A study of the Efficacy and Safety of SHP647 as Induction Therapy in Subjects with Moderate to Severe Ulcerative Colitis

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Main Information

Primary registry identifying number
LBCTR2019090238

Protocol number
SHP647-302

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

Primary sponsor: Country of origin
USA

Date of registration in primary registry
24/12/2019

Date of registration in national regulatory agency

Public title
A study of the Efficacy and Safety of SHP647 as Induction Therapy in Subjects with Moderate to Severe Ulcerative Colitis

Acronym
FIGARO UC 302

Scientific title
A Phase 3 Randomized, Double-blind, Placebo-controlled, Parallel-group Efficacy and Safety Study of SHP647 as Induction Therapy in Subjects with Moderate to Severe Ulcerative Colitis

Acronym
FIGARO UC 302

Brief summary of the study: English
The purpose of this study, which involves research, is to determine whether an investigational drug, SHP647, is safe and effective in the treatment of moderate to severe UC, compared with placebo (dummy treatment)

Brief summary of the study: Arabic
الهدف من هذه الدراسة هو SHP647 امنا و فعالا لعلاج التهاب القولون التقرحي المعتدل الى الحاد مقارنة بدواء وهمي (علاج غير فعال)
تحديد ما اذا كان الدواء البحثي

Health conditions/problem studied: Specify
Moderate to severe Ulcerative Colitis

Interventions: Specify
The study consists of a screening period up to 6 weeks and a 12-week treatment period. After the screening period, eligible subjects will be randomly assigned to receive 1 of 3 treatments (25 mg SHP647, 75 mg SHP647, or placebo) in a 2:2:1 ratio. Randomization will be stratified based upon the subject's status of prior anti-tumor necrosis factor (TNF) treatment (naïve or experienced) and glucocorticoid use at baseline (on glucocorticoids at baseline versus not on glucocorticoids at baseline). Subjects will receive SC injections of SHP647 or placebo, using a prefilled syringe (PFS), on Week 0/Day 1 (Visit 2), Week 4 (Visit 4), and Week 8 (Visit 5). Subjects will undergo efficacy, biomarker, PK, safety, and health outcome assessments at these visits
At the end of the 12-week treatment period, eligible subjects will be offered the opportunity to participate in a double-blind maintenance study

(SHP647-303; for subjects who achieve clinical response) or a long-term safety extension (LTS) study (SHP647-304; for subjects who do not achieve a clinical response). Subjects who withdraw early from the 12-week treatment period or who do not wish to enter the maintenance study (SHP647-303) or LTS study (SHP647-304) will continue into a 16-week safety follow-up period. Only those subjects who complete the full course of investigational product treatment in the induction studies (SHP647-302) will be eligible to continue in the maintenance study or LTS study.

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 be between ≥16 and ≤80 years of age at the time of the signing of the informed consent/assent form (for Lebanon must be ≥ 18 and ≤80 years of age).

NOTE: Subjects <18 years of age must weigh ≥40 kg and must have body mass index (BMI) ≥16.5. (NA for Lebanon)

4. Subjects must have a documented diagnosis (radiologic or endoscopic with histology) of UC for ≥ 3 months before screening. The following must be available in each subject's source documentation:
•A biopsy report to confirm the histological diagnosis.

•A report documenting disease duration based upon prior colonoscopy.

NOTE: If this documentation is not available at the time of screening, a colonoscopy with biopsy to confirm the diagnosis is required during the screening period.

5. Subjects must be willing to undergo a flexible sigmoidoscopy or colonoscopy (if preferred), including biopsy sample collection, during screening after all other inclusion criteria have been met.

6. Subjects must have moderate to severe active UC, defined as a total Mayo score of ≥ 6, including a centrally read endoscopic subscore ≥ 2, rectal bleeding subscore ≥1, and stool frequency subscore ≥ 1 at baseline (Visit 2).

7. Subjects must have evidence of UC extending proximal to the rectum (ie, not limited to proctitis).

8. Subjects must have had an inadequate response to, or lost response to, or had an intolerance to at least 1 conventional treatment such as mesalamine (5-ASA), glucocorticoids, immunosuppressants (azathioprine [AZA], 6-mercaptopurine [6-MP], or methotrexate [MTX]), or anti-TNF (refer to Appendix 4 for guidance).

9. Subjects receiving any treatment(s) for UC described in Section 5.2.1 of the protocol are eligible provided they have been, and are anticipated to be, on a stable dose for the designated period of time.

10. Subjects are males or nonpregnant, nonlactating females who, if sexually active, agree to comply with the contraceptive requirements of the protocol, or females of nonchildbearing potential. Males and females of reproductive potential who are sexually active must agree to use appropriate contraception for the duration of the study.

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 with indeterminate colitis, microscopic colitis, non-steroidal anti-inflammatory drug-induced colitis, ischemic colitis, infectious colitis, or clinical/histologic findings suggestive of Crohn's disease.

2.Subjects with colonic dysplasia or neoplasia. (Subjects with prior history of adenomatous polyps will be eligible if the polyps have been completely removed.)

3.Subjects with past medical history or presence of toxic megacolon.

4.Subjects with colonic stricture, past medical history of colonic resection, a history of bowel surgery within 6 months before screening, or who are likely to require surgery for UC during the treatment period.

5.Subjects at risk for colorectal cancer must have a colonoscopy (Eaden and Mayberry 2002) performed during the screening period with results available within 10 days before the baseline visit (Visit 2), unless the subject has had a surveillance colonoscopy performed within 1 year prior to screening, and any adenomatous polyps found at that examination have been excised. Colonoscopy report and pathology report (if biopsies are obtained) from the colonoscopy performed during screening or in the prior year confirming no evidence of dysplasia and colon cancer must be available in the source documents.

Subjects at risk for colorectal cancer include, but are not limited to:

•Subjects with extensive colitis for ≥8 years or disease limited to left side of colon (ie, distal to splenic flexure) for ≥10 years before screening, regardless of age.

•Subjects ≥50 years of age at the time of signing of the informed consent form.

6.Subjects have had prior treatment with SHP647 (formerly PF-00547659).

7.Subjects with known or suspected intolerance or hypersensitivity to the investigational product(s), closely related compounds, or any of the stated ingredients.

8.Subjects have received anti-TNF treatment within 60 days before baseline (Visit 2).

9.Subjects have received any biologic with immunomodulatory properties (other than anti-TNFs) within 90 days before baseline (Visit 2).

10. Subjects have received any nonbiologic treatment with immunomodulatory properties (other than their current background UC treatment) within 30 days before baseline (Visit 2).

11. Subjects have ever received anti-integrin/adhesion molecule treatment (eg, natalizumab, vedolizumab, efalizumab, etrolizumab, or any other investigational anti-integrin/adhesion molecule).

12. Subjects have received parenteral or rectal glucocorticoids, or rectal 5-ASA, within 14 days before screening endoscopic procedure.

13. Subjects have received leukocyte apheresis or selective lymphocyte, monocyte, or granulocyte apheresis or plasma exchange within 30 days before baseline (Visit 2).

14. Subjects have participated in other investigational studies within either 30 days or 5 half-lives of investigational product used in the study (whichever is longer) before baseline (Visit 2).

15. Subjects have received a live (attenuated) vaccine within 30 days before the baseline visit (Visit 2).

16. Subjects with active enteric infections (positive stool culture and sensitivity), Clostridium difficile infection or pseudomembranous colitis [subjects with C. difficile infection at screening may be allowed re-test after treatment], evidence of active cytomegalovirus infection or Listeria monocytogenes, known active invasive fungal infections such as histoplasmosis or parasitic infections, clinically significant underlying disease that could predispose the subjects to infections, or a history of serious infection (requiring parenteral antibiotic and/or hospitalization) within 4 weeks before the baseline visit (Visit 2).

17. Subjects with abnormal chest x-ray findings at screening (Visit 1), such as presence of active tuberculosis (TB), general infections, heart failure, or malignancy. (A chest x-ray performed up to 12 weeks before study entry [screening, Visit 1] may be used if available; documentation of the official reading must be located and available in the source documentation.)

18. Subjects with evidence of active or latent infection with Mycobacterium tuberculosis (TB) or subjects with this history who have not completed a generally accepted full course of treatment before randomization are excluded. All other subjects must have either the Mantoux (purified protein derivative [PPD]) tuberculin skin test or interferon gamma release assay (IGRA) performed.

Subjects who have no history o f previously diagnosed active or latent tuberculosis are excluded if they have a positive Mantoux (PPD) tuberculin skin test (ie ≥5 mm induration) or a positive IGRA (the latter to be tested at the site's local laboratory) during screening or within 12 weeks before randomization. If IGRA test cannot be performed locally, a central laboratory may be used, with prior agreement from the sponsor.

•An IGRA is strongly recommended for subjects with a prior Bacillus Calmette-Guérin (BCG) vaccination, but may be used for any subject. Documentation of IGRA product used and the test result must be in the subject's source documentation if performed locally. Acceptable IGRA products include QuantiFERON TB Gold Plus In-Tube Test.

•If the results of the IGRA are indeterminate, the test may be repeated, and if a negative result is obtained, enrollment may proceed. In subjects with no history of treated active or latent tuberculosis, a positive test on repeat will exclude the subject.

Subjects with a history of active or latent tuberculosis infection must follow instructions for "Subjects with a prior diagnosis of active or latent tuberculosis are excluded unless both of the following criteria are met" in this criterion.

•Subjects with repeat indeterminate IGRA results, with no prior TB history, may be enrolled after consultation with a pulmonary or infectious disease specialist who determines low risk of infection (ie, subject would be acceptable for immunosuppressant [eg, anti-TNF] treatment without additional action). This consultation must be included in source documentation.

Results from a chest x-ray, taken within the 3 months before or during screening (Visit 1) must show no abnormalities suggestive of active TB infection as determined by a qualified medical specialist.

Subjects with a prior diagnosis of active or latent tuberculosis are excluded unless both of the following criteria are met:

•The subject has previously received an adequate course of treatment for either latent
(eg, 9 months of isoniazid or an acceptable alternative regimen, in a locale where rates of primary multidrug TB resistance are <5%. Subjects from regions with higher rates of primary multidrug TB resistance are excluded) or active (acceptable multidrug regimen) TB infection. Evidence of diagnosis and treatment must be included in source documentation. Consultation with a pulmonary or infectious disease specialist to confirm adequate treatment (ie, subject would be acceptable for immunosuppressant [eg,
anti-TNF] treatment without additional action) must be performed during the screening period. The consultation report must be included in source documentation prior to enrollment.

•A chest x-ray performed within 3 months prior to screening (Visit 1) or during screening (Visit 1) indicates no evidence of active or recurrent disease, and documentation of interpretation by a qualified medical specialist must be included in source documentation.

19. Subjects with a pre-existing demyelinating disorder such as multiple sclerosis or new onset seizures, unexplained sensory motor, or cognitive behavioral, neurological deficits, or significant abnormalities noted during screening.

20. Subjects with any unexplained symptoms suggestive of progressive multifocal leukoencephalopathy (PML) based on the targeted neurological assessment during the screening period (see Section 7.2.3.3).

21. Subjects with a transplanted organ. Skin grafts to treat pyoderma gangrenosum are allowed.

22. Subjects with a significant concurrent medical condition at the time of screening (Visit 1) or baseline (Visit 2), including, but not limited to, the following:

•Any major illness/condition or evidence of an unstable clinical condition (eg, renal, hepatic, hematologic, GI (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.

•Cancer or history of cancer or lymphoproliferative disease within the previous 5 years (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).

•Presence of acute coronary syndrome (eg, acute myocardial infarction, unstable angina pectoris) within 24 weeks before screening (Visit 1).

•History of significant cerebrovascular disease within 24 weeks before screening (Visit 1).

23. Subjects who have had significant trauma or major surgery within 4 weeks before the screening visit (Visit 1), or with any major elective surgery scheduled to occur during the study.

24. Subjects with evidence of cirrhosis with or without decompensation.

25. Subjects with primary sclerosing cholangitis.

26. Subjects with evidence of positive hepatitis B surface antigen (HBsAg) or hepatitis B core antibody (HBcAb). NOTE: if a subject tests negative for HBsAg, but positive for HBcAb, the subject would be considered eligible if no presence of HBV DNA is confirmed by HBV DNA PCR reflex testing performed in the central laboratory.

27. Subjects with chronic hepatitis C (HCV) (positive HCVAb and HCVRNA). Note: Subjects who are HCVAb positive without evidence of HCVRNA may be considered eligible (spontaneous viral clearance or previously treated and cured [defined as no evidence of HCVRNA at least 12 weeks prior to baseline]).

