A Study Evaluating the Efficacy and Safety of Etrasimod in the Treatment of Patients With Moderately to Severely Active Crohn's Disease

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Main Information

Primary registry identifying number
LBCTR2020114568

Protocol number
APD334-202

MOH registration number

Study registered at the country of origin
Yes

Study registered at the country of origin: Specify

Type of registration
Prospective

Type of registration: Justify
N/A

Date of registration in national regulatory agency

Primary sponsor
Arena Pharmaceuticals Inc.

Primary sponsor: Country of origin
United States of America

Date of registration in primary registry
20/04/2022

Date of registration in national regulatory agency

Public title
A Study Evaluating the Efficacy and Safety of Etrasimod in the Treatment of Patients With Moderately to Severely Active Crohn's Disease

Acronym

Scientific title
A Phase 2b, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study to Assess the Efficacy and Safety of Oral Etrasimod as Induction Therapy in Subjects With Moderately to Severely Active Crohn's Disease

Acronym

Brief summary of the study: English
The purpose of this study is to evaluate the dose-response relationship of two doses of Etrasimod versus placebo as induction therapy in participants with moderately to severely active Crohn's disease and to select an oral Etrasimod dose, based on efficacy and safety, for continued development.

Brief summary of the study: Arabic
الغرض من هذه الدراسة هو تقييم العلاقة بين الجرعة والاستجابة لجرعتين من Etrasimod مقابل الدواء الوهمي كعلاج تحريضي في المشاركين المصابين بمرض كرون النشط بشكل معتدل إلى شديد، واختيار جرعة Etrasimod عن طريق الفم، بناءً على الفعالية والسلامة، من أجل التطوير المستمر.

Health conditions/problem studied: Specify
Crohn's Disease

Interventions: Specify
Drug: Etrasimod (APD334)
Drug: Placebo

Key inclusion and exclusion criteria: Inclusion criteria

1. Subjects 18 to 80 years of age, inclusive, at the time of consent.
2. Ability to provide written informed consent and to be compliant with the schedule of protocol assessments.
3. Have CD for ≥ 3 months prior to randomization, involving the ileum and/or colon, at a minimum; diagnosis may be confirmed at any time in the past by endoscopy and/or histopathology. The screening endoscopy and histopathology reports may serve as source documents for subjects who do not have diagnostic endoscopy reports in their medical chart.
4. Have moderately to severely active CD at Screening, defined as:
a. CDAI score ≥ 220 and ≤ 450, AND
b. Unweighted average worst daily AP score ≥ 2 OR unweighted average daily loose/watery SF score ≥ 4, AND
c. SES-CD of ≥ 6 or SES-CD ≥ 4 for subjects with isolated ileal disease
5. Demonstrated inadequate response, loss of response to, or intolerance to ≥ 1 of the following therapies for the treatment of CD:
a. Oral corticosteroids (eg, prednisone or its equivalent, budesonide)
b. Immunosuppressants (eg, azathioprine [AZA], 6-mercaptopurine [6-MP], or methotrexate [MTX])
c. Tumor necrosis factor alpha (TNFα) antagonists (eg, infliximab, adalimumab, certolizumab pegol, or biosimilars)
d. Integrin receptor antagonist (eg, vedolizumab)
e. Interleukin-12/-23 antagonist (eg, ustekinumab)
6. Females of childbearing potential must be nonpregnant evidenced by a negative serum beta-human chorionic gonadotropin (β-hCG) pregnancy test at Screening and negative urine dipstick pregnancy test at Day 1.
7. 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 and confirmed by follicle-stimulating hormone (FSH) within postmenopausal range according to local standards;
− Permanent sterilization procedure, such as hysterectomy, bilateral salpingectomy, or bilateral oophorectomy.
b. A female who is of childbearing potential must agree to using a highly effective contraception method during treatment and for 4 weeks 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 (IUS).
− Bilateral tubal occlusion.
− Vasectomized partner, provided that partner is the sole sexual partner of the woman of childbearing potential (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.

Key inclusion and exclusion criteria: Gender

Both

Key inclusion and exclusion criteria: Specify gender

Key inclusion and exclusion criteria: Age minimum

18

Key inclusion and exclusion criteria: Age maximum

80

Key inclusion and exclusion criteria: Exclusion criteria

1. History of inadequate response (ie, primary non-response) to agents from ≥ 2 classes of biologics marketed for the treatment of CD (ie, TNFα antagonists, interleukin-12/-23 antagonist, and integrin receptor antagonist).
2. Have stopped, started, or changed the dosage of oral 5-ASA compounds ≤ 2 weeks prior to randomization or do not intend to maintain the same dose during the study.
3. Have stopped, started, or changed the dosage of oral corticosteroids (prednisone ≤ 20 mg/day or its equivalent, budesonide ≤ 9 mg/day) ≤ 2 weeks prior to randomization.
4. Have a confirmed absolute lymphocyte count < 800 cells/mm3 (< 0.8 × 109 cells/L) at Screening or confirmed absolute neutrophil count < 1000 cells/mm3 (< 1.0 × 109 cells/L) at

Screening.
5. Have confirmed aspartate aminotransferase (AST) or alanine aminotransferase (ALT) > 2 × upper limit of normal (ULN) and total bilirubin > 1.5 × ULN (unless consistent with a history of Gilbert's syndrome) at Screening.
6. Used any of the following therapies within the timeframes prior to randomization indicated below:
• Within 2 weeks: AZA, 6-MP, MTX, adalimumab or biosimilar (unless there is documentation of an undetectable biologic level), antibiotics (eg, metronidazole, ciprofloxacin) used for the treatment of CD.
• Within 4 weeks: Infliximab, certolizumab, vedolizumab, ustekinumab or biosimilars (unless there is documentation of an undetectable or subtherapeutic biologic trough level according to the American Gastroenterological Association 2017 Guidelines for Therapeutic Drug Monitoring, or in the Investigator's opinion, if target trough concentrations have not been proposed), therapeutic apheresis, total parenteral nutrition, IV corticosteroids, or medications that are known to be moderate or strong inhibitors or inducers of cytochrome P450 (CYP) 2C8, CYP2C9, or UGT1A7.
• Within 8 weeks: 6-Thioguanine, systemic lymphocyte suppressive therapy (eg, cyclosporine, mycophenolate mofetil), or intravenous (IV) immunoglobulin
• Within 12 weeks: Any investigational agent or device
• Within 48 weeks: Mesenchymal stem cell transplant (eg, Prochymal)
• Any time prior to randomization: Sphingosine-1 phosphate receptor modulators (eg, fingolimod, siponimod), α4β1-integrin receptor antagonist (eg, natalizumab), lymphocyte-depleting therapies (eg, rituximab, cyclophosphamide, bone marrow transplantation, total body irradiation)
7. Have a known hypersensitivity to etrasimod or any of the excipients.
8. Have ulcerative colitis, indeterminate colitis, microscopic colitis, ischemic colitis, radiation colitis, diverticular disease-associated colitis, toxic megacolon, or active infectious colitis or test positive for Clostridium difficile (C. difficile) toxin at Screening. NOTE: Subjects with C. difficile colitis who have been treated with documented evidence of C. difficile toxin clearance ≥ 2 weeks prior to randomization and are symptomatically stable, in the opinion of the Investigator, are eligible for enrollment.
9. Have functional or post-operative short bowel syndrome (ie, have > 3 small bowel resections) or any associated complications that may require surgery or interfere with efficacy assessments (eg, intestinal stricture with obstructive symptoms, colonic stenoses that are not passable with an adult colonoscope, active perianal/intra-abdominal abscess, active fistula [except for perianal fistula], fulminant colitis).
10. Had surgical treatment for intra-abdominal abscesses ≤ 8 weeks prior to randomization or surgical treatment for perianal abscesses ≤ 4 weeks prior to randomization.
11. Had intestinal resection ≤ 24 weeks prior to randomization or other intra-abdominal surgeries ≤ 12 weeks prior to randomization.
12. Have an ileostomy or a colostomy.
13. Have a serious infection requiring IV antibiotics/medication(s) ≤ 4 weeks prior to randomization.
14. Have any of the following conditions or risk factors:
a. Primary or secondary immunodeficiency syndromes (eg, hereditary immunodeficiency syndrome, AIDS)
b. History of organ transplant (except corneal transplant)
c. History of an opportunistic infection (eg, cryptococcal meningitis, progressive multifocal leukoencephalopathy)
d. History of disseminated herpes simplex or herpes zoster or ≥ 2 episodes of herpes zoster
e. Known to have or test positive for human immunodeficiency virus (HIV; positive HIV antibody), hepatitis B virus (HBV; positive hepatitis B surface antigen or core IgM antibody), or active hepatitis C virus (HCV; positive hepatitis C antibody with detectable HCV RNA)
NOTE: If the Investigator suspects false positive hepatitis serology results, such as an antibody pattern indicating acute hepatitis infection but no corresponding elevated liver enzymes and no signs or symptoms of liver disease, an infectious disease expert may be consulted. If the infectious disease expert finds no evidence of acute or chronic hepatitis infection and considers the serology results false positive and not clinically relevant, the Investigator may document (in source data and in the electronic case report form [eCRF]) that the serology results are considered false positive and may randomize the subject.
f. History of active or latent tuberculosis (TB). The following is the EXCEPTION to this exclusion criterion.
− Subjects with treated latent TB or latent TB diagnosed at Screening who have received ≥ 2 weeks of TB prophylaxis treatment prior to randomization, ruled out for active TB, and have not had recent close contact with a person with active TB. It is the responsibility of the Investigator to verify the adequacy of TB prophylaxis treatment and provide appropriate documentation. NOTE: The exception to the exclusion criterion outlined above does NOT apply to subjects residing in countries identified by the World Health Organization (WHO) as a high multi-drug resistance (MDR) TB burden country due to the risk of latent infection with MDR TB.
15. Received a live or live-attenuated vaccine (except the influenza vaccine) ≤ 4 weeks prior to randomization.
16. Have not received varicella zoster virus (VZV) vaccination prior to randomization, unless the

subject has a documented positive VZV immunoglobulin (Ig) G status. NOTE: VZV vaccination requirement is applicable to subjects residing in countries where the vaccine is approved/licensed and can be safely administered per product labeling (refer to indication/usage/warnings/contraindications).
17. Subjects with high risk for colorectal cancer (eg, family history, CD duration, disease involving ≥ 30% of the colon), who have not had a surveillance colonoscopy ≤ 12 months prior to randomization to rule out polyps, colorectal dysplasia/neoplasia. In the absence of a recent history of surveillance colonoscopy, this may be done as part of the screening colonoscopy. Any visualized adenomatous polyps must be removed, and any suspicious lesions must be confirmed free of dysplasia and/or malignancy prior to baseline.
18. History of malignancy of any organ system (other than localized basal cell carcinoma of the skin that have been excised or resolved), treated or untreated, within the past 5 years, regardless of whether there is evidence of local recurrence or metastases.
19. Have active epilepsy.
20. Have any of the following conditions or receiving treatments that may affect cardiovascular function:
a. Myocardial infarction, unstable angina, stroke/transient ischemic attack, decompensated heart failure requiring hospitalization or Class III/IV heart failure ≤ 8 weeks prior to randomization.
b. 2nd degree or 3rd degree atrioventricular (AV) block, sick sinus syndrome without a functional pacemaker, or periods of asystole for > 3 seconds without an implanted cardiac defibrillator.
c. Recurrent symptomatic bradycardia or recurrent cardiogenic syncope.
d. Screening and Day 1 pre-randomization vital signs (taken in the sitting position) with a heart rate (HR) < 50 beat per minute (bpm) AND systolic blood pressure (BP) < 90 mm Hg OR diastolic BP < 55 mm Hg. Vital signs may be repeated up to 3 times during a visit to confirm abnormal readings.
e. Screening and Day 1 pre-randomization electrocardiogram (ECG) with PR interval ≥ 220 ms or Fridericia's corrected QT interval (QTcF) ≥ 450 ms in males or ≥ 470 ms in females.
f. Receiving Class Ia or Class III anti-arrhythmic drugs.
g. Start, stop, or change dosage of Class Ib, II, or IV anti-arrhythmic drugs within 1 week of randomization.
21. Have active retinopathy or macular edema.
22. Have active severe pulmonary disease (eg, chronic obstructive pulmonary disease, pulmonary fibrosis) or have a chronic pulmonary disease requiring IV corticosteroid or hospitalization ≤ 12 months prior to Screening.
23. Have forced expiratory volume at 1 second (FEV1) or forced vital capacity (FVC) < 70% of predicted values at Screening.
24. Lactating female who is breastfeeding.
25. Any acute illnesses or medical conditions including cognitive impairment and alcohol/drug abuse/dependence, or signs/symptoms suspicious for a serious disease that, in the Investigator’s opinion, could put the subject at increased risk for safety event(s) or interfere with protocol-specified procedures or adherence with study treatment.
Note:
A confirmed result means there have been 2 consecutive assessments showing similar findings.
If a subject fails ≥ 1 screening laboratory criteria, the laboratory assessment(s) may be repeated once at the discretion of the Investigator, and the subject may be enrolled if the laboratory criteria are then met, provided that laboratory assessments are completed within the Screening Period. Any screening laboratory assessments repeated beyond 1 time will need to be discussed with the Medical Monitor before proceeding.

Type of study

Interventional

Type of intervention

Pharmaceutical

Type of intervention: Specify type

N/A

Trial scope

Safety

Trial scope: Specify scope

N/A

Study design: Allocation

Randomized controlled trial

Study design: Masking

Blinded (masking used)

Study design: Control

Placebo

Study phase

2

Study design: Purpose

Study design: Specify purpose

Treatment

N/A

Study design: Assignment

Parallel

Study design: Specify assignment

N/A

IMP has market authorization

No

IMP has market authorization: Specify

Name of IMP

Etrasimod APD334

Year of authorization

Month of authorization

Type of IMP

Others

Pharmaceutical class

Highly selective sphingosine 1-phosphate (S1P) receptor modulator

Therapeutic indication

Crohn's Disease

Therapeutic benefit

Clinical remission of moderately to severely active Crohn’s Disease

Study model

N/A

Study model: Explain model

N/A

Study model: Specify model

N/A

Time perspective

N/A

Time perspective: Explain time perspective

N/A

Time perspective: Specify perspective

N/A

Target follow-up duration

Target follow-up duration: Unit

Number of groups/cohorts

Biospecimen retention

Samples with DNA**

Biospecimen description

Both Samples with DNA and Samples without DNA will be processed

Target sample size

2

Actual enrollment target size

4

Date of first enrollment: Type

Date of first enrollment: Date

Actual

15/07/2021

Date of study closure: Type

Actual

Date of study closure: Date

02/12/2026

Recruitment status

Recruiting

Recruitment status: Specify

Date of completion

IPD sharing statement plan

No

IPD sharing statement description

N/A

Additional data URL

Admin comments

Trial status

Approved

Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
Clinicaltrials.gov	NCT04173273
EudraCT Number	2019-002895-14

Sources of Monetary or Material Support

Name
Arena Pharmaceuticals Inc. USA

Secondary Sponsors

Name
N/A

Contact for Public/Scientific Queries

Contact type	Contact full name	Address	Country	Telephone	Email	Affiliation
Public	Hasan Dakkak	Wahat Al Arab Bldg. 3rd floor- Al Arab Street – Barbir – Beirut	Lebanon	+96170027779	hasan.dakkak@iqvia.com	IQVIA
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Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
Hotel Dieu de France Hospital	Dr. Cesar Yaghi	Gastroenterology	Approved
Hammoud Hospital University Medical Center	Dr. Hasan Atwi	Gastroenterology	Approved
Saint Georges University Medical Center	Dr. Said Farhat	Gastroenterology	Approved
Rafik Hariri University Hospital	Dr. Hala Zantout	Gastroenterology	Approved
Nini Hospital	Dr. Mahmoud Othman	Gastroenterology	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
Hotel Dieu de France	04/02/2020	Pr. Sami Richa	cue@usj.edu.lb	+9611421229
Saint George Hospital University Medical Center	27/02/2020	Dr. Michel Daher	N/A	+9611441000
Hammoud Hospital University Medical Center	09/01/2020	Dr. Ahmad Zaatari	medical@hammoudhospital.org	+9617721021
Rafic Hariri University Hospital	03/03/2021	Dr. Gladys Gemayel	N/A	+9611830000
Nini Hospital	04/04/2022	Dr. Nabil Kabbara	NA	+9616431400

Countries of Recruitment

Name
Lebanon
United States of America

Belgium
Brazil
Bulgaria
Canada
Chile
Czech Republic
France
Germany
Greece
Hungary
Italy
Republic of Korea
Netherlands
Norway
Philippines
Poland
Portugal
Russian Federation
Republic of Serbia
Slovakia
South Africa
Spain
Sweden
Ukraine
United Kingdom

Health Conditions or Problems Studied

Condition	Code	Keyword
Crohn's Disease	Crohn s disease [regional enteritis] (K50)	Inflammatory Bowel Diseases Gastroenteritis Gastrointestinal Diseases Digestive System Diseases Intestinal Diseases

Interventions

Intervention	Description	Keyword
Drug	Etrasimod APD334	N/A
Drug	Placebo	N/A

Primary Outcomes

Name	Time Points	Measure
Proportion of Participants Who Achieve Endoscopic Response	Week 14	Endoscopic response is defined as ≥ 50% decrease from baseline in simple endoscopic score in Crohn's disease (SES-CD)

Key Secondary Outcomes

Name	Time Points	Measure
Proportion of Participants Who Achieve Clinical Remission Worst Daily Abdominal Pain	Week 14	Loose/Watery Stool Frequency Scores (APSF)
Number and Severity of Adverse Events	Up to Week 66	Number and Severity of Adverse Events

Trial Results

Summary results

Study results globally

Date of posting of results summaries

Date of first journal publication of results

Results URL link

Baseline characteristics

Participant flow

Adverse events

Outcome measures

URL to protocol files