A study on the Efficacy and Safety of SHP647 as Maintenance Therapy in Subjects With Moderate to Severe Crohn's Disease (CARMEN CD 307)

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Main Information

Primary registry identifying number
LBCTR2019090265

Protocol number
SHP647-307

MOH registration number
3009243/23423

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
12/12/2019

Primary sponsor
Shire Human Genetic Therapies, Inc. ("Shire")

Primary sponsor: Country of origin
USA

Date of registration in primary registry
07/01/2020

Date of registration in national regulatory agency
12/12/2019

Public title
A study on the Efficacy and Safety of SHP647 as Maintenance Therapy in Subjects With Moderate to Severe Crohn's Disease (CARMEN CD 307)

Acronym
CARMEN CD 307

Scientific title
A Phase 3 Randomized, Double-blind, Placebo-controlled, Parallel-group Efficacy and Safety Study of SHP647 as Maintenance Therapy in Subjects With Moderate to Severe Crohn's Disease (CARMEN CD 307)

Acronym
CARMEN CD 307

Brief summary of the study: English
This study is designed to evaluate the efficacy of SHP647 as maintenance therapy in subjects with moderate to severe CD who fulfilled the efficacy entry criteria of this study including the clinical and/or endoscopic response criteria defined in induction study SHP647-306.

Brief summary of the study: Arabic
تم تصميم هذه الدراسة لتقييم فعالية دواء الدراسة كعلاج الصيانة لدى الأشخاص الذين يعانون من مرض كرون المعتدل إلى الشديد والذين استوفوا معايير دخول فعالية هذه الدراسة بما في ذلك معايير الاستجابة السريرية و / أو SHP647-306 بالمنظار المحددة في الدراسة الحثية .

Health conditions/problem studied: Specify
Moderate to Severe Crohn Disease

Interventions: Specify
This study consists of a 52-week, double-blind treatment period, followed by a 16-week safety follow-up period for subjects who either

discontinue treatment early or complete the treatment period and do not enter the long-term safety extension (LTS) study (SHP647-304).
Eligible subjects who received active treatment in the induction study and fulfilled the efficacy entry criteria of this study, including achieving endoscopic and/or clinical response, will be randomized as follows: subjects who received 25 mg SHP647 in the induction study will be randomized (1:1) to receive either 25 mg SHP647 or placebo, and subjects who received 75 mg SHP647 in the induction study will be randomized (1:1) to receive either 75 mg SHP647 or placebo.
Eligible subjects who received placebo in the induction study and fulfilled the efficacy entry criteria of this study, including achieving endoscopic and/or clinical response, will be randomized in a 2:2:1 ratio to receive 1 of 3 treatments (25 mg SHP647, 75 mg SHP647, or placebo, respectively) during this maintenance study.
Subjects enrolled in this study (SHP647-307) will receive double-blind maintenance treatment in the form of SC injections, using a prefilled syringe (PFS), every 4 weeks for 52 weeks. Subjects will undergo efficacy, biomarker, pharmacokinetic (PK), safety, and health outcome assessments.
Subjects who complete the double-blind treatment period in this maintenance study may be eligible to enter the LTS study (SHP647-304).
Subjects who are withdrawn from the study prior to completing the double-blind treatment period due to fulfilling the criteria for treatment failure also may be eligible to enter the LTS study. The intent of providing rescue treatment in the LTS study rather than in this maintenance study following “treatment failure” is to maintain study integrity.
Offering treatment in the LTS study after exiting this maintenance study allows non-responder subjects on placebo, as well as subjects on active study drug, to potentially benefit from a prolonged or different dose of active treatment. Subjects will enter a 16-week safety follow-up period if they withdraw early from the treatment period, are treatment failures and do not choose to enter the LTS study (SHP647-304), or who complete the study and do not wish to enter the LTS study. Treatment failure is defined in Section 4.5.1.

