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 Ulcerative Colitis (FIGARO UC 303)

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Primary: To evaluate the efficacy of ontamalimab as maintenance treatment of remission, based on composite score of patient reported symptoms and centrally read endoscopy, in subjects with moderate to severe ulcerative colitis (UC).Key Secondary:*...

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

Summary

ID

NL-OMON50472

Source
ToetsingOnline

Brief title
SHP647-303

Condition

- Gastrointestinal inflammatory conditions

Synonym
chronic inflammation of the mucosa of the colon and rectum, Ulcerative Colitis

Research involving

Human

Sponsors and support

Primary sponsor: Shire
Source(s) of monetary or material Support: Shire

Intervention

Keyword: Maintenance therapy, Ontamalimab, Phase 3, Ulcerative Colitis

Outcome measures

Primary outcome

To evaluate the efficacy of ontamalimab as maintenance treatment of remission, based on composite score of patient reported symptoms and centrally read endoscopy, in subjects with moderate to severe ulcerative colitis (UC).

Secondary outcome

* To evaluate the efficacy of ontamalimab on endoscopic remission, based on centrally read endoscopy.

* To evaluate the efficacy of ontamalimab on clinical remission, based on composite score of patient reported symptoms.

* To evaluate the efficacy of ontamalimab on maintenance of remission among subjects in remission at baseline of the SHP647-303 study, based on composite score of patient reported symptoms and centrally read endoscopy.

* To evaluate the efficacy of ontamalimab on clinical response, based on composite score of patient reported symptoms and centrally read endoscopy.

* To evaluate the efficacy of ontamalimab on mucosal healing, based on a centrally read endoscopic and histological assessment using the Geboes Score grading system.

* To evaluate the efficacy of ontamalimab on glucocorticoid free clinical remission.

* To evaluate the efficacy of ontamalimab on glucocorticoid free remission.

* To evaluate the safety and tolerability of ontamalimab as maintenance treatment.

* To evaluate the effect of ontamalimab maintenance treatment on other clinical and endoscopic outcomes (including Mayo-based remission, Mayo-based clinical response, partial Mayo score over time, clinical remission over time, endoscopic remission, deep remission, sustained endoscopic remission, sustained mucosal healing, sustained deep remission, sustained clinical remission, sustained endoscopic remission, sustained remission, sustained clinical remission over time, and glucocorticoid-free clinical remission over time).

* To evaluate the effect of ontamalimab on abdominal pain, urgency, diarrhea, and absolute stool frequency and bleeding scores.

* To evaluate the effect of ontamalimab maintenance treatment on health-related quality of life (as measured by the Inflammatory Bowel Disease Questionnaire [IBDQ] and the Short Form-36 Health Survey [SF-36]).

* To evaluate the impact of ontamalimab maintenance treatment on incidence of hospitalizations and total inpatient days.

Study description

Background summary

Ulcerative colitis (UC) is a chronic, relapsing disease marked by ulceration and inflammation of the colonic mucosa and submucosa. Initially it usually

involves the rectum but may extend proximally to involve a portion of, or the entirety of, the colon. In the early stages, hemorrhagic and erythematous tissue is observed, progressing to mucosal ulceration with purulent exudates in severe cases. The ulceration pattern is continuous and may extend the entire length of the colon. Perforation of the bowel wall causing ileus and peritonitis can occur with transmural extension of the ulceration. Bloody diarrhea with or without mucus and lower abdominal pain with periods of remission and exacerbation are the most common symptoms.
Although UC can occur at any age, peak incidence has been observed in the second to fourth decades of life. UC is a lifelong condition with a serious effect on the quality of life. Current treatment primarily consists of symptomatic management with dietary modifications and opiates, as well as disease modifying agents, systemic glucocorticoids, immunosuppressive agents, and biologic therapy. Despite recent advances, there is still an unmet need for an effective pharmacological treatment that will induce and maintain remission.
The selectivity of lymphocyte homing to specialized lymphoid tissue and mucosal sites of the gastrointestinal (GI) tract is influenced by the endothelial expression of mucosal addressin cell adhesion molecule (MAdCAM). MAdCAM plays a role in gut immune surveillance, and also appears to facilitate excessive lymphocyte infiltration under conditions of chronic GI inflammation.
Ontamalimab is a fully human immunoglobulin G2 kappa (IgG2k) monoclonal antibody that binds to human MAdCAM to reduce lymphocyte homing to the gut and GI inflammation.

Study objective

Primary: To evaluate the efficacy of ontamalimab as maintenance treatment of remission, based on composite score of patient reported symptoms and centrally read endoscopy, in subjects with moderate to severe ulcerative colitis (UC).

Key Secondary:
* To evaluate the efficacy of ontamalimab on endoscopic remission, based on centrally read endoscopy.
* To evaluate the efficacy of ontamalimab on clinical remission, based on composite score of patient reported symptoms.
* To evaluate the efficacy of ontamalimab on maintenance of remission among subjects in remission at baseline of the SHP647-303 study, based on composite score of patient reported symptoms and centrally read endoscopy.
* To evaluate the efficacy of ontamalimab on clinical response, based on composite score of patient reported symptoms and centrally read endoscopy.
* To evaluate the efficacy of ontamalimab on mucosal healing, based on a centrally read endoscopic and histological assessment using the Geboes Score grading system.
* To evaluate the efficacy of ontamalimab on glucocorticoid free clinical remission.
* To evaluate the efficacy of ontamalimab on glucocorticoid free remission.

Other Secondary:
* To evaluate the safety and tolerability of ontamalimab as maintenance treatment.
* To evaluate the effect of ontamalimab maintenance treatment on other clinical and endoscopic outcomes (including Mayo-based remission, Mayo-based clinical response, partial Mayo score over time, clinical remission over time, endoscopic remission, deep remission, sustained endoscopic remission, sustained mucosal healing, sustained deep remission, sustained clinical remission, sustained endoscopic remission, sustained remission, sustained clinical remission over time, and glucocorticoid-free clinical remission over time).
* To evaluate the effect of ontamalimab on abdominal pain, urgency, diarrhea, and absolute stool frequency and bleeding scores.
* To evaluate the effect of ontamalimab maintenance treatment on health-related quality of life (as measured by the Inflammatory Bowel Disease Questionnaire [IBDQ] and the Short Form-36 Health Survey [SF-36]).
* To evaluate the impact of ontamalimab maintenance treatment on incidence of hospitalizations and total inpatient days.

Study design

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 who complete the treatment period and do not enter the long-term safety extension (LTS) study (SHP647-304).
The eligibility of a subject for the study will be assessed based on the study data collected at the Week 12 visit of the induction studies (SHP647-301), which will be considered as the baseline visit for this maintenance study.
Subjects enrolled in this study (SHP647-303) will receive double-blind maintenance treatment in the form of SC injections, using a PFS, every 4 weeks for 52 weeks. Subjects will undergo efficacy, biomarker, pharmacokinetic, safety, and health outcome assessments.
Patient-reported UC signs and symptom data (including stool frequency, rectal bleeding severity and frequency, diarrhea frequency, urgency frequency, and abdominal pain worst severity) will be collected using a daily e diary for 10 days before each visit. The Mayo score is a measure of UC disease activity consisting of the following 4 subscores: stool frequency, rectal bleeding, findings of endoscopy, and physician global assessment (PGA). The partial Mayo score consists of the Mayo score without the endoscopic subscores. The composite score is a recommended measure consisting of the Mayo score without the PGA subscore, and will be used for the primary efficacy endpoint. The Mayo scores and composite score will be based on subject daily e-diary entries.
Subjects who complete the double-blind treatment period in this maintenance study may be eligible to enter the LTS study (SHP647-304). Subjects will enter a 16 week safety follow up period if they withdraw early from the treatment period, are treatment failures and do not enter the LTS study (SHP647-304), or who complete the study and do not wish to enter the LTS study.

Intervention

The participants receive a subcutaneous injection every 4 weeks; 1 group with 25 mg ontamalimab, 1 group with 75 mg ontamalimab, and 1 group with placebo.

Study burden and risks

Ontamalimab may cause side effects. The most frequently reported side effects (in more than 1 out of every 10 subjects) are: joint pain, headache, pain in the belly, nausea, fever and nasopharyngitis. If the patient receives placebo there is a possibility that symptoms of the disease may return or get worse. Also the study procedures may be accompanied by risks and discomforts. In addition the study drug, the study procedures and the combination of these may lead to risks that are as yet unknown.

Ulcerative colitis (UC) is a chronic, relapsing disease marked by ulceration and inflammation of the colonic mucosa and submucosa. Ulcerative colitis is a lifelong condition with a serious effect on the quality of life. Current treatment primarily consists of symptomatic management. Despite recent advances, there is still an unmet need for an effective pharmacological treatment that will induce and maintain remission.

Considering the chronic and relapsing characteristics of this lifelong disease, we feel these side effects and the burden associated with participation, are in proportion considering the positive effects that participation in the study might have on the patients disease.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Subjects must meet all of the following inclusion criteria to be eligible for enrollment into the study.
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 to participate in the study.,
3. Subjects must have completed the 12-week induction treatment period from study SHP647-301 or SHP647-302. ,
4. Subjects must have achieved clinical response in induction study SHP647-301 or SHP647-302. Clinical response is defined as:
1) A decrease from the induction study (SHP647-301 or SHP647-302) 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
OR
2) A decrease from the induction study (SHP647-301 or SHP647-302) baseline in total Mayo score of at least 3 points and at least 30%, with an accompanying decrease in the rectal bleeding subscore of at least 1 point or an absolute rectal bleeding subscore of 0 or 1.
For eligibility assessment, clinical response will be determined based on the centrally read endoscopy performed during screening and at Week 12 of induction study SHP647-301 or SHP647-302.,
5. 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.

Exclusion criteria

Subjects are excluded from the study if any of the following criteria are met:,
1. Subjects who had major protocol deviation(s) (as determined by the sponsor) in induction study SHP647-301 or SHP647-302.
2. Subjects who permanently discontinued investigational product because of an adverse event, regardless of relatedness to investigational product, in induction study SHP647-301 or SHP647-302.
3. Subjects who are likely to require surgery for UC during the study period.
4. Subjects are females who became pregnant during induction study SHP647-301 or SHP647-302, females who are planning to become pregnant during the study period, or males or females of childbearing potential not agreeing to continue appropriate contraception methods (ie, highly effective methods for female and medically appropriate methods for male study subjects) through the conclusion of study participation.
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, 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.
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 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).
8. 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.
9. 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.
10. Subjects with known exposure to Mycobacterium tuberculosis (TB) since testing at screening in induction study SHP647-301 or SHP647-302 and who are without a generally accepted course of treatment.
11. 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.

12. Subjects who are participating in or plan to participate in other investigational studies (other than induction study SHP647-301 or SHP647-302) during study SHP647-303.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	11-02-2019
Enrollment:	14
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ontamalimab
Generic name:	-

Ethics review

Approved WMO

Date:	02-11-2017
Application type:	First submission
Review commission:	METC Brabant (Tilburg)

Approved WMO Date:	15-03-2018
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	06-07-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	25-09-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	26-09-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	10-10-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	20-12-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	30-01-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	20-02-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	27-02-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO	

Date:	17-06-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	20-06-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	23-09-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	30-09-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	16-03-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	18-03-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	10-09-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	23-09-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	10-12-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO	

Date:	14-12-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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	EUCTR2017-000573-37-NL
ClinicalTrials.gov	NCT03290781
CCMO	NL62886.028.17

Study results

Date completed:	09-02-2021
Results posted:	25-01-2022

First publication
22-11-2021