



Clinical trial results:

Asthma Exacerbation Profile in patients on open label treatment with Benralizumab for severe eosinophilic asthma - an exploratory cohort study

Summary

EudraCT number	2018-003699-11
Trial protocol	GB
Global end of trial date	23 April 2024

Results information

Result version number	v1 (current)
This version publication date	13 August 2026
First version publication date	13 August 2026

Trial information

Trial identification

Sponsor protocol code	GN17RM684
-----------------------	-----------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04102800
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	NHS Greater Glasgow and Clyde
Sponsor organisation address	1055 Great Western Road, Glasgow, United Kingdom, G12 0XH
Public contact	Dr Lynsey Gillespie , NHS Greater Glasgow and Clyde, 0044 (0)141 201 9316 , Lynsey.Gillespie@ggc.scot.nhs.uk
Scientific contact	Dr Lynsey Gillespie , NHS Greater Glasgow and Clyde, 0044 (0)141 201 9316 , Lynsey.Gillespie@ggc.scot.nhs.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 March 2026
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 April 2024
Global end of trial reached?	Yes
Global end of trial date	23 April 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the inflammatory and physiological characteristics of an asthma exacerbation whilst on treatment with benralizumab for severe eosinophilic asthma.

Protection of trial subjects:

All investigators and key trial personnel will complete GCP training.

PI at each site will assign tasks to staff to the Delegation log depending on their skills and training.

Correct Inclusion of participants - A delegated study doctor will sign off the check of inclusion and exclusion criteria prior to administration of the study drug.

Investigational drug - The drug is benralizumab, which is licensed in Europe and is being used in its licensed indication with no change in dose or regimen in this study. The risk is no greater than using other clinically available monoclonal antibodies for asthma.

The risk of anaphylaxis is very unlikely as no cases were recorded in clinical trials, but will advise patients of symptoms of anaphylaxis and have emergency medication available at sites.

Patients will be asked to wait at site for observation for at least 2 hours after the first injection and 1 hour after the next 3 injections.

Hypersensitivity reactions - have occurred following administration of benralizumab. These reactions generally occur within hours of administration, but in some instances have a delayed onset (i.e. days). In the event of a hypersensitivity reaction that the PI records as benralizumab related the drug will be discontinued.

All AE's will be collected and reported as per protocol.

A Drug Safety Monitoring Committee is not planned as it is a Phase 4 study of a licensed medication and the known risk in terms of expected serious adverse events is not significant. The Trial Management Group and Trial Steering Committees will monitor safety.

AE's will be collected for up to 3 months after the last study injection.

Study procedures: Blood tests, spirometry - All procedures will be carried out by trained staff. Potential risks of procedures will be outlined in the patient information sheet. There is no particularly invasive procedure in this study.

Induced sputum Hypertonic saline will be used if the baseline FEV1 is above 50% predicted and 1L

Background therapy:

participants own asthma treatment - high dose inhaled corticosteroid + 1 other additional drug for asthma (e.g. long acting beta2 agonist (LABA), leukotriene receptor antagonist (LTRA) such as montelukast, theophylline, long acting muscarinic antagonist (LAMA) such as tiotropium).

Evidence for comparator:

N/A

Actual start date of recruitment	30 September 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 156
--------------------------------------	---------------------

Worldwide total number of subjects	156
EEA total number of subjects	0

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	122
From 65 to 84 years	34
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were identified from severe asthma clinics across the UK at 15 participating sites from 30th Sept 2019 unto 2nd Dec 2022

Pre-assignment

Screening details:

Informed consent was obtained at the screening visit for 176 participants. 157 were enrolled and had Baseline assessments included spirometry, induced sputum, FeNO, full blood count [FBC] and asthma-related questionnaires. After a two-week run-in period, 156 participants started open-label benralizumab [Fasenra®] 30mg via subcutaneous injection.

Period 1

Period 1 title	Baseline and final Analysis (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Arm - Experienced an exacerbation

Arm description:

Benralizumab

Arm type	Experimental
Investigational medicinal product name	Benralizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in dose-dispenser cartridge
Routes of administration	Subcutaneous use

Dosage and administration details:

Benralizumab 30mg by subcutaneous injection every 4 weeks for the first 3 doses and then every 8 weeks thereafter.

Arm title	Treatment Arm - Did not experience an exacerbation
------------------	--

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Benralizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in dose-dispenser cartridge
Routes of administration	Subcutaneous use

Dosage and administration details:

Benralizumab 30mg by subcutaneous injection every 4 weeks for the first 3 doses and then every 8 weeks thereafter.

Number of subjects in period 1	Treatment Arm - Experienced an exacerbation	Treatment Arm - Did not experience an exacerbation
Started	91	65
Completed	91	65

Baseline characteristics

Reporting groups

Reporting group title	Baseline and final Analysis
-----------------------	-----------------------------

Reporting group description: -

Reporting group values	Baseline and final Analysis	Total	
Number of subjects	156	156	
Age categorical Units: Subjects			
Adults (18-64 years)	122	122	
From 65-84 years	34	34	
Gender categorical Units: Subjects			
Female	90	90	
Male	66	66	

Subject analysis sets

Subject analysis set title	Primary endpoint - Experienced an exacerbation
----------------------------	--

Subject analysis set type	Full analysis
---------------------------	---------------

Subject analysis set description:

Total analysis - Primary endpoint - To assess the inflammatory [blood cell counts, exhaled nitric oxide] and physiological [FEV1, ACQ-6] characteristics of an asthma exacerbation whilst on treatment with benralizumab for severe eosinophilic asthma.

Subject analysis set title	Primary endpoint - Did not experience an exacerbation
----------------------------	---

Subject analysis set type	Full analysis
---------------------------	---------------

Subject analysis set description:

Total analysis - Primary endpoint - To assess the inflammatory [blood cell counts, exhaled nitric oxide] and physiological [FEV1, ACQ-6] characteristics of an asthma exacerbation whilst on treatment with benralizumab for severe eosinophilic asthma.

Reporting group values	Primary endpoint - Experienced an exacerbation	Primary endpoint - Did not experience an exacerbation	
Number of subjects	91	65	
Age categorical Units: Subjects			
Adults (18-64 years)	122		
From 65-84 years	34		
Gender categorical Units: Subjects			
Female	90		
Male	66		

End points

End points reporting groups

Reporting group title	Treatment Arm - Experienced an exacerbation
Reporting group description:	
Benralizumab	
Reporting group title	Treatment Arm - Did not experience an exacerbation
Reporting group description: -	
Subject analysis set title	Primary endpoint - Experienced an exacerbation
Subject analysis set type	Full analysis
Subject analysis set description:	
Total analysis - Primary endpoint - To assess the inflammatory [blood cell counts, exhaled nitric oxide] and physiological [FEV1, ACQ-6] characteristics of an asthma exacerbation whilst on treatment with benralizumab for severe eosinophilic asthma.	
Subject analysis set title	Primary endpoint - Did not experience an exacerbation
Subject analysis set type	Full analysis
Subject analysis set description:	
Total analysis - Primary endpoint - To assess the inflammatory [blood cell counts, exhaled nitric oxide] and physiological [FEV1, ACQ-6] characteristics of an asthma exacerbation whilst on treatment with benralizumab for severe eosinophilic asthma.	

Primary: To study the nature of asthma exacerbation events while on treatment with benralizumab - FeNO

End point title	To study the nature of asthma exacerbation events while on treatment with benralizumab - FeNO
End point description:	
End point type	Primary
End point timeframe:	
Between September 30th 2019 to April 23rd Apr 2024	

End point values	Treatment Arm - Experienced an exacerbation	Treatment Arm - Did not experience an exacerbation	Primary endpoint - Experienced an exacerbation	Primary endpoint - Did not experience an exacerbation
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	91	65	91	65
Units: ppb	43	65	43	65

Statistical analyses

Statistical analysis title	Change from stable on IMP to first exacerbation
Comparison groups	Treatment Arm - Experienced an exacerbation v Treatment Arm - Did not experience an exacerbation

Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	other ^[1]
P-value	= 0.014
Method	Regression, Linear
Parameter estimate	Median difference (final values)

Notes:

[1] - Baseline

Adverse events

Adverse events information

Timeframe for reporting adverse events:

September 8 30th 2019 and April 23rd 2024

Assessment type	Non-systematic
-----------------	----------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	28
--------------------	----

Reporting groups

Reporting group title	Adverse events - SAEs and ARs
-----------------------	-------------------------------

Reporting group description: -

Serious adverse events	Adverse events - SAEs and ARs		
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 156 (13.46%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 156 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Non-small cell lung cancer stage III			
subjects affected / exposed	1 / 156 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Prostate cancer			
subjects affected / exposed	1 / 156 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 156 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Arteriovenous fistula thrombosis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 156 (0.64%) 0 / 1 0 / 0		
Cardiac disorders Atrioventricular block complete subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 156 (0.64%) 0 / 1 0 / 0		
Palpitations subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 156 (0.64%) 0 / 1 0 / 0		
Surgical and medical procedures Cholecystectomy subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 156 (0.64%) 0 / 1 0 / 0		
Skin neoplasm excision subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 156 (0.64%) 0 / 1 0 / 0		
Nervous system disorders Hemiplegic migraine subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 156 (0.64%) 0 / 1 0 / 0		
Seizure subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 156 (0.64%) 0 / 1 0 / 0		
General disorders and administration site conditions Chest pain			

subjects affected / exposed	2 / 156 (1.28%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Eosinophilic granulomatosis with polyangiitis			
subjects affected / exposed	1 / 156 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis ischaemic			
subjects affected / exposed	1 / 156 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 156 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 156 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 156 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Arthritis bacterial			
subjects affected / exposed	1 / 156 (0.64%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19			

subjects affected / exposed	1 / 156 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	1 / 156 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diabetic foot infection			
subjects affected / exposed	1 / 156 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	2 / 156 (1.28%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	2 / 156 (1.28%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonia viral			
subjects affected / exposed	1 / 156 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 156 (0.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Adverse events - SAEs and ARs		
Total subjects affected by non-serious adverse events subjects affected / exposed	18 / 156 (11.54%)		
Investigations Eosinophil count increased subjects affected / exposed occurrences (all)	2 / 156 (1.28%) 2		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Lethargy subjects affected / exposed occurrences (all) Migraine subjects affected / exposed occurrences (all)	4 / 156 (2.56%) 4 2 / 156 (1.28%) 2 2 / 156 (1.28%) 2		
General disorders and administration site conditions Adverse drug reaction subjects affected / exposed occurrences (all) Chills subjects affected / exposed occurrences (all) Injection site erythema subjects affected / exposed occurrences (all) Injection site pain subjects affected / exposed occurrences (all) Injection site pallor subjects affected / exposed occurrences (all)	1 / 156 (0.64%) 1 1 / 156 (0.64%) 1 1 / 156 (0.64%) 1 1 / 156 (0.64%) 1 1 / 156 (0.64%) 1		
Immune system disorders Hypersensitivity			

subjects affected / exposed occurrences (all)	1 / 156 (0.64%) 1		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	1 / 156 (0.64%) 1		
Musculoskeletal and connective tissue disorders Bone pain subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	1 / 156 (0.64%) 1 1 / 156 (0.64%) 1		
Infections and infestations Herpes zoster subjects affected / exposed occurrences (all)	1 / 156 (0.64%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 November 2019	Discrepancy in the PIS/ICF revised to reflect that the name and telephone number of participants is provided for the purposes of the electronic diary.
14 April 2020	Changes needed in line with the current COVID-19 pandemic to limit attendance at hospital sites Patients will continue to receive benralizumab injections in the study. The device will change from the pre-filled syringe to an auto-injector during this period and patients taught to self-inject so that they will not need to attend hospital during the COVID crisis. Patients will receive the same dose / formulation in the pen device. Patients will not be attending for study visits so only limited study data can be collected during this period. This will be collected via phone with the patient in line with the visit schedule of assessments. Patients will be advised not to attend for exacerbations visits. At present there are a limited number of patients in the study so although some of the data will be missed this is expected to have a minimal effect on the overall study. The study statistician has reviewed and agreed the changes.
21 October 2020	Changes to reduce the onsite visits. Handheld devices provided to patients to allow measurements and sample collection to be done off site for some visits. Key study visits will still be conducted onsite but samples can be collected prior to attending. Selected study visits will be conducted with the study team via video call. Patients will be provided with handheld Spirometer and vivatmo me devices and consumables for collection of samples. In line with changes to routine practice, option for participants to switch from study specific benralizumab supplies to usual local NHS supply arrangements for benralizumab which includes use of homecare services. To facilitate participant self-administration, participants will now be provided with pre-filled pen presentation. Handheld devices to be purchased/ donated and provided for patient use at home. Exacerbation kits and sample consumable will be provided to patients to allow for sample collection off site where appropriate. Study recruitment was suspended due to the COVID-19 pandemic. The duration of the study will be extended by 10 months, with the agreement of the funder, to allow for the delay. Given that only one of the study sites was open and actively recruiting there should be no resource implications for the other sites. Patient instructions to be provided to assist with the sample collection and outcome measures by patients at home. Addition to exclusion: 13. Current malignancy, or history of malignancy, except for: a) Patients who have had non-melanoma skin cancers or in situ carcinoma of the cervix – these patients are eligible provided that the patient is in remission and curative therapy was completed at least 12 months prior to the date informed consent is obtained; b) Patients who have had other malignancies are eligible provided that the patient is in remission and curative therapy was completed at least 5 years prior to the date informed consent is obtained

07 April 2021	Minor changes to the protocol for clarification. Addition to the Patient Information Sheet / Informed Consent Form to include collection of patient date of birth. The current electronic diary provider is unable to continue to support the service moving forward and this is needed for the new provider. Addition to the PIS/ICF to include that data, including postcode, will be held by the Robertson Centre, University of Glasgow and that consent forms will be uploaded. Tracked and clean copies of all affected documents, and a summary of the protocol changes, have been included with the submission.
08 June 2021	Minor changes to the protocol and PIS to include clarification on COVID vaccination and considerations in relation to timing and administration of benralizumab where applicable . Clarification in the protocol on reporting of COVID vaccine as a concomitant medication. Addition to the Patient Information Sheet / Informed Consent form to include collection of NHS number. This is needed for initiation of patients into the new electronic diary service. Patient identifiers are already being collected for the purposes of the electronic diary and this has been reviewed and approved by REC previously. Tracked and clean copies of all documents have been included with the submission.
21 June 2021	Minor change to the patient instruction regarding the electronic diary provider. This is due to a change to the service provider and the instructions have been updated in line with the wording used by the new provider. A tracked and clean version of the revised document is attached with the submission.
05 January 2022	Revisions to the protocol to include clarification on the sputum endpoints requested by the Sponsor. Changes to the breathomics sampling timepoints / reduction in number of samples collected. Changes to the inclusion criteria in relation to a new inhaler Enerzair.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported