A 52-week, randomized, double-blind, double-dummy, parallel-group, multi-centre, non-inferiority study to investigate the efficacy and safety of depemokimab compared with mepolizumab in adults with relapsing or refractory Eosinophilic Granulomatosis with Polyangiitis (EGPA) receiving standard of care (SoC) therapy

Published: 15-09-2022
Last updated: 05-10-2024

This study has been transitioned to CTIS with ID 2023-510019-20-00 check the CTIS register for the current data. Primary:To evaluate the efficacy of depemokimab 200 mg SC every 26 weeks compared with mepolizumab 300 mg SC every 4 weeks in...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON53511

Source
ToetsingOnline

Brief title
OCEAN (depemokimab efficacy eosinophilic granulomatosis with polyangiitis)

Condition

- Autoimmune disorders

Synonym
EGPA, Eosinophylic Granulomatosis with Polyangiitis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: depemokimab, EGPA, mepolizumab, phase 3

Outcome measures

Primary outcome

Remission (i.e., a Birmingham Vasculitis Activity Score (BVAS)=0 and a dose of

oral corticosteroids (OCS) <=4mg/day) at both Week 36 and Week 52

Secondary outcome

•Total accrued duration of remission, i.e., the accrued number of weeks where

BVAS=0 plus OCS dose <=4 mg /day over the 52-week intervention period

categorised as zero weeks; >0 to <12 weeks; 12 to <24 weeks; 24 to <36 weeks or

>=36 weeks

•Total accrued duration of remission, i.e., the accrued number of weeks where

BVAS=0 plus OCS dose <=4 mg /day over the 52-week intervention period

•Time to first EGPA relapse

• Mean OCS dose during the last 4 weeks of the study treatment period (Weeks 49

to 52) categorised as 0, >0 to <=4, >4 to <=7.5 or >7.5 mg/day

• Remission (BVAS=0 and OCS <=4mg/day) within the first 24 weeks with continued remission until Week 52

• Remission using the European League against Rheumatism (EULAR) definition; BVAS=0 and OCS <=7.5 mg/day at both Week 36 and Week 52

• Total accrued duration of remission according to the EULAR definition of remission, i.e., the accrued number of weeks where BVAS=0 plus OCS <=7.5 mg/day over the 52-week intervention period categorised as zero weeks; >0 to <12 weeks; 12 to <24 weeks; 24 to <36 weeks or >=36 weeks

• Total accrued duration of remission according to the EULAR definition of remission, i.e., the accrued number of weeks where BVAS=0 plus OCS <=7.5 mg/day over the 52-week intervention period

• Remission (BVAS=0 and OCS <=7.5 mg/day) within the first 24

Study description

Background summary

Eosinophilic granulomatosis with polyangiitis, formerly known as Churg-Strauss syndrome, is a rare hypereosinophilic syndrome characterised by small vessel necrotizing vasculitis in association with asthma, sinusitis, and pulmonary infiltrates. Eosinophilic Granulomatosis with Polyangiitis can be life-threatening and multiple organs can be affected including the heart, lungs, skin, gastrointestinal tract, kidneys, and nervous system. EGPA is associated with a positive status for antineutrophil cytoplasmic antibodies (ANCAs), typically antineutrophil cytoplasmic antibodies (ANCA)-Myeloperoxidase and ANCA-Proteinase 3, in approximately 40% of subjects. Overall, the incidence of EGPA across the world ranges from 0.18 to 4.0 cases per million person-years. The prevalence of EGPA across the world ranges from 2.0 to 30.4 cases per million persons. In a systematic review and meta analysis of 35 observational studies describing the incidence and prevalence of EGPA, the pooled global estimate of EGPA was 1.22 cases per million person-years and 15.27 cases per million persons, respectively.

Disease onset typically occurs in people aged 40-60 years, and there is no known sex, familial, or ethnic predisposition to EGPA. EPGA is a relapsing, remitting disease, and it is estimated that 10% to 35% of participants will relapse after achieving initial remission. The predominance of eosinophils in the peripheral blood and tissues in patients with EGPA has suggested a central role for eosinophils in the pathogenesis of this disease by means of tissue and vascular infiltration and inflammation through a variety of mediators.

Disease management relies on the EGPA Consensus Task Force recommendations for the treatment of EGPA and the recent recommendations endorsed by the American College of Rheumatology (ACR) and the Vasculitis Foundation for the management of antineutrophil cytoplasmic antibody-associated vasculitis (AAV) which are aimed at remission-induction and prevention of relapse. Treatment of EGPA is adjusted according to disease severity with systemic corticosteroids and immunosuppressive agents being the SoC therapies.

Treatment of EGPA patients with mepolizumab 300 mg SC provided strong evidence of efficacy, a favourable safety profile and an overall positive benefit:risk profile. Furthermore, a comprehensive systemic review by the ACR on benefits and harms of common treatment of EGPA and the ACR Guideline for the Management of Antineutrophil Cytoplasmic Antibody-Associated Vasculitis recommended the use of mepolizumab for the treatment of non-severe EGPA.

Depemokimab is a humanised IgG1 monoclonal antibody that is directed against the same cytokine, IL-5, and binds to the same epitope on IL-5 as mepolizumab. It is therefore expected to demonstrate comparable efficacy and safety compared to mepolizumab and other biologics in its class, with the added convenience of an extended duration of action and, therefore, a reduced healthcare and patient burden due to the less frequent SC dosing (i.e. once every 26 weeks).

This study has been designed to investigate the efficacy and safety profile of depemokimab as an add on to SoC therapy compared with mepolizumab as an add on to SoC therapy.

Study objective

This study has been transitioned to CTIS with ID 2023-510019-20-00 check the CTIS register for the current data.

Primary:
To evaluate the efficacy of depemokimab 200 mg SC every 26 weeks compared with mepolizumab 300 mg SC every 4 weeks in participants with relapsing or refractory EGPA receiving SoC therapy

Secondary:
- To evaluate the efficacy of depemokimab 200 mg SC every 26 weeks compared with mepolizumab 300 mg SC every 4 weeks on additional efficacy assessments in

participants with relapsing or refractory EGPA receiving SoC therapy

Study design

This is a 52-week, randomized, double-blind, double-dummy, parallel-group, multi-centre, non-inferiority study to investigate the efficacy and safety of depemokimab compared with mepolizumab in adult participants with a history of relapsing or refractory EGPA who are on stable corticosteroid therapy with or without concomitant stable immunosuppressant therapy.

Participants are required to be on a stable dose of OCS, i.e., >=7.5 mg/day prednisolone/prednisone (but not >50 mg/day), for at least 4 weeks prior to baseline (Randomization/Visit 2). Participants receiving other immunosuppressive therapy must be on a stable dose for at least 4 weeks prior to baseline (Randomization/Visit 2) and should continue with the immunosuppressive therapy for the duration of the study.

Participants will be randomly assigned in a 1:1 ratio to receive either 200 mg depemokimab SC administered every 26 weeks as an add on to SoC therapy or 300 mg mepolizumab SC administered every 4 weeks as an add on to SoC therapy.

The study will comprise a screening/run-in period (1 to 4 weeks), intervention period (52 weeks) and a follow-up period (4 weeks).

Intervention

Participants will receive treatment with either depemokimab 200 mg every 26 weeks (at Week 0 and Week 26) or mepolizumab 300 mg every 4 weeks, administered SC using a pre-filled safety syringe (PFS) while continuing their SoC EGPA therapy. The treatment duration is 52 weeks followed by a non-treatment 4-week follow-up period. The final dose of depemokimab will be administered at Week 26 and the final dose of mepolizumab will be administered at Week 48.

Study burden and risks

Please refer to the study schedule in the protocol (p.15-24)

Participating in this study is 1 year and 2 months. Subjects will visit the hospital every 4 weeks, with exception of visit 3 which takes place 2 weeks following visit 2. Subjects can decide to stop receiving the study drug, but continue with participation and undergo all tests and procedures.

During this study, the following tests and assessments can be done, but not necessarily during every visit:
- Check your concomitant medications
- Physical examination

- Electrocardiogram (ECG)
- A breathing test (Spirometry).
- Blood test
- Urine samples for safety tests
- If you are a woman of childbearing potential, you will be asked to provide some urine for a pregnancy test.
- Fill in questionnaires

If a subject decides to participate in optional biomarker analysis and/or genetic testing, additional blood and urine will be collected during visits.

Contacts

Public
GlaxoSmithKline

Great West Road 980
Brentford, Middlesex TW8 9GS
GB
Scientific
GlaxoSmithKline

Great West Road 980
Brentford, Middlesex TW8 9GS
GB

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Participant (male or female) must be 18 years or older at the time of signing the informed consent.
2. Participants who are >= 40 kg at Screening Visit 1.
3. Participants with a documented diagnosis of EGPA for at least 6 months based on the history or presence of: asthma plus eosinophilia defined in this study as >1.0x109/L and/or >10% of leucocytes plus at least 2 of the following additional features of EGPA:
• a biopsy showing histopathological evidence of eosinophilic vasculitis, or perivascular eosinophilic infiltration, or eosinophil-rich granulomatous inflammation
• neuropathy, mono or poly (motor deficit or nerve conduction abnormality)
• pulmonary infiltrates, non-fixed
• sino-nasal abnormality
• cardiomyopathy (established by echocardiography or magnetic resonance imaging [MRI])
• glomerulonephritis (haematuria, red cell casts, proteinuria)
• alveolar haemorrhage (by bronchoalveolar lavage)
• palpable purpura
• ANCA positive Myeloperoxidase (MPO) or Proteinase 3 (PR3).
4. History of relapsing OR refractory disease defined as:
• Relapsing disease: Participants must have a history of at least one confirmed EGPA relapse (i.e., requiring increase in oral corticosteroid (OCS) dose, initiation/increased dose of immunosuppressive therapy or inpatient hospitalisation due to EGPA) within the past 2 years. EGPA relapse should have occurred at least 12 weeks or more prior to Screening (Visit 1) whilst receiving a dose of prednisolone (or equivalent of) >=7.5 mg/day.
• China and Japan only definition of Relapsing disease: Participant must have a history of at least one confirmed EGPA relapse (i.e., requiring increase in OCS dose, initiation of IV prednisolone (or equivalent), initiation/increased dose of immunosuppressive therapy, initiation/increased dose of intravenous immunoglobulin (IVIG) or hospitalisation) within the past 2 years which occurred at least 12 weeks prior to Screening (Visit 1) whilst receiving a dose of prednisolone (or equivalent of) >=7.5 mg/day.
• Refractory disease: Defined as either:
o Failure to attain remission (BVAS=0 and OCS dose <=7.5 mg/day prednisolone or equivalent) within the last 6 months prior to Screening Visit 1 and following induction treatment with a standard OCS regimen, administered for at least 3 months
OR
o Participants with recurrence of EGPA symptoms within 6 months prior to Screening (Visit 1) whilst tapering OCS and occurring at any dose level >=7.5 mg/day prednisolone or equivalent.
5. Corticosteroid therapy: Participants must be on a stable dose of oral prednisolone or prednisone of >=7.5 mg/day (but not >50 mg/day) for at least 4

weeks prior to Baseline (Visit 2).
6. Immunosuppressive therapy: If receiving immunosuppressive therapy (excluding cyclophosphamide) the dosage must be stable for the 4 weeks prior to Baseline (Visit 2) and during the study.
7. A female participant is eligible to participate if she is not pregnant or breastfeeding, and one of the following conditions applies:
• Is a woman of nonchildbearing potential (WONCBP)
• Is a woman of childbearing potential (WOCBP) and using a contraceptive method that is highly effective, with a failure rate of <1%, from at least 14 days prior to the first dose of study intervention until the following durations (whichever is greater):
o 30 weeks after the last potential administration of depemokimab at Week 1 or Week 26,
o 16 weeks after the last potential administration of mepolizumab (remaining administrations).
8. Capable of giving signed informed consent as described in Section 10.1 which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in this protocol.
French participants: In France, a participant will be eligible for inclusion in this study only if he/she is either affiliated to or a beneficiary of a social security category.

Exclusion criteria

1. Diagnosed with granulomatosis with polyangiitis (GPA; previously known as Wegener's granulomatosis) or microscopic polyangiitis (MPA).
2. EULAR defined organ-threatening EGPA: Organ-threatening EGPA as per EULAR criteria, i.e., organ failure due to active vasculitis, creatinine >5.8 g/dL (>513 µmol/L) within 3 months prior to Screening (Visit 1).
3. Imminently life-threatening EGPA disease defined as any of the following within 3 months prior to Screening (Visit 1):
• Intensive care required
• Severe alveolar haemorrhage or haemoptysis requiring transfusion or ventilation or haemoglobin <8 g/dL (<80 g/L) or drop in haemoglobin >2 g/dL (>20 g/L) over a 48 hours period due to alveolar haemorrhage
• Rapidly progressive glomerulonephritis (RPGN) with creatinine >2.5 mg/dL (>221 µmol/L) or rise in creatinine >2 mg/dL (>177 µmol/L) over a 48 hour period
• Severe gastrointestinal (GI) involvement, e.g., gangrene, bleeding requiring surgery
• Severe central nervous system (CNS) involvement
• Severe cardiac involvement, e.g., life-threatening arrhythmia, cardiac failure: ejection fraction <20%, New York Heart Association Class III/IV, acute myocardial infarction.
4. A current malignancy or previous history of cancer in remission for less than 12 months prior to screening. Participants that had localised carcinoma of

the skin which was resected for cure will not be excluded.
5. Liver Disease:
• Alanine aminotransferase (ALT) >2x upper limit of normal (ULN) or if participant is on background methotrexate or azathioprine >3x ULN
• AST >2x ULN or if participant is on background methotrexate or azathioprine >3x ULN
• Alkaline Phosphatase >=2.0x ULN
• Total bilirubin >1.5x ULN (isolated bilirubin >1.5xULN is acceptable if bilirubin is fractionated and direct bilirubin <35%)
• Cirrhosis or current unstable liver or biliary disease per investigator assessment defined by the presence of ascites, encephalopathy, coagulopathy, hypoalbuminaemia, oesophageal or gastric varices, persistent jaundice.
6. Participants who have severe or clinically significant cardiovascular disease uncontrolled with standard treatment including but not limited to:
• Known ejection fraction of <20%, OR
• Severe heart failure that meets New York Heart Association Class IV, OR
• Hospitalised in the 12 months prior to Visit 1 for severe heart failure meeting New York Heart Association Class III OR
• Myocardial infarction or angina diagnosed less than 3 months prior to or at Screening Visit 1 OR
• Uncontrolled life threatening arrythmia within 3 months prior to or at Screening Visit 1).
7. Participants who have known, pre-existing, clinically significant cardiac, endocrine, autoimmune, metabolic, neurological, renal, gastrointestinal, hepatic, haematological, respiratory or any other system abnormalities that are not associated with EGPA and are uncontrolled with standard treatment.
8. Evidence of clinically significant abnormality in the haematological, biochemical or urinalysis screen at Visit 1, as judged by the investigator.
9. Infectious disease: Chronic or ongoing active infectious disease requiring systemic treatment.
10. Participants with a known, pre-existing parasitic infestation within 6 months prior to Screening Visit 1.
11. A known immunodeficiency (e.g. HIV), other than that explained by the use of OCS or other immunosuppressants taken as therapy for EGPA.
12. COVID-19: Participants that, according to the investigator's medical judgment, are likely to have active COVID-19 infection. Participants with known COVID-19 positive contacts within the past 14 days must be excluded for at least 14 days following the exposure during which the participant must remain symptom-free.
13. Hypersensitivity: Participants with a known allergy or intolerance to a monoclonal antibody or biologic therapy or any of the excipients of the investigational products listed in Section 6.1.
14. Monoclonal antibodies targeting IL-5/5R:
-Participants who have a previous documented failure with anti-IL-5/5R therapy based on investigator's discretion
-Participants who have received mAb who have not undergone the required washout

periods prior to visit 1.
15. Investigational Medications/clinical study:
• Participants who have received treatment with investigational drug within the past 30 days or 5 terminal phase half-lives of the drug whichever is longer, prior to Visit 1 (this also includes investigational formulations of marketed products).
• Participants who are currently participating in any other interventional clinical study.
16. Participants receiving other prohibited medications
17. Previous participation in any study with mepolizumab, reslizumab, or benralizumab and received study intervention (including placebo) within 6 months prior to Screening Visit 1.
18. ECG Assessment: QTcF >=450 msec or QTcF >=480 msec for participants with Bundle Branch Block in the 12-lead ECG central over-read from Screening Visit 1.
19. Alcohol/Substance Abuse
20. Pregnancy
21. Participants who have known evidence of lack of adherence to controller medications and/or ability to follow physician's recommendations

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-07-2023
Enrollment:	4
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	15-09-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-12-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-01-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-02-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-04-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	27-11-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-04-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-04-2024
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	CTIS2023-510019-20-00
EudraCT	EUCTR2021-005726-15-NL
ClinicalTrials.gov	NCT05263934
CCMO	NL81758.056.22