Clinical trial results:
A Multicentre, Randomised, Open-label, Parallel-group, Functionality, and Performance Study of an Accessorised Pre-filled Syringe and Autoinjector with Home-administered Subcutaneous Tezepelumab in Adolescent and Adult Subjects with Severe Asthma (PATH-HOME)

Summary

EudraCT number	2018-004588-30
Trial protocol	PL
Global end of trial date	05 June 2020

Results information

Result version number	v1 (current)
This version publication date	18 December 2020
First version publication date	18 December 2020

Trial information

Trial identification

Sponsor protocol code	D5180C00011

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03968978
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	151 85, Södertälje, Sweden,
Public contact	Global Clinical Head, AstraZeneca, +1 8772409479, information.center@astrazeneca.com
Scientific contact	AstraZeneca Clinical Study Information, AstraZeneca, 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 July 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 June 2020
Global end of trial reached?	Yes
Global end of trial date	05 June 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of the study is to assess the successful administration, performance, and functionality of a single-use accessorized pre-filled syringe (APFS) and autoinjector (AI) with a fixed 210 mg dose of tezepelumab administered subcutaneously (SC) in clinic and an at-home setting.

Protection of trial subjects:

Data safety monitoring board is not utilized for this study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 May 2019
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	Canada: 37
Country: Number of subjects enrolled	Japan: 17
Country: Number of subjects enrolled	Poland: 78
Country: Number of subjects enrolled	United States: 84
Worldwide total number of subjects	216
EEA total number of subjects	78

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)	24
Adults (18-64 years)	152
From 65 to 84 years	40

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

266 subjects enrolled in the study. 50 subjects were screen failure, and 216 randomized.

Pre-assignment

Screening details:

216 subjects randomized to tezepelumab 210 mg Q4W via APFS and tezepelumab 210 mg Q4W via AI. All randomized subjects were treated. 111 (51.4%) were randomized to tezepelumab 210 mg Q4W via APFS and 105 (48.6%) were randomized to tezepelumab 210 mg Q4W via AI.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Teze 210 mg Q4W via APFS

Arm description:

Accessorized pre-filled syringe every 4 weeks administered subcutaneously

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:

210 mg

Arm title	Teze 210 mg Q4W via AI

Arm description:

Autoinjector every 4 weeks administered subcutaneously

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

Dosage and administration details:

210 mg

Number of subjects in period 1	Teze 210 mg Q4W via APFS	Teze 210 mg Q4W via AI
Started	111	105
Completed	110	105
Not completed	1	0
Adverse event, non-fatal	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Teze 210 mg Q4W via APFS
Reporting group description:	
Accessorized pre-filled syringe every 4 weeks administered subcutaneously	
Reporting group title	Teze 210 mg Q4W via AI
Reporting group description:	
Autoinjector every 4 weeks administered subcutaneously	

Reporting group values	Teze 210 mg Q4W via APFS	Teze 210 mg Q4W via AI	Total
Number of subjects	111	105	216
Age Categorical Units: Participants			
Adolescents (>=12 to <18 years)	13	11	24
Adults (>=18 to <65 years)	79	73	152
Adults (>=65 years)	19	21	40
Age Continuous			
Measure analysis population description for: Full Analysis Set			
Units: Years			
arithmetic mean	48.5	45.8	
standard deviation	± 18.1	± 18.3	-
Sex: Female, Male Units: Participants			
Female	56	52	108
Male	55	53	108
Race/Ethnicity, Customized Units: Subjects			
White	87	82	169
Black or African American	8	8	16
Asian	16	15	31
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	12	13	25
Not Hispanic or Latino	99	92	191

End points

End points reporting groups

Reporting group title	Teze 210 mg Q4W via APFS
Reporting group description:	
Accessorized pre-filled syringe every 4 weeks administered subcutaneously	
Reporting group title	Teze 210 mg Q4W via AI
Reporting group description:	
Autoinjector every 4 weeks administered subcutaneously	

Primary: Proportions of HCPs and subjects/caregivers who successfully administered tezepelumab in clinic or at home by device type

End point title	Proportions of HCPs and subjects/caregivers who successfully administered tezepelumab in clinic or at home by device type[1]
End point description:	
Successful administration is defined as an injection completed, based on a used/returned (HCP or subject/caregiver) answer of YES to all 5 questions in the administration questionnaire, and satisfactory in vitro evaluation of returned/evaluated devices.	
End point type	Primary
End point timeframe:	
Week 0, Week 4, Week 8, Week 12, Week 16, Week 20	

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: According to the protocol the primary analysis in this study was not a comparison between treatments, it was to assess the functionality in each treatment arm separately. Therefore no statistical analysis is included in this form. The proportions and confidence intervals within treatment arms are however provided.

End point values	Teze 210 mg Q4W via APFS	Teze 210 mg Q4W via AI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	105		
Units: Proportion of Participants				
number (confidence interval 95%)				
Week 0 (in clinic)	98.2 (93.7 to 99.5)	100.0 (96.5 to 100.0)		
Week 4 (in clinic)	100.0 (96.6 to 100.0)	97.1 (91.9 to 99.0)		
Week 8 (in clinic)	100.0 (96.6 to 100.0)	98.1 (93.3 to 99.5)		
Week 12 (at home)	100.0 (96.6 to 100.0)	99.0 (94.8 to 99.8)		
Week 16 (at home)	95.4 (89.7 to 98.0)	97.1 (91.9 to 99.0)		
Week 20 (in clinic)	96.3 (90.9 to 98.6)	97.1 (91.9 to 99.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportions of used/returned devices that pass functional tests and visual inspection and showed no evidence of malfunction

End point title	Proportions of used/returned devices that pass functional tests and visual inspection and showed no evidence of malfunction

End point description:

Devices that passed functional tests and visual inspection and showed no evidence of malfunction will be evaluated as functional.
Percentages have been calculated by using the number of used and returned devices at specified visit as denominator.

End point type	Secondary

End point timeframe:

Week 0, Week 4, Week 8, Week 12, Week 16, Week 20

End point values	Teze 210 mg Q4W via APFS	Teze 210 mg Q4W via AI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	105		
Units: Proportion of Devices				
number (confidence interval 95%)				
Week 0 (in clinic)|	98.2 (93.7 to 99.5)	100.0 (96.5 to 100.0)		
Week 4 (in clinic)	100.0 (96.6 to 100.0)	97.2 (93.4 to 99.5)		
Week 8 (in clinic)	100.0 (96.6 to 100.0)	98.1 (93.3 to 99.5)		
Week 12 (at home)|	100.0 (96.6 to 100.0)	100.0 (96.4 to 100.0)		
Week 16 (at home)	97.2 (92.1 to 99.0)	100.0 (96.4 to 100.0)		
Week 20 (in clinic)	99.1 (94.8 to 99.8)	100.0 (96.4 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportions of devices that have been reported as malfunctioning (Product Complaints)

End point title	Proportions of devices that have been reported as malfunctioning (Product Complaints)

End point description:

Performance is measured by the proportion of APFS or AI devices that have been reported as malfunctioning (i.e. via Product Complaints).
Percentages have been calculated by using the number of used and returned devices at specified visit as denominator.

End point type	Secondary

End point timeframe:

Week 0, Week 4, Week 8, Week 12, Week 16, Week 20

End point values	Teze 210 mg Q4W via APFS	Teze 210 mg Q4W via AI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	105		
Units: Proportion of Devices				
number (confidence interval 95%)				
Week 0 (in clinic)	1.8 (0.5 to 6.3)	0.0 (0.0 to 3.5)		
Week 4 (in clinic)	0.0 (0.0 to 3.3)	2.8 (1.0 to 8.0)		
Week 8 (in clinic)	0.0 (0.0 to 3.4)	1.9 (0.5 to 6.7)		
Week 12 (at home)|	0.0 (0.0 to 3.4)	0.0 (0.0 to 3.6)		
Week 16 (at home)|	2.8 (1.0 to 7.9)	0.0 (0.0 to 3.6)		
Week 20 (in clinic)	0.9 (0.2 to 5.1)	0.0 (0.0 to 3.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Asthma Control Questionnaire-6 (ACQ-6) score

End point title	Change from baseline in Asthma Control Questionnaire-6 (ACQ-6) score

End point description:

The ACQ-6 captures asthma symptoms and short-acting β2-agonist use via subject-report. Questions are weighted equally and scored from 0 (totally controlled) to 6 (severely uncontrolled). The ACQ-6 score is the mean of the responses.

End point type	Secondary

End point timeframe:

Baseline (Week 0), Week 4, Week 8, Week 12, Week 16, Week 20 and Week 24

End point values	Teze 210 mg Q4W via APFS	Teze 210 mg Q4W via AI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	105		
Units: Score				
arithmetic mean (standard deviation)				
ACQ-6 score at Baseline (Week 0)	2.227 (± 0.732)	2.081 (± 0.625)		
ACQ-6 score at Week 4	1.629 (± 0.791)	1.492 (± 0.715)		
Change from Baseline of ACQ-6 score at Week 4	-0.598 (± 0.702)	-0.589 (± 0.694)		
ACQ-6 score at Week 8	1.401 (± 0.859)	1.316 (± 0.744)		
Change from Baseline of ACQ-6 score at Week 8	-0.826 (± 0.833)	-0.765 (± 0.793)		
ACQ-6 score at Week 12	1.197 (± 0.751)	1.143 (± 0.745)		

Change from Baseline of ACQ-6 score at Week 12	-1.011 (± 0.805)	-0.938 (± 0.805)		
ACQ-6 score at Week 16	1.226 (± 0.845)	1.171 (± 0.782)		
Change from Baseline of ACQ-6 score at Week 16	-0.986 (± 0.893)	-0.910 (± 0.867)		
ACQ-6 score at Week 20	1.230 (± 0.832)	1.238 (± 0.795)		
Change from Baseline of ACQ-6 score at Week 20	-0.978 (± 0.866)	-0.843 (± 0.910)		
ACQ-6 score at Week 24	1.072 (± 0.755)	1.140 (± 0.765)		
Change from Baseline of ACQ-6 score at Week 24	-1.141 (± 0.845)	-0.941 (± 0.775)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum trough concentrations

End point title	Serum trough concentrations

End point description:

PK serum samples were collected pre-dose on dosing visits

End point type	Secondary

End point timeframe:

Baseline (Week 0), Week 4, Week 20 and Week 24 (EOT)

End point values	Teze 210 mg Q4W via APFS	Teze 210 mg Q4W via AI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	105		
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Baseline (Week 0)	0 (± 0)	0 (± 0)		
Week 4	10.9764 (± 48.3948)	10.5690 (± 57.0076)		
Week 20	18.9653 (± 69.0785)	20.3206 (± 56.5858)		
Week 24 (EOT)	19.6274 (± 58.2660)	19.9264 (± 54.3198)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-drug antibodies (ADA)

End point title	Anti-drug antibodies (ADA)

End point description:

Anti-drug antibodies (ADA) responses at baseline and/or post baseline. Treatment-induced ADA positive is defined as ADA negative at baseline and post-baseline ADA positive. Treatment-boosted ADA positive is defined as baseline positive ADA titre that was boosted to a 4-fold or higher-level following IP administration. Treatment-emergent ADA (TE-ADA) positive is defined as either treatment-induced ADA positive or treatment-boosted ADA positive. ADA incidence is the proportion of TE-ADA positive subjects in a population. Persistently positive is defined as ADA positive at >=2 post-baseline assessments (with >=16 weeks between first and last positive) or ADA positive at last post-baseline assessment. Transiently positive is defined as having at least one post-baseline ADA positive assessment and not fulfilling the conditions of persistently positive

End point type	Secondary

End point timeframe:

Pre-treatment on dosing days until end of follow-up (Week 36) per protocol

End point values	Teze 210 mg Q4W via APFS	Teze 210 mg Q4W via AI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	105		
Units: Participants				
ADA prevalence	2	11		
TE-ADA positive (ADA incidence)	2	8		
Treatment-induced ADA positive	2	8		
Treatment-boosted ADA positive	0	0		
ADA persistently positive	1	7		
ADA transiently positive	1	3		
Only baseline ADA positive	0	1		
Both baseline and at least one post-baseline ADA +	0	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose till end of study (Week 36)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups	
Reporting group title	Teze 210 mg Q4W via APFS
Reporting group description:	
Accessorized pre-filled syringe every 4 weeks administered subcutaneously	
Reporting group title	Teze 210 mg Q4W via AI
Reporting group description:	
Autoinjector every 4 weeks administered subcutaneously	

Serious adverse events	Teze 210 mg Q4W via APFS	Teze 210 mg Q4W via AI	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 111 (4.50%)	4 / 105 (3.81%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Nervous system disorders			
Psychogenic seizure			
subjects affected / exposed	0 / 111 (0.00%)	1 / 105 (0.95%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 111 (0.00%)	1 / 105 (0.95%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 111 (0.90%)	0 / 105 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			

Asthma			
subjects affected / exposed	0 / 111 (0.00%)	3 / 105 (2.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	1 / 111 (0.90%)	0 / 105 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 111 (0.00%)	1 / 105 (0.95%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	1 / 111 (0.90%)	0 / 105 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Diverticulitis			
subjects affected / exposed	2 / 111 (1.80%)	0 / 105 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	1 / 111 (0.90%)	0 / 105 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Genitourinary tract infection			
subjects affected / exposed	1 / 111 (0.90%)	0 / 105 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia escherichia			
subjects affected / exposed	1 / 111 (0.90%)	0 / 105 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Varicella			
subjects affected / exposed	0 / 111 (0.00%)	1 / 105 (0.95%)	
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	Teze 210 mg Q4W via APFS	Teze 210 mg Q4W via AI	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 111 (26.13%)	29 / 105 (27.62%)	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	6 / 111 (5.41%)	5 / 105 (4.76%)	
occurrences (all)	9	5	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	12 / 111 (10.81%)	15 / 105 (14.29%)	
occurrences (all)	13	15	
Pharyngitis			
subjects affected / exposed	4 / 111 (3.60%)	4 / 105 (3.81%)	
occurrences (all)	4	6	
Upper respiratory tract infection			
subjects affected / exposed	9 / 111 (8.11%)	8 / 105 (7.62%)	
occurrences (all)	11	9	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 July 2019	Added exclusion criterion of non-leukocyte depleted whole blood transfusion in 120 days prior to Visit 1
03 July 2019	Language was updated from "Prior to the date of randomisation, a history of continuous treatment with medium or high dose ICS plus a second controller medication for at least six months prior to Visit 1 should be documented in source documents and recorded in the eCRF." to "Prior to the date of randomisation, a history of continuous treatment with medium or high dose ICS for at least six months prior to Visit 1 plus a second controller medication for at least three months prior to Visit 1 should be documented in source documents and recorded in the eCRF."

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported