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-1 (depemokimAb iN CHrOnic Rhinosinusitis)

Summary

EudraCT number	2021-005037-16
Trial protocol	FR BE DE ES
Global end of trial date	27 August 2024

Results information

Result version number	v1
This version publication date	15 August 2025
First version publication date	15 August 2025

Trial information

Trial identification

Sponsor protocol code	217095

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05274750
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	01 October 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 July 2024
Global end of trial reached?	Yes
Global end of trial date	27 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	22 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	Belgium: 4
Country: Number of subjects enrolled	France: 15
Country: Number of subjects enrolled	Germany: 29
Country: Number of subjects enrolled	Netherlands: 18
Country: Number of subjects enrolled	Spain: 22
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	United States: 21
Country: Number of subjects enrolled	Argentina: 71
Country: Number of subjects enrolled	Canada: 18
Country: Number of subjects enrolled	China: 31
Country: Number of subjects enrolled	Japan: 38
Worldwide total number of subjects	276
EEA total number of subjects	88

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	57
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 276 participants were randomized, of which 271 participants were included in Full analysis set (FAS). The FAS included all randomized participants who received at least 1 dose of study drug excluding 4 participants from 1 site with GCP/data integrity issues. One participant was randomized in error and did not receive any study drug.

Pre-assignment

Screening details:

A total of 276 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	Investigator, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Depemokimab

Arm description:

Participants received a 100 milligram (mg) dose of depemokimab SC injection once every 26 weeks (week 0 and week 26) over a treatment period of 52 weeks. Participants were to be maintained on their existing baseline maintenance for 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 of 52 weeks. Participants were to be maintained on their existing baseline maintenance for 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	143	128
Completed	128	115
Not completed	15	13
Physician decision	3	-
Consent withdrawn by subject	10	9
Adverse event, non-fatal	-	1
Lost to follow-up	2	3

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 276 participants who were randomized, 4 participants from 1 site was excluded from the full analysis population due to data integrity concerns & GCP violations, and one randomized participant did not receive any study intervention. Hence, a total of 271 participants 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 SC injection once every 26 weeks (week 0 and week 26) over a treatment period of 52 weeks. Participants were to be maintained on their existing baseline maintenance for 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 of 52 weeks. Participants were to be maintained on their existing baseline maintenance for CRSwNP SOC treatment throughout the study.

Reporting group values	Depemokimab	Placebo	Total
Number of subjects	143	128	271
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	54.1	52.9	
standard deviation	± 13.37	± 13.49	-
Sex: Female, Male Units: Participants			
Female	45	38	83
Male	98	90	188
Race/Ethnicity, Customized			
"All Other Races" category (Black or African American or Asian and Unknown where 0<n<11) are combined into one category to maintain participant confidentiality and privacy			
Units: Subjects			
WHITE	97	88	185
All Other Races	42	36	78
Missing	4	4	8

Subject analysis sets

Subject analysis set title	Pooled Depemokimab
Subject analysis set type	Sub-group 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.

Subject analysis set title	Pooled Placebo
Subject analysis set type	Sub-group 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 (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.

Reporting group values	Pooled Depemokimab	Pooled Placebo	
Number of subjects	272	256	
Age categorical Units: Subjects			
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 (Black or African American or Asian and Unknown where 0<n<11) are combined into one category to maintain participant confidentiality and privacy			
Units: Subjects			
WHITE	196	186	
All Other Races	72	66	
Missing	4	4	

End points

End points reporting groups

Reporting group title	Depemokimab

Reporting group description:

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

Subject analysis set title	Pooled Depemokimab
Subject analysis set type	Sub-group 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.

Subject analysis set title	Pooled Placebo
Subject analysis set type	Sub-group 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 (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.

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 1 site 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	139	127		
Units: Scores on a Scale				
least squares mean (standard error)	-0.6 (± 0.14)	0.2 (± 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	Depemokimab v Placebo
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Difference in Least Square Means
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	-0.3

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 change from baseline in the mean nasal obstruction score using a Verbal Response Scale (VRS) from Week 49 through to Week 52. Participants used 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 and severe symptoms. This was scored on a scale ranging from 0 (no symptoms) to 3 (severe symptoms). The average of daily scores in 4-weekly intervals were calculated & data are for Weeks 49-52. Baseline was defined as the average score from the 28 days of eDairy data collected prior to Day 1. Change from Baseline = Post-baseline value minus Baseline value. The analysis was performed on FAS population. The number of participants analyzed represents evaluable participants at specified time points.	
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	142	128		
Units: Scores on a Scale				
least squares mean (standard error)	-0.76 (± 0.079)	-0.53 (± 0.083)		

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	270
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.047
Method	Mixed models analysis
Parameter estimate	Difference in Least Square Means
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	0

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 indicate the worse status. The average of daily scores in 4-weekly intervals were calculated and data are presented for Weeks 49-52. Baseline was defined as Day 1 value. Change from Baseline = Post-baseline value minus Baseline value. The analysis was performed on the FAS population excluding participants from 1 site due to GCP violation. The number of participants analyzed represents evaluable participants at 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	142	128		
Units: Scores on a Scale				
least squares mean (standard error)	-0.71 (± 0.084)	-0.49 (± 0.087)		

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 49 to Week 52 in participants with a diagnosis of CRSwNP

Comparison groups	Placebo v Depemokimab
Number of subjects included in analysis	270
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.074
Method	Mixed models analysis
Parameter estimate	Difference in Least Square Means
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	0.02

Secondary: Change from Baseline in Mean Symptom Score for Loss of Smell Using Verbal Response Scale from Week 49 Through to Week 52

End point title	Change from Baseline in Mean Symptom Score for Loss of Smell Using Verbal Response Scale 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 score indicates worse status. The average of daily scores in 4-weekly intervals were calculated and data are presented for Weeks 49-52. Baseline was defined as the average score from the 28 days of eDiary data collected prior to Day 1. The analysis was performed on the FAS population excluding participants from 1 site due to GCP violation. The number of participants analyzed represents evaluable participants at 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	142	128		
Units: Scores on a Scale				
least squares mean (standard error)	-0.48 (± 0.069)	-0.29 (± 0.072)		

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	270
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.055
Method	Mixed models analysis
Parameter estimate	Difference in Least Square Means
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.39
upper limit	0

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

End point title	Change from Baseline in Lund Mackay Computerized 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 were 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. 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 analysis was performed on the FAS population excluding participants from 1 site due to GCP violation. The number of participants analyzed represents evaluable participants at 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	127	119		
Units: Scores on a Scale				
least squares mean (standard error)	-2.8 (± 0.45)	-0.8 (± 0.46)		

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	246
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.002
Method	ANCOVA
Parameter estimate	Difference in Least Square Means
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	-0.8

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:	
Sino-nasal outcome test-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 0-5 including: 0 = Not present/no problem; 1 = Very mild problem; 2 = Mild or slight problem; 3 = Moderate problem; 4 = Severe problem; 5 = Problem as "bad as it can be". The scores for each question were summed up to derive the total score range for the SNOT-22 was from 0 (high quality of life) to 110 (worst quality of life), where higher scores indicate worse quality of life. Baseline was defined as Day 1 value. Change from Baseline = Post-baseline value minus Baseline value. The analysis was performed on the FAS population excluding participants from 1 site due to GCP violation. The number of participants analyzed represents evaluable participants at 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	139	125		
Units: Scores on a Scale				
least squares mean (standard error)	-13.3 (± 2.96)	-6.5 (± 3.08)		

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	264
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.113
Method	Mixed models analysis
Parameter estimate	Difference in Least Square Means
Point estimate	-6.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.2
upper limit	1.6

Secondary: Change from Baseline in Mean Nasal Obstruction Score from Week 21 Through to Week 24

End point title	Change from Baseline in Mean Nasal Obstruction Score 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 score indicated more severe status. The average of daily scores in 4-weekly intervals were calculated and data are presented for Weeks 21-24. Baseline was defined as Day 1 value. Change from Baseline = Post-baseline value minus Baseline value. The analysis was performed on the FAS population excluding participants from 1 site due to GCP violation. The number of participants analyzed represents evaluable participants at 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	142	128		
Units: Scores on a Scale				
least squares mean (standard error)	-0.74 (± 0.071)	-0.57 (± 0.074)		

Statistical analyses

Statistical analysis title	Statistical Analysis 7

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	270
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.094
Method	Mixed models analysis
Parameter estimate	Difference in Least Square Means
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.37
upper limit	0.03

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

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

End point description:

Total endoscopic nasal polyps score evaluated the size and extent of nasal polyps via endoscopy. The right & left nostrils were scored from 0 - 4 (0 = No polyps; 1 = Small polyps in the middle meatus not reaching below the inferior border of the middle concha; 2 = Polyps reaching below the lower border of the middle turbinate; 3 = Large polyps reaching the lower border of the inferior turbinate or polyps medial to the middle concha; and 4 = Large polyps causing complete obstruction of the inferior meatus). The scores were recorded as sum of the right & left nostril scores ranging from 0 (no polyps) to 8 (large polyps), calculated by summing scores (0 - 4) in each nostril; with higher scores indicating worse status. Change from Baseline = Post-baseline value minus Baseline value. FAS population excluding participants from 1 site due to GCP violation. The number of participants analyzed represents evaluable subjects at specified time points.

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	139	127		
Units: Scores on a Scale				
least squares mean (standard error)	-0.6 (± 0.13)	0.1 (± 0.13)		

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	266
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Difference in Least Square Means
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	-0.4

Secondary: Percentage of Participants Requiring First Nasal Surgery (Actual or Entry on Waiting List) or Disease-Modulating Medication for Chronic Rhinosinusitis with Nasal Polyps 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 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) and 218079 (2021-005055-36). Percentage of participants with nasal surgery or course of systemic CS for CRSwNP and corresponding 95% CI have been presented, calculated using the Kaplan-Meier method. For pooled studies of 217095 and 218079, the analysis was performed on the FAS population. The FAS included all randomized participants who took at least 1 dose of study treatment excluding participants from 1 site for 217095 and 2 sites for 218079 respectively with GCP violation.	
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 Depemokimab v Pooled Placebo
Number of subjects included in analysis	528
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.128
Method	Cox proportional hazards
Parameter estimate	Hazard ratio (HR)
Point estimate	0.735
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.495
upper limit	1.092

Notes:

[1] - Cox Proportional Hazards Model with covariates of treatment, baseline total endoscopic nasal polyps score, baseline nasal obstruction score (VRS), log(e) baseline blood eosinophil count, region, study and previous surgery for nasal polyps. The covariate for study is removed for the individual-study analyses. If the hierarchy is broken, subsequent endpoints will be evaluated for nominal significance in a descriptive manner, using a 5% reference level.

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

End point title	Percentage of Participants Requiring First Nasal Surgery (Actual) or Disease-Modulating Medication for Chronic Rhinosinusitis with Nasal Polyps 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 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). Percentage of participants with nasal surgery or course of systemic CS for CRSwNP and corresponding 95% CI have been presented, calculated using the Kaplan-Meier method. For pooled studies of 217095 and 218079, the analysis was performed on the FAS population. The FAS included all randomized participants who took at least 1 dose of study treatment excluding participants from 1 site for 217095 and 2 sites for 218079 respectively with GCP violation.

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 Depemokimab v Pooled Placebo
Number of subjects included in analysis	528
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.146
Method	Cox proportional hazards
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: Percentage of Participants Requiring at Least One Course of Systemic Corticosteroids or Disease-Modulating 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-Modulating 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 will be assessed in a pre-specified pooled analysis across replicate studies 217095 (2021-005037-16) and 218079 (2021-005055-36). For pooled studies of 217095 and 218079, the analysis was performed on the FAS population. The FAS included all randomized participants who took at least 1 dose of study treatment excluding participants from 1 site for 217095 and 2 sites for 218079 respectively with GCP violation.	
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
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

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(i.e. partially or not well-controlled asthma) 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 population from study 217095 & 218079 excluding participants from 3 sites with GCP violation. Participants analyzed represents evaluable participants at specified time points.	
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 a 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:	
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	206
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.004
Method	Mixed models analysis
Parameter estimate	Difference in Least Square Means
Point estimate	-0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.26
upper limit	-0.25

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 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 1 site with GCP violation. AEs were reported treatment-wise.

Assessment type	Systematic

Dictionary used

Dictionary name	27.1
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 mg dose of depemokimab 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.

Serious adverse events	Placebo	Depemokimab	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 128 (4.69%)	5 / 143 (3.50%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	1 / 128 (0.78%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	1 / 128 (0.78%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			

subjects affected / exposed	0 / 128 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Parkinson's disease			
subjects affected / exposed	1 / 128 (0.78%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 128 (0.78%)	0 / 143 (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 / 128 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 128 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Diverticulitis			
subjects affected / exposed	1 / 128 (0.78%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 128 (0.78%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of bronchiectasis			

subjects affected / exposed	0 / 128 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	0 / 128 (0.00%)	1 / 143 (0.70%)	
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	72 / 128 (56.25%)	71 / 143 (49.65%)	
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 128 (6.25%)	6 / 143 (4.20%)	
occurrences (all)	12	6	
Gastrointestinal disorders			
Toothache			
subjects affected / exposed	4 / 128 (3.13%)	4 / 143 (2.80%)	
occurrences (all)	4	4	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 128 (4.69%)	3 / 143 (2.10%)	
occurrences (all)	8	4	
Epistaxis			
subjects affected / exposed	1 / 128 (0.78%)	5 / 143 (3.50%)	
occurrences (all)	1	6	
Nasal congestion			
subjects affected / exposed	4 / 128 (3.13%)	4 / 143 (2.80%)	
occurrences (all)	5	5	
Nasal polyps			
subjects affected / exposed	8 / 128 (6.25%)	8 / 143 (5.59%)	
occurrences (all)	10	11	
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	4 / 128 (3.13%)	3 / 143 (2.10%)	
occurrences (all)	4	3	
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	4 / 128 (3.13%)	7 / 143 (4.90%)	
occurrences (all)	4	9	
Bronchitis			
subjects affected / exposed	4 / 128 (3.13%)	6 / 143 (4.20%)	
occurrences (all)	4	6	
COVID-19			
subjects affected / exposed	9 / 128 (7.03%)	12 / 143 (8.39%)	
occurrences (all)	9	12	
Gastroenteritis			
subjects affected / exposed	4 / 128 (3.13%)	2 / 143 (1.40%)	
occurrences (all)	5	2	
Influenza			
subjects affected / exposed	10 / 128 (7.81%)	3 / 143 (2.10%)	
occurrences (all)	13	4	
Nasopharyngitis			
subjects affected / exposed	23 / 128 (17.97%)	21 / 143 (14.69%)	
occurrences (all)	26	28	
Sinusitis			
subjects affected / exposed	7 / 128 (5.47%)	5 / 143 (3.50%)	
occurrences (all)	8	7	
Upper respiratory tract infection			
subjects affected / exposed	14 / 128 (10.94%)	14 / 143 (9.79%)	
occurrences (all)	17	18	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

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

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported