A Phase 2 Randomized, Double-Blind, Placebo-Controlled Study to Assess the Safety and Efficacy of Etrasimod in Adult Subjects with Eosinophilic Esophagitis

Published: 26-11-2020
Last updated: 08-04-2024

Primary:* To evaluate the effects of etrasimod on esophageal eosinophilia in adult subjects with active eosinophilic esophagitis (EoE)* To evaluate the dose-response relationship of 2 doses of etrasimod versus placebo in adult subjects with active...

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

Summary

ID

NL-OMON52257

Source
ToetsingOnline

Brief title
APD334-206

Condition

- Gastrointestinal inflammatory conditions

Synonym
EoE, Eosinophilic Esophagitis

Research involving
Human

Sponsors and support

Primary sponsor: Arena Pharmaceuticals Inc.

Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: Efficacy, Eosinophilic Esophagitis, Etrasimod, Safety

Outcome measures

Primary outcome

Percent change from Baseline in esophageal PEC at Week 16

Secondary outcome

* Absolute change from Baseline in DSQ score at Week 16

* Absolute change from Baseline in esophageal PEC at Week 16

* Proportion of subjects with esophageal PEC < 15 eos/hpf at Week 16

* Proportion of subjects with esophageal PEC * 6 eos/hpf at Week 16

Study description

Background summary

EoE is a chronic and progressive, allergen-driven, immune-mediated disease of the esophagus, with risk factors including atopy and other allergic diseases, including asthma, allergic rhinitis, and atopic dermatitis. Histologically, EoE is characterized by the accumulation of eosinophils in the lining of the esophagus, a tissue that under normal conditions lacks these cells. The presence of these eosinophils has been shown to have a direct effect on immune function and tissue damage. The eosinophilic predominant inflammation characteristic of EoE results in a variety of symptoms including but not limited to difficulty swallowing (dysphagia and/or odynophagia) and regurgitation, central chest pain, upper abdominal pain, food impaction, food refusal, and malnutrition. Current treatment options for EoE are dietary, pharmacologic, or endoscopic in nature. These treatments are subject to a variety of disadvantages including difficulty in adhering to dietary therapy, potential safety concerns associated with long-term use of systemic corticosteroids, lack of efficacy of topical steroids in some steroid-refractory patients, and invasiveness and risks of endoscopic treatment, including esophageal dilation. Therefore, there is a need to develop and find new long-term, safe and effective treatments for people with

EoE.
Etrasimod (APD334) is an orally administered, selective modulator of S1P receptors 1, 4, 5 that is being developed to treat immune-mediated inflammatory disorders (IMIDs). Etrasimod is a substance designed to block the movement of lymphocytes to areas of inflammation. By blocking this movement etrasimod may reduce inflammation of the esophagus, leading to an improvement in the symptoms of EoE.

Study objective

Primary:
* To evaluate the effects of etrasimod on esophageal eosinophilia in adult subjects with active eosinophilic esophagitis (EoE)
* To evaluate the dose-response relationship of 2 doses of etrasimod versus placebo in adult subjects with active EoE
* To select an etrasimod dose based on efficacy and safety for continued development
Secondary:
* To evaluate the effect of etrasimod on dysphagia symptoms in adult subjects with active EoE

Study design

This Phase 2, randomized, double-blind, multi-center study will evaluate the efficacy, safety, and pharmacokinetics (PK) of etrasimod compared with placebo in adults with active EoE.
The study will consist of a Screening Period of up to 28 days, 24 weeks of double-blind treatment (Double-Blind Treatment Period), 28 weeks of active extended treatment (Extension Treatment Period), and 4 weeks of follow-up (Safety Follow-Up Period) for a total study duration of up to 60 weeks.
Eligible subjects will be randomized in a double-blind fashion (3:3:2 ratio) to etrasimod 1 mg, etrasimod 2 mg, or matching placebo once daily. Randomization will be stratified by baseline history of esophageal dilation (yes/no) and concurrent proton pump inhibitor (PPI) therapy (yes/no).

Intervention

During the Double-Blind Treatment Period, eligible subjects will be randomized in a double-blind fashion (3:3:2 ratio) to etrasimod 1 mg, etrasimod 2 mg, or matching placebo once daily. Subjects who were in the etrasimod 1 mg or etrasimod 2 mg groups in the Double-Blind Treatment Period will continue the same etrasimod dose in the Extension Treatment Period. Subjects who were in the placebo group during the Double-Blind Treatment Period will be re-randomized (1:1 ratio) to etrasimod 1 mg or etrasimod 2 mg at entry into the Extension Treatment Period.

Study burden and risks

Subject's participation will last a total of approximately 57 weeks (1 year and 1 month) and consists of 4 periods: a screening period to determine eligibility to participate, a 24-week treatment period, a 28-week extension treatment period, and a 4-week follow-up period. Aside from the intervention described above, participation in this study involves blood draws at multiple visits, biopsy and endoscopies. Participants will also be subjected to: questions regarding medical history, use of concomitant medications/procedures and adverse events; measurement of vital signs; physical examination; eye tests; pulmonary functions tests; ECGs, Esophagogastroduodenoscopy (EGD); eDiary reporting and patient reported outcomes questionnaires.

The most common side effects seen in healthy volunteers were headache, dizziness, mouth ulcers, skin rash caused by direct contact of the skin with a substance, constipation, diarrhea, and a reduction in white blood cell counts (the blood cells that help to fight infection). There were episodes of slower heart rate after the first dose and changes in heart rhythm, but participants did not feel any symptoms. This effect of etrasimod on the heart is a known effect and it generally improved over time. The most common side effects seen in patients with UC were upper respiratory tract infection, nasopharyngitis (the common cold), anemia (low numbers of red blood cells), and headache. Slower heart rate without feeling symptoms after the first dose, changes in heart rhythm, and a reduction in white blood cell counts were also observed. When patients with UC received etrasimod for longer (up to 52 weeks), some of the patients experienced increased anemia and increased gamma-glutamyl transferase (GGT).

The safety profile of etrasimod coupled with a potent effect on the lymphocyte count demonstrate that etrasimod may be an effective oral treatment option for IMIDs such as EoE. Based on the favorable clinical safety and efficacy data that has been generated from etrasimod studies in healthy adults and subjects with UC, the precautions outlined above, and the current lack of safe and effective long-term oral medications for the treatment of EoE, the benefit/risk assessment justifies the further clinical development of etrasimod in subjects with EoE and the current Phase 2 study multi-center, randomized, double-blind, placebo-controlled study.

Contacts

Public
Arena Pharmaceuticals Inc.

Nancy Ridge Drive 6154

San Diego, California 92121
US
Scientific
Arena Pharmaceuticals Inc.

Nancy Ridge Drive 6154
San Diego, California 92121
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Key Inclusion Criteria
* Men or women between 18 and 65 years of age at the time of informed consent (IC)
* Have an EoE diagnosis prior to screening and histologically active disease with an esophageal peak eosinophil count (PEC) of * 15 eosinophils (eos)/high power field (hpf) (~60 eos/mm2) from any level (proximal, mid, or distal) of the esophagus at the Screening esophagogastroduodenoscopy (EGD).
* Have dysphagia, defined as solid food going down slowly or getting stuck in the throat with an average frequency of * 2 episodes per week over 2 weeks (as documented using the Dysphagia Symptom Questionnaire (DSQ) during the Screening period)

Exclusion criteria

Key Exclusion Criteria
* History of any of the following non-EoE conditions or procedures that may interfere with the evaluation of or affect the histologic, endoscopic, or symptom endpoints of the study:
a. Conditions that substantially contribute to esophageal eosinophilia (eg

eosoinophilic, gastroenteritis, or enteritis [ie, eosinophilic duodenitis or colitis] with esophageal involvement, achalasia, hypereosinophilic syndrome, Crohn's disease [CD] with esophageal involvement, esophageal infection [fungal, viral], eosinophilic granulomatosis with polyangitis (formally known as Churg-Strauss Syndrome), pemphigus with esophageal involvement, pill esophagitis, graft versus host disease, Mendelian disorders [eg, Marfan syndrome Type II, hyper-immunoglobulin E (IgE) syndrome, phosphatase and tensin homolog (PTEN) hamartoma tumor syndrome, Netherton syndrome, severe atopy metabolic wasting (SAM) syndrome])
b. Conditions that interfere with the evaluation of the esophagus (eg, esophageal varices with risk of spontaneous bleed, high-grade esophageal stenosis where an 8- to 10-mm endoscope could not pass through the stricture without dilation at the time of Screening EGD)
c. Conditions or procedures substantially contribute to dysphagia (eg, histologically active Barrett's, active, esophagitis, erosive esophagitis Los Angeles Grade B or above, significant hiatal hernia [* 4 cm], esophageal resection)
* Undergone dilation of an esophageal stricture within 12 weeks prior to Screening EGD.
* Use of corticosteroids for the treatment of EoE within 8 weeks prior to Screening EGD.
* Discontinue, initiate, or change dosing (dosage/frequency) of the following therapies for EoE within 8 weeks prior to Screening EGD.
Subjects on any of the following therapy need to stay on a stable regimen during study participation:
a. Elemental diet
b. EoE food trigger elimination diet
c. PPI therapy

Study design

Design

Study phase:	2
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):	22-02-2021
Enrollment:	5
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	26-11-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-02-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-04-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-05-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-04-2022

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-04-2022
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	EUCTR2020-003226-23-NL
CCMO	NL74899.056.20