Key inclusion and exclusion criteria: Inclusion criteria

1. Subjects and/or their parent or legally authorized representative must have an understanding, ability, and willingness to fully comply with study procedures and restrictions.
2. Subjects must be able to voluntarily provide written, signed, and dated (personally or via a legally authorized representative) informed consent and/or assent, as applicable, to participate in the study.
3. Subjects must have completed the 16-week induction treatment period from study SHP647-306 and met the following criteria at baseline in maintenance Study SHP647-307:
a) Meet endoscopic response criteria of a reduction in SES-CD from induction study SHP647-306 baseline by ≥25% at Week 16 of induction study SHP647-306
OR
b) Meet at least 1 of the following 4 criteria at baseline in maintenance study SHP647-307, in addition to no worsening of endoscopic score as measured by SES-CD relative to induction study SHP647-306 baseline:
i. Achieving clinical remission as determined by meeting the criteria for clinical remission using the 2-item PRO, ie, 2-item PRO subscores of average worst daily abdominal pain ≤3 (based on 11-point numerical rating scale [NRS]) over the 7 most recent days* and average daily stool type frequency ≤2 of type 6/7 (very soft stools/liquid stools) as shown in the BSFS over the 7 most recent days*
ii. A decrease of at least 100 points in CDAI score (CDAI-100) from induction study SHP647-306 baseline.
iii. A decrease of ≥30% and at least 2 points from induction study SHP647-306 baseline in the average daily worst abdominal pain over the 7 most
recent days*, with the average daily stool frequency of type 6/7 (very soft stools/liquid stools) either: (i) not worsening from induction study SHP647-306 baseline and/or (ii) meeting the criteria for clinical remission, ie, 2-item PRO subscore of average daily stool frequency ≤2 of type 6/7 (very soft
stools/liquid stools) as shown in the BSFS over the 7 most recent days*
iv. A decrease of ≥30% from induction study SHP647-306 baseline in the average daily stool frequency of type 6/7 (very soft stools/liquid stools) as shown in the BSFS over the 7 most recent days*, with the average daily worst abdominal pain either: (i) not worsening from induction study SHP647-306 baseline and/or (ii) meeting the criteria for clinical remission, ie, 2-item PRO subscore of average worst daily abdominal pain ≤3 (based on 11-point NRS) over the 7 most recent days*
*Note: The 7 days may or may not be contiguous during the 10 days of data collection before colonoscopy preparation, depending on days to be excluded because of missing data. If fewer than 7 days are available, the criterion will be calculated on all available most recent 6 or 5 days. If fewer than 5 days are available, the criterion will be treated as missing.
4. Subjects receiving any treatment(s) for CD described in Section 5.2.1 are eligible provided they have been, and are anticipated to be, on a stable dose for the designated period of time.

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. Subjects who had major protocol deviation(s) (as determined by the sponsor) in induction study SHP647-306.
2. Subjects who permanently discontinued investigational product because of an AE, regardless of relatedness to investigational product, in induction study SHP647-306.
3. Subjects who are likely to require surgery for CD during the study period, except minor interventions (eg, seton placement for anal fistulas).
4. Subjects are females who became pregnant during induction study SHP647-306, females who are planning to become pregnant during the study period, or males or females of childbearing potential not agreeing to continue using appropriate contraception methods through the conclusion of study participation (Section 4.4).
5. Subjects who do not agree to postpone donation of any organ or tissue, including male subjects who are planning to bank or donate sperm, or female subjects who are planning to harvest or donate eggs, for the duration of the study and through 16 weeks after last dose of investigational product.
6. Subjects who, in the opinion of the investigator or the sponsor, will be uncooperative or unable to comply with study procedures.
7. Subjects who have developed obstructive colonic stricture, or enterovesical or enterovaginal fistulae during the induction study SHP647-306.

8. Subjects who have a newly diagnosed malignancy or recurrence of malignancy (other than resected cutaneous basal cell carcinoma, squamous cell carcinoma, or carcinoma in situ of the uterine cervix that has been treated with no evidence of recurrence).
9. Subjects who have developed any major illness/condition or evidence of an unstable clinical condition (eg, renal, hepatic, hematologic, gastrointestinal [except disease under study], endocrine, cardiovascular, pulmonary, immunologic [eg, Felty's syndrome], or local active infection/infectious illness) that, in the investigator's judgment, will substantially increase the risk to the subject if he or she participates in the study.
10. Subjects with any other severe acute or chronic medical or psychiatric condition or laboratory or electrocardiogram (ECG) abnormality that may increase the risk associated with study participation or investigational product administration or may interfere with the interpretation of study results and, in the judgment of the investigator, would make the subject inappropriate for entry into this study.
11. Subjects with known exposure to Mycobacterium tuberculosis since testing at screening in induction study SHP647-306 and who have been advised to require treatment for latent or active disease but who are without a generally accepted course of treatment.
12. Subjects with any of the following abnormalities in hematology and/or serum chemistry profiles during the evaluation of the last visit in the SHP647-306 study.
If the results are considered by the investigator to be transient and inconsistent with the subject's clinical condition, may be repeated once prior to enrolment in Study SHP647-307.
 Alanine aminotransferase and aspartate aminotransferase levels > ou = 3 × the upper limit of normal (ULN)
 Total bilirubin level > ou =1.5 × ULN or >2 × ULN if the subject has a known documented history of Gilbert's syndrome
 Hemoglobin level < ou = 80 g/L (8.0 g/dL)
 Platelet count < ou = 100 × 109/L (100,000 cells/mm3) or > ou = 1000 × 109/L (1,000,000 cells/mm3)*
 White blood cell count < ou = 3.5 × 109/L (3500 cells/mm3)
 Absolute neutrophil count<2 × 109/L (<2000 cells/mm3)
 Serum creatinine level >1.5 × ULN or estimated glomerular filtration rate <30 mL/min/1.73 m2 based on the abbreviated Modification of Diet in Renal Disease Study Equation.
*Note: If platelet count is <150,000 cells/mm3, a further evaluation should be performed to rule out cirrhosis, unless another etiology has already been identified.
13. Subjects who are investigational site staff members or relatives of those site staff members or subjects who are sponsor employees directly involved in the conduct of the study.
14. Subjects who are participating in other investigational studies (other than induction study SHP647-306 or plan to participate in other investigational studies during Study SHP647-307.

Type of study

Interventional

Type of intervention

Pharmaceutical

Type of intervention: Specify type

N/A

Trial scope

Therapy

Trial scope: Specify scope

N/A

Study design: Allocation

Randomized controlled trial

Study design: Masking

Blinded (masking used)

Study design: Control

Active

Study phase

3

Study design: Purpose

Treatment

Study design: Specify purpose

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

Ontamalimab

Year of authorization

Month of authorization

Type of IMP

Immunological

Pharmaceutical class

IgG2 Monoclonal antibody

Therapeutic indication

Crohn Disease

Therapeutic benefit

This study is designed to evaluate the efficacy of SHP647 as maintenance therapy in subjects with moderate to severe CD who fulfilled the efficacy entry criteria of this study including the clinical and/or endoscopic response criteria defined in induction study SHP647-306.
The design of the maintenance study (SHP647-307) for those who completed active treatment in the induction study SHP647-306 and met entry criteria is one of randomized withdrawal, whereby a subject may be randomized to continue treatment on the same dose of active treatment or switched to placebo. This design allows for the assessment of the total and multidimensional benefits of a new drug, which encompass efficacy, safety, convenience, and other factors like the durability of the effect of the drug.
As one of the coprimary objectives of this study is clinical remission, rerandomizing placebo-treated subjects from the induction study SHP647-306 who meet entry criteria for the maintenance study (SHP647-307) allows for the greatest number of subjects to potentially be in clinical remission.
Rerandomizing placebo-treated subjects who qualify for the maintenance study allows for the greatest number of subjects to potentially benefit from treatment with active treatment.
Additionally, randomized withdrawal of subjects on active treatment and rerandomization of placebo-treated subjects entering the maintenance study allows for a full and separate investigation of the induction of clinical remission and maintenance of clinical remission effects of any potential new treatment for CD, such as SHP647. Rerandomizing placebo-treated subjects allows for further investigation of long-term safety of SHP647.

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 without DNA

Biospecimen description

N/A

Target sample size

4

Actual enrollment target size

Date of first enrollment: Type

Actual

Date of first enrollment: Date

30/03/2020

Date of study closure: Type

Date of study closure: Date

Actual

31/01/2023

Recruitment status

Other

Recruitment status: Specify

Study not initiated yet

Date of completion

26/08/2022

IPD sharing statement plan

No

IPD sharing statement description

Not decided yet

Additional data URL

Admin comments

Trial status

Approved

Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
No Numbers	No numbers

Sources of Monetary or Material Support

Name
Shire Human Genetic Therapies, Inc. ("Shire")

Secondary Sponsors

Name
None

Contact for Public/Scientific Queries

Contact type	Contact full name	Address	Country	Telephone	Email	Affiliation
Public	Aziz Zoghbi	MCT Lebanon s.a.r.l.	Lebanon	01--612500 ext2040	Zog_Az@Mctcro.com	CRO
Scientific	Shire Human Genetic Therapies, Inc. US US	300 Shire Way Lexington Post code MA 02421	United States of America	+1 781 482 0852	chantal.letourneau@shire.com	sponsor "Clinical Trial Information Desk"

Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
Al Zahraa University Hospital	Dr. Mahmoud Hallal	Gastroenterologist	NA
Hammoud Hospital University Medical Center	Dr. Majed Bahlawan	Gastroenterologist	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
Hammoud Hospital University Medical Center	15/07/2019	ghada aoun	medical@hammoudhospital.org	+9617721021

Countries of Recruitment

Name
Lebanon
Australia
United States of America
Austria
Belgium
Bulgaria
Croatia
Czech Republic
Estonia
Germany

Hungary
Ireland
Italy
Lithuania
Netherlands
Poland
Portugal
Slovakia
Spain
United Kingdom
Bosnia and Herzegovina
Canada
Colombia
Japan
Mexico
New Zealand
Russian Federation
Republic of Serbia
South Africa
Democratic People Republic of Korea
Ukraine

Health Conditions or Problems Studied

Condition	Code	Keyword
Crohn Disease	Crohn s disease, unspecified (K50.9)	CD

Interventions

Intervention	Description	Keyword
SHP647 25 mg	SHP647 will be administered subcutaneously in a PFS 1ml	subjects who received 25 mg SHP647 in one of the induction studies will be randomized (1:1) to receive either 25 mg SHP647 or placebo
SHP647 75 mg	SHP647 will be administered subcutaneously in a PFS 1ml	subjects who received 75 mg SHP647 in one of the induction studies will be randomized (1:1) to receive either 75 mg SHP647 or placebo.
Placebo	The placebo solution will contain the same sterile aqueous buffered solution as the test product but will not contain SHP647	Subjects who fulfill all eligibility criteria and who received placebo in the induction study will be randomized in a 2:2:1 ratio to receive 1 of 3 treatments (25 mg SHP647, 75 mg SHP647, or placebo, respectively) during this maintenance study.

Primary Outcomes

Name	Time Points	Measure
Clinical remission	week 52	Clinical remission, as measured by a decrease below prespecified thresholds in the 2-item PRO (abdominal pain severity and very soft stool/liquid stool frequency [as shown in the BSFS]).
Enhanced endoscopic response	week 52	Enhanced endoscopic response, as measured by a decrease in SES-CD.

Key Secondary Outcomes

Name	Time Points	Measure
Clinical Remission defined by CDAI score	week 52	Clinical Remission defined by CDAI score at week 52
Glucocorticoid-free Clinical Remission Based on Patient-reported Clinical Signs and Symptoms (2-item PRO)	Week 52	Glucocorticoid-free Clinical Remission at week 52
Clinical Remission Defined by Average Daily Abdominal Pain ≤1 (Based on the 4-point Scale) and Average Daily Stool Frequency ≤3 of Type 6/7	Week 52	Clinical Remission at week 52
Clinical Remission Among Subjects in Clinical Remission at Baseline of the SHP647-307 Study, Based on Patient-reported Clinical Signs and Symptoms (2-Item PRO)	Week 52	Clinical Remission at week 52
Enhanced Endoscopic Response Among Subjects with Enhanced Endoscopic Response at Baseline of the SHP647-307 Study	Week 52	Enhanced Endoscopic Response at week 52
Clinical Remission as Well as Enhanced Endoscopic Response in the Same Subject	Week 52	Clinical Remission as Well as Enhanced Endoscopic Response at week 52
Complete Endoscopic Healing	week 52	Complete Endoscopic Healing at week 52

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