A Multi-center, Randomized, Double-blind, Parallel-group, Placebo-controlled 3-Part Phase 3 Study to Demonstrate the Efficacy and Safety of Benralizumab in Patients with Eosinophilic Gastritis and/or Gastroenteritis (The HUDSON GI Study)

Published: 14-06-2021
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The objective of this Phase 3 study is to investigate the safety and efficacy of benralizumab as a treatment for patients with eosinophilic gastritis and/or gastro-enteritis.

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

Summary

ID

NL-OMON50900

Source
ToetsingOnline

Brief title
HUDSON GI

Condition

- Gastrointestinal inflammatory conditions

Synonym
Eosinophilic gastritis and/or gastroenteritis allergic gastritis and/or gastroenteritis

Research involving
Human

Sponsors and support

Primary sponsor: Astra Zeneca
Source(s) of monetary or material Support: AstraZeneca

Intervention

Keyword: Benralizumab, Eosinophilic gastritis and/or Gastroenteritis, IL-5R&alfa, monoklonaal antilichaam

Outcome measures

Primary outcome

Primary objective Part A/B: To compare the effect of benralizumab 30 mg every 4 weeks (Q4W) with placebo on histologic signs and gastrointestinal symptoms in patients with eosinophilic gastritis and/or gastroenteritis.

Histology-based Dual-primary endpoints/variables: Proportion of patients achieving a histological response (defined as <=6 eosinophils/hpf in the stomach and/or, <=15 eosinophils/hpf in the duodenum) at Week 24.
Symptom-based dual primary endpoint: Symptom Endpoint: Absolute change from baseline in SAGED Score at Week 24

Symptom based Endpoint: Absolute change from baseline in SAGED Score at Week 24

Secondary outcome

Secondary objectives Part A/B: To compare the effect of benralizumab 30 mg Q4W with placebo on clinical features of eosinophilic gastritis/ gastroenteritis and disease activity.

Key secondary endpoint: :

* Percentage change from baseline in tissue eosinophils (stomach and/or duodenum if applicable) at Week 24.

* Proportion of patients who achieve treatment response: tissue remission (<=6 eosinophils/hpf in the stomach and <=15 eosinophils/hpf in the duodenum, if applicable) and improvement in symptoms at Week 24

* Change from baseline in proportion of vomiting free days, and change from baseline in frequency of vomiting episodes

* Change from baseline in proportion of diarrheafree days, and change from baseline in frequency of diarrhea episodes

* Change from baseline in proportion of days both diarrhea and constipation free

* Time to clinically meaningful improvement in SAGED score

* Change from baseline in PROMIS Fatigue 7a score and PAGI-SYM score at Week 24

Safety objective: To assess the safety of benralizumab in patients with eosinophilic gastritis and/or gastroenteritis.

Safety endpoint: Adverse Events, vital signs, physical exam, and laboratory parameters.

Study description

Background summary

Eosinophilic gastritis and eosinophilic gastroenteritis (EG/EGE) are rare chronic allergic inflammatory disorders of the gastrointestinal tract characterized by increased infiltration of eosinophils in the stomach and duodenum tissues and accompanying gastrointestinal

symptoms, such as nausea, vomiting, abdominal pain, and diarrhea. Although these disorders have been increasingly recognized and diagnosed in both adults and adolescents, there are currently neither established diagnostic criteria nor treatment guidelines and no approved treatments. Histopathology of affected tissue demonstrates high numbers of eosinophils and evidence of eosinophilic degranulation. This increase, especially when associated with aggregation, degranulation and infiltration of squamous epithelium along with architectural changes in the mucosa, indicates a pathologic process, and the histopathology of affected tissue demonstrates high numbers of eosinophils and evidence of eosinophilic degranulation (Egan and Furuta 2018). Currently there are no established treatment guidelines and no approved treatments for EG/EGE. Dietary elimination therapy and corticosteroids (systemic and topical) are the most common treatments but are suboptimal and have limitations. Benralizumab is a humanized, afucosylated, monoclonal antibody that binds specifically to the IL-5Rα on target cells, resulting in the depletion of eosinophils through antibody-dependent cell-mediated cytotoxicity. This mechanism of action makes benralizumab a potential treatment for patients with symptomatic and histologically active EG/EGE. This 3-part Phase 3 study will 1) validate a patient-reported outcome (PRO) instrument for EG/EGE symptoms while providing preliminary efficacy and safety data (24-week Part A), 2) provide pivotal efficacy and safety data for EG/EGE for the registration of this indication (24-week Part B), and 3) provide long-term efficacy and safety data of benralizumab (Part C) during an open label extension.

Study objective

The objective of this Phase 3 study is to investigate the safety and efficacy of benralizumab as a treatment for patients with eosinophilic gastritis and/or gastro-enteritis.

Study design

This is a 3-part study. Part A and Part B have identical designs (ie, parallel-group, randomized, double-blinded, placebo-controlled with 24-week treatment periods), with enrollment/randomization performed sequentially. Part A will be enrolled first, followed by Part B. Parts A and Parts B will include approximately 70 and 150 unique participants in total with eosinophilic gastritis (with or without eosinophilic duodenitis) or duodenal-only disease, including a minimum of at least 50 and 110 patients with EG (with or without duodenal involvement) in each part, respectively. After a 4-week to 8-week run-in period, symptomatic participants with EG with or without duodenitis and patients with eosinophilic duodenitis only, on stable background medications and diet, with histologically-confirmed disease will be randomized 1:1 to benralizumab or placebo treatments. Part A will be enrolled first, followed by

Part B. After completing Part A or Part B, participants will continue to Part C, an extended open-label benralizumab treatment period. Participants will remain on stable background medication and diet throughout the first 52 weeks of the study (including Part A/B and the
first 28 weeks of Part C). After 52 weeks of treatment with stable diet and medications, investigators may adjust background medication and diet restrictions as clinically indicated.

Intervention

After a 4-week to 8-week run-in period, eligible patients with gastritis and/or gastro-enteritis will be randomized 1:1 to24 weeks of subcutaneous treatment with benralizumab 30 mg Q4W or matching placeboQ4W, in either Part A or Part B. Subsequently, all participants will receive benralizumab 30 mg Q4W subcutaneously in an open-label period, Part C, which is intended to allow patients at least 1 year of treatment with open-label benralizumab treatment. Patients will maintain stable background medication and diet regimen for EG/EGE treatment through Week 52. After this timepoint investigators may consider clinically appropriate adjustments to background medications and dietary restrictions.

Study burden and risks

For the double-blind treatment period, the subject is asked to visit the hospital at least 8 times. Each visit will last 1-4 hours. For the open label treatment period, the subject may self-administer the study drug at home during two consecutive visits. (from week 32) This will then be a telephone appointment. The next (third) visit will take place in the hospital. The subject will receive study drug 14 times for 52 weeks. If the subject participates in the study extension, the subject will receive study drug 20 times over 76 weeks. Thereafter, the subject can participate in an extension period and receive the study drug every 4 weeks. For the open label extension treatment period from week 76, it is also possible to administer benralizumab at home for 2 visits and then again during a hospital visit. This visit will last 1-2 hours.
The study drug can cause allergic reactions. A study physician will be present during the administration of the studydrug and will observe the subject for at least one hour after administration of the studydrug. In addition, the subject may suffer from side effects of the studydrug. Blood samples will be taken during the study. The total blood volume to be collected during the first year is 190 ml. The subject will receive a physical examination at each visit. The subject will undergo an endoscopy including biopsies at least 3 times during the study. Endoscopies involve risks and inconveniences, but the number of endoscopies is equal to the number of endoscopies in standard practice. An ECG is made during one visit. Women of childbearing potential will be required to provide a urine sample to take a pregnancy test during the screening visit and

each time prior to study drug administration, The subject is asked to complete questionnaires during each hospital visit. The subject will complete daily, weekly and monthly questionnaires in an electronic diary. This will take about 10 minutes per day.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

· Aged >= 12 years of age at the time of signing the ICF or informed consent or assent form.
· Confirmed diagnosis of EG/EGE for at least 3 months prior to screening.
· Baseline Eosinophilic gastritis, with or without duodenitis, or eosinophilic duodenitis alone confirmed by biopsy
with a gastric count of >=30 eosinophils/hpf in at least 5 hpfs and/or duodenal eosinophil count >=30 eosinophils/hpf in at least 3 hpfs without any other cause

for the gastrointestinal eosinophilia.
· Symptoms including at least moderate abdominal pain, nausea, bloating, early satiety, and/or loss of appetite
· Must be adherent to daily PRO assessments including at least 8 of 14 symptom assessments in the 14 days prior to randomization
· If on background medications for EG/EGE, the medications should be stable at least 4 weeks prior to the run-in period.
· Willing and able to comply with all study procedures and visit schedule including follow-up visits
· Women of childbearing potential must agree to use a highly effective form of birth control (confirmed by the Investigator) from randomization throughout the study duration and within 12 weeks after last dose if IP.

Exclusion criteria

· Other gastrointestinal disorders such as active Helicobacter pylori infection, history of achalasia, esophageal varices, Crohn's disease, ulcerative colitis, inflammatory bowel disease, or celiac disease.
· Hypereosinophilic syndrome or eosinophilic granulomatosis with polyangiitis.
· Current malignancy, or history of malignancy, except for patients who have had basal
cell, localized squamous cell carcinoma of the skin, or in situ carcinoma of the cervix are
eligible provided that the patient is in remission and curative therapy was completed at
least 12 months prior to the date of informed consent.
· History of anaphylaxis to any biologic therapy or vaccine.
· Current active liver disease.
· Helminth parasitic infection diagnosed within 24 weeks prior to the date informed that has not been treated with or has failed to respond to standard of care therapy.
· Known immunodeficiency disorder including testing positive for HIV.
· Concomitant use of immunosuppressive medication.
· Receipt of live attenuated vaccines 30 days prior to date of informed consent or assent.
· Receipt of inactive vaccines within 7 days of informed consent or assent.
· Initiation or change of a food-elimination diet regimen or re-introduction of a previously
eliminated food group from 6 weeks prior to start of the run-in period and unable or
unwilling to remain on a stable diet until the completion of Week 52.
· Currently pregnant or breast-feeding.

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:	Recruiting
Start date (anticipated):	21-03-2022
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Fasenra
Generic name:	Benralizumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	14-06-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-09-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO Date:	29-11-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-12-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-04-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-05-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-05-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-06-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-01-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-02-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2021-000085-14-NL
ClinicalTrials.gov	NCTnummervolgt
CCMO	NL77322.018.21