To Evaluate Efficacy and Long-term Safety of Ozanimod in Japanese Subjects With Moderately to Severely Active Ulcerative Colitis

CLINICALTRIALS.GOV IDENTIFIER	RECRUITMENT STATUS	FIRST POSTED	LAST UPDATE POSTED
NCT03915769	RECRUITING	APRIL 16, 2019	FEBRUARY 8, 2022

STUDY DESCRIPTION

Brief Summary

Japanese patients with moderate or severe active ulcerative colitis as a subject when ozanimod 0.46 mg or 0.92 mg is orally administered is evaluated about dose response, efficacy and safety with placebo as a control.

Condition or Disease: Colitis, Ulcerative

Intervention/treatment: Drug: Ozanimod
Other: Placebo

Phase: Phase 3

DETAILED DESCRIPTION

Following the 4-week Screening Period, eligible subjects will be randomized to enter the 12 weeks placebo-controlled Induction Period (IP). Subjects who are responders at Week 12 will continue on their assigned treatment in the 52-week Maintenance Period (MP). Non responders at Week 12 have the option to enter the Open-label Extension (OLE). Subjects who complete the MP will be given the option to participate in the OLE. Subjects that enter the MP and experience disease relapse will also have the option to enter the OLE. The OLE will continue until marketing launch (about 4 years of ozanimod for Ulcerative colitis (UC), or until the Sponsor discontinues the development program.

STUDY DESIGN

Study Type: Interventional

Estimated Enrollment : 195 participants

Intervention Model : Parallel Assignment

Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)

Primary Purpose: Treatment

Official Title: To Evaluate Efficacy and Long-term Safety of Ozanimod in Japanese Subjects With Moderately to Severely Active Ulcerative Colitis

Actual Study Start Date: June 2019

Estimated Primary Completion Date: February 2023

Estimated Study Completion Date: March 2025

ARMS AND INTERVENTIONS

Arm	Intervention/treatment
Experimental: 0.46 mg ozanimod oral capsule once daily (QD) It will be a 7-day dose escalation regimen in the IP consisting of 4 days of treatment with 0.23 mg ozanimod, followed by 3 days of treatment with 0.46 mg ozanimod, followed by 0.46 mg ozanimod.	Drug: Ozanimod Ozanimod is an orally bioavailable, small molecule compound that activates the sphingosine 1-phosphate 1 receptor (S1P1) and the S1P 5 receptor (S1P5), although it is more selective towards S1P1 over S1P5
Experimental: 0.92 mg ozanimod oral capsule QD It will be a 7-day dose escalation regimen in the IP consisting of 4 days of treatment with 0.23 mg ozanimod, followed by 3 days of treatment with 0.46 mg ozanimod, followed by 0.92 mg ozanimod.	Drug: Ozanimod Ozanimod is an orally bioavailable, small molecule compound that activates the sphingosine 1-phosphate 1 receptor (S1P1) and the S1P 5 receptor (S1P5), although it is more selective towards S1P1 over S1P5
Placebo Comparator: Placebo oral capsule QD It will be a 7-day dose escalation regimen in the IP consisting of 4 days of treatment with a placebo capsule, followed by 3 days of treatment with two placebo capsules, followed by two placebo capsules.	Other: Placebo The placebo is a capsule that contains no study medication but looks exactly like the study medication capsule.

OUTCOME MEASURES

Primary Outcome Measures:
1. Proportion of subjects with clinical response [Time Frame: At Week 12]
Defined as a reduction from Baseline in the complete Mayo score of ≥ 3 points and ≥ 30%, and a reduction from Baseline in the rectal bleeding subscore of ≥ 1 point or an absolute rectal bleeding subscore of ≤ 1 point

Secondary Outcome Measures:
1. Proportion of subjects with clinical remission [Time Frame: At Week 12 and Week 52]
Defined as: Definition 1. Complete Mayo score of ≤ 2 points with no individual subscore of > 1 point, Definition 2. Rectal bleeding subscore = 0 and stool frequency subscore ≤ 1 (and a decrease of ≥ 1 point from the Baseline stool frequency subscore) and endoscopy subscore ≤ 1
2. Proportion of subjects in clinical remission measured at week 12- Rectal Bleeding [Time Frame: Up to week 12]
Defined as Rectal bleeding subscore = 0 and stool frequency subscore ≤ 1 (and a decrease of ≥ 1 point from the Baseline stool frequency subscore) and endoscopy subscore ≤ 1
3. Proportion of subjects with endoscopic improvement [Time Frame: At Week 12 and Week 52]
Defined as an endoscopy subscore of ≤ 1 point

4. Proportion of subjects with mucosal healing [Time Frame: At Week 12 and Week 52]
Defined as an endoscopy subscore of ≤ 1 point and a Geboes index score < 2.0
5. Proportion of subjects with a clinical response [Time Frame: At Week 9]
Defined as a reduction from Baseline in the partial Mayo score of ≥ 2 points and ≥ 30%, and a reduction from Baseline in the rectal bleeding subscore of ≥ 1 point or an absolute rectal bleeding subscore of ≤ 1 point
6. Change in the EuroQol-5 Dimension (EQ-5D) from baseline [Time Frame: At Week 12]
Is a quality of life questionnaires and will be collected from all subjects at visits
7. Proportion of subjects in clinical remission measured at week 52 - Mayo Score [Time Frame: Up to week 52]
Complete Mayo score of ≤ 2 points with no individual subscore of > 1 point
8. Proportion of subject with clinical response [Time Frame: At week 52]
Defined as a reduction from Baseline in the complete Mayo score of ≥ 3 points and ≥ 30%, and a reduction from Baseline in the rectal bleeding subscore of ≥ 1 point or an absolute rectal bleeding subscore of ≤ 1 point
9. Proportion of subjects in remission while off corticosteroids for any length of time [Time Frame: Up to week 52]
Proportion of subjects in remission while off corticosteroids for any length of time
10. Change in partial Mayo score from Baseline [Time Frame: Up to week 64]
Change in partial Mayo score from Baseline
11. Adverse Event (AE) [Time Frame: From enrollment until at least 75 days after completion of study treatment]
Number of participants with adverse event.
12. Proportion of subjects in clinical remission measured at week 52- Rectal Bleeding [Time Frame: Up to week 52]
Defined as an endoscopy subscore of ≤ 1 point
13. Proportion of subject with clinical response at week 52 [Time Frame: Up to week 52]
Defined as a reduction from Baseline in the complete Mayo score of ≥ 3 points and ≥ 30%, and a reduction from Baseline in the rectal bleeding subscore of ≥ 1 point or an absolute rectal bleeding subscore of ≤ 1 point
14. Proportion of subjects with endoscopic improvement [Time Frame: Up to week 52]
Defined as an endoscopy subscore of ≤ 1 point
15. Proportion of subjects with mucosal healing [Time Frame: Up to week 52]
Defined as an endoscopy subscore of ≤ 1 point and a Geboes index score < 2.0

ELIGIBILITY CRITERIA

Ages Eligible for Study: 18 to 75 Years (Adult, Older Adult)

Sexes Eligible for Study: All

Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:
Main Inclusion Criteria for Induction and Maintenance Periods
Subject is a Japanese male or female subjects aged 18 to 75 years at the time of signing the informed consent form (ICF) at Screening. Subject has had Ulcerative Colitis (UC) diagnosed at least 3 months prior to first investigational product administration. The diagnosis should be confirmed by clinical and endoscopic evidence and corroborated by a histopathology report. Subject has evidence of UC extending ≥ 15 cm from the anal verge as determined by Baseline endoscopy (flexible sigmoidoscopy or colonoscopy). Subject has active UC defined as Mayo score of 6 to 12 inclusive, with endoscopic subscore of ≥ 2, a rectal bleeding score of ≥ 1, and a stool frequency score ≥ 1.
Main Inclusion Criteria for Open-label Extension Period
Subjects must satisfy the following criteria to be enrolled in the study:
1. Subject must have completed through the Week 12 Visit in the Induction Period (IP) AND either:
Completed participation through the last study treatment visit at Week 64 and maintained clinical response in the Maintenance Period (MP), OR Experiencing disease relapse eligible for Open-label Extension (OLE).
Exclusion Criteria:
Main Exclusion Criteria
Subject has severe extensive colitis Subject has diagnosis of Crohn's disease or indeterminate colitis or the presence or history of a fistula consistent with Crohn's disease or microscopic colitis or radiation colitis or ischemic colitis. Subject has positive stool examination for pathogens (ova and parasites, bacteria) or positive test for toxin producing Clostridium difficile (C. difficile) at Screening.4. Subject is pregnant or breastfeeding
5. Subject has clinically relevant cardiovascular conditions

CONTACTS AND LOCATIONS

Contacts

Contact: BMS Study Connect Contact Center www.BMSStudyConnect.com 855-907-3286 Clinical.Trials@bms.com
Contact: First line of the email MUST contain the NCT# and Site #.

Locations

Japan	Kokikai Tokatsu-Tsujinaka Hospital	Abiko
Japan	Mazda Hospital of Mazda Motor Corporation	Aki-gun
Japan	Tokyo Medical and Dental University Hospital	Bunkyo-ku
Japan	Fukuoka University Chikushi Hospital	Chikushino
Japan	Sai Clinic	Fujiidera
Japan	Fukui Prefectural Hospital	Fukui
Japan	Fukui-ken Saiseikai Hospital	Fukui
Japan	Saiseikai Fukuoka General Hospital	Fukuoka
Japan	Harasanshin Hospital	Fukuoka
Japan	Japanese Red Cross Fukuoka Hospital	Fukuoka

Japan	Gifu Prefectural General Medical Center	Gifu
Japan	Hakodate Goryokaku Hospital	Hakodate
Japan	Hirosaki University Hospital	Hirosaki
Japan	Hiroshima Prefectural Hospital	Hiroshima
Japan	Hiroshima University Hospital	Hiroshima
Japan	Hitachi General Hospital	Hitachi, Ibaraki
Japan	Aso Iizuka Hospital	Iizuka
Japan	Saitama Medical University Hospital	Iruma-gun
Japan	Tokai University Hospital	Isehara City, Kanagawa
Japan	Kanazawa Medical University Hospital	Kahoku-gun
Japan	Mitoyo General Hospital	Kannonji
Japan	Nara Medical University Hospital	Kashihara
Japan	Tsujinaka Hospital Kashiwanoha	Kashiwa
Japan	Saitama Medical Center	Kawagoe
Japan	Medical Corporation Aoyama Clinic	Kobe
Japan	Kobe University Hospital	Kobe
Japan	Komatsu Municipal Hospital	Komatsu
Japan	Hoshi General Hospital	Koriyama
Japan	Kurume University Hospital	Kurume, Fukuoka
Japan	Our Lady of the Snow Social Medical Corporation St. Mary's Hospital	Kurume
Japan	Hidaka Coloproctology Clinic	Kurume
Japan	University Hospital, Kyoto Prefectural University of Medicine	Kyoto-city
Japan	Ehime Prefectural Central Hospital	Matsuyama
Japan	Jikei University Hospital	Minato-ku
Japan	Kitasato University Kitasato Institute Hospital	Minato-ku
Japan	Kyorin University Hospital	Mitaka
Japan	Iwate Medical University Uchimaru Medical Center	Morioka
Japan	Nagaoka Chuo General Hospital	Nagaoka
Japan	Nagoya University Hospital	Nagoya-shi
Japan	Hyogo College of Medicine Hospital	Nishinomiya
Japan	Ogaki Municipal Hospital	Ogaki
Japan	Ishida Clinic of IBD and Gastroenterology	Oita
Japan	Okayama Saiseikai Outpatient Center Hospital	Okayama
Japan	Okayama University Hospital	Okayama
Japan	Iseikai Hospital	Osaka
Japan	Osaka City University Hospital	Osaka
Japan	Osaki Citizen Hospital	Osaki-shi
Japan	Shiga University of Medical Science Hospital	Otsu
Japan	Saga University Hospital	Saga
Japan	Tokitokai Tokito Clinic	Saitama
Japan	Osaka Rosai Hospital	Sakai
Japan	Toho University Medical Center Sakura Hospital	Sakura
Japan	Sapporo Medical University Hospital	Sapporo, Hokkaidô
Japan	JA Sapporo Kosei General Hospital	Sapporo
Japan	Japan Community Health care Organization Hokkaido Hospital	Sapporo

Japan	IMS Meirikai Sendai General Hospital	Sendai
Japan	NTT Medical Center Tokyo	Shinagawa-ku, Tokyo
Japan	Tokyo Yamate Medical Center	Shinju-ku
Japan	Shizuoka City Shizuoka Hospital	Shizuoka-shi
Japan	National Hospital Organization Shizuoka Medical Center	Sunto-gun
Japan	Kagawa Prefectural Central Hospital	Takamatsu
Japan	Medical Corporation Shoyu-Kai Fujita Gastroenterology Hospital	Takatsuki
Japan	Takatsuki Red Cross Hospital	Takatsuki
Japan	Hiratsuka Gastroenterological hospital	Toshima-ku
Japan	Toyama City Hospital	Toyama
Japan	Mie University hospital	Tsu
Japan	Kanke Gastrointestinal Clinic	Utsunomiya

Sponsors and Collaborators

Celgene

Investigator

Study Director :	Bristol-Myers Squibb	Bristol-Myers Squibb

MORE INFORMATION

Responsible Party :	Celgene
ClinicalTrials.gov Identifier :	NCT03915769
Other Study ID Numbers :	RPC01-3103, U1111-1230-3228
First Posted :	April 16, 2019
Last Update Posted :	February 8, 2022
Last Verified :	February 2022
Individual Participant Data (IPD) Sharing Statement:	
Plan to Share IPD:	Yes
Plan Description:	https://www.celgene.com/research-development/clinical-trials/clinical-trials-data-sharing/
Supporting Materials:	Study Protocol, Statistical Analysis Plan (SAP), Informed Consent Form (ICF), Clinical Study Report (CSR), Analytic Code
Time Frame:	See Plan Description
Access Criteria:	See Plan Description
URL:	https://www.celgene.com/research-development/clinical-trials/clinical-trials-data-sharing/
Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No
Product Manufactured in and Exported from the U.S.:	Yes
Keywords provided by Celgene:	*Ulcerative colitis* *Ozanimod colitis* *Ulcerative*

Additional relevant MeSH terms :

Colitis	*Digestive System Diseases*
Colitis, Ulcerative	*Colonic Diseases*
Ulcer	*Intestinal Diseases*
Gastroenteritis	*Pathologic Processes*
Gastrointestinal Diseases	*Inflammatory Bowel Diseases*