Clinical trial results:
A 52-week, Randomised, Double-blind, Placebo-controlled, Parallel-group, Multi-centre Study of the Efficacy and Safety of GSK3511294 Adjunctive Therapy in Adult and Adolescent Participants With Severe Uncontrolled Asthma With an Eosinophilic Phenotype

Summary

EudraCT number	2020-003632-25
Trial protocol	DE FR CZ PL IT ES IE
Global end of trial date	21 November 2023

Results information

Result version number	v1
This version publication date	06 June 2024
First version publication date	06 June 2024

Trial information

Trial identification

Sponsor protocol code	206713

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04719832
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford,Middlesex, United Kingdom, TW8 9GS
Public contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002836-PIP01-20
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 January 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 November 2023
Global end of trial reached?	Yes
Global end of trial date	21 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of GSK3511294 100 mg (SC) every 26 weeks versus placebo in participants with severe uncontrolled asthma with an eosinophilic phenotype on top of existing asthma therapy

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 March 2021
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	Czechia: 34
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 38
Country: Number of subjects enrolled	Ireland: 3
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	Poland: 74
Country: Number of subjects enrolled	Spain: 74
Country: Number of subjects enrolled	United Kingdom: 12
Country: Number of subjects enrolled	United States: 49
Country: Number of subjects enrolled	Canada: 9
Country: Number of subjects enrolled	China: 59
Country: Number of subjects enrolled	Russian Federation: 21
Worldwide total number of subjects	382
EEA total number of subjects	232

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)	8
Adults (18-64 years)	276
From 65 to 84 years	98
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Out of 395 participants randomized, 382 participants received at least one dose of study intervention and included in the full analysis set population. Eleven participants were excluded due to concerns about data integrity and GCP violations; and 2 participants were randomized in error but did not receive any study drug.

Pre-assignment

Screening details:

In this study, out of 622 participants enrolled, 395 participants were randomized the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received subcutaneous (SC) injection of matching placebo once every 26 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Matching Placebo once every 26 weeks

Arm title	GSK3511294

Arm description:

Participants received a SC injection of GSK3511294 100 milligrams (mg) once every 26 weeks.

Arm type	Experimental
Investigational medicinal product name	GSK3511294
Investigational medicinal product code	
Other name	Depemokimab
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

100 milligram (mg) once every 26 weeks

Number of subjects in period 1	Placebo	GSK3511294
Started	132	250
Completed	122	237
Not completed	10	13
Consent withdrawn by subject	5	5
Physician decision	-	1
Adverse event, non-fatal	2	-
Pregnancy	1	1
Lost to follow-up	-	2
Lack of efficacy	2	4

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received subcutaneous (SC) injection of matching placebo once every 26 weeks.	
Reporting group title	GSK3511294
Reporting group description:	
Participants received a SC injection of GSK3511294 100 milligrams (mg) once every 26 weeks.	

Reporting group values	Placebo	GSK3511294	Total
Number of subjects	132	250	382
Age categorical Units: Participants			
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)	5	3	8
Adults (18-64 years)	91	185	276
From 65-84 years	36	62	98
85 years and over	0	0	0
Sex: Female, Male Units: Participants			
Female	79	144	223
Male	53	106	159
Race/Ethnicity, Customized Units: Subjects			
ASIAN	20	38	58
BLACK OR AFRICAN AMERICAN	3	5	8
WHITE	109	207	316
Age, Continuous Units: YEARS			
arithmetic mean	53.6	54.1	
standard deviation	± 14.91	± 13.82	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received subcutaneous (SC) injection of matching placebo once every 26 weeks.	
Reporting group title	GSK3511294
Reporting group description:	
Participants received a SC injection of GSK3511294 100 milligrams (mg) once every 26 weeks.	

Primary: Annualized Rate of Clinically Significant Exacerbations Over 52 Weeks

End point title	Annualized Rate of Clinically Significant Exacerbations Over 52 Weeks

End point description:

Clinically significant exacerbations of asthma were defined by worsening of asthma which required use of systemic corticosteroids and/or hospitalization and/or Emergency Department (ED) visit. Exacerbations occurring from the start of randomized study treatment up to the Week 52 visit, including exacerbations reported after early discontinuation from study treatment by participants who remained in the study, were included in the analysis. Annualized rate of exacerbations was analyzed using a generalized linear model assuming a negative binomial distribution. The analysis was performed on the Full Analysis Set which comprised of all randomized participants who received at least one dose of study intervention excluding participants from one study site due to concerns about data integrity and GCP violation.

End point type	Primary

End point timeframe:

From first dose of study treatment up to Week 52

End point values	Placebo	GSK3511294		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	132	249		
Units: Exacerbation per participant per year				
number (confidence interval 95%)	1.11 (0.86 to 1.43)	0.46 (0.37 to 0.58)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

To demonstrate the superiority of GSK3511294 100 mg SC + SoC following two doses (at Week 0 and at Week 26) compared with placebo + SoC, assessed by the annualized rate of clinically significant exacerbations measured over the study intervention period of 52 weeks.

Comparison groups	Placebo v GSK3511294

Number of subjects included in analysis	381
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.001
Method	Negative binomial distribution
Parameter estimate	Rate Ratio
Point estimate	0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	0.59

Notes:

[1] - Analysis performed using a negative binomial model with covariates of treatment, exacerbation history (2, 3, 4+), baseline ICS dose (medium, high), geographical region, baseline percent predicted FEV1, and offset of log (total time in the study in years)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality, Serious adverse events (SAEs) and non-serious adverse events (Non-SAEs) were collected were collected from the start of the study intervention till follow up week 56 .

Adverse event reporting additional description:

All-cause mortality, SAEs and Non-SAEs were reported for the Safety Population which included all participants who received at least 1 dose of study treatment excluding participants from one study site due to concerns about data integrity and GCP violation. AEs were reported treatment-wise.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	GSK3511294

Reporting group description:

Participants received a 100 mg dose of GSK3511294 subcutaneously once every 26 weeks

Reporting group title	Placebo

Reporting group description:

Participants received placebo subcutaneously once every 26 weeks

Serious adverse events	GSK3511294	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 250 (6.00%)	22 / 132 (16.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 250 (0.40%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 250 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid cancer			
subjects affected / exposed	0 / 250 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Uterine leiomyoma			
subjects affected / exposed	1 / 250 (0.40%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Mass			
subjects affected / exposed	0 / 250 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernia			
subjects affected / exposed	0 / 250 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 250 (0.40%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Genital prolapse			
subjects affected / exposed	0 / 250 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	0 / 250 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp			
subjects affected / exposed	0 / 250 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			

subjects affected / exposed	0 / 250 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	3 / 250 (1.20%)	5 / 132 (3.79%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Rib fracture			
subjects affected / exposed	0 / 250 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 250 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 250 (0.40%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	0 / 250 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	1 / 250 (0.40%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 250 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cerebrovascular disorder			
subjects affected / exposed	0 / 250 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Rhegmatogenous retinal detachment			
subjects affected / exposed	1 / 250 (0.40%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	0 / 250 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	1 / 250 (0.40%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 250 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Jaundice cholestatic			
subjects affected / exposed	1 / 250 (0.40%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 250 (0.40%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			

subjects affected / exposed	1 / 250 (0.40%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 250 (0.40%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 250 (0.40%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint range of motion decreased			
subjects affected / exposed	0 / 250 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	1 / 250 (0.40%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 250 (0.40%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 250 (0.40%)	3 / 132 (2.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis A			
subjects affected / exposed	1 / 250 (0.40%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

COVID-19			
subjects affected / exposed	0 / 250 (0.00%)	2 / 132 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 250 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	1 / 250 (0.40%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 250 (0.40%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	GSK3511294	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	145 / 250 (58.00%)	78 / 132 (59.09%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	9 / 250 (3.60%)	7 / 132 (5.30%)	
occurrences (all)	10	7	
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 250 (4.80%)	10 / 132 (7.58%)	
occurrences (all)	17	13	
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 250 (0.80%)	4 / 132 (3.03%)	
occurrences (all)	3	4	
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	9 / 250 (3.60%)	6 / 132 (4.55%)	
occurrences (all)	23	7	
Rhinitis allergic			
subjects affected / exposed	11 / 250 (4.40%)	4 / 132 (3.03%)	
occurrences (all)	15	4	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	6 / 250 (2.40%)	7 / 132 (5.30%)	
occurrences (all)	6	11	
Infections and infestations			
Laryngitis			
subjects affected / exposed	9 / 250 (3.60%)	4 / 132 (3.03%)	
occurrences (all)	9	4	
Influenza			
subjects affected / exposed	19 / 250 (7.60%)	2 / 132 (1.52%)	
occurrences (all)	21	2	
Nasopharyngitis			
subjects affected / exposed	29 / 250 (11.60%)	25 / 132 (18.94%)	
occurrences (all)	37	32	
Pharyngitis			
subjects affected / exposed	8 / 250 (3.20%)	2 / 132 (1.52%)	
occurrences (all)	8	2	
Respiratory tract infection			
subjects affected / exposed	8 / 250 (3.20%)	6 / 132 (4.55%)	
occurrences (all)	9	11	
Rhinitis			
subjects affected / exposed	15 / 250 (6.00%)	10 / 132 (7.58%)	
occurrences (all)	17	16	
Sinusitis			
subjects affected / exposed	11 / 250 (4.40%)	6 / 132 (4.55%)	
occurrences (all)	14	6	
Upper respiratory tract infection			
subjects affected / exposed	25 / 250 (10.00%)	14 / 132 (10.61%)	
occurrences (all)	39	22	
Lower respiratory tract infection			

subjects affected / exposed	10 / 250 (4.00%)	5 / 132 (3.79%)	
occurrences (all)	10	7	
COVID-19			
subjects affected / exposed	51 / 250 (20.40%)	27 / 132 (20.45%)	
occurrences (all)	51	30	
Bronchitis			
subjects affected / exposed	12 / 250 (4.80%)	5 / 132 (3.79%)	
occurrences (all)	18	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 August 2021	Amendment 1
08 April 2022	Amendment 2

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.

Data has not been disclosed for secondary endpoints for this study. We will disclose data for all pre-specified secondary endpoints by 21-Nov-2024.

Notes: