A Phase 2 Long-Term Extension (LTE) Study to Evaluate The Safety and Efficacy of Efavaleukin Alfa in Subjects With Moderately to Severely Active Ulcerative Colitis

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This study has been transitioned to CTIS with ID 2023-506046-24-00 check the CTIS register for the current data. Main:To evaluate the long-term safety and tolerability of efavaleukin alfa in subjects with moderate to severe ulcerative colitis (UC)...

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

Summary

ID

NL-OMON56326

Source
ToetsingOnline

Brief title
20210210

Condition

- Gastrointestinal inflammatory conditions

Synonym
Colitis gravis, Inflammatory bowel disease

Research involving
Human

Sponsors and support

Primary sponsor: Amgen
Source(s) of monetary or material Support: Ministerie van OC&W,Amgen

Intervention

Keyword: inflammation, interleukin, treatment, Ulcerative Colitis

Outcome measures

Primary outcome

Treatment-emergent adverse events

Secondary outcome

- Clinical response at week 52 and 104

- Clinical remission at week 52 and 104

- Durable clinical remission at week 52 and 104

- Endoscopic remission at week 52 and 104

- Histologic remission at week 52 and 104

- Corticosteroid-free remission at week 52 and 104 in subjects receiving

corticosteroids at randomization of Study 20170104

- Combined endoscopic and histologic remission at week 52 and 104

- Symptomatic remission at week 52 and 104

- Change from baseline of Study 20170104 in histological score (Geboes) at week

52 and 104

Study description

Background summary

Ulcerative colitis is a chronic inflammatory bowel disease (IBD) with symptoms

of abdominal pain, bloody diarrhea, and fecal urgency, which can occur without warning, placing a significantburden on daily life. There is an increased risk of colorectal cancer, with risk factors such as long duration of disease, extensive colonic involvement, severe inflammation and epithelialdysplasia, and childhood-onset disease.

Conventional treatment consists of oral or topical aminosalicylates (5-ASAs) or topical steroids for induction of remission and oral and/or topical 5-ASAs for maintenance (Rubin et al 2019).Advanced therapies for treatment include immunosuppressants, biologic therapies such as anti-TNF inhibitors, anti-integrins (ie, vedolizumab), and interleukin-12 and -23 antagonists (ie,ustekinumab) as well as small molecule JAK inhibitors (eg, tofacitinib). Despite this there is a lack of effective treatment, with patients becoming intolerant or nonresponsive with a proportionof patients being unsuitable for treatment. Therefore, there continues to be unmet need for new therapies with better safety and efficacy, particularly for achieving long term, steroid-free,remission and mucosal healing.

A loss of homeostatic balance between Treg and other lymphocytes is considered a causative factor in many inflammatory conditions, with ulcerative colitis associated with geneticpolymorphisms in the IL-2 gene. Efavaleukin alfa is an IL-2 mutein Fc fusion protein that has been developed to preferentially expand Tregs in patients with inflammatory diseases. Thisgreater selectivity of efavaleukin alfa may provide for greater efficacy and a wider therapeutic margin in inflammatory diseases relative to low dose recombinant IL-2 based modalities and,therefore,
supports the investigation of efavaleukin alfa for the treatment of UC with lower side effects.

This study is a phase 2 LTE study for subjects who completed the 52 week phase 2 dose-finding study (Study 20170104). Subjects will enroll into the LTE in a blinded manner on the same dose they were receiving at the completion of their participation in Study 20170104. This study will evaluate the long-term safety and clinical efficacy of efavaleukin alfa in subjects entering Study 20170104 with moderately to severely active UC.

Study objective

This study has been transitioned to CTIS with ID 2023-506046-24-00 check the CTIS register for the current data.

Main:
To evaluate the long-term safety and tolerability of efavaleukin alfa in subjects with moderate to severe ulcerative colitis (UC)

Secondary:
- To evaluate the effect of efavaleukin alfa long-term treatment on clinical

response
- To evaluate the effect of efavaleukin alfa long-term treatment on clinical remission
- To evaluate the effect of efavaleukin alfa long-term treatment on durable clinical remission
- To evaluate the effect of efavaleukin alfa long-term treatment on endoscopic remission
- To evaluate the effect of efavaleukin alfa long-term treatment on histologic remission
- To evaluate the effect of efavaleukin alfa long-term treatment on corticosteroid-free remission - To evaluate the effect of efavaleukin alfa long-term treatment on combined endoscopic and histologic remission
- To evaluate the effect of efavaleukin alfa long-term treatment on symptomatic remission
- To evaluate the effect of efavaleukin alfa long-term treatment on change in histological score

Study design

This phase 2 long-term extension (LTE) study will assess the long-term safety and efficacy of efavaleukin alfa in subjects with moderately to severely active ulcerative colitis (UC). Efavaleukin alfa may be a viable treatment option for patients with moderately to severely active UC who have failed at least one of the following: conventional therapy (eg, immunomodulators, corticosteroids), biologic therapy, or targeted small molecule therapy (ie, Janus kinase [JAK] inhibitor).

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Intervention

Subjects will enroll into the LTE in a blinded manner on the same dose they were receiving at the completion of their participation in study 20170104.

Study burden and risks

See responses to questions E2 / E4 / E6 / E9 and E9a.

The safety of efavaleukin alfa has been evaluated in healthy subjects and in subjects with rheumatoid arthritis (RA), chronic graft versus host disease(cGvHD), and systemic lupus erythematosus (SLE). See Section 2.3 of the

protocol for more information on these studies. Efavaleukin alfa has been well tolerated in clinical studies and has an acceptable safety profile. Based upon the totality of available safety data to date, the benefit/risk profile of efavaleukin alfa is favorable. The benefit risk assessment detailed in Section 2.3 supports the conduct of this phase 2 clinical trial in subjects with UC. Reference should be made to the latest version of the Investigator*s Brochure for further safety data on efavaleukin alfa.

Contacts

Public
Amgen

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

101 Subject has provided informed consent prior to initiation of any study specific activities/procedures.
102 Subject has completed the week 52 endoscopy in the phase 2 parent

dose-finding study (20170104) and who in the opinion of the investigator may benefit from continued treatment.

Exclusion criteria

201 Permanent discontinuation of investigational product during the 52-week phase 2 dose finding study (20170104) for any reason. Disease Related
202 Adenoma and dysplasia exclusion criteria:
o Any current sporadic adenoma without dysplasia (adenomatous polyps occurring proximal to known areas of colitis) that has not been removed.
o Dysplasia occurring in flat mucosa, sporadic adenomas containing dysplasia, and dysplasia-associated lesions or masses will be managed as follows:
* 1. Any history or current evidence of high-grade dysplasia.
* 2. Any history or current evidence of dysplasia occurring in flat mucosa. This includes histopathology reporting indefinite for dysplasia, low-grade dysplasia, and high-grade dysplasia.
* 3. Any history or current evidence of a nonadenoma like dysplasia associated lesions or masses, with or without evidence of dysplasia.
* 4. Any current sporadic adenoma containing dysplasia or any current adenoma-like dysplasia-associated lesions or masses that has not been removed.

Other Medical Conditions
203 Any malignancy diagnosed during Study 20170104, including evidence of cutaneous basal or squamous cell carcinoma or melanoma
204 Active infection (including chronic, acute, recurrent, opportunistic infections) at the time of eligibility evaluation requiring intravenous (IV)anti-infectives or hospitalization (infections requiring oral and/or topicalanti-infective[s] for > 7 days may be allowed in consultation with the Amgen physician).
205 Required systemic corticosteroid use for any indication other than UC. The only exception is corticosteroids used for the treatment of adrenal insufficiency are allowed. Prior/Concomitant Therapy
206 Plan to receive a live (attenuated) vaccine during the treatment period and up to 6 weeks after the last dose of investigational product inthe LTE study.

Prior/Concurrent Clinical Study Experience
207 Currently receiving treatment in another investigational device or drug study. Other investigational procedures while participating in this study are excluded.

Other Exclusions
208 Female subjects who are pregnant or breastfeeding or planning to become pregnant or breastfeed during study and for an additional 6 weeks after the

last dose of investigational product.
209 Female subjects of childbearing potential unwilling to use protocol specified method of contraception see Appendix 5 (Section 11.5) during treatment and for an additional 6 weeks after the last dose of investigational product.
210 Subject has known sensitivity to any of the products to be administered during dosing with the exception of subjects who exhibitedsensitivity in Study 20170104 but did not result in treatment discontinuation.
211 Subject likely to not be available to complete all protocol-required study visits or procedures, and/or to comply with all required study procedures (e.g., Clinical Outcome Assessments) to the best of the subject and investigator's knowledge.
212 Subject has a history or evidence of any other clinically significant disorder (including laboratory abnormalities), condition, or disease that, in the opinion of the investigator or Amgen physician, if consulted would pose a risk to subject safety, or interfere with the study evaluation, procedures, or completion.
214 Female subjects of reproductive potential must agree not to donate eggs during the study and for 6 weeks after receiving the last dose of investigational product.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	29-03-2024
Enrollment:	6
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	efavaleukin alfa
Generic name:	efavaleukin alfa

Ethics review

Approved WMO Date:	28-11-2022
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	22-02-2023
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	10-03-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	21-03-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	02-06-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	06-06-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	10-10-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

Approved WMO Date:	26-10-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	04-01-2024
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-01-2024
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
EU-CTR	CTIS2023-506046-24-00
EudraCT	EUCTR2022-001686-12-NL
ClinicalTrials.gov	NCT-nummernognietbekend.hetnummervolgt
CCMO	NL82759.028.22