A Phase 3, 52-week, open-label, single arm study to investigate the efficacy and safety of mepolizumab SC in participants aged 6 to 17 years with hypereosinophilic syndrome.

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This study has been transitioned to CTIS with ID 2023-510110-36-00 check the CTIS register for the current data. Primary objective: To evaluate the efficacy of mepolizumab SC given every 4 weeks in participants aged 6 to 17 years with HESSecondary...

Ethical review	Approved WMO
Status	Pending
Health condition type	Haematopoietic neoplasms (excl leukaemias and lymphomas)
Study type	Interventional

Summary

ID

NL-OMON51313

Source
ToetsingOnline

Brief title
Study in Paediatrics with HypEREosinophilic syndrome (SPHERE)

Condition

- Haematopoietic neoplasms (excl leukaemias and lymphomas)

Synonym
HES, Hypereosinophilic syndrome

Research involving
Human

Sponsors and support

Primary sponsor: GlaxoSmithKline
Source(s) of monetary or material Support: GlaxoSmithKline Research & Development Limited

Intervention

Keyword: hypereosinophilic syndrome, mepolizumab, pediatric, phase 3

Outcome measures

Primary outcome

Frequency of HES flares over the 52-week study treatment period

Secondary outcome

- Change in the mean daily OCS dose (prednisone/prednisolone or equivalent)

from Weeks 0 to 4 to Weeks 48 to 52

- Reduction of >=50% in mean daily OCS dose (prednisone/prednisolone or

equivalent) from Weeks 0 to 4 compared with Weeks 48 to 52

- Achieving a mean daily OCS dose (prednisone/prednisolone or equivalent) of

<=7.5 mg during Weeks 48 to 52

- Achieving a mean daily OCS dose (prednisone/prednisolone or equivalent) of

<=7.5 mg during Weeks 48 to 52

- Change from baseline in fatigue severity based on weekly average score of

Brief Fatigue Inventory (BFI) item 3 (worst level of fatigue during past 24

hours) for Week 52

- Occurrence of anti-drug antibodies (ADA) and neutralising antibodies (NAb)

- Ratio to baseline in absolute blood eosinophil count at discrete time points

during the 52-week study treatment period

- Mepolizumab plasma concentration at discrete time points during the 52-week

study treatment period

Study description

Background summary

Hypereosinophilic syndrome (HES) is a group of rare haematological disorders without a known cause in which eosinophils are overproduced in the bone marrow for prolonged periods of time. The goal of HES treatment is to relieve symptoms and to reverse or delay progression of any further organ damage caused by activated eosinophils. Mepolizumab has been shown to be efficacious and well tolerated in patients with HES.

The purpose of this study is to investigate the efficacy and safety of mepolizumab SC in children (aged 6 to 11 years) and adolescents (aged 12 to 17 years) with HES who are receiving standard of care (SoC) therapy. The primary objective of the study is to evaluate the efficacy of mepolizumab SC given every 4 weeks in participants aged 6 to 17 years with HES.

Study objective

This study has been transitioned to CTIS with ID 2023-510110-36-00 check the CTIS register for the current data.

Primary objective: To evaluate the efficacy of mepolizumab SC given every 4 weeks in participants aged 6 to 17 years with HES

Secondary objectives:
- To assess the effect of mepolizumab SC given every 4 weeks on the change in oral corticosteroid (OCS) dose in participants aged 6 to 17 years with HES that are taking OCS at baseline
- To assess the effect of mepolizumab SC given every 4 weeks on the change in oral corticosteroid (OCS) dose in participants aged 6 to 17 years with HES
- To assess the efficacy of mepolizumab SC given every 4 weeks on fatigue in participants aged 12 to 17 years with HES
- To evaluate the immunogenicity of mepolizumab SC given every 4 weeks in participants aged 6 to 17 years with HES
- To assess the effect of long-term use of mepolizumab SC on a pharmacodynamics (PD) marker in participants aged 6 to 17 years with HES.
- To assess the pharmacokinetics (PK) of mepolizumab SC in participants aged 6 to 17 years with HES

Study design

This is a 52-week, open-label, single arm, multicentre study of SC mepolizumab in children and adolescent participants with HES receiving SoC therapy.

Intervention

participants receive mepolizumab as 1-3 injections every 4 weeks over a treatment period of 52 weeks (last dose at week 48). The amount depends on a participants age and weight. In this period, participants will also take their regular medicine (standard of care)

Study burden and risks

Please refer to the schedule of activities in the protocol, table 1 (p14-19)

This study takes up to 1 year and 3 months. Participants visit the hospital every 4 weeks during the treatment period. The treatment period takes 52 weeks in total.

During the treatment period, the following tests and procedures can be done during a visit, but not necessarily during each visit.
- Do a physical examination including height and weight
- Do a HES core assessment, which means the study doctor will look and write down your HES symptoms.
- Ask about concomitant medication including Oral Corticosteroids (OCS)
- Review the Healthcare Resource Utilisation (HCRU) worksheet in which you write down any other doctor visits or treatments you have received.
- Fill in some questionnaires
- Ask your parents/guardians to fill in some questionnaires.
- Do a ung test (Spirometry)
- Do an echocardiogram
- Do an AE/SAE assessment
- Measure your vital signs
- Perform an ECG
- Take some blood
- Collect some urine
- Administer the study drug

Contacts

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Scientific
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GB

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

Age:
1. Participant must be aged 6 to 17 years inclusive, at Screening (Visit 1);

Type of Participant and Disease Characteristics:
2. Participants who have been diagnosed with HES for at least 6 months prior to enrolment (Visit 2);
3. A history of 2 or more HES flares within the past 12 months prior to Screening (Visit 1);
4. Participants must have blood eosinophil count >=1000 cells/µL present at Screening;
5. Participants must be on a stable dose of HES therapy for the 4 weeks prior to the first dose of mepolizumab (Visit 2);

Sex and Contraceptive/Barrier Requirements:
6. Male and/or female [(according to their reproductive organs and functions assigned by chromosomal complement)] [FDA, 2016].
• Contraception and barriers as well as pregnancy testing is required as

appropriate for the age and sexual activity of paediatric participants and as required by local regulations.
A female participant is eligible to participate if she is either:
• Premenarcheal or
• Not pregnant as confirmed by a negative urine (or serum if required by local regulations) human chorionic gonadotrophin [hCG] test if of reproductive potential.
Females of childbearing potential must commit to consistent and correct use of an acceptable method of contraception (see Section 10.4, Appendix 4 of the study protocol) for the duration of the trial and 16weeks after the last dose of investigational product. A urine pregnancy test is required of females of childbearing potential.

Informed Consent and Assent
7. The investigator, or a person designated by the investigator, will obtain written informed consent from each study participant's (legal guardian as defined in Section 10.1.3 of the study protoocol) and the participant's assent, when applicable, before any study-specific activity is performed (unless a waiver of informed consent has been granted by an Institutional Review Board [IRB]/Ethics Committee [EC]). All legal guardians should be fully informed, and participants should be informed to the fullest extent possible, about the study in language and terms they are able to understand.
8. The participant capable of providing signed and dated written assent signs and dates a written assent form (age appropriate) and the parent/guardian signs and dates a written informed consent form (ICF) for study participation prior to the initiation of any study-related activities.

Other
9. A legal guardian or primary caregiver must be available to help the study-site personnel ensure follow-up; support the participant to attended assessment days according to the SoA (e.g., able to comply with scheduled visits, treatment plan, laboratory tests, and other study procedures); consistently and consecutively be available to provide information on the participant using the rating scales during the scheduled study visits; accurately and reliably dispense study intervention as directed.

Exclusion criteria

Medical Conditions:
1. Life-threatening HES or life-threatening HES co-morbidities:
Imminently life threatening HES disease severity such that (a) likelihood of death is high unless the course of the disease is interrupted within 12 weeks prior to Visit 2 (b) likelihood of severe deterioration of HES is high unless immediate therapeutic intervention is provided.
2. Other concurrent medical conditions that may affect the participant's safety:

Participants who have known, pre-existing, clinically significant endocrine, autoimmune, metabolic, neurological, renal, gastrointestinal, hepatic, haematological, respiratory, or any other system abnormalities that are not associated with HES and are uncontrolled with standard treatment.
3. Eosinophilia of unknown significance
4. FIP1L1-PDGFRα (F/P) Status: Participants who test positive for F/P
5. Clinical diagnosis of EGPA
6. Infection:
• Participants with chronic or ongoing active infections requiring systemic treatment, as well as participants who have experienced clinically significant infections due to viruses, bacteria, and fungi within 4 weeks prior to enrolment (Visit 2).
• Participants with a pre-existing parasitic infestation within 6 months prior to enrolment (Visit 2).
7. Participants with a known immunodeficiency (e.g., HIV), other than that explained by the use of OCS or other therapy taken for HES.
8. Participants with documented history of any clinically significant cardiac damage prior to Screening (Visit 1) that, in the opinion of the investigator, would impact the participant's participation during the study.
9. Malignancy:
• Participants with a history of or current lymphoma
• Participants with current malignancy or previous history of cancer in remission for less than 12 months prior to Screening (Visit 1).
Participants that had localised carcinoma (i.e., basal or squamous cell) of the skin that was resected for cure will not be excluded.
10. Participants who are not responsive to OCS based on clinical response or blood eosinophil counts.

Prior/Concomitant Therapy:
11. Participants who have previously received mepolizumab in the 4 months prior to enrolment (Visit 2).
12. Participants receiving any of the following:
• IV or SC corticosteroids in the 4-week period prior to enrolment (Visit 2).
• Any other monoclonal antibodies within 30 days or 5 half-lives, whichever is longer, of enrolment (Visit 2).

Other investigational product/clinical study:
13. Participants who have received treatment with an investigational agent (biologic or non-biologic) within the past 30 days or 5 drug half lives, whichever is longer, prior to enrolment (Visit 2). The term "investigational" applies to any drug not approved for sale in the country in which it is being used or investigational formulations of marketed products
14. Use of candidate COVID-19 vaccines that have not received limited, accelerated, or full authorisation/approval, and are only in use as part of a clinical trial
15. Participants who are currently participating in any other interventional

clinical study

Contraindications:
16. Participants with any history of hypersensitivity to any monoclonal antibody (including mepolizumab)

Other Exclusions:
17. 12-lead ECG finding:
For all participants:
• An abnormal ECG finding from the 12-lead ECG conducted at Visit 1 if considered to be clinically significant and would impact the participant's participation during the study based on the evaluation of the investigator.
For participants aged 6 to 11 years:
• QT interval corrected using Fridericia's formula (QTcF) > 450 msec.
• Left bundle branch block
For participant aged 12 to 17 years:
• QTcF > 450 msec or QT interval corrected for heart rate (QTc) > 480 msec in participants with bundle branch block
18. Liver abnormality/disease
19. Other laboratory abnormalities

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	31-01-2023
Enrollment:	3
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Nucala
Generic name:	Mepolizumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	07-09-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-03-2023
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-05-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-07-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-08-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-11-2023
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-05-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	CTIS2023-510110-36-00
EudraCT	EUCTR2021-000933-15-NL
ClinicalTrials.gov	NCT04965636
CCMO	NL81252.056.22