Clinical trial results:
A Multicenter, Randomized, Double-blind, Parallel Group, Placebo controlled, Phase IIIb Study to Evaluate the Potential Effect of Tezepelumab on the Humoral Immune Response to Seasonal Quadrivalent Influenza Vaccination in Adolescent and Young Adult Participants with Moderate to Severe Asthma (VECTOR)

Summary

EudraCT number	2022-003286-37
Trial protocol	Outside EU/EEA
Global end of trial date	18 July 2022

Results information

Result version number	v1 (current)
This version publication date	21 January 2023
First version publication date	21 January 2023

Trial information

Trial identification

Sponsor protocol code	D5180C00031

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05062759
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	Södertälje, Södertälje, Sweden, 151 85
Public contact	Global Clinical Head, AstraZeneca Clinical Study Information Center, +1 87724094 79, information.center@astrazeneca.com
Scientific contact	Global Clinical Head, AstraZeneca Clinical Study Information Center, +1 87724094 79, information.center@astrazeneca.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 July 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of tezepelumab on the humoral immune response following seasonal influenza virus vaccination in adolescent and young adult participants with moderate to severe asthma

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with ICH/GCP, applicable regulatory requirements, and the AstraZeneca policy on Bioethics. The Principal Investigator or designee ensured that each patient (or parent/legally authorised representative) was given full and adequate oral and written information about the nature, purpose, possible risk, and benefit of the study. Informed consent/assent was obtained from all patients (and some parents/legally authorised representatives) before performing any study tests or procedures.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 August 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 70
Worldwide total number of subjects	70
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	43
Adults (18-64 years)	27
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted in 15 study centres in the United States between 23 August 2021 and 18 July 2022.

Pre-assignment

Screening details:

The Screening period was 2 to 3 weeks before randomisation. 81 patients signed informed consent and 70 patients were randomized. Patients were randomised in a 1:1 ratio to receive tezepelumab or placebo. All the study assessments were performed as per the Schedule of Activities.

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, Monitor, Subject, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Tezepelumab

Arm description:

Patients received at least 1 injection of tezepelumab 210 mg administered subcutaneously every 4 weeks by accessorized pre-filled syringe (APFS).

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

Dosage and administration details:

Patients received 1 injection of tezepelumab 210mg administered subcutaneously every 4 weeks by APFS.

Arm title	Placebo

Arm description:

Patients received at least 1 injection of placebo administered subcutaneously every 4 weeks by APFS.

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

Dosage and administration details:

Patients received 1 injection of placebo administered subcutaneously every 4 weeks by APFS.

Number of subjects in period 1	Tezepelumab	Placebo
Started	35	35
Completed	34	34
Not completed	1	1
Adverse event, serious fatal	-	1
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Tezepelumab
Reporting group description:	
Patients received at least 1 injection of tezepelumab 210 mg administered subcutaneously every 4 weeks by accessorized pre-filled syringe (APFS).	
Reporting group title	Placebo
Reporting group description:	
Patients received at least 1 injection of placebo administered subcutaneously every 4 weeks by APFS.	

Reporting group values	Tezepelumab	Placebo	Total
Number of subjects	35	35	70
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)	22	21	43
Adults (18-64 years)	13	14	27
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	16.3	16.6	
standard deviation	± 2.3	± 3.1	-
Gender Categorical			
Units: Subjects			
Female	14	11	25
Male	21	24	45
Race			
Units: Subjects			
White	24	23	47
Black or African American	8	12	20
Asian	1	0	1
American Indian or Alaska	2	0	2
Ethnic group			
Units: Subjects			
Hispanic or Latino	8	10	18
Not Hispanic or Latino	27	25	52

End points

End points reporting groups

Reporting group title	Tezepelumab
Reporting group description:	
Patients received at least 1 injection of tezepelumab 210 mg administered subcutaneously every 4 weeks by accessorized pre-filled syringe (APFS).	
Reporting group title	Placebo
Reporting group description:	
Patients received at least 1 injection of placebo administered subcutaneously every 4 weeks by APFS.	

Primary: Post-vaccination strain-specific hemagglutination inhibition (HAI) antibody geometric mean fold rises (GMFRs)

End point title	Post-vaccination strain-specific hemagglutination inhibition (HAI) antibody geometric mean fold rises (GMFRs)
End point description:	
Effect of tezepelumab on the humoral immune response following seasonal influenza virus vaccination in adolescent and young adult participants with moderate to severe asthma was assessed. Vaccine immunogenicity analysis set consisted of all randomised patients who received the influenza vaccine plus at least 1 dose of tezepelumab or placebo, had pre and post vaccination HAI or Microneutralization antibody measurements, had no influenza infection prior to Visit 7 (Week 16), and had no protocol deviation, judged to have the potential to interfere with the generation or interpretation of an antibody response.	
End point type	Primary
End point timeframe:	
From Week 12 to Week 16	

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	33		
Units: Fold change				
geometric mean (geometric coefficient of variation)				
Influenza A H1N1	7.34 (± 1.361)	4.75 (± 1.455)		
Influenza B Yamagata Lineage	1.76 (± 0.955)	1.46 (± 0.937)		
Influenza B Victoria Lineage	2.94 (± 1.054)	2.90 (± 0.841)		

Statistical analyses

Statistical analysis title	Influenza A H1N1, Placebo vs Teze
Statistical analysis description:	
Ratio of placebo over tezepelumab. Results based on ANCOVA model	
Comparison groups	Tezepelumab v Placebo

Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometric Least square (LS) mean ratio
Point estimate	0.65
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.43
upper limit	0.98

Statistical analysis title	Influenza B Yamagata Lineage, Placebo vs Teze
Statistical analysis description:	
Ratio of placebo over tezepelumab. Results based on ANCOVA model	
Comparison groups	Tezepelumab v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometeric LS mean ratio
Point estimate	0.83
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.6
upper limit	1.15

Statistical analysis title	Influenza B Victoria Lineage, Placebo vs Teze
Statistical analysis description:	
Ratio of placebo over tezepelumab. Results based on ANCOVA model	
Comparison groups	Tezepelumab v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometric LS mean ratio
Point estimate	0.99
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.71
upper limit	1.37

Primary: Post-vaccination strain-specific microneutralization (MN) antibody GMFRs

End point title	Post-vaccination strain-specific microneutralization (MN) antibody GMFRs

End point description:

Effect of tezepelumab on the humoral immune response following seasonal influenza virus vaccination in adolescent and young adult participants with moderate to severe asthma was assessed.

Vaccine immunogenicity analysis set consisted of all randomised patients who received the influenza vaccine plus at least 1 dose of tezepelumab or placebo, had pre and post vaccination HAI or MN antibody measurements, had no influenza infection prior to Visit 7 (Week 16), and had no protocol deviation, judged to have the potential to interfere with the generation or interpretation of an antibody response.

End point type	Primary

End point timeframe:

From Week 12 to Week 16

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	33		
Units: Fold change				
geometric mean (geometric coefficient of variation)				
Influenza A H1N1	14.56 (± 2.581)	10.62 (± 2.409)		
Influenza A H3N2	4.73 (± 1.509)	5.90 (± 3.180)		
Influenza B Yamagata Lineage	4.00 (± 1.541)	3.56 (± 2.206)		
Influenza B Victoria Lineage	4.08 (± 2.279)	5.04 (± 1.723)		

Statistical analyses

Statistical analysis title	Influenza A H1N1, Placebo vs Teze

Statistical analysis description:

Ratio of placebo over tezepelumab.
Results based on ANCOVA model

Comparison groups	Tezepelumab v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometeric LS mean ratio
Point estimate	0.73
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.42
upper limit	1.28

Statistical analysis title	Influenza A H3N2, Placebo vs Teze

Statistical analysis description: Ratio of placebo over tezepelumab. Results based on ANCOVA model	
Comparison groups	Tezepelumab v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometeric LS mean ratio
Point estimate	1.25
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.72
upper limit	2.17

Statistical analysis title	Influenza B Victoria Lineage, Placebo vs Teze
Statistical analysis description: Ratio of placebo over tezepelumab. Results based on ANCOVA model	
Comparison groups	Tezepelumab v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometric LS mean ratio
Point estimate	1.23
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.73
upper limit	2.07

Statistical analysis title	Influenza B Yamagata Lineage, Placebo vs Teze
Statistical analysis description: Ratio of placebo over tezepelumab. Results based on ANCOVA model	
Comparison groups	Tezepelumab v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometeric LS mean ratio
Point estimate	0.89
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.54
upper limit	1.48

Primary: Post-vaccination strain-specific serum HAI antibody geometric mean titers (GMTs)

End point title	Post-vaccination strain-specific serum HAI antibody geometric mean titers (GMTs)

End point description:

Effect of tezepelumab on the humoral immune response following seasonal influenza virus vaccination in adolescent and young adult participants with moderate to severe asthma was assessed.

Vaccine immunogenicity analysis set consisted of all randomised patients who received the influenza vaccine plus at least 1 dose of tezepelumab or placebo, had pre and post vaccination HAI or MN antibody measurements, had no influenza infection prior to Visit 7 (Week 16), and had no protocol deviation, judged to have the potential to interfere with the generation or interpretation of an antibody response.

End point type	Primary

End point timeframe:

Week 16

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	33		
Units: Geometric Mean Titer				
geometric mean (geometric coefficient of variation)				
Influenza A H1N1	809.23 (± 0.921)	596.76 (± 1.076)		
Influenza B Yamagata Lineage	167.46 (± 0.925)	161.56 (± 0.688)		
Influenza B Victoria Lineage	194.68 (± 1.089)	200.55 (± 0.948)		

Statistical analyses

Statistical analysis title	Influenza A H1N1, Placebo vs Teze

Statistical analysis description:

Ratio of placebo over tezepelumab.
Results based on ANCOVA model

Comparison groups	Tezepelumab v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometeric LS mean ratio
Point estimate	0.74
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.52
upper limit	1.04

Statistical analysis title	Influenza B Yamagata Lineage, Placebo vs Teze
Statistical analysis description: Ratio of placebo over tezepelumab. Results based on ANCOVA model	
Comparison groups	Tezepelumab v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometeric LS mean ratio
Point estimate	0.96
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.72
upper limit	1.29

Statistical analysis title	Influenza B Victoria Lineage, Placebo vs Teze
Statistical analysis description: Ratio of placebo over tezepelumab. Results based on ANCOVA model	
Comparison groups	Tezepelumab v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometric LS mean ratio
Point estimate	1.03
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.73
upper limit	1.46

Primary: Post-vaccination strain-specific serum MN antibody GMTs

End point title	Post-vaccination strain-specific serum MN antibody GMTs

End point description:

Effect of tezepelumab on the humoral immune response following seasonal influenza virus vaccination in adolescent and young adult participants with moderate to severe asthma was assessed.

Vaccine immunogenicity analysis set consisted of all randomised patients who received the influenza vaccine plus at least 1 dose of tezepelumab or placebo, had pre and post vaccination HAI or MN antibody measurements, had no influenza infection prior to Visit 7 (Week 16), and had no protocol deviation, judged to have the potential to interfere with the generation or interpretation of an antibody response.

End point type	Primary

End point timeframe:

Week 16

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	33		
Units: Geometric Mean Titer				
geometric mean (geometric coefficient of variation)				
Influenza A H1N1	382.55 (± 1.469)	303.63 (± 1.667)		
Influenza A H3N2	600.92 (± 2.154)	457.33 (± 2.336)		
Influenza B Yamagata Lineage	355.44 (± 1.076)	366.81 (± 1.270)		
Influenza B Victoria Lineage	125.67 (± 4.687)	124.35 (± 3.515)		

Statistical analyses

Statistical analysis title	Influenza A H1N1, Placebo vs Teze
Statistical analysis description:	
Ratio of placebo over tezepelumab. Results based on ANCOVA model	
Comparison groups	Tezepelumab v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometeric LS mean ratio
Point estimate	0.79
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.51
upper limit	1.25

Statistical analysis title	Influenza A H3N2, Placebo vs Teze
Statistical analysis description:	
Ratio of placebo over tezepelumab. Results based on ANCOVA model	
Comparison groups	Tezepelumab v Placebo

Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometeric LS mean ratio
Point estimate	0.76
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.42
upper limit	1.28

Statistical analysis title	Influenza B Victoria Lineage, Placebo vs Teze
Statistical analysis description:	
Ratio of placebo over tezepelumab. Results based on ANCOVA model	
Comparison groups	Tezepelumab v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometric LS mean ratio
Point estimate	0.99
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.49
upper limit	1.99

Statistical analysis title	Influenza B Yamagata Lineage, Placebo vs Teze
Statistical analysis description:	
Ratio of placebo over tezepelumab. Results based on ANCOVA model	
Comparison groups	Tezepelumab v Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometeric LS mean ratio
Point estimate	1.03
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.7
upper limit	1.52

Primary: Percentage of patients with post-vaccination strain-specific antibody

response at Week 16 with antibody response defined as a ≥ 4-fold rise in HAI antibody titer

End point title	Percentage of patients with post-vaccination strain-specific antibody response at Week 16 with antibody response defined as a ≥ 4-fold rise in HAI antibody titer[1]

End point description:

Effect of tezepelumab on the humoral immune response following seasonal influenza virus vaccination in adolescent and young adult participants with moderate to severe asthma was assessed.

Vaccine immunogenicity analysis set consisted of all randomised patients who received the influenza vaccine plus at least 1 dose of tezepelumab or placebo, had pre and post vaccination HAI or MN antibody measurements, had no influenza infection prior to Visit 7 (Week 16), and had no protocol deviation, judged to have the potential to interfere with the generation or interpretation of an antibody response.

End point type	Primary

End point timeframe:

Week 16

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal hypothesis testing was performed, as this is a descriptive study

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	33		
Units: Percentage				
number (confidence interval 90%)				
Influenza A H1N1	78.8 (63.82 to 89.60)	51.5 (36.07 to 66.74)		
Influenza B Yamagata Lineage	15.2 (6.17 to 29.25)	15.2 (6.17 to 29.25)		
Influenza B Victoria Lineage	30.3 (17.46 to 45.96)	39.4 (25.11 to 55.18)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of patients with post-vaccination strain-specific antibody response at Week 16 with antibody response defined as a ≥ 4-fold rise in MN antibody titer

End point title	Percentage of patients with post-vaccination strain-specific antibody response at Week 16 with antibody response defined as a ≥ 4-fold rise in MN antibody titer[2]

End point description:

Effect of tezepelumab on the humoral immune response following seasonal influenza virus vaccination in adolescent and young adult participants with moderate to severe asthma was assessed.

Vaccine immunogenicity analysis set consisted of all randomised patients who received the influenza vaccine plus at least 1 dose of tezepelumab or placebo, had pre and post vaccination HAI or MN antibody measurements, had no influenza infection prior to Visit 7 (Week 16), and had no protocol deviation, judged to have the potential to interfere with the generation or interpretation of an antibody response.

End point type	Primary

End point timeframe:

Week 16

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal hypothesis testing was performed, as this is a descriptive study

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	33		
Units: Percentage				
number (confidence interval 90%)				
Influenza A H1N1	81.8 (67.24 to 91.77)	75.8 (60.49 to 87.32)		
Influenza A H3N2	60.6 (44.82 to 74.89)	51.5 (36.07 to 66.74)		
Influenza B Yamagata Lineage	51.5 (36.07 to 66.74)	36.4 (22.50 to 52.16)		
Influenza B Victoria Lineage	54.5 (38.94 to 69.51)	63.6 (47.84 to 77.50)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of patients with post-vaccination strain-specific HAI antibody titer ≥ 40

End point title	Percentage of patients with post-vaccination strain-specific HAI antibody titer ≥ 40[3]

End point description:

Effect of tezepelumab on the humoral immune response following seasonal influenza virus vaccination in adolescent and young adult participants with moderate to severe asthma was assessed.

Vaccine immunogenicity analysis set consisted of all randomised patients who received the influenza vaccine plus at least 1 dose of tezepelumab or placebo, had pre and post vaccination HAI or MN antibody measurements, had no influenza infection prior to Visit 7 (Week 16), and had no protocol deviation, judged to have the potential to interfere with the generation or interpretation of an antibody response.

End point type	Primary

End point timeframe:

Week 16

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal hypothesis testing was performed, as this is a descriptive study.

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	33		
Units: Percentage				
number (confidence interval 90%)				
Influenza A H1N1	100 (91.32 to 100.00)	100 (91.32 to 100.00)		

Influenza B Yamagata Lineage	97 (86.41 to 99.84)	100 (91.32 to 100.00)		
Influenza B Victoria Lineage	100 (91.32 to 100.00)	97.0 (86.41 to 99.84)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of patients with post-vaccination strain-specific MN antibody titer ≥ 40

End point title	Percentage of patients with post-vaccination strain-specific MN antibody titer ≥ 40[4]

End point description:

Effect of tezepelumab on the humoral immune response following seasonal influenza virus vaccination in adolescent and young adult participants with moderate to severe asthma was assessed.

Vaccine immunogenicity analysis set consisted of all randomised patients who received the influenza vaccine plus at least 1 dose of tezepelumab or placebo, had pre and post vaccination HAI or MN antibody measurements, had no influenza infection prior to Visit 7 (Week 16), and had no protocol deviation, judged to have the potential to interfere with the generation or interpretation of an antibody response.

End point type	Primary

End point timeframe:

Week 16

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal hypothesis testing was performed, as this is a descriptive study

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	33		
Units: Percentage				
number (confidence interval 90%)				
Influenza A H1N1	100 (91.32 to 100.00)	93.9 (82.13 to 98.91)		
Influenza A H3N2	93.9 (82.13 to 98.91)	97 (86.41 to 99.84)		
Influenza B Yamagata Lineage	97 (86.41 to 99.84)	100 (91.32 to 100.00)		
Influenza B Victoria Lineage	78.8 (63.82 to 89.60)	81.8 (67.24 to 91.77)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum tezepelumab concentrations

End point title	Serum tezepelumab concentrations[5]

End point description:

Tezepelumab serum concentrations were summarized using descriptive statistics at each visit.

Pharmacokinetic (PK) analysis set consisted of all patients who received tezepelumab and from whom PK blood samples were obtained and assumed not to be affected by factors such as protocol deviations.

Here, the arbitrary value 9999.9999 represent "Not calculated as > 50% of concentrations are below Lower limit of quantification (0.010 ug/mL)"

End point type	Secondary

End point timeframe:

Week 0, Week 12, Week 16 and Week 28

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The Placebo arm did not receive Tezepelumab, therefore serum concentration for tezepelumab cannot be measured in placebo arm.

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: microgram/milliliter (µg/mL)				
geometric mean (geometric coefficient of variation)				
Week 0 (n=32)	9999.9999 (± 9999.9999)			
Week 12 (n=30)	27.00 (± 0.5421)			
Week 16 (n=32)	20.76 (± 3.6969)			
Week 28 (n=31)	2.79 (± 1.0705)			

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity

End point title	Immunogenicity

End point description:

Immunogenicity assessments were performed.
ADA prevalence was defined as patients who are ADA positive at any time including baseline. Persistently positive was defined as having at least two post-baseline ADA positive measurements (with ≥16 weeks between first and last positive) or an ADA positive result at the last available post-baseline assessment. Transiently positive was defined as having at least one post-baseline ADA positive measurement and not fulfilling the conditions for persistently positive. Treatment boosted ADA was defined as baseline positive ADA titre that was boosted to a 4-fold or higher-level following treatment. Treatment emergent ADA (ADA incidence) was defined as the sum of treatment induced ADA and treatment boosted ADA.

Safety analysis set consisted of all patients who received at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

From Baseline to Week 28

End point values	Tezepelumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: Patients				
number (not applicable)				
ADA prevalence	0	4		
Only baseline ADA positive	0	0		
Both baseline and post-baseline ADA positive	0	0		
Any baseline ADA positive	0	0		
Any post-baseline ADA positive	0	4		
Treatment-induced ADA positive	0	4		
ADA persistently positive	0	4		
ADA transiently positive	0	0		
Treatment-boosted ADA positive	0	0		
TE-ADA positive (ADA incidence)	0	4		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the date of the first dose of study drug, throughout the treatment period up to the follow-up period or end of the study visit (Week 28)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Patients received at least 1 injection of placebo administered subcutaneously every 4 weeks by APFS.	
Reporting group title	Tezepelumab
Reporting group description:	
Patients received at least 1 injection of tezepelumab 210 mg administered subcutaneously every 4 weeks by APFS.	

Serious adverse events	Placebo	Tezepelumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Injury, poisoning and procedural complications			
Stab wound			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

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

Non-serious adverse events	Placebo	Tezepelumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 35 (42.86%)	14 / 35 (40.00%)	
Injury, poisoning and procedural complications			
Skin laceration			
subjects affected / exposed	0 / 35 (0.00%)	2 / 35 (5.71%)	
occurrences (all)	0	2	

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 35 (5.71%)	1 / 35 (2.86%)	
occurrences (all)	2	2	
Infections and infestations			
COVID-19			
subjects affected / exposed	8 / 35 (22.86%)	8 / 35 (22.86%)	
occurrences (all)	8	8	
Acute sinusitis			
subjects affected / exposed	0 / 35 (0.00%)	3 / 35 (8.57%)	
occurrences (all)	0	3	
Ear infection			
subjects affected / exposed	2 / 35 (5.71%)	1 / 35 (2.86%)	
occurrences (all)	2	1	
Pharyngitis			
subjects affected / exposed	2 / 35 (5.71%)	0 / 35 (0.00%)	
occurrences (all)	2	0	
Sinusitis			
subjects affected / exposed	2 / 35 (5.71%)	0 / 35 (0.00%)	
occurrences (all)	2	0	
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 35 (5.71%)	1 / 35 (2.86%)	
occurrences (all)	2	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 February 2022	The primary rationale for this amendment is to introduce a primary database lock after the end of treatment at Visit 7 (Week 16) and to update safety information based on the most recent Investigator's Brochure, Version 5.0, dated 21 Oct 2021. Additional changes include APFS device malfunction, medical device deficiencies, and Appendix F Medical Device Adverse Events (AEs) to align with International Organisation for Standardisation 14155 and European Medical Device Regulation. In addition, the vaccine immunogenicity analysis set definition was updated to exclude patients who experience influenza infection prior to Visit 7 (Week 16). Other minor changes included clarification of Schedule of Assessments for participants who prematurely discontinue study intervention. In addition, minor formatting and editorial administrative revisions were made throughout the protocol for clarification purposes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported