A Phase 3 Long-term Safety Extension Study of SHP647 in Subjects with Moderate to Severe Ulcerative Colitis or Crohn's Disease (AIDA)

Published: 02-11-2017
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To evaluate the safety and tolerability of long term treatment with ontamalimab in subjects with moderate to severe UC or CD.

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

Summary

ID

NL-OMON54678

Source
ToetsingOnline

Brief title
SHP647-304

Condition

- Gastrointestinal inflammatory conditions

Synonym
a type of IBD that may affect any part of the gastroinestinal tract from mouth to anus, chronic inflammation of the mucosa of the colon and rectum; Crohn's Disease, Ulcerative Colitis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Crohn's Disease, Long-term extension study, Ontamalimab, Ulcerative Colitis

Outcome measures

Primary outcome

To evaluate the safety and tolerability of long term treatment with

ontamalimabin subjects with moderate to severe UC or CD.

Secondary outcome

Secondary Objectives - Subjects with Ulcerative Colitis

• To evaluate the maintenance of response to long-term treatment with

ontamalimab as measured by clinical composite score and biomarkers, with or

without endoscopy.

Secondary Objective - Subjects with Crohn's Disease:

• To evaluate the maintenance of response to long-term treatment with

ontamalimab as measured by Crohn's Disease Activity Index (CDAI) score and

biomarkers, with or without endoscopy

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. Ulcerative colitis 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.

Crohn*s disease (CD) is a chronic, relapsing disease marked by granulomatous inflammation of the gastrointestinal (GI) tract. Although the terminal ileum and right colon are the most commonly involved sites, CD can affect any part of the GI tract, from the mouth to the perianal
region. Inflammation is typically transmural (full-thickness), segmental, and discontinuous, and symptoms are predominantly determined by the part of bowel or organ involved. Patients typically present with symptoms including abdominal pain, diarrhea, rectal bleeding, which may
be persistent and lead to anemia, and weight loss due to pain on eating and malabsorption. As the disease progresses, extraintestinal manifestations and associated conditions can develop, including bowel obstruction, fistulas, and stenosis, as well as painful skin ulcerations, eye pain, and arthritis.
Crohn*s disease is a lifelong condition with a serious effect on quality of life. The traditional approach to therapy of CD has been the step-up approach usually represented as a pyramid where, progressing from mild to severe disease, therapeutic choices proceed step by step from
less potent drugs at the base of the pyramid to more potent but also more toxic drugs at the top. Despite recent advances, there is still an
unmet need for a safe, effective, and durable 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

To evaluate the safety and tolerability of long term treatment with ontamalimab in subjects with moderate to severe UC or CD.

Study design

This is a Phase 3, multicenter extension study designed to evaluate the long-term safety and efficacy of ontamalimab in subjects with moderate to severe UC or CD. The study will enroll subjects from 6 separate Phase 3 studies: 4 multicenter, randomized, double-blind, placebo-controlled, parallel group study studies evaluating SHP647 as an induction therapy in subjects with moderate to severe UC (SHP647-301 and SHP647-302) or CD (SHP647-305 and SHP647-306); and 2 multicenter, double-blind, randomized, placebo-controlled, parallel-group studies evaluating SHP647 as maintenance therapy in subjects with moderate to severe UC (SHP647-303) or CD (SHP647-307).
Additionally, the study will directly enroll subjects with moderate to severe UC who had not participated in any of the Phase 3 induction studies (SHP647-301, SHP647-302) or the maintenance study (SHP647-303). Direct-entry subjects include UC subjects who were ineligible for an induction study due to previous treatment with ontamalimab during a Phase 1 or Phase 2 study or previous treatment with vedolizumab, or subjects who had met the eligibility criteria for induction study SHP647-301 or SHP647-302 but were unable to enroll because of an enrollment cap in their particular country.
Eligible subjects entering study SHP647-304 will be assigned to receive either 25 mg or 75 mg of ontamalimab every 4 weeks. Allocation is dependent on how the subject entered into this study:
• Subjects who completed maintenance study SHP647-303 or SHP647-307 without treatment failure and received either 25 mg or 75 mg of ontamalimab every 4 weeks will continue to receive the same dose of SHP647 in this long term safety extension study.
• All other subjects will be randomized using a 1:1 allocation. Randomization will be stratified by whether the subjects are entering this study following (1) non-response in induction study ; (2) treatment failure in maintenance study; or (3) maintenance study completion for subjects receiving placebo, to facilitate balance of treatment assignment within each stratum.

Intervention

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

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.

Crohn*s disease (CD) is a chronic, relapsing disease marked by granulomatous inflammation of the gastrointestinal (GI) tract. Although the terminal ileum and right colon are the most commonly involved sites, CD can affect any part of the GI tract, from the mouth to the perianal region. Crohn*s disease is a lifelong condition with a serious effect on quality of life. Despite recent advances, there is still an unmet need for a safe, effective, and durable pharmacological treatment that will induce and maintain remission.

Considering the chronic and relapsing characteristics of these lifelong diseases, 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
Shire

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Subjects with Ulcerative Colitis:
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 been enrolled previously in Study SHP647-301 and are in the treatment period of Study SHP647-303, completed the ET or Week 52 visit in maintenance study SHP647 303, had responded to ontamalimab treatment (in the induction and/or maintenance studies), and meet one of the following criteria:
• Subjects are on placebo at the maintenance study ET or Week 52 visit: they received ontamalimab in the induction studies and fulfilled the maintenance study response criteria, OR
• Subjects have received ontamalimab at the maintenance study ET or Week 52 visit:
* Clinical composite score that has decreased by >=2 points and >=30%, with an accompanying decrease in the subscore for RB >=1 point or a subscore for RB <=1, compared to the baseline value for induction studies, and/or
* Composite score that has decreased by >=30% and >=3 points compared to the baseline value for induction studies.
4. Subjects receiving any treatment(s) for UC described in Section 5.1.2.1 are eligible provided they have been, and are anticipated to be, on a stable dose for the designated period of time.

Subjects with Crohn*s Disease:
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 been enrolled previously in Study SHP647-305 and are in the treatment period of Study SHP647-307, completed the ET or Week 52 visit in maintenance study SHP647 307, had responded to ontamalimab treatment (in the induction and/or maintenance studies), and meet one of the following criteria:
• Subjects are on placebo at the maintenance study ET or Week 52 visit: they received ontamalimab in the induction study and fulfilled the maintenance study response criteria, OR
• Subjects have received ontamalimab at the maintenance study ET or Week 52 visit:
* CDAI score that has decreased by >=100 points at EOT visit compared to the baseline value for induction studies, and/or
* SES-CD that has decreased by >=25% compared to the baseline value for induction studies.
4. Subjects receiving any treatment(s) for CD described in Section 5.2.2.1 are eligible provided they have been, and are anticipated to be, on a stable dose for the designated period of time.

Exclusion criteria

Subjects with UC Entering from an Induction or Maintenance Study/Subjects with CD
1. Subjects who had major protocol deviation(s) (as determined by the sponsor) in previous studies.
2. Subjects who permanently discontinued investigational product because of an AE, regardless of relatedness to investigational product, in previous studies.
3. Subjects who are likely to require major surgery for UC/CD.
4. Subjects are females who became pregnant during the previous UC/CD studies, females who are lactating, 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 (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
8. Subjects who have developed any major illness/condition or evidence of an unstable clinical condition (except disease under study) 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 *.tuberculosis (TB) since testing at screening in previous UC/CD studies and who have been advised to require treatment for latent or active disease, but who are without a generally accepted course of treatment.

Subjects with UC Entering directly
1. Subjects with indeterminate colitis, microscopic colitis, nonsteroidal anti-inflammatory drug-induced colitis, ischemic colitis, infectious colitis, or clinical/histologic findings suggestive of CD.
2. Subjects with colonic dysplasia or neoplasia.
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 1), 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.
6. Subjects with known or suspected intolerance or hypersensitivity to the investigational product(s), closely related compounds, or any of the stated ingredients.
7. Subjects have received anti-TNF treatment within 60 days or vedolizumab within 120 days before baseline
8. Subjects have received any biologic with immunomodulatory properties (other than anti-TNFs) within 90 days before baseline
9. Subjects have received any nonbiologic treatment with immunomodulatory properties within 30 days before baseline.
10. Subjects have ever received anti-integrin/adhesion molecule treatment (eg, natalizumab, efalizumab, etrolizumab, or any other investigational anti-integrin/adhesion molecule) with the exception of vedolizumab.
11. Subjects have received parenteral or rectal glucocorticoids, or rectal 5-ASA, within 14 days before screening endoscopic procedure.
12. Subjects have received leukocyte apheresis or selective lymphocyte, monocyte, or granulocyte apheresis or plasma exchange within 30 days before baseline
13. Subjects have participated in other investigational studies within either 30 days or 5 half-lives of investigational product used in the study before baseline

14. Subjects have received a live (attenuated) vaccine within 30 days before the baseline
15. Subjects with active enteric infections, Clostridium difficile infectionor pseudomembranous colitis, evidence of active cytomegalovirus infection or Listeria monocytogenes, known active invasive fungal infections, clinically significant underlying disease that could predispose the subjects to infections, or a history of serious infection within 4 weeks before the baseline

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-01-2019
Enrollment:	9
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:	31-05-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	11-06-2018
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:	21-12-2018
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:	17-11-2020
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)
Approved WMO Date:	03-05-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	24-11-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	13-12-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	05-04-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	30-06-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	18-07-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO	

Date:	18-07-2023
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	EUCTR2017-000574-11-NL
ClinicalTrials.gov	NCT03283085
CCMO	NL62887.028.17