28. Subjects with any of the following abnormalities in hematology and/or serum chemistry profiles during screening. NOTE: Screening laboratory tests, if the results are considered by the investigator to be transient and inconsistent with the subject's clinical condition, may be repeated once during the screening period for confirmation. Results must be reviewed for eligibility prior to the screening endoscopy procedure.
•Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels ≥ 3.0 × the upper limit of normal (ULN).

•Total bilirubin level ≥1.5 ×ULN or >2.0×ULN if the subject has a known documented history of Gilbert's syndrome.

•Hemoglobin level ≤ 80 g/L (8.0 g/dL).

•Platelet count ≤ 100 × 1 000 000 000/L (100,000 cells/mm3) or ≥1000 × 1 000 000 000/L (1,000,000 cells/mm3).*

• White blood cell count ≤ 3.5 × 1 000 000 000/L (3500 cells/mm3).

• Absolute neutrophil count (ANC) <2 × 1 000 000 000/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.

29. Subjects with known human immunodeficiency (HIV) infection based on documented history, with positive serological test, or positive HIV serologic test at screening, tested at the site's local laboratory in accordance with country requirements or tested at the central laboratory. Note: A documented negative HIV test within 6 months of screening is acceptable and does not need to be repeated.

30. Subjects who have, or who have a history of (within 2 years before screening [Visit 1]), serious psychiatric disease, alcohol dependency, or substance/drug abuse or dependency of any kind, including abuse of medical marijuana (cannabis).

31. 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.

32. Female subjects who are planning to become pregnant during the study period.

33. Subjects who do not agree to postpone donation of any organ or tissue, including male subjects who are planning to bank or donate sperm and 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.

34. Subjects who are investigational site staff members or relatives of those site staff members or subjects who are Shire employees directly involved in the conduct of the study.

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

Placebo

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 (SHP647)

Year of authorization

Month of authorization

Type of IMP

Immunological

Pharmaceutical class

IgG2 monoclonal antibody

Therapeutic indication

Ulcerative Colitis

Therapeutic benefit

SHP647, in doses of 7.5 mg, 22.5 mg, and 75 mg, appears to increase the rate of remission in subjects with UC.

Study model

N/A

Study model: Explain model

Study model: Specify model

N/A

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
12

Actual enrollment target size

Date of first enrollment: Type
Actual

Date of first enrollment: Date
01/11/2019

Date of study closure: Type
Actual

Date of study closure: Date
10/12/2020

Recruitment status
Other

Recruitment status: Specify
Study is not initiated yet

Date of completion

IPD sharing statement plan
No

IPD sharing statement description
Not decided yet

Additional data URL
NA

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@ct-CRO.com	CRO
Scientific	Shire Human Genetic Therapies, Inc. 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
Rafik Hariri University Hospital	Dr. Iyad Issa	Gastroenterology	Approved
Al Zahraa University Hospital	Dr. Mahmoud Hallal	Gastroenterology	NA
Hammoud Hospital University Medical Center	Dr. Hassan Atwi	Gastroenterology	Approved
Hammoud Hospital University Medical Center	Dr. Majed Bahlawan	Gastroenterology	Approved
Hotel Dieu De France	Dr. Cesar Yaghi	Gastroenterology	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
Rafic Hariri University Hospital	29/05/2019	Abir Sinno	abir.sinno@crurhuh.com	+961 1 830000 ext 2037
Hotel Dieu de France	06/06/2019	Virginia El Khoury	Virginia.elkhoury@usj.edu.lb	+961 1 421229
Hammoud Hospital University Medical Center	15/07/2019	ghada aoun	medical@hammoudhospital.org	+9617721021
Al Zahraa University Hospital	05/12/2019	Dr. Bassam Mansour	dr.bassammansour@gmail.com	+96176171272

Countries of Recruitment

Name
Lebanon
Belgium
Bulgaria
Estonia
France
Greece
Hungary
Ireland
Slovakia
Portugal
Spain
Argentina
Bosnia and Herzegovina
Canada
Colombia
Japan
Mexico
Democratic People Republic of Korea
Switzerland
Ukraine
United States of America

Health Conditions or Problems Studied

Condition	Code	Keyword
Ulcerative Colitis	Ulcerative colitis (K51)	Ulcerative Colitis

Interventions

Intervention	Description	Keyword
SHP647 25 mg	SHP647 will be administered subcutaneously in a PFS 1ml	randomization ratio: 2:2:1 for SHP647 25mg, 75mg and Placebo respectively
SHP647 75 mg	SHP647 will be administered subcutaneously in a PFS 1ml	randomization ratio: 2:2:1 for SHP647 25mg, 75mg and Placebo respectively
Placebo	The placebo solution will contain the same sterile aqueous buffered solution as the test product but will not contain SHP647	randomization ratio: 2:2:1 for SHP647 25mg, 75mg and Placebo respectively

Primary Outcomes

Name	Time Points	Measure
Remission is defined as a composite score of patient-reported symptoms using daily e-diary and centrally read endoscopy as follows: •stool frequency subscore of 0 or 1 with at least a 1-point change from baseline AND •rectal bleeding subscore of 0 AND •endoscopic subscore of 0 or 1 (modified, excludes friability).	Week 12	Remission at week 12

Key Secondary Outcomes

Name	Time Points	Measure
Endoscopic remission, as defined by centrally read endoscopic subscore 0 or 1 (modified, excludes friability)	Week 12	Endoscopic remission at week 12
Clinical remission, as defined by stool frequency subscore of 0 or 1 with at least a 1-point change from baseline in stool frequency subscore, and rectal bleeding subscore of 0	Week 12	Clinical remission at week 12
Clinical response based on composite score. It is defined as a decrease from baseline in the composite score of patient-reported symptoms using daily e-diary and centrally read endoscopy of at least 2 points and at least 30%, with an accompanying decrease in the subscore for rectal bleeding ≥1 point or a subscore for rectal bleeding ≤1.	Week 12	Clinical response at week 12
Mucosal healing based on endoscopic and histological assessment. it s defined by centrally read endoscopic subscore 0 or 1 (modified, excludes friability) and centrally read Geboes score of ≤2.	Week 12	Mucosal Healing at week 12
Remission, defined as a total Mayo score ≤2 with no individual subscore (stool frequency, rectal bleeding, endoscopy [modified, excludes friability], and physician's global assessment) exceeding 1	Week 12	Remission at week 12
Clinical response based on total Mayo score. Clinical response (Mayo) is defined as a decrease from baseline in the total Mayo score of at least 3 points and at least 30%, with an accompanying decrease in the subscore for rectal bleeding ≥1 point or a subscore for rectal bleeding ≤1.	Week 12	Clinical response based on Mayo score at week 12
Partial Mayo score ≤2 with no individual subscore >1. The partial Mayo score does not include the endoscopy subscore.	Weeks 4, 8 and 12	Partial Mayo score at weeks 4, 8 and 12
Clinical remission as defined by stool frequency subscore of 0 or 1 with at least a 1-point change from baseline in stool frequency subscore, and rectal bleeding subscore of 0.	weeks 4 and 8	Clinical Remission at weeks 4 and 8
Endoscopic remission with endoscopic subscore of 0.	Week 12	Endoscopic Remission at week 12
Clinical remission with both rectal bleeding and stool frequency subscores of 0.	Weeks 4, 8 and 12	Clinical remission at Weeks 4, 8 and 12
Deep remission. It is defined as both endoscopic and rectal bleeding subscores of 0, and stool frequency subscore ≤1 and a centrally read Geboes score of ≤2.	Week 12	Deep remission at Week 12
Change in abdominal pain, urgency and diarrhea item scores, absolute stool frequency, absolute rectal bleeding and total sign/symptom score based on subject daily e-diary entries (sum of rectal bleeding, stool frequency, abdominal pain, diarrhea, and urgency).	Week 0 and Week 12	Week 0 and Week 12
Change from baseline in IBDQ domain and total (absolute) scores).	Week 0, Week 8, up to Week 12, or early termination	Change in IBDQ and total scores Week 0, Week 8, up to Week 12, or early termination
Change in SF-36, version 2, acute (physical and mental component summary scores and individual domain scores).	From Baseline to the Week 12/ET visit	Change in SF-36, version 2, acute (physical and mental component summary scores and individual domain scores).
Incidence of all-cause hospitalizations and total inpatient days.	From Baseline to week 12	Incidence of all-cause hospitalizations and total inpatient days.

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