A Multicentre, Randomised, Double-blind, Parallel-group, Placebo controlled, 24-week Phase 3 Study with an Open-label Extension to Evaluate the Efficacy and Safety of Benralizumab in Patients with Hypereosinophilic Syndrome (HES)

Published: 03-11-2021
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This study has been transitioned to CTIS with ID 2023-510455-28-00 check the CTIS register for the current data. This study is being carried out to investigate the treatment with benralizumab in patients with active HES.The purpose of this study is...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	White blood cell disorders
Study type	Interventional

Summary

ID

NL-OMON54266

Source
ToetsingOnline

Brief title
Evaluation of the Efficacy and Safety of Benralizumab in patients with HES

Condition

- White blood cell disorders

Synonym
Hypereosinophilic Syndrome

Research involving

Human

Sponsors and support

Primary sponsor: Astra Zeneca
Source(s) of monetary or material Support: Industry;by the sponsor AstraZeneca

Intervention

Keyword: Benralizumab, HES, NATRON

Outcome measures

Primary outcome

Primary endpoint:

- To evaluate the effect of benralizumab on the time to first HES worsening/flare

For more details, please see Protocol V6.0, part 3 Objectives and Endpoints

Secondary outcome

Secundary Endpoints of the Open-Label Treatment: - To evaluate the effect of benralizumab on the time to first haematological relapse - To evaluate the effect of benralizumab on the proportion of patients who experience HES worsening/flare - To evaluate the effect of benralizumab on the proportion of patients with haematologic relapse - To evaluate the effect of benralizumab on the number of patients who maintain AEC < 500 cells/µL for 24 weeks - To evaluate the effect of benralizumab on corticosteroid use - To evaluate the effect of benralizumab on patient-reported measure of fatigue - To evaluate the

effect of benralizumab on health status/health-related quality of life (HRQoL)

measures For more details, please see Protocol V6.0, part 3 Objectives and

Endpoints

Study description

Background summary

Benralizumab is an antibody (i.e. biologic drug) that has been made to reduce the number of eosinophils in the body. A previous benralizumab HES study showed that benralizumab may reduce eosinophils in blood and tissues in patients with severe HES that is not well controlled by standard of care medications. Benralizumab is not approved by any health authority for treatment of HES, except for use in research studies like this. Health authorities are authorities who supervise the study, who approve the commercialisation of the drug or who receive the adverse events reporting, whether in your country or in other countries. Benralizumab is an approved treatment for severe eosinophilic asthma in the US, Europe, Canada and other countries under the trade name Fasenra.

Study objective

This study has been transitioned to CTIS with ID 2023-510455-28-00 check the CTIS register for the current data.

This study is being carried out to investigate the treatment with benralizumab in patients with active HES.
The purpose of this study is to see if benralizumab, given as injections under the skin, can help control your HES better if it is added to available standard of care HES medications which you are currently taking.

Study design

This is a multicentre, randomised, Double-blind, parallel-group, placebo-controlled, 24-week Phase 3 study to compare the efficacy and safety of benralizumab 30 mg versus placebo administered by SC injection Q4W in patients with HES.

The study is double-blind for the first 24 weeks, with 1:1 randomization to benralizumab or placebo.
This is followed by an open-label part, at least 1 year for each participant, in which benralizumab is given.

See Protocol V6.0 Part 4 Study Design

Intervention

The Treatment options includes:

- Treatment with 1 investigational product; Benrazilumab vs placebo

See Protocol V6.0 Part 6 Study Treatment

Study burden and risks

Safety and tolerability data from the Phase 2 study of benralizumab in patients with HES showed that benralizumab was well-tolerated, with similar rates of AEs observed between active and placebo groups.

Total AEs, Grade 3 AEs, and the number of patients reporting an AE were similar between the benralizumab and placebo groups. No new safety signals for benralizumab were identified in this study of patients with HES.

Given the initial study results for benralizumab in HES, potential benefits of this similarly designed Phase 3 study include: reduction in the incidence of HES worsening/flare, reduction in haematological relapse, and improvement in patient symptoms while exhibiting a safety profile similar to placebo.

Given the extensive safety data already available at the dosing regimen to be studied, the benefit/risk profile in patients with HES is expected to continue to be favourable, commensurate with that observed in the benralizumab asthma pivotal trials and the HES Phase 2 study. Risk minimisation measures include exclusion of patients with life-threatening HES and/or HES complication(s), patients with a history of thrombotic complications, stroke, or significant cardiac damage related to HES, untreated parasitic infection, a history of anaphylaxis to any biologic therapy, active or recent malignancy, and exclusion of pregnant women. Risk minimisation measures will be maintained during the conduct of this study, in conjunction with the performance of the Sponsor*s routine pharmacovigilance activities.

See protocol V6.0, Part 2.3 Benefit/Risk and Investigator Brochure Ed 19

Contacts

Public
Astra Zeneca

n/a n/a
Södertälje SE-151 85
SE
Scientific
Astra Zeneca

n/a n/a
Södertälje SE-151 85
SE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Adults with documented diagnosis of HES
* Stable HES treatment dose(s) and regimen for >= 4 weeks at the time of Visit 1
* Signs or symptoms of HES worsening/flare and/or laboratory abnormalities indicative of HES worsening/flare (other than isolated eosinophilia) at Visit 1.
OR
A documented history of 2 or more HES worsening/flares within 12 months prior to Visit 1 requiring an escalation in therapy.
* At least one flare within the past 12 months must not be related to a decrease in HES therapy during the 4 weeks prior to the flare.

For more details, see protocol section 5.1

Exclusion criteria

* Life-threatening HES and/or HES complication(s) as judged by the Investigator
* Current malignancy, or history of malignancy
* A history of known immunodeficiency disorder other than that explained by the

use of OCS or other therapy taken for HES. Positive human immunodeficiency virus (HIV) test.

For more details, see protocol Section 5.2

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):	13-01-2023
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Benralizumab
Generic name:	MEDI-563, FASENRA
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	03-11-2021

Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-05-2022
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-10-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-11-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-04-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-06-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-10-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-10-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	07-11-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-11-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	CTIS2023-510455-28-00
EudraCT	EUCTR2019-002039-27-NL
ClinicalTrials.gov	NCT04191304
CCMO	NL79083.078.21