
a. Subjects previously enrolled in Study APD334-301 must have either:
I. Completed the Week 12 visit whose UC condition in the opinion of the Investigator has not improved or has worsened, compared with baseline (Week 0/Day 1), may be eligible to entroll provided their ES is is * 2 and they meet one of the following criteria:

* Rectal bleeding (RB) subscore * 2 at 2 timepoints at least 7 days and no more than 14 days apart
* RB + stool frequency (SF) subscore * 4 at 2 timepoints at least 7 days and no more than 14 days apart
* RB subscore * 2 or RB + SF subscores * 4 (in any order) at 2 timepoints at least 7 days and no more than 14 days apart
or
II. Completed the Week 52 visit
Note: For subjects discontinuing prior to Week 52, an endoscopic evaluation is required to confirm eligibility for the OLE. An endoscopy should be scheduled upon the appearance of UC symptoms but no more than 14 days after the second timepoint for entry criteria above. A proctosigmoidoscopy does not need to be repeated if performed within the last 4 weeks
b. Subjects previously enrolled in APD334-302 must have completed the Week 12 visit
2. Eligible women of childbearing potential must fulfill the following on Day 1:
a. Have a negative urine beta human chorionic gonadotropin (*-hCG) pregnancy test
b. Not breastfeeding
3. Females must meet either a or b of the following criteria and males must meet criterion c to qualify for the study:
a. A female who is not of childbearing potential must meet 1 of the following:
- Postmenopausal, defined as no menses for 12 months without an alternative medical cause;
- Permanent sterilization procedure, such as hysterectomy, bilateral salpingectomy, or bilateral oophorectomy.
b. A female of childbearing potential must agree to using a highly effective contraception method during treatment and for 30 days following treatment that can achieve a failure rate of less than 1% per year when used consistently and correctly.
The following are considered highly effective birth control methods:
- Combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation, which may be oral, intravaginal, or transdermal.
- Progestogen-only hormonal contraception associated with inhibition of ovulation, which may be oral, injected, or implanted.
- Intrauterine device (IUD).
- Intrauterine hormone-releasing system.
- Bilateral tubal occlusion.
- Vasectomized partner, provided that partner is the sole sexual partner of the WOCBP trial participant and that the vasectomized partner has received medical assessment of the surgical success.
- Sexual abstinence (complete sexual abstinence defined as refraining from heterosexual intercourse for the entire period of risk associated with study treatments). The reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical study and the preferred and usual lifestyle of the subject.

Periodic abstinence (calendar, symptothermal, post-ovulation methods) is not acceptable.
c. A male must agree to using condoms during treatment and for 4 weeks following treatment.
4. Ability to provide written informed consent or assent (parent or legal guardian must provide consent for a subject < 18 years of age or as required per local regulations who has assented to participate in the study) and to be compliant with the schedule of protocol assessments. Enrollment of subjects < 18 years should be conducted only if acceptable according to local laws and regulations.

Exclusion criteria

Subjects who meet ANY of the following exclusion criteria will NOT be eligible for enrollment into the study:
1. If the Investigator considers the subject to be unsuitable for any reason to participate in the OLE study

Exclusions related to general health:
2. Experienced an adverse event that led to discontinuation (except when such an event is related to UC flare) from parent study
3. Day 1 pre-dose sitting vital sign assessment: heart rate (HR) < 50 bpm OR systolic blood pressure (BP) < 90 mm Hg OR diastolic BP < 55 mm Hg
4. Day 1 pre-dose 12-lead electrocardiogram (ECG) in the supine position showing a second or third-degree AV block, periods of asystole > 3 seconds, PR interval > 200 ms, or Fridericia's corrected QT interval (QTcF) * 450 ms (men) or QTcF * 470 ms (women)
5. Subjects requiring partial or total colectomy during the parent study
6. Subjects requiring treatment with prohibited concomitant medications as defined in the parent 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):	17-11-2019
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Etrasimod
Generic name:	Etrasimod

Ethics review

Approved WMO Date:	22-08-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-10-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-05-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-08-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-12-2020

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-03-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-11-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-11-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2018-003987-29-NL
Other	IND 125154
CCMO	NL70302.056.19