A 52-week, randomised, double-blind, double-dummy, parallel group,multi-centre, non-inferiority study assessing exacerbation rate, additional measures of asthma control and safety in adult and adolescent severe asthmatic participants with an eosinophilic phenotype treated with GSK3511294 (depemokimab) compared with mepolizumab or benralizumab

Published: 15-07-2021
Last updated: 19-09-2024

This study has been transitioned to CTIS with ID 2023-510230-84-00 check the CTIS register for the current data. To evaluate the efficacy of GSK3511294 100 mg (SC) every 26 weeks versus maintaining existing treatment with either mepolizumabor…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Interventional

Summary

ID

NL-OMON54219

Source
ToetsingOnline

Brief title
206785 (NIMBLE)

Condition

- Bronchial disorders (excl neoplasms)

Synonym
asthma, severe asthma

Research involving
Human

Sponsors and support

Primary sponsor: GlaxoSmithKline (Ireland) Limited
Source(s) of monetary or material Support: Pharmacuetical Industry

Intervention

Keyword: asthma, eosinophilic phenotype, GSK3511294

Outcome measures

Primary outcome

Annualised rate of clinically significant exacerbations over 52 weeks

Secondary outcome

1.Weighted mean change from baseline in St. George's Respiratory Questionnaire

(SGRQ) total score calculated over 52 weeks

2.Weighted mean change from baseline in Asthma Control Questionnaire-5 (ACQ-5)

score calculated over 52 weeks

3.Weighted mean change from baseline in pre-bronchodilator forced expiratory

volume in one second (FEV1) calculated over 52 weeks

Study description

Background summary

Asthma is a chronic disease in which airways of the lungs are inflamed and

narrowed triggering difficulty in breathing among other symptoms.
It was estimated that more than 339 million people had asthma globally in 2016.
Persistent eosinophil inflammation is a feature of more than 50% of patients with severe asthma.
A variety of drugs and combination treatments have been evaluated and found effective in managing asthma. Clinical trial data over more than 10 years combined with real-world evidence, have demonstrated that treatments targeting the IL-5 pathway are both highly effective and well-tolerated. Based on this established efficacy and safety, anti-IL-5/5R therapies are now a cornerstone of severe asthma management and are endorsed by international guidelines for appropriate patients that continue to exacerbate despite optimized care. Three antagonists of IL-5 (mepolizumab and reslizumab) or its receptor (IL-5R) (benralizumab) are approved for severe asthma with an eosinophilic phenotype, as an add-on treatment administered every 4 to 8 weeks.

Study objective

This study has been transitioned to CTIS with ID 2023-510230-84-00 check the CTIS register for the current data.

To evaluate the efficacy of GSK3511294 100 mg (SC) every 26 weeks versus maintaining existing treatment with either mepolizumab or benralizumab in participants with severe asthma with an eosinophilic phenotype who have previously benefited from anti-IL-5/5R therapy

Study design

This is a multi-centre, randomised, double-blind, double-dummy, parallel group noninferiority trial of GSK3511294 100 mg SC compared with continuation of mepolizumab or benralizumab treatment in participants with severe asthma with an eosinophilic phenotype.

Intervention

Participants will be randomised in a 1:1 ratio to receive either:
• GSK3511294 100 mg SC administered every 26 weeks plus placebo SC treatment matching the active comparator.
• Active comparator (either mepolizumab every 4 weeks or benralizumab every 8 weeks) according to the participants treatment prior to randomisation plus placebo SC matching GSK3511294 administered every 26 weeks.

Study burden and risks

Participation will last approximately 66 weeks, during which time the subjects will visit the hospital up to 18 times. Subjects will be subjected to:
questions regarding medical history, use of concomitant medications/procedures

and adverse events; urine sampling; measurement of vital signs; physical examination; pulmonary functions tests; ECGs and patient reported outcomes questionnaires. Subjects will be expected to not take part in other medical studies, keep their appointments for visits, follow instructions from the study team, keep a patient card with them at all times, not donate blood/sperm/ova and to use appropriate forms of contraception. Subjects will also be asked to complete a diary daily with questions about their asthma. Furthermore, blood samples will collected up to 13 times.

The most commonly reported side effects in astudy in participants who received GSK3511294 were nasopharyngitis (common cold) and headache, and in participants who received placebo were rhinitis (inflammation in the lining of the nose) and cough. No severe allergic reactions were reported in the study. Possible side effects of the study drug include an allergic reaction and/or reaction at the injection site (for example pain, redness swelling or itchiness).

Although no additional clinical benefit is expected for recruited participants who are already receiving anti-IL-5/5R therapy, the overall benefit: risk balance of this study for participants with severe asthma with an eosinophilic phenotype is considered acceptable. Potential risks will be minimised with the risk mitigation strategy.

Contacts

Public
GlaxoSmithKline (Ireland) Limited

Riverwalk, Citywest Business Campus 12
Dublin 24 N/A
IE
Scientific
GlaxoSmithKline (Ireland) Limited

Riverwalk, Citywest Business Campus 12
Dublin 24 N/A
IE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Age: Adults and adolescents >=12 years of age, at the time of signing the informed consent/assent.[For countries where local regulations or the regulatory status of study medication permit enrolment of adults only, participants recruited will be >=18 years of age] Note for Germany, UK and Norway Participants: In Germany, UK and Norway, only adult participants (>=18 years) are to be included in this clinical trial. Note for Austrian Participants: In Austria, participants who are >=16 years are to be included in this clinical trial.
2. Asthma: Participants who have a documented physician diagnosis of asthma for >=2 years that meets the National Heart, Lung, and Blood Institute guidelines [NHLBI, 2007] or GINA guidelines [GINA, 2020].
3. Anti-IL-5/5R Therapy: Receiving either mepolizumab 100 mg SC or benralizumab 30 mg SC for >=12 months prior to Screening and have a documented benefit to therapy assessed by either:
• >=50% reduction in exacerbation frequency since initiating treatment, ORhttps://www.toetsingonline.nl/to/ccmo_monitor.nsf/europe.gif?OpenImageResource
• >=50% reduction in maintenance OCS use since initiating treatment, OR
• no exacerbations in the past 6 months whilst receiving anti-IL-5/5R therapy and an ACQ-5 score of <=1.5 at Screening.
4. Inhaled Corticosteroid: A well-documented requirement for regular treatment with medium to high dose ICS in the 12 months prior to Visit 1 with or without maintenance OCS. The maintenance ICS dose must be >=440 mcg fluticasone propionate [FP] hydrofluoroalkane product [HFA] daily, or clinically comparable [GINA, 2020; see Appendix 10 of the protocol]. Participants who are treated with medium dose ICS will also need to be treated with a Long-acting beta-agonist (LABA) to qualify for inclusion.
5. Additional Controller Medication: Current treatment with at least one additional controller medication, besides ICS [e.g., LABA, LAMA, leukotriene receptor antagonist (LTRA), or theophylline].
6. Male or eligible female.
• A female participant is eligible to participate if she is not pregnant or breastfeeding, and 1 of the following conditions applies:
o Is a woman of non-childbearing potential (WONCBP) as defined in Section 10.4.1 of the protocol
OR

o Is a woman of childbearing potential (WOCBP) and using a contraceptive method that is highly effective, with a failure rate of <1%,as described in Section 10.4.2 of the protocol from at least 14 days prior to the first dose of study intervention until at least 30 weeks after either: the first dose (if study intervention was permanently discontinued prior to Week 26), or the dose at Week 26.
• A WOCBP must have a negative highly sensitive serum pregnancy test at screening Visit 1 and a negative highly sensitive urine pregnancy test within 24 hours before the first dose of study intervention. Additional requirements for pregnancy testing during and after study intervention are located in Section 8.3.5 of the protocol.
• Contraceptive use by women should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies.
• The investigator should evaluate the potential for contraceptive method failure (e.g., noncompliance, recently initiated in relationship to the first dose of study intervention).
• The investigator is responsible for review of medical history, menstrualhistory, and recent sexual activity to decrease the risk for inclusion of awoman with an early undetected pregnancy.
• Note: If the childbearing potential changes after start of the study (e.g., a premenarcheal female participant experiences menarche) or the risk of pregnancy changes (e.g., a female participant who is not heterosexually active becomes active), the participant must discuss this with the investigator, who should determine if a female participant must begin a highly effective method of contraception. If reproductive status is questionable, additional evaluation should be considered.
7. Informed Consent: Capable of giving signed informed consent/assent as described in Section 10.1 of the protocol which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in the protocol.French participants: In France, a participant will be eligible for inclusion in this study only if either affiliated to or a beneficiary of a social securitycategory.

Exclusion criteria

1. Concurrent Respiratory Disease: Presence of a known pre-existing, clinically important lung condition other than asthma. This includes (but is not limited to) current infection, bronchiectasis, pulmonary fibrosis, XML File Identifier: 8gn94WbuVgZQJdjuTL83BkI1PnI=Page 24/38bronchopulmonary aspergillosis, or diagnoses of emphysema or chronic bronchitis (chronic obstructive pulmonary disease other than asthma) or a history of lung cancer.
2. Eosinophilic Diseases: Participants with other conditions that could lead to elevated eosinophils such as hyper-eosinophilic syndromes including (but not limited to) Eosinophilic Granulomatosis with Polyangiitis (EGPA, formerly known

as Churg-Strauss Syndrome) or Eosinophilic Esophagitis.
3. Parasitic Infection: Participants with a known, pre-existing parasitic infestation within 6 months prior to Visit 1 are to be excluded.
4. Immunodeficiency: A known immunodeficiency (e.g. human immunodeficiency virus - HIV), other than that explained by the use of CSs taken as therapy for asthma.
5. Malignancy: 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).
6. Liver Disease: 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.
NOTE: Stable non-cirrhotic chronic liver disease (including Gilbert's syndrome, asymptomatic gallstones, and chronic stable hepatitis B or C) are acceptable if participant otherwise meets entry criteria.
7. Other Concurrent Medical Conditions: Participants who have known, preexisting, clinically significant cardiac, endocrine, autoimmune, metabolic, neurological, renal, gastrointestinal, hepatic, haematological or any other system abnormalities that are uncontrolled with standard treatment.
8. Vasculitis: Participants with current diagnosis of vasculitis. Participants with high clinical suspicion of vasculitis at screening will be evaluated and current vasculitis excluded prior to enrolment.
9. COVID-19: Participants that, according to the investigator's medical judgment, are likely to have active COVID-19 infection should be excluded. Participants with known COVID-19 positive contacts within the past 14 days should be excluded for at least 14 days following the exposure during which the participant should remain symptom-free.
10. Other mAbs used in the treatment of asthma: Participants who have received omalizumab (Xolair), dupilumab (Dupixent), reslizumab (Cinqair/Cinqaero) or Tezepelumab (Tezspire) within 130 days prior to Visit 1.
11. Other mAbs not used for the treatment of asthma: Participants who have received any mAb within 5 half-lives of Visit 1. Authorised treatments for COVID-19 are permitted and should be used in line with local regulatory guidance.
12. Investigational Medications: Participants who have received treatment with an investigational drug within the past 30 days or five terminal phase half-lives of the drug whichever is longer, prior to visit 1 (this also includes investigational formulations of marketed products).
13. ECG Assessment: QTcF >=450msec or QTcF >=480 msec for participants with Bundle Branch Block in the central over-read 12-lead ECG at screening Visit 1.
14. Smoking history: Current smokers or former smokers with a smokinghistory of >=20 pack years (number of pack years = (number of cigarettesper day / 20) x number of years smoked). A former smoker is defined as a participant who quit smoking at least 6 months prior to Visit 1. Pipes and/or cigars and/or electronic cigarettes/vaping use cannot be used to calculate pack-year history. Current and former use of these is exclusionary.

15. Alcohol/Substance Abuse: A history (or suspected history) of alcoholmisuse or substance abuse within 2 years prior to Visit 1.XML File Identifier: 8gn94WbuVgZQJdjuTL83BkI1PnI=Page 25/38
16. Hypersensitivity: Participants with allergy/intolerance to a mAb or biologic or any of the excipients of the investigational products listed in section 6.1 of the protocol.
17. Pregnancy: Participants who are pregnant or breastfeeding. Participants should not be enrolled if they plan to become pregnant during the time of study participation. Requirements for pregnancy testing are located in Section 8.3.5 of the protocol.
18. Adherence: 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):	26-04-2022
Enrollment:	34
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Fasenra

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

Ethics review

Approved WMO Date:	15-07-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-10-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-12-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-02-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-02-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	23-05-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-05-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-11-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-11-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-04-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-09-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-12-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-01-2024

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	CTIS2023-510230-84-00
EudraCT	EUCTR2020-003612-28-NL
CCMO	NL77988.056.21