EU Clinical Trials Register

Clinical trial results:
A Phase I, Open Label Study to Evaluate the Pharmacokinetics of Tezepelumab in Children 5 to 11 Years of Age with Mild, Moderate, or Severe Asthma

Summary

EudraCT number	2020-000554-97
Trial protocol	GB HU
Global end of trial date	27 September 2022

Results information

Result version number	v1 (current)
This version publication date	28 March 2023
First version publication date	28 March 2023

Trial information

Trial identification

Sponsor protocol code	D5180C00025

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04673630
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	Karlebyhusentren, B674 Astraallen, Södertälje, Sweden, 151 85
Public contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001613-PIP01-14
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	27 September 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 September 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to describe the Pharmacokinetic (PK) parameters following a single subcutaneous (SC) administration of tezepelumab in children with mild, moderate, or 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 International Council for Harmonisation/Good Clinical Practice, applicable regulatory requirements, and the AstraZeneca policy on Bioethics.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 February 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 Kingdom: 8
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	South Africa: 8
Worldwide total number of subjects	18
EEA total number of subjects	2

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)	18
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This Phase I open-label study was conducted in pediatric participants with mild, moderate, or severe asthma at 6 investigational sites.

Pre-assignment

Screening details:

This study consists a screening period (14 days), and a single dose treatment (Day 1) and follow-up period (85 days). A total of 18 participants were treated in the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Tezepelumab

Arm description:

Participants received a single dose of tezepelumab SC injection on Day 1.

Arm type	Experimental
Investigational medicinal product name	Tezepelumab
Investigational medicinal product code	
Other name	MEDI9929, AMG 157
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single SC injection of tezepelumab administered by a healthcare professional on Day 1.

Number of subjects in period 1	Tezepelumab
Started	18
Completed	18

Baseline characteristics

Reporting groups

Reporting group title	Tezepelumab

Reporting group description:

Participants received a single dose of tezepelumab SC injection on Day 1.

Reporting group values	Tezepelumab	Total	
Number of subjects	18	18	
Age Categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	7.9		
standard deviation	± 1.78	-	
Gender Categorical			
Units: Subjects			
Female	7	7	
Male	11	11	
Race			
Units: Subjects			
Asian	2	2	
Black or African American	1	1	
White	6	6	
Other	9	9	
Ethnicity			
Units: Subjects			
Not Hispanic or Latino	18	18	

End points

End points reporting groups

Reporting group title	Tezepelumab
Reporting group description:	
Participants received a single dose of tezepelumab SC injection on Day 1.	

Primary: Maximum Observed Serum Concentration (Cmax) of Tezepelumab

End point title	Maximum Observed Serum Concentration (Cmax) of Tezepelumab[1]

End point description:

Blood samples were collected to determine the Cmax of tezepelumab. The PK parameters were estimated using non-compartmental analysis method. The PK analysis set included participants in the Safety Analysis set that had at least 1 detectable tezepelumab serum concentration from a sample collected postdose that was assumed not to be affected by factors such as important protocol deviations (eg, incorrect dose of study drug received).

End point type	Primary

End point timeframe:

Predose and within ± 1 hour of postdose on Day 1; on Days 3, 7, 11, 15, 29, 57 and 85

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: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: microgram per milliliter (mcg/mL)				
arithmetic mean (standard deviation)	27.1 (± 11.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Time to Achieve Maximum Observed Serum Concentration (tmax) of Tezepelumab

End point title	Time to Achieve Maximum Observed Serum Concentration (tmax) of Tezepelumab[2]

End point description:

Blood samples were collected to determine the tmax of tezepelumab. The PK parameters were estimated using non-compartmental analysis method. The PK analysis set included participants in the Safety Analysis set that had at least 1 detectable tezepelumab serum concentration from a sample collected postdose that was assumed not to be affected by factors such as important protocol deviations (eg, incorrect dose of study drug received).

End point type	Primary

End point timeframe:

Predose and within ± 1 hour of postdose on Day 1; on Days 3, 7, 11, 15, 29, 57 and 85

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: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: day				
median (full range (min-max))	3.47 (1.92 to 9.96)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Concentration-Time Curve From Time Zero to The Last Measurable Concentration (AUC0-last) of Tezepelumab

End point title	Area Under the Concentration-Time Curve From Time Zero to The Last Measurable Concentration (AUC0-last) of Tezepelumab[3]

End point description:

Blood samples were collected to determine the AUC0-last of tezepelumab and calculated by linear up/log down trapezoidal summation. The PK parameters were estimated using non-compartmental analysis method. The PK analysis set included participants in the Safety Analysis set that had at least 1 detectable tezepelumab serum concentration from a sample collected postdose that was assumed not to be affected by factors such as important protocol deviations (eg, incorrect dose of study drug received).

End point type	Primary

End point timeframe:

Predose and within ± 1 hour of postdose on Day 1; on Days 3, 7, 11, 15, 29, 57 and 85

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: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: day*mcg/mL				
arithmetic mean (standard deviation)	872 (± 285)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Concentration-Time Curve From Time Zero Extrapolated to Infinity (AUC0-inf) of Tezepelumab

End point title	Area Under the Concentration-Time Curve From Time Zero Extrapolated to Infinity (AUC0-inf) of Tezepelumab[4]

End point description:

Blood samples were collected to determine the AUC0-inf of tezepelumab and calculated by linear up/log down trapezoidal summation and extrapolated to infinity by the addition of the last quantifiable concentration divided by the terminal rate constant. The PK parameters were estimated using non-compartmental analysis method. The PK analysis set included participants in the Safety Analysis set that had at least 1 detectable tezepelumab serum concentration from a sample collected postdose that was assumed not to be affected by factors such as important protocol deviations (eg, incorrect dose of study drug received).

End point type	Primary

End point timeframe:

Predose and within ± 1 hour of postdose on Day 1; on Days 3, 7, 11, 15, 29, 57 and 85

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: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: day*mcg/mL				
arithmetic mean (standard deviation)	974 (± 320)			

Statistical analyses

No statistical analyses for this end point

Primary: Terminal Phase Elimination Half-Life (t1/2) of Tezepelumab

End point title	Terminal Phase Elimination Half-Life (t1/2) of Tezepelumab[5]

End point description:

Blood samples were collected to determine the t1/2 of tezepelumab and calculated as $\ln(2)/\lambda Z$, where λZ is the first-order rate constant associated with the terminal (log-linear) elimination phase. The PK parameters were estimated using non-compartmental analysis method. The PK analysis set included participants in the Safety Analysis set that had at least 1 detectable tezepelumab serum concentration from a sample collected postdose that was assumed not to be affected by factors such as important protocol deviations (eg, incorrect dose of study drug received).

End point type	Primary

End point timeframe:

Predose and within ± 1 hour of postdose on Day 1; on Days 3, 7, 11, 15, 29, 57 and 85

Notes:

[5] - 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: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: day				
arithmetic mean (standard deviation)	25.7 (± 5.94)			

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Clearance (CL/F) of Tezepelumab

End point title	Apparent Clearance (CL/F) of Tezepelumab[6]

End point description:

Blood samples were collected to determine the CL/F of tezepelumab and estimated as dose divided by AUC0-inf. The PK parameters were estimated using non-compartmental analysis method. The PK analysis set included participants in the Safety Analysis set that had at least 1 detectable tezepelumab serum concentration from a sample collected postdose that was assumed not to be affected by factors such as important protocol deviations (eg, incorrect dose of study drug received).

End point type	Primary

End point timeframe:

Predose and within ± 1 hour of postdose on Day 1; on Days 3, 7, 11, 15, 29, 57 and 85

Notes:

[6] - 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: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: liter per day				
arithmetic mean (standard deviation)	0.0802 (± 0.0295)			

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Steady-State Volume of Distribution (Vss/F) of Tezepelumab

End point title	Apparent Steady-State Volume of Distribution (Vss/F) of Tezepelumab[7]

End point description:

Blood samples were collected to determine the Vss/F of tezepelumab and estimated as CL/F*mean residence time (MRT), where MRT=Area under the moment curve of the analyte in the sampled matrix from zero (predose) extrapolated to infinite time/(AUC0-inf). The PK parameters were estimated using non-compartmental analysis method. The PK analysis set included participants in the Safety Analysis set that had at least 1 detectable tezepelumab serum concentration from a sample collected postdose that was assumed not to be affected by factors such as important protocol deviations (eg, incorrect dose of study drug received).

End point type	Primary

End point timeframe:

Predose and within ± 1 hour of postdose on Day 1; on Days 3, 7, 11, 15, 29, 57 and 85

Notes:

[7] - 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: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: liter				
arithmetic mean (standard deviation)	3.08 (± 1.32)			

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Volume of Distribution (Vz/F) of Tezepelumab

End point title	Apparent Volume of Distribution (Vz/F) of Tezepelumab[8]

End point description:

Blood samples were collected to determine the Vz/F of tezepelumab and estimated as CL/F*1/ λZ. The PK parameters were estimated using non-compartmental analysis method. The PK analysis set included participants in the Safety Analysis set that had at least 1 detectable tezepelumab serum concentration from a sample collected postdose that was assumed not to be affected by factors such as important protocol deviations (eg, incorrect dose of study drug received).

End point type	Primary

End point timeframe:

Predose and within ± 1 hour of postdose on Day 1; on Days 3, 7, 11, 15, 29, 57 and 85

Notes:

[8] - 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: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: liter				
arithmetic mean (standard deviation)	2.98 (± 1.26)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Anti-Drug Antibody (ADA) Response to Tezepelumab

End point title	Number of Participants With Anti-Drug Antibody (ADA) Response to Tezepelumab

End point description:

Blood samples were analyzed for the presence of ADAs for tezepelumab using validated assays. ADA prevalence was defined as ADA positive at baseline and/or post baseline. ADA incidence was defined as the percentage of treatment-emergent ADA positive participants in a population. Treatment induced ADA positive was defined as ADA negative at baseline and post-baseline ADA positive. Treatment-boosted ADA positive was defined as baseline positive ADA titre that was boosted to a 4-fold or higher level following study drug administration. Treatment-emergent ADA positive was defined as either treatment-induced ADA positive or treatment-boosted ADA positive. The Safety analysis set included all participants who received at least 1 dose of tezepelumab.

End point type	Secondary

End point values	Tezepelumab			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: participants				
number (not applicable)				
ADA prevalence	3			
Only baseline ADA positive	2			
Baseline and at least 1 post-baseline ADA positive	1			
Baseline ADA positive regardless of post-baseline	3			
Any post-baseline ADA positive	1			
Treatment-induced ADA positive	0			
Treatment-boosted ADA positive	0			
Treatment-emergent ADA positive	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose administration (Day 1) up to study completion (End of Study/Day 85 visit) or withdrawal date

Adverse event reporting additional description:

The Safety analysis set included all participants who received at least 1 dose of tezepelumab.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Tezepelumab

Reporting group description:

Participants received a single dose of tezepelumab SC injection on Day 1.

Serious adverse events	Tezepelumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Tezepelumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 18 (38.89%)		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Contusion			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Nervous system disorders			
Headache			

subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Nasopharyngitis			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 July 2020	Clarified that study start occur only when it is acceptable and safe to do so in accordance with local and national guidelines. Testing for Coronavirus Disease 2019 (COVID-19) and additional visits added. Addition of new exclusion criteria for participants that were positive for COVID-19 and/or had signs and/or symptoms indicative of present or past multisystem inflammatory syndrome. Screening classification for participants with a positive COVID-19 test clarified. Volume of blood clarified for severe acute respiratory syndrome coronavirus 2 serology to allow for testing of COVID 19. Details of mitigations added that could be employed to ensure study continuity in the event of a civil crisis, natural disaster or public health crisis. New section added for COVID-19 safety assessment procedure. New section added for pandemic impact assessment for COVID-19. New requirements for performing spirometry added, including the procedure for participants testing positive for COVID-19, and clarification regarding the safety of performing spirometry. New requirements for conducting the fractional exhaled nitric oxide test added, including the procedure for participants testing positive for COVID 19, and clarification regarding the safety of performing the test. Updated text to clarify that approximately 14 participants will receive a single SC dose of tezepelumab. Additional information added to clarify replacement of participants who did not receive tezepelumab or complete all required evaluations.
13 May 2021	The COVID-19 viral testing procedure updated to rapid test at local laboratory instead of at central laboratory at Visit 1 and Visit 2. Removed exclusion for use of systemic or intra-articular glucocorticosteroids for conditions other than asthma for 3 months prior to Visit 2 and discouraged until end of study. Change evidence of asthma by removing post-bronchodilator spirometry or historical reversibility criteria and adding to physician diagnosis of asthma as defined by regional guidelines and Investigator review of medical history. Change in participant's pre-bronchodilator forced expiratory volume in one second criteria from ≥ 70% to ≥ 50% of predicted normal value. Updated to allow more than 1 rescreen attempt per participant, as long as the study physician had deemed the reason for rescreen was valid.
06 January 2022	Removed inclusion criteria for body mass index for age at both screening and Day 1 to include full span of growth percentiles. Updated exclusion criteria around a history of a deterioration in asthma, asthma exacerbation requiring glucocorticoids, and systemic corticosteroid use for the maintenance treatment of asthma to decrease time restriction from 3 months to 6 weeks. Updated exclusion criteria around a history of overnight hospitalisation for asthma from 6 months to 3 months prior to Visit 1, up to and including Visit 2 (Day 1). Updated location where the study was conducted to include approximately 10 study sites globally. Exclusion criteria added relating to COVID-19. Restricted medications updated to allow administration of COVID-19 vaccinations during study conduct.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

 None reported