Clinical trial results:
A Multi-center, Randomized, Double-blind, Parallel-group, Placebo-controlled 3-Part Phase 3 Study to Demonstrate the Efficacy and Safety of Benralizumab in Patients with Eosinophilic Gastritis and/or Gastroenteritis

Summary

EudraCT number	2021-000085-14
Trial protocol	DE ES NL PL IT FR BE
Global end of trial date	13 February 2024

Results information

Result version number	v1 (current)
This version publication date	18 August 2024
First version publication date	18 August 2024

Trial information

Trial identification

Sponsor protocol code	D3258C00001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05251909
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca KK
Sponsor organisation address	3-1 Ofuka-cho, Kita-ku,, Osaka, Japan, 530-011
Public contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com
Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	151 85, Södertälje, Sweden,
Public contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com

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	03 June 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 February 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To compare the effect of benralizumab 30 mg every 4 weeks (Q4W) with placebo on histologic signs and gastrointestinal symptoms in patients with eosinophilic gastritis and/or gastroenteritis

Protection of trial subjects:

Participants’ confidentiality and personal information will be protected throughout the study to the same standard as all other coded data in the study.

Background therapy:

Medications for EG/EGE (eg, systemic and topical ingested or swallowed corticosteroids, PPIs) and steroid treatments used for asthma or allergies that are inhaled or administered intranasally

Evidence for comparator: -

Actual start date of recruitment	18 January 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 2
Country: Number of subjects enrolled	United States: 9
Country: Number of subjects enrolled	Italy: 1
Worldwide total number of subjects	12
EEA total number of subjects	1

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)	1
Adults (18-64 years)	9
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients ages 12 and above with EG/EGE that are
symptomatic and histologically active on stable background medication and diet

Pre-assignment

Screening details:

The study had a 4-8 week screening period

Period 1

Period 1 title	Double Blind
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Carer, Data analyst, Assessor, Monitor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Benralizumab

Arm description:

Patients received benralizumab every 4 weeks for the 24 weeks treatment period

Arm type	Experimental
Investigational medicinal product name	Benralizumab
Investigational medicinal product code	MEDI-563
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Benralizumab 30mg SC injection was administered Q4W

Arm title	Placebo

Arm description:

Patients received matching Placebo every 4 weeks for the 24 weeks treatment period

Arm type	Placebo
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

30 mg every 4 weeks

Number of subjects in period 1	Benralizumab	Placebo
Started	6	6
Completed	6	3
Not completed	0	3
Consent withdrawn by subject	-	3

Period 2

Period 2 title	OLE Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Benralizumab

Arm description:

Open label Benralizumab 30mg q4 weekly

Arm type	Experimental
Investigational medicinal product name	Benralizumab
Investigational medicinal product code	MEDI-563
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Benralizumab 30mg SC injection was administered Q4W

Number of subjects in period 2	Benralizumab
Started	9
Completed	7
Not completed	2
Consent withdrawn by subject	2

Baseline characteristics

Reporting groups	
Reporting group title	Benralizumab
Reporting group description:	
Patients received benralizumab every 4 weeks for the 24 weeks treatment period	
Reporting group title	Placebo
Reporting group description:	
Patients received matching Placebo every 4 weeks for the 24 weeks treatment period	

Reporting group values	Benralizumab	Placebo	Total
Number of subjects	6	6	12
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	1	1
Adults (18-64 years)	5	4	9
From 65-84 years	1	1	2
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	51.17	39.17	
full range (min-max)	39 to 68	17 to 72	-
Gender Categorical Units: Subjects			
Female	5	1	6
Male	1	5	6
Race Units: Subjects			
White	5	3	8
Asian	1	1	2
Black or African American	0	1	1
Other	0	1	1
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic of Latino	6	6	12

Subject analysis sets	
Subject analysis set title	Benralizumab
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Patients received benralizumab 30mg every 4 weeks for the 24 weeks treatment period

Subject analysis set title	Placebo
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Patients received matching Placebo every 4 weeks for the 24 weeks treatment period

Reporting group values	Benralizumab	Placebo	
Number of subjects	6	6	
Age Categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	1	
Adults (18-64 years)	5	4	
From 65-84 years	1	1	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	51.17	39.17	
full range (min-max)	39 to 68	17 to 72	
Gender Categorical Units: Subjects			
Female	5	1	
Male	1	5	
Race Units: Subjects			
White	5	3	
Asian	1	1	
Black or African American	0	1	
Other	0	1	
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic of Latino	6	6	

End points

End points reporting groups

Reporting group title	Benralizumab
Reporting group description:	
Patients received benralizumab every 4 weeks for the 24 weeks treatment period	
Reporting group title	Placebo
Reporting group description:	
Patients received matching Placebo every 4 weeks for the 24 weeks treatment period	
Reporting group title	Benralizumab
Reporting group description:	
Open label Benralizumab 30mg q4 weekly	
Subject analysis set title	Benralizumab
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Patients received benralizumab 30mg every 4 weeks for the 24 weeks treatment period	
Subject analysis set title	Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Patients received matching Placebo every 4 weeks for the 24 weeks treatment period	

Primary: Proportion of patients with a histologic response at Week 24

End point title	Proportion of patients with a histologic response at Week 24[1]
End point description:	
For the first primary endpoint, the proportion of patients achieving a histological response at Week 24, is defined as below: ≤6 eosinophils/hpf in the stomach for the patients with only gastric disease at baseline. ≤6 eosinophils/hpf in the stomach and ≤15 eosinophils/hpf in the duodenum for the patients with gastric + duodenal disease at baseline. ≤15 eosinophils/hpf in the duodenum for the patients with only duodenal disease at baseline.	
End point type	Primary
End point timeframe:	
at week 24	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No analysis was performed due to study termination prior to sufficient patient randomization.

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: percentage				

Notes:

[2] - No analysis was performed due to study termination prior to sufficient patient randomization.

[3] - No analysis was performed due to study termination prior to sufficient patient randomization.

Statistical analyses

No statistical analyses for this end point

Primary: CFB in SAGED score at Week 24

End point title	CFB in SAGED score at Week 24[4]

End point description:

The Symptom Assessment for Gastrointestinal Eosinophilic Diseases (SAGED) instrument was developed to measure gastrointestinal symptoms in participants diagnosed with EG/EGE. The SAGED instrument, comprising 8 items, measures the severity of abdominal pain, nausea, bloating, early satiety, lack of appetite, vomiting, diarrhea, and frequency of vomiting. Severity for each concept is assessed using an 11-point numerical rating scale (where 0 = 'none' and 10 = 'worst imaginable'). Frequency of vomiting is reported as number of episodes of vomiting within the past 24 hours.

End point type	Primary

End point timeframe:

at week 24

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No analysis was performed due to study termination prior to sufficient patient randomization.

End point values	Benralizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[5]	0[6]		
Units: score				

Notes:

[5] - No analysis was performed due to study termination prior to sufficient patient randomization.

[6] - No analysis was performed due to study termination prior to sufficient patient randomization.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events are reported from the first dose administration up to 30 days after the last dose of study drug.	
Adverse event reporting additional description:	
The Safety Analysis Set included all participants who received at least 1 dose of study drug	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups	
Reporting group title	Benra 30 mg
Reporting group description:	
Patients received benralizumab 30mg every 4 weeks for the 24 weeks treatment period.	
Reporting group title	Placebo
Reporting group description:	
Patients received matching Placebo every 4 weeks for the 24 weeks treatment period	

Serious adverse events	Benra 30 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Benra 30 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	3 / 6 (50.00%)	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Injection site reaction			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast			

disorders			
Menstrual discomfort			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Eating disorder			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Fall			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Foot fracture			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Migraine			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Eosinophilia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Myopic chorioretinal degeneration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	2 / 6 (33.33%)	0 / 6 (0.00%)	
occurrences (all)	3	0	
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	2 / 6 (33.33%)	1 / 6 (16.67%)	
occurrences (all)	2	1	
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	2 / 6 (33.33%)	0 / 6 (0.00%)	
occurrences (all)	2	0	

Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Arthritis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Neck pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Bronchitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Bacterial infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Fungal infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Herpes zoster			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Parotitis			

subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Sialoadenitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Tooth abscess			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Genitourinary tract infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 March 2023	This amendment is considered to be substantial based on the criteria set forth in Article 10(a) of Directive 2001/20/EC of the European Parliament and the Council of the European Union. Following the decision to close recruitment to this study early, the primary rationale for this amendment is to fulfill a commitment to participants as they enrolled in the trial, of open-label access to benralizumab following double-blind treatment. This amendment will make available a streamlined 24-week open-label trial of benralizumab with the addition of a Part D, contingent on the Investigator's clinical judgement and the potential for benefit.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to early termination of study limited number of patients was randomized and thus data was not analysed on group level.

Notes: