Clinical trial results:
A Randomised, Double-blind, Parallel Group Phase III Study to Assess the Efficacy and Safety of 100 mg SC Depemokimab in Patients With Chronic Rhinosinusitis With Nasal Polyps (CRSwNP) - ANCHOR-2 (depemokimAb iN CHrOnic Rhinosinusitis)

Summary

EudraCT number	2021-005055-36
Trial protocol	IT SE ES PL
Global end of trial date	06 August 2024

Results information

Result version number	v1
This version publication date	25 July 2025
First version publication date	25 July 2025

Trial information

Trial identification

Sponsor protocol code	218079

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05281523
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)	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	04 September 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 July 2024
Global end of trial reached?	Yes
Global end of trial date	06 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of depemokimab 100 milligram (mg) subcutaneous + standard of care (SOC) compared to placebo + SoC at Week 52 in participants with a diagnosis of CRSwNP

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 April 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	Italy: 23
Country: Number of subjects enrolled	Poland: 60
Country: Number of subjects enrolled	Romania: 31
Country: Number of subjects enrolled	Spain: 42
Country: Number of subjects enrolled	Sweden: 10
Country: Number of subjects enrolled	United States: 20
Country: Number of subjects enrolled	China: 32
Country: Number of subjects enrolled	Japan: 28
Country: Number of subjects enrolled	Türkiye: 18
Worldwide total number of subjects	264
EEA total number of subjects	166

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)	219
From 65 to 84 years	45
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 264 participants were randomized of which 257 participants were included in Full Analysis Set (FAS) population. The FAS included all randomized participants who received at least 1 dose of study intervention excluding 7 participants from 2 sites with good clinical practice (GCP)/data integrity issues.

Pre-assignment

Screening details:

A total of 264 participants were enrolled in 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	Depemokimab

Arm description:

Participants received a 100 milligram (mg) dose of depemokimab subcutaneous (SC) injection once every 26 weeks (week 0 and week 26) over a treatment period for 52-weeks. Participants were to be maintained on their existing baseline maintenance Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) standard of care (SOC) treatment throughout the study.

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

Dosage and administration details:

100 milligram (mg) once every 26 weeks

Arm title	Placebo

Arm description:

Participants received placebo SC injection once every 26 weeks (week 0 and week 26) over a treatment period for 52-weeks. Participants were to be maintained on their existing baseline maintenance CRSwNP SOC treatment throughout the study.

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

Number of subjects in period 1[1]	Depemokimab	Placebo
Started	129	128
Completed	122	111
Not completed	7	17
Physician decision	1	1
Consent withdrawn by subject	5	15
Adverse event, non-fatal	1	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Of 264 participants who were randomized, 7 participants from 2 sites were excluded from the full analysis population due to data integrity concerns & GCP violations, A total of 257 participants received treatment and were included in the Full analysis set population

Baseline characteristics

Reporting groups	
Reporting group title	Depemokimab
Reporting group description:	
Participants received a 100 milligram (mg) dose of depemokimab subcutaneous (SC) injection once every 26 weeks (week 0 and week 26) over a treatment period for 52-weeks. Participants were to be maintained on their existing baseline maintenance Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) standard of care (SOC) treatment throughout the study.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo SC injection once every 26 weeks (week 0 and week 26) over a treatment period for 52-weeks. Participants were to be maintained on their existing baseline maintenance CRSwNP SOC treatment throughout the study.	

Reporting group values	Depemokimab	Placebo	Total
Number of subjects	129	128	257
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	0	0
Adults (18-64 years)	110	104	214
From 65-84 years	19	24	43
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	50.5	50.4	
standard deviation	± 12.95	± 12.98	-
Sex: Female, Male Units: Participants			
Female	40	40	80
Male	89	88	177
Race/Ethnicity, Customized			
"All Other Races" category (American Indian or Alaska Native and Black or African American where 0<n<11) are combined into one category to maintain participant confidentiality and privacy			
Units: Subjects			
ALL OTHER RACES	3	4	7
ASIAN	27	26	53
WHITE	99	98	197

Subject analysis sets	
Subject analysis set title	Pooled Depemokimab
Subject analysis set type	Full analysis

Subject analysis set description:

This reporting arm contains the pooled population of treated participants from the clinical trial groups "Depemokimab" study intervention from protocol 217095 (2021-005037-16) and protocol 218079 (2021-005055-36). Participants received a 100 mg dose of depemokimab SC injection once every 26 weeks (week 0 and week 26). Participants were to be maintained on their existing baseline maintenance CRSwNP SOC treatment throughout the study. Due to EudraCT template restriction, the number of subjects entered cannot exceed the number of subjects enrolled in 218079, ANCHOR-2 study (264). However, a total of 272 participants were included in the pooled analysis comprising of 143 participants from 217095 study and 129 participants from 218079 study who received depemokimab as study intervention.

Subject analysis set title	Pooled Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

This reporting arm contains the pooled population of participants from the clinical trial groups "Placebo" study intervention from protocol 217095 and protocol 218079. Participants received a placebo SC injection once every 26 weeks (week 0 and week 26). Participants were to be maintained on their existing baseline maintenance CRSwNP SOC treatment throughout the study.

Reporting group values	Pooled Depemokimab	Pooled Placebo	
Number of subjects	264	256	
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	0	
Adults (18-64 years)	223	205	
From 65-84 years	49	51	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	52.4	51.6	
standard deviation	± 13.27	± 13.27	
Sex: Female, Male			
Units: Participants			
Female	85	78	
Male	187	178	
Race/Ethnicity, Customized			
"All Other Races" category (American Indian or Alaska Native and Black or African American where 0<n<11) are combined into one category to maintain participant confidentiality and privacy			
Units: Subjects			
ALL OTHER RACES	1	1	
ASIAN	64	56	
WHITE	196	186	

End points reporting groups

Reporting group title	Depemokimab

Reporting group description:

Participants received a 100 milligram (mg) dose of depemokimab subcutaneous (SC) injection once every 26 weeks (week 0 and week 26) over a treatment period for 52-weeks. Participants were to be maintained on their existing baseline maintenance Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) standard of care (SOC) treatment throughout the study.

Reporting group title	Placebo

Reporting group description:

Participants received placebo SC injection once every 26 weeks (week 0 and week 26) over a treatment period for 52-weeks. Participants were to be maintained on their existing baseline maintenance CRSwNP SOC treatment throughout the study.

Subject analysis set title	Pooled Depemokimab
Subject analysis set type	Full analysis

Subject analysis set description:

This reporting arm contains the pooled population of treated participants from the clinical trial groups "Depemokimab" study intervention from protocol 217095 (2021-005037-16) and protocol 218079 (2021-005055-36). Participants received a 100 mg dose of depemokimab SC injection once every 26 weeks (week 0 and week 26). Participants were to be maintained on their existing baseline maintenance CRSwNP SOC treatment throughout the study. Due to EudraCT template restriction, the number of subjects entered cannot exceed the number of subjects enrolled in 218079, ANCHOR-2 study (264). However, a total of 272 participants were included in the pooled analysis comprising of 143 participants from 217095 study and 129 participants from 218079 study who received depemokimab as study intervention.

Subject analysis set title	Pooled Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

This reporting arm contains the pooled population of participants from the clinical trial groups "Placebo" study intervention from protocol 217095 and protocol 218079. Participants received a placebo SC injection once every 26 weeks (week 0 and week 26). Participants were to be maintained on their existing baseline maintenance CRSwNP SOC treatment throughout the study.

Primary: Change From Baseline in Total Endoscopic Nasal Polyps (NP) Score at Week 52 (Centrally Read)

End point title	Change From Baseline in Total Endoscopic Nasal Polyps (NP) Score at Week 52 (Centrally Read)

End point description:

Total endoscopic nasal polyps (NP) score evaluated the size and extent of nasal polyps via endoscopy. The assessments were performed by central video image recordings. The right & left nostrils were scored from 0 to 4 (0 = No polyps; 1 = Small polyps in the middle meatus; 2 = Polyps reaching below the lower border of the middle turbinate; 3 = Large polyps reaching the lower border of the inferior turbinate; and 4 = Large polyps causing complete obstruction of the inferior meatus). The scores were graded based on NP size, recorded as sum of the right and left nostril scores & ranges from 0 (no polyps) to 8 (large polyps), calculated by summing the scores in each nostril; with higher scores indicating worse status. Baseline=Day 1 value. Change from Baseline = Post-baseline value minus Baseline value. FAS population excluding participants from 2 sites with GCP violation. Only those participants with data available at specified time points have been analyzed.

End point type	Primary

End point timeframe:

Baseline (Day 1) and at Week 52

End point values	Depemokimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	127		
Units: Scores on scale				
least squares mean (standard error)	-0.5 (± 0.14)	0.1 (± 0.15)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 52 in participants with a diagnosis of CRSwNP	
Comparison groups	Placebo v Depemokimab
Number of subjects included in analysis	255
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.004
Method	Mixed models analysis
Parameter estimate	LS Mean
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	-0.2

Primary: Change From Baseline in Mean Nasal Obstruction Score Using Verbal Response Scale from Week 49 Through to Week 52

End point title	Change From Baseline in Mean Nasal Obstruction Score Using Verbal Response Scale from Week 49 Through to Week 52

End point description:

This endpoint evaluated the change from baseline in the mean nasal obstruction score using a VRS from Week 49 through Week 52. Participants used a VRS to rate nasal obstruction severity, with scores averaged over the specified period to assess treatment impact on nasal obstruction symptoms. Participants were asked to indicate the severity of nasal obstruction at their worst over the last 24 hours using a 4-point VRS, with options of no symptoms, mild symptoms, moderate symptoms, and severe symptoms. This was scored on a scale ranging from 0 (no symptoms) to 3 (severe symptoms). Baseline was defined as the average score from the 28 days of eDiary data collected prior to Day 1. Change from Baseline = Post-baseline value minus Baseline value. The FAS included all randomized participants who received at least 1 dose of study treatment excluding participants from 2 sites due to GCP violation. Only those participants with data available at specified time points have been analyzed.

End point type	Primary

End point timeframe:

Baseline (Day 1) and from Week 49 to Week 52

End point values	Depemokimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	127		
Units: Scores on scale				
least squares mean (standard error)	-0.77 (± 0.076)	-0.53 (± 0.078)		

Statistical analyses

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 52 in participants with a diagnosis of CRSwNP

Comparison groups	Placebo v Depemokimab
Number of subjects included in analysis	256
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.025
Method	Mixed models analysis
Parameter estimate	LS Mean
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	-0.03

Secondary: Change from Baseline in Mean Symptom Score for Rhinorrhea (Runny Nose) Using Verbal Response Scale from Week 49 Through to Week 52

End point title	Change from Baseline in Mean Symptom Score for Rhinorrhea (Runny Nose) Using Verbal Response Scale from Week 49 Through to Week 52

End point description:

Participants were asked to indicate the severity of rhinorrhea (runny nose) at their worst over the last 24 hours using a 4-point VRS, with options of no symptoms, mild symptoms, moderate symptoms, and severe symptoms. This was scored on a scale ranging from 0 (no symptoms) to 3 (severe symptoms). Higher scores indicated the worst status. Baseline was defined as the average score from the 28 days of eDiary data collected prior to Day 1. Change from Baseline = Post-baseline value minus Baseline value. The FAS included all randomized participants who received at least 1 dose of study treatment excluding participants from 2 sites due to GCP violation. Participants were analyzed according to the treatment they were allocated at randomization. Only those participants who were measured and analyzed (i.e., contributed data reported in the table) were included in the Overall Number of Participants Analyzed field. 'Number Analyzed' signifies participants evaluable for specified time points.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and from Week 49 to Week 52

End point values	Depemokimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	127		
Units: Scores on scale				
least squares mean (standard error)	-0.72 (± 0.080)	-0.54 (± 0.082)		

Statistical analyses

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 49 to Week 52 in participants with a diagnosis of CRSwNP

Comparison groups	Placebo v Depemokimab
Number of subjects included in analysis	256
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.125
Method	Mixed models analysis
Parameter estimate	LS Mean
Point estimate	-0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.05

Secondary: Change From Baseline in Mean Symptom Score for Loss of Smell From Week 49 Through to Week 52

End point title	Change From Baseline in Mean Symptom Score for Loss of Smell From Week 49 Through to Week 52

End point description:

Participants were asked to indicate the severity of loss of smell at their worst over the last 24 hours using a 4-point VRS, with options of no symptoms, mild symptoms, moderate symptoms, and severe symptoms. This was scored on a scale ranging from 0 (no symptoms) to 3 (severe symptoms. Higher scores indicated worse status. Baseline was defined as the average score from the 28 days of eDiary data collected prior to Day 1. Change from Baseline = Post-baseline value minus Baseline value. The FAS included all randomized participants who received at least 1 dose of study treatment excluding participants from 2 sites with GCP violation. Only those participants who were measured and analyzed (i.e., contributed data reported in the table) were included in the Overall Number of Participants Analyzed field. 'Number Analyzed' signifies participants evaluable for specified time points.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and from Week 49 to Week 52

End point values	Depemokimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	127		
Units: Scores on scale				
least squares mean (standard error)	-0.56 (± 0.066)	-0.30 (± 0.068)		

Statistical analyses

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 49 to Week 52 in participants with a diagnosis of CRSwNP

Comparison groups	Placebo v Depemokimab
Number of subjects included in analysis	256
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.007 [1]
Method	Mixed models analysis
Parameter estimate	LS Mean
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.45
upper limit	-0.07

Notes:

[1] - Nominal significance (i.e., p<0.05 without multiplicity control). However, statistical significance was not achieved due to a break in the multiplicity-controlled testing hierarchy.

Secondary: Change from Baseline in Lund Mackay (LMK) Computed Tomography (CT) Score at Week 52

End point title	Change from Baseline in Lund Mackay (LMK) Computed Tomography (CT) Score at Week 52

End point description:

The LMK CT scoring system is based on CT imaging of the sinuses with points given for degree of opacification: 0 =normal, 1 = partial opacification, 2 = total opacification. These points are then applied to the maxillary, anterior ethmoid, posterior ethmoid, sphenoid, frontal sinus on each side (right and left). The osteomeatal complex (OC) is graded as 0 = not occluded, or 2 = occluded deriving a maximum score of 12 per side. The range for the total LMK CT score is therefore 0 (normal) to 24 (total opacification) when summed across both sides. Higher scores indicated more severe disease. Baseline was defined as Day 1 value. Change from Baseline = Post-baseline value minus Baseline value. The FAS included all randomized participants who received at least 1 dose of study treatment excluding participants from 2 sites with GCP violation. Only those participants with data available at specified time points have been analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Week 52

End point values	Depemokimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	121	111		
Units: Scores on scale				
least squares mean (standard error)	-3.5 (± 0.42)	-0.3 (± 0.44)		

Statistical analyses

Statistical analysis title	Statistical Analysis 5

Statistical analysis description:

To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 52 in participants with a diagnosis of CRSwNP

Comparison groups	Placebo v Depemokimab
Number of subjects included in analysis	232
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001 [2]
Method	ANCOVA
Parameter estimate	LS Mean
Point estimate	-3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.4
upper limit	-2

Notes:

[2] - Nominal significance (i.e., p<0.05 without multiplicity control). However, statistical significance was not achieved due to a break in the multiplicity-controlled testing hierarchy.

Secondary: Change from Baseline in Sino-nasal Outcome Test (SNOT)-22 Total Score at Week 52

End point title	Change from Baseline in Sino-nasal Outcome Test (SNOT)-22 Total Score at Week 52

End point description:

SNOT-22 is a 22-item measure of disease specific health related quality of life (HRQoL). Participants were asked to rate the severity of their condition on each of the 22 items over the previous 2 weeks using a 6-point rating scale of 0 (not present/no problem) to 5 (Problem as bad as it can be). The total score range for the SNOT-22 is 0-110, where higher scores indicate greater disease impact. Baseline was defined as Day 1 value. Change from Baseline = Post-baseline value minus Baseline value. The full analysis set included all randomized participants who received at least 1 dose of study treatment excluding participants from 2 sites with GCP violation. Only those participants who were measured and analyzed (i.e., contributed data reported in the table) were included in the Overall Number of Participants Analyzed field. 'Number Analyzed' signifies participants evaluable for specified time points.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Week 52

End point values	Depemokimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	126	126		
Units: Scores on scale				
least squares mean (standard error)	-15.9 (± 2.83)	-6.0 (± 2.87)		

Statistical analyses

Statistical analysis title	Statistical Analysis 6

Statistical analysis description:

To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 52 in participants with a diagnosis of CRSwNP

Comparison groups	Placebo v Depemokimab
Number of subjects included in analysis	252
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.015 [3]
Method	Mixed models analysis
Parameter estimate	LS Mean
Point estimate	-9.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.9
upper limit	-2

Notes:

[3] - Nominal significance (i.e., p<0.05 without multiplicity control). However, statistical significance was not achieved due to a break in the multiplicity-controlled testing hierarchy.

Secondary: Change from Baseline in Total Endoscopic Nasal Polyps Score at Week 26

End point title	Change from Baseline in Total Endoscopic Nasal Polyps Score at Week 26

End point description:

Total endoscopic nasal polyps (NP) score evaluated the size and extent of nasal polyps via endoscopy. The right & left nostrils were scored from 0 to 4 (0 = No polyps; 1 = Small polyps in the middle meatus; 2 = Polyps reaching below the lower border of the middle turbinate; 3 = Large polyps reaching the lower border of the inferior turbinate; and 4 = Large polyps causing complete obstruction of the inferior meatus). The scores were graded based on NP size, recorded as sum of the right & left nostril scores & ranges from 0 (no polyps) to 8 (large polyps), calculated by summing the scores in each nostril; with higher scores indicating worse status. Baseline was defined as Day 1 value. Change from Baseline = Post-baseline value minus Baseline value. The FAS included all randomized participants who received at least 1 dose of study treatment excluding participants from 2 sites due to GCP violation. Only those participants with data available at specified time points have been analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Week 26

End point values	Depemokimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	127		
Units: Scores on scale				
least squares mean (standard error)	-0.5 (± 0.12)	-0.1 (± 0.12)		

Statistical analyses

Statistical analysis title	Statistical Analysis 8

Statistical analysis description:

To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 26 in participants with a diagnosis of CRSwNP

Comparison groups	Placebo v Depemokimab
Number of subjects included in analysis	255
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.066
Method	Mixed models analysis
Parameter estimate	LS Mean
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0

Secondary: Change From Baseline in Mean Nasal Obstruction Score (VRS) From Week 21 Through to Week 24

End point title	Change From Baseline in Mean Nasal Obstruction Score (VRS) From Week 21 Through to Week 24

End point description:

Participants were asked to indicate the severity of nasal obstruction at its worst over the previous 24 hours using a 4-point VRS. The response options were no symptoms, mild symptoms, moderate symptoms, and severe symptoms, scored on a scale ranging from 0 (no symptoms) to 3 (severe symptoms). Higher scores indicated more severe status. Baseline was defined as the average score from the 28 days of eDiary data collected prior to Day 1. Change from Baseline = Post-baseline value minus Baseline value. The full analysis set included all randomized participants who received at least 1 dose of study treatment excluding participants from 2 sites with GCP violation. Only those participants who were measured and analyzed (i.e., contributed data reported in the table) were included in the Overall Number of Participants Analyzed field. 'Number Analyzed' signifies participants evaluable for specified time points.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and from Week 21 to Week 24

End point values	Depemokimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	127		
Units: Scores on scale				
least squares mean (standard error)	-0.78 (± 0.068)	-0.54 (± 0.069)		

Statistical analyses

Statistical analysis title	Statistical Analysis 6

Statistical analysis description:

To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 21 to Week 24 in participants with a diagnosis of CRSwNP

Comparison groups	Placebo v Depemokimab
Number of subjects included in analysis	256
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.016 [4]
Method	Mixed models analysis
Parameter estimate	LS Mean
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.43
upper limit	-0.04

Notes:

[4] - Nominal significance (i.e., p<0.05 without multiplicity control). However, statistical significance was not achieved due to a break in the multiplicity-controlled testing hierarchy.

Secondary: Percentage of Participants Requiring First Nasal Surgery (Actual or Entry on Waiting List) or Disease-Modulating Medication for Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) Up to Week 52

End point title	Percentage of Participants Requiring First Nasal Surgery (Actual or Entry on Waiting List) or Disease-Modulating Medication for Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) Up to Week 52

End point description:

Nasal polyp surgery is defined as any procedure involving instruments resulting in incision & removal of tissue from the nasal cavity. Time to first nasal surgery (actual or entry on waiting list) or disease-modulating medication for CRSwNP up to Week 52 was assessed in a pre-specified pooled analysis across replicate studies 217095 (2021-005037-16) & 218079 (2021-005055-36). The percentage of participants with corresponding 95%CI have been presented, calculated using the Kaplan-Meier method. Analysis was performed on FAS which consisted of all randomized participants from study 217095 and 218079 (Pooled analysis) & who had at least 1 dose of study drug excluding participants from 3 sites with GCP violation. Due to EudraCT template restriction, the number of subjects (N) entered cannot exceed subjects 264 enrolled in 218079 study. But the depemokimab pooled arm included 272 participants comprising 143 participants from 217095 & 129 participants from 218079 & for all pooled analysis.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Pooled Depemokimab	Pooled Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	272	256		
Units: Percentage of participants				
number (confidence interval 95%)	15.0 (11.3 to 19.9)	21.9 (17.2 to 27.7)		

Statistical analyses

Statistical analysis title	Statistical Analysis 9
Statistical analysis description:	
To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 52 in participants with a diagnosis of CRSwNP (pooled analysis)	
Comparison groups	Pooled Placebo v Pooled Depemokimab
Number of subjects included in analysis	528
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.128
Method	Cox Proportional Hazards Model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.735
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.495
upper limit	1.092

Secondary: Percentage of Participants Requiring at Least One Course of Systemic Corticosteroids or Disease-Modifying Medication for CRSwNP or Nasal Surgery (Actual) During the Week 52 Treatment Period

End point title	Percentage of Participants Requiring at Least One Course of Systemic Corticosteroids or Disease-Modifying Medication for CRSwNP or Nasal Surgery (Actual) During the Week 52 Treatment Period

End point description:

Percentage of participants requiring at least 1 course of systemic corticosteroids or disease-modulating medication for CRSwNP or nasal surgery (actual) during the Week 52 treatment period was assessed in a pre-specified pooled analysis across replicate studies 217095 (2021-005037-16) and 218079 (2021-005055-36). Analysis was performed on the FAS which consisted of all randomized participants from study 217095 and 218079 (Pooled analysis) and who had at least 1 dose of study treatment excluding participants from 3 sites with GCP violation. Due to template limitations, the number of subjects (N) entered cannot exceed subjects 264 enrolled in 218079 study. But depemokimab pooled arm included 272 participants comprising 143 participants (217095 study) and 129 participants (218079 study) and for all pooled analysis.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Pooled Depemokimab	Pooled Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	272	256		
Units: Percentage of participants	26	36		

Statistical analyses

Statistical analysis title	Statistical Analysis 11

Statistical analysis description:

To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 52 in participants with a diagnosis of CRSwNP (pooled analysis)

Comparison groups	Pooled Depemokimab v Pooled Placebo
Number of subjects included in analysis	528
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.006 [5]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	0.86

Notes:

[5] - Nominal significance (i.e., p<0.05 without multiplicity control) was achieved. However, statistical significance was not achieved due to a break in the multiplicity-controlled testing hierarchy.

Secondary: Percentage of Participants Requiring First Nasal Surgery (Actual) or Disease-Modulating Medication for CRSwNP up to Week 52

End point title	Percentage of Participants Requiring First Nasal Surgery (Actual) or Disease-Modulating Medication for CRSwNP up to Week 52

End point description:

Nasal polyp surgery is defined as any procedure involving instruments resulting in incision & removal of tissue from the nasal cavity (e.g. polypectomy).Time to first nasal surgery (actual) or disease-modulating medication for CRSwNP up to Week 52 was assessed in a pre-specified pooled analysis across replicate studies 217095 (2021-005037-16) and 218079 (2021-005055-36). The percentage of participants with corresponding 95%CI have been presented, calculated using the Kaplan-Meier method. Analysis was performed on the FAS which consisted of all randomized participants from study 217095 and 218079 (Pooled analysis) and who had at least 1 dose of study treatment excluding participants from 3 sites with GCP violation. Due to EudraCT template restriction, the number of subjects (N) entered cannot exceed subjects 264 enrolled in 218079 study. But depemokimab pooled arm included 272 participants comprising 143 participants (217095) and 129 participants (218079) and for all pooled analysis.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Pooled Depemokimab	Pooled Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	272	256		
Units: Percentage of participants				
number (confidence interval 95%)	12.2 (8.8 to 16.8)	16.7 (12.6 to 22.0)		

Statistical analyses

Statistical analysis title	Statistical Analysis 10

Statistical analysis description:

To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 52 in participants with a diagnosis of CRSwNP (pooled analysis)

Comparison groups	Pooled Placebo v Pooled Depemokimab
Number of subjects included in analysis	528
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.146
Method	Cox Proportional Hazards Model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.713
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.453
upper limit	1.124

Secondary: Change from Baseline in Asthma Control Questionnaire (ACQ-5) score at Week 52

End point title	Change from Baseline in Asthma Control Questionnaire (ACQ-5) score at Week 52

End point description:

The ACQ-5 is a 5-item questionnaire which enquires about the frequency and/or severity of asthma signs over the previous week (nocturnal awakening on waking in morning, activity limitation, & shortness of breath, wheeze). Each question is scored from 0 (no impairment) to 6 (total impairment). Higher scores indicate more limitations. Impact on asthma control in participants with an ACQ-5 score > 0.75 at baseline was assessed across replicate studies 217095 (2021-005037-16) and 218079 (2021-005055-36). Baseline was defined as Day 1 value. Change from Baseline = Post-baseline value minus Baseline value. FAS = randomized participants from study 217095 & 218079 excluding participants from 3 sites with GCP violation. Due to template limitations, the number of subjects (N) entered cannot exceed subjects 264 enrolled in 218079 study. But depemokimab pooled arm included 272 participants comprising 143 participants (217095 study) and 129 participants (218079 study) and for all pooled analysis.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Week 52

End point values	Pooled Depemokimab	Pooled Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	104	102		
Units: Scores on scale				
least squares mean (standard error)	-0.75 (± 0.182)	0.00 (± 0.182)		

Statistical analyses

Statistical analysis title	Statistical Analysis 12

Statistical analysis description:

The pooled statistical analyses will be performed using a Mixed Models Repeated Measures (MMRM) model with covariates of treatment group, baseline score, log(e) baseline blood eosinophil count, region, previous surgery for nasal polyps, study, visit and interaction terms for visit by baseline score and visit by treatment group.

Comparison groups	Pooled Depemokimab v Pooled Placebo
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.004 [6]
Method	Mixed models analysis
Parameter estimate	Adjusted mean difference
Point estimate	-0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.26
upper limit	-0.25

Notes:

[6] - Nominal significance (i.e., $p<0.05$ without multiplicity control) was achieved. However, statistical significance was not achieved due to a break in the multiplicity-controlled testing hierarchy.

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 from the start of the study intervention (Day 1) until follow up at week 56.

Adverse event reporting additional description:

All-cause mortality, SAEs and Non-SAEs were reported for the Safety Population which included all randomized participants who received at least 1 dose of study treatment excluding participants from 2 site with GCP violation. AEs were reported treatment-wise.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received placebo SC injection once every 26 weeks (week 0 and week 26) over a treatment period for 52-weeks. Participants were to be maintained on their existing baseline maintenance CRSwNP SOC treatment throughout the study.

Reporting group title	Depemokimab

Reporting group description:

Participants received a 100 milligram (mg) dose of depemokimab subcutaneous (SC) injection once every 26 weeks (week 0 and week 26) over a treatment period for 52-weeks. Participants were to be maintained on their existing baseline maintenance CRSwNP standard of care (SOC) treatment throughout the study.

Serious adverse events	Placebo	Depemokimab	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 128 (7.81%)	6 / 129 (4.65%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	0 / 128 (0.00%)	1 / 129 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sternal fracture			
subjects affected / exposed	1 / 128 (0.78%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			

subjects affected / exposed	1 / 128 (0.78%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	1 / 128 (0.78%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 128 (0.00%)	1 / 129 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocarditis			
subjects affected / exposed	0 / 128 (0.00%)	1 / 129 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 128 (0.00%)	1 / 129 (0.78%)	
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 / 128 (0.78%)	0 / 129 (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			
Ischaemic stroke			
subjects affected / exposed	0 / 128 (0.00%)	1 / 129 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular insufficiency			
subjects affected / exposed	1 / 128 (0.78%)	0 / 129 (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	1 / 128 (0.78%)	0 / 129 (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			
Heavy menstrual bleeding			
subjects affected / exposed	1 / 128 (0.78%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary dilatation			
subjects affected / exposed	1 / 128 (0.78%)	0 / 129 (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 / 128 (0.78%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 128 (1.56%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal polyps			
subjects affected / exposed	1 / 128 (0.78%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	1 / 128 (0.78%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Pneumonia			
subjects affected / exposed	1 / 128 (0.78%)	1 / 129 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peri-implantitis			
subjects affected / exposed	0 / 128 (0.00%)	1 / 129 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic sinusitis			
subjects affected / exposed	1 / 128 (0.78%)	0 / 129 (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 / 128 (0.00%)	1 / 129 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Depemokimab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	78 / 128 (60.94%)	75 / 129 (58.14%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 128 (3.91%)	2 / 129 (1.55%)	
occurrences (all)	6	2	
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 128 (10.16%)	11 / 129 (8.53%)	
occurrences (all)	17	15	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 128 (1.56%)	6 / 129 (4.65%)	
occurrences (all)	2	6	
Respiratory, thoracic and mediastinal disorders			

Oropharyngeal pain			
subjects affected / exposed	4 / 128 (3.13%)	4 / 129 (3.10%)	
occurrences (all)	7	4	
Nasal polyps			
subjects affected / exposed	11 / 128 (8.59%)	7 / 129 (5.43%)	
occurrences (all)	15	12	
Nasal congestion			
subjects affected / exposed	14 / 128 (10.94%)	5 / 129 (3.88%)	
occurrences (all)	16	8	
Epistaxis			
subjects affected / exposed	4 / 128 (3.13%)	6 / 129 (4.65%)	
occurrences (all)	6	6	
Cough			
subjects affected / exposed	8 / 128 (6.25%)	5 / 129 (3.88%)	
occurrences (all)	10	6	
Asthma			
subjects affected / exposed	6 / 128 (4.69%)	2 / 129 (1.55%)	
occurrences (all)	8	3	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	8 / 128 (6.25%)	3 / 129 (2.33%)	
occurrences (all)	9	3	
Arthralgia			
subjects affected / exposed	6 / 128 (4.69%)	3 / 129 (2.33%)	
occurrences (all)	11	4	
Infections and infestations			
COVID-19			
subjects affected / exposed	11 / 128 (8.59%)	9 / 129 (6.98%)	
occurrences (all)	11	9	
Upper respiratory tract infection			
subjects affected / exposed	15 / 128 (11.72%)	14 / 129 (10.85%)	
occurrences (all)	22	20	
Pharyngitis			
subjects affected / exposed	5 / 128 (3.91%)	4 / 129 (3.10%)	
occurrences (all)	5	4	
Nasopharyngitis			

subjects affected / exposed	15 / 128 (11.72%)	28 / 129 (21.71%)	
occurrences (all)	22	39	
Influenza			
subjects affected / exposed	5 / 128 (3.91%)	3 / 129 (2.33%)	
occurrences (all)	5	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 February 2022	Amendment 1
26 October 2022	Amendment 2
17 October 2023	Amendment 3
12 March 2024	Amendment 4
26 June 2024	Amendment 5

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported