EU Clinical Trials Register

Clinical trial results:
A Phase 1, Open-label Study to Evaluate the Pharmacokinetics of MEDI9929 in Adolescents with Mild to Moderate Asthma

Summary

EudraCT number	2014-005450-19
Trial protocol	PL
Global end of trial date	02 May 2016

Results information

Result version number	v1 (current)
This version publication date	20 January 2017
First version publication date	20 January 2017

Trial information

Trial identification

Sponsor protocol code	D5180C00002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02512900
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	MedImmune, LLC
Sponsor organisation address	One MedImmune Way, Gaithersburg, United States,
Public contact	Rene van der Merwe, Senior Director, Clinical Development, Respiratory, and Inflammation, MedImmune, LLC, 011 3013980000 x, information.center@astrazeneca.com
Scientific contact	Rene van der Merwe, Senior Director, Clinical Development, Respiratory, and Inflammation, MedImmune, LLC, 011 3013980000 x, 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 May 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 May 2016
Global end of trial reached?	Yes
Global end of trial date	02 May 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the PK profile of a single-dose administration of MEDI9929 in adolescent subjects with mild to moderate asthma

Protection of trial subjects:

The conduct of this clinical study met all local and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and are consistent with International Conference on Harmonization guideline: Good Clinical Practice, and applicable regulatory requirements. Participants signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy:

Participants in this study continued to receive asthma controller medications consistent with those described at Step 2 to Step 4 of GINA guidelines (GINA, 2014) as prescribed by their physician.

Evidence for comparator: -

Actual start date of recruitment	01 September 2015
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	Poland: 21
Worldwide total number of subjects	21
EEA total number of subjects	21

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)	21

Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Adolescent participants (12 to 17 years, inclusive) with mild to moderate asthma were recruited in an open-label fashion to receive a single-dose of MEDI9929 (also known as tezepelumab or AMG 157) at two study centers in Poland from Sep 2015 to May 2016.

Pre-assignment

Screening details:

A total of 26 participants were screened in this study. Of which 21 participants completed the study. Additional 5 participants signed the informed consent but were not enrolled in the study as they were screen failures. The reason for screen failures were not meeting the inclusion/exclusion criteria, lost to follow-up, and/or consent withdrawal.

Period 1

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

Blinding implementation details:

This is an Open-label study

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1

Arm description:

On Day 1, a single dose of MEDI9929 was administered subcutaneously to all participants.

Arm type	Experimental
Investigational medicinal product name	MEDI9929
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single-dose subcutaneous

Arm title	Cohort 2

Arm description:

On Day 1, a single dose of MEDI9929 was administered subcutaneously to all participants.

Arm type	Experimental
Investigational medicinal product name	MEDI9929
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single-dose subcutaneous

Number of subjects in period 1	Cohort 1	Cohort 2
Started	11	10
Completed	11	10

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1
Reporting group description:	
On Day 1, a single dose of MEDI9929 was administered subcutaneously to all participants.	
Reporting group title	Cohort 2
Reporting group description:	
On Day 1, a single dose of MEDI9929 was administered subcutaneously to all participants.	

Reporting group values	Cohort 1	Cohort 2	Total
Number of subjects	11	10	21
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)	11	10	21
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous				
Units: Years			
arithmetic mean	13.5	15.9	
standard deviation	± 0.8	± 0.7	-
Gender, Male/Female			
Units: Participants			
Male	10	5	15
Female	1	5	6

Subject analysis sets

Subject analysis set title	MEDI9929
Subject analysis set type	Per protocol
Subject analysis set description:	
On Day 1, a single dose of MEDI9929 was administered subcutaneously to participants, aged 12 to 17 years, inclusive.	

Reporting group values	MEDI9929		
Number of subjects	21		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		

Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	21		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous	Units: Years			
arithmetic mean	14.7		
standard deviation	± 1.4		
Gender, Male/Female Units: Participants			
Male	15		
Female	6		

End points

End points reporting groups

Reporting group title	Cohort 1
Reporting group description:	
On Day 1, a single dose of MEDI9929 was administered subcutaneously to all participants.	
Reporting group title	Cohort 2
Reporting group description:	
On Day 1, a single dose of MEDI9929 was administered subcutaneously to all participants.	
Subject analysis set title	MEDI9929
Subject analysis set type	Per protocol
Subject analysis set description:	
On Day 1, a single dose of MEDI9929 was administered subcutaneously to participants, aged 12 to 17 years, inclusive.	

Primary: Area Under the Concentration-time Curve From Zero to Infinity (AUC [0-infinity])

End point title	Area Under the Concentration-time Curve From Zero to Infinity (AUC [0-infinity])[1]
End point description:	
The pharmacokinetic (PK) parameter AUC (0 to infinity) was estimated based on the serum concentrations of MEDI9929. Serum concentrations of MEDI9929 were measured by enzyme-linked immunosorbent assay.	
End point type	Primary
End point timeframe:	
Day 1 (predose) and postdose.	

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: Statistical analysis was not applicable since there was no formal statistical testing or modeling performed.

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: µg•day/mL				
arithmetic mean (standard deviation)	1020 (± 355)	881 (± 185)		

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Concentration-Time Curve From Zero to Last Observation (AUC [0-t])

End point title	Area Under the Concentration-Time Curve From Zero to Last Observation (AUC [0-t])[2]
End point description:	
The PK parameter AUC (0-t) was estimated based on the serum concentrations of MEDI9929. Serum concentrations of MEDI9929 were measured by enzyme-linked immunosorbent assay.	
End point type	Primary

End point timeframe:

Day 1 (predose) and postdose.

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: Statistical analysis was not applicable since there was no formal statistical testing or modeling performed.

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: µg•day/mL				
arithmetic mean (standard deviation)	906 (± 284)	780 (± 171)		

Statistical analyses

No statistical analyses for this end point

Primary: Dose-normalized AUC (0-infinity) (AUC [0 infinity]/D)

End point title	Dose-normalized AUC (0-infinity) (AUC [0 infinity]/D)[3]

End point description:

The AUC (0-infinity)/D is the area under concentration-time curve extrapolated to infinity postdose normalized by MEDI9929 dose. The PK parameter was estimated based on the serum concentrations of MEDI9929. Serum concentrations of MEDI9929 were measured by enzyme-linked immunosorbent assay.

End point type	Primary

End point timeframe:

Day 1 (predose) and postdose.

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: Statistical analysis was not applicable since there was no formal statistical testing or modeling performed.

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: µg•day/mL/mg				
arithmetic mean (standard deviation)	7.27 (± 2.54)	6.29 (± 1.32)		

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Serum Concentration (Cmax)

End point title	Maximum Observed Serum Concentration (Cmax)[4]

End point description:

The PK parameter Cmax was estimated based on the serum concentrations of MEDI9929. Serum concentrations of MEDI9929 were measured by enzyme-linked immunosorbent assay.

End point type	Primary

End point timeframe:

Day 1 (predose) and postdose.

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: Statistical analysis was not applicable since there was no formal statistical testing or modeling performed.

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: µg/mL				
arithmetic mean (standard deviation)	24.6 (± 6.65)	23.4 (± 6.82)		

Statistical analyses

No statistical analyses for this end point

Primary: Dose-normalized Cmax (Cmax/D)

End point title	Dose-normalized Cmax (Cmax/D)[5]

End point description:

The Cmax/D is the maximum observed concentration post dose normalized by MEDI9929 dose. The PK parameter was estimated based on the serum concentrations of MEDI9929. Serum concentrations of MEDI9929 were measured by enzyme-linked immunosorbent assay.

End point type	Primary

End point timeframe:

Day 1 (predose) and postdose.

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: Statistical analysis was not applicable since there was no formal statistical testing or modeling performed.

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: µg/mL/mg				
arithmetic mean (standard deviation)	0.176 (± 0.0475)	0.167 (± 0.0487)		

Statistical analyses

No statistical analyses for this end point

Primary: Time to Reach Cmax (Tmax)

End point title	Time to Reach Cmax (Tmax)[6]

End point description:

The Tmax is the time to maximum observed serum concentration of MEDI9929. The PK parameter was estimated based on the serum concentrations of MEDI9929. Serum concentrations of MEDI9929 were measured by enzyme-linked immunosorbent assay.

End point type	Primary

End point timeframe:

Day 1 (predose) and postdose.

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: Statistical analysis was not applicable since there was no formal statistical testing or modeling performed.

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: Day				
median (full range (min-max))	5.98 (0.99 to 9.97)	4.44 (1.4 to 19.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Terminal Phase Elimination Half Life (t1/2,z)

End point title	Terminal Phase Elimination Half Life (t1/2,z)[7]

End point description:

The t½,z is the time measured for the serum drug concentration of MEDI9929 to decrease by one half. The PK parameter was estimated based on the serum concentrations of MEDI9929. Serum concentrations of MEDI9929 were measured by enzyme-linked immunosorbent assay.

End point type	Primary

End point timeframe:

Day 1 (predose) and postdose.

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: Statistical analysis was not applicable since there was no formal statistical testing or modeling performed.

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: Day				
arithmetic mean (standard deviation)	24 (± 4.09)	26.7 (± 5.13)		

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Clearance (CL/F)

End point title	Apparent Clearance (CL/F)[8]

End point description:

The PK parameter CL/F was estimated based on the serum concentrations of MEDI9929. Serum concentrations of MEDI9929 were measured by enzyme-linked immunosorbent assay.

End point type	Primary

End point timeframe:

Day 1 (predose) and postdose.

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: Statistical analysis was not applicable since there was no formal statistical testing or modeling performed.

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: Liter/day				
arithmetic mean (standard deviation)	0.153 (± 0.0507)	0.166 (± 0.0376)		

Statistical analyses

No statistical analyses for this end point

Primary: Apparent steady-state volume of distribution (Vss/F)

End point title	Apparent steady-state volume of distribution (Vss/F)[9]

End point description:

The PK parameter Vss/F was estimated based on the serum concentrations of MEDI9929. Serum concentrations of MEDI9929 were measured by enzyme-linked immunosorbent assay.

End point type	Primary

End point timeframe:

Day 1 (predose) and postdose.

Notes:

[9] - 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: Statistical analysis was not applicable since there was no formal statistical testing or modeling performed.

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: Liter				
arithmetic mean (standard deviation)	5.65 (± 1.6)	6.55 (± 2.19)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Reporting Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events

End point title	Number of Participants Reporting Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events

End point description:

An adverse event (AE) is any unfavorable and unintended sign, symptom, or disease temporally associated with the use of study drug, whether or not considered related to the study drug. A serious adverse event (SAE) is any AE resulting in any of the following outcomes such as death; initial or prolonged inpatient hospitalization; life-threatening; persistent or significant disability/incapacity; congenital anomaly or birth defect, or is an important medical event that may jeopardize the participant or may require medical intervention to prevent one of the outcomes listed above. A TEAE is defined as events present at baseline that worsened in intensity after administration of study drug or events absent at baseline that emerged after administration of study drug. The AEs were summarized using Medical Dictionary for Regulatory Activities version 19.0

End point type	Secondary

End point timeframe:

From the start of study drug administration up to end of follow-up period

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: Participants				
Participants with TEAEs	4	4		
Participants with treatment-emergent SAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment-emergent Adverse Events Related to Vital Sign Parameters and Physical Findings

End point title	Treatment-emergent Adverse Events Related to Vital Sign Parameters and Physical Findings

End point description:

Vital signs (blood pressure, temperature, pulse, and respiratory rate) were performed throughout the study. The TEAEs related to vital signs in participants were reported.

End point type	Secondary

End point timeframe:

From the start of study drug administration up to end of follow-up period

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment-emergent Adverse Events Related to Laboratory Parameters

End point title	Treatment-emergent Adverse Events Related to Laboratory Parameters

End point description:

Laboratory evaluations of blood and urine samples were performed, including hematology (white blood cell count with differential, red blood cell count, hematocrit, hemoglobin and platelet count); serum chemistry: calcium, chloride, potassium, sodium, bicarbonate, aspartate transaminase, alanine transaminase, albumin, uric acid, creatinine, total bilirubin, glucose, alkaline phosphatase, blood urea nitrogen, total protein, and gamma glutamyl transferase; and urinalysis (nitrites, protein, glucose, ketones, urine drug screen, blood, and bilirubin). Number of participants with TEAEs related to laboratory evaluations were reported.

End point type	Secondary

End point timeframe:

From the start of study drug administration up to end of follow-up period

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment-emergent Adverse Events Related to Electrocardiogram Evaluations

End point title	Treatment-emergent Adverse Events Related to Electrocardiogram Evaluations

End point description:

Computerized triplicate 12-lead ECGs as well as Qualitative 12-lead ECGs were obtained during the study. ECG parameters included heart rate, PR, QRS, QT, and corrected QT (QTc) intervals. Number of participants with TEAEs related to ECG after the start of study drug were to be reported.

End point type	Secondary

End point timeframe:

From the start of study drug administration up to end of followup period

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	10		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Positive for Anti-drug Antibodies and With Neutralizing Antibodies for MEDI9929 at any Visit

End point title	Number of Participants Positive for Anti-drug Antibodies and With Neutralizing Antibodies for MEDI9929 at any Visit

End point description:

Blood samples for immunogenicity assessment included the determination of anti-drug antibodies (ADA) for MEDI9929. The incidence rate of positive serum antibodies to MEDI9929 were presented. Neutralizing antibody was tested only for the positive ADA samples. Combined immunogenicity data are presented for Cohort 1 and Cohort 2, i.e., for all participants.

End point type	Secondary

End point timeframe:

Day 1 (predose), and postdose.

End point values	MEDI9929			
Subject group type	Subject analysis set			
Number of subjects analysed	21			
Units: Participants				
Baseline: ADA positive, n=21	1			
Baseline: Positive neutralizing antibody, n=1	0			
Post-baseline: ADA positive, n=21	1			
Post-baseline: Positive neutralizing antibody, n=1	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:	
From the start of study drug administration up to end of followup period.	
Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Cohort 1
Reporting group description:	
On Day 1, a single dose of MEDI9929 was administered subcutaneously to all participants.	
Reporting group title	Cohort 2
Reporting group description:	
On Day 1, a single dose of MEDI9929 was administered subcutaneously to all participants.	

Serious adverse events	Cohort 1	Cohort 2	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Cohort 1	Cohort 2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 11 (36.36%)	4 / 10 (40.00%)	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Ligament sprain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	2	
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Bronchitis			
subjects affected / exposed	2 / 11 (18.18%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Nasopharyngitis			
subjects affected / exposed	2 / 11 (18.18%)	1 / 10 (10.00%)	
occurrences (all)	3	1	
Pharyngitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 June 2015	Protocol Amendment 1: The major changes were made in response to feedback from the Polish regulatory authorities Office for Registration of Medicinal Products, Medical Devices, and Biocidal Products regarding the period of contraception following administration of investigational product. Minor editing and correction of typographical errors were also addressed.
10 February 2016	Protocol Amendment 2: The purpose of this amendment was to change the Medical Monitor of the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported