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

Summary

EudraCT number	2011-005503-33
Trial protocol	PL
Global end of trial date	09 January 2013

Results information

Result version number	v2 (current)
This version publication date	07 May 2016
First version publication date	05 August 2015
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CD-RI-CAT-354-1054

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01592396
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	MedImmune, LLC
Sponsor organisation address	Milstein Building, Grant Park, Cambridge, United Kingdom, CB21 6GH
Public contact	Meena Jain, MB BChir/Associate Medical Director, MedImmune, LLC, jainm@medimmune.com
Scientific contact	Meena Jain, MB BChir/Associate Medical Director, MedImmune, LLC, jainm@medimmune.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000782-PIP01-09
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	09 January 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 January 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the pharmacokinetic (PK) profile of a single 300 milligram (mg) of subcutaneous (SC) dose of tralokinumab in adolescent subjects with asthma.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Participating participant 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: -

Evidence for comparator: -

Actual start date of recruitment	19 June 2012
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: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	20
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Twenty (20) participants enrolled and completed the study as planned. An additional 10 participants signed informed consent but were not enrolled in the study. The reasons for screen failures were not meeting the inclusion/exclusion criteria, and/or consent withdrawal.

Pre-assignment

Screening details:

Screening Details: A total of 20 participants participated in the study at 3 investigative sites in Poland.

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	Tralokinumab 300 mg (Participants aged 12-14 years) - Cohort 1

Arm description:

Participants aged 12 to 14 years received a single dose of tralokinumab (CAT-354) 300 milligram (mg), subcutaneously on Day 1.

Arm type	Experimental
Investigational medicinal product name	Tralokinumab
Investigational medicinal product code	CAT-354
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

300 mg and Subcutaneous use

Arm title	Tralokinumab 300 mg (Participants aged 15-17 years) - Cohort 2

Arm description:

Participants aged 15 to 17 years received a single dose of tralokinumab (CAT-354) 300 mg, subcutaneously on Day 1.

Arm type	Experimental
Investigational medicinal product name	Tralokinumab
Investigational medicinal product code	CAT-354
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

300 mg and Subcutaneous use

Number of subjects in period 1	Tralokinumab 300 mg (Participants aged 12-14 years) - Cohort 1	Tralokinumab 300 mg (Participants aged 15-17 years) - Cohort 2
Started	10	10
Completed	10	10

Baseline characteristics

Reporting groups

Reporting group title	Tralokinumab 300 mg (Participants aged 12-14 years) - Cohort 1

Reporting group description:

Participants aged 12 to 14 years received a single dose of tralokinumab (CAT-354) 300 milligram (mg), subcutaneously on Day 1.

Reporting group title	Tralokinumab 300 mg (Participants aged 15-17 years) - Cohort 2

Reporting group description:

Participants aged 15 to 17 years received a single dose of tralokinumab (CAT-354) 300 mg, subcutaneously on Day 1.

Reporting group values	Tralokinumab 300 mg (Participants aged 12-14 years) - Cohort 1	Tralokinumab 300 mg (Participants aged 15-17 years) - Cohort 2	Total
Number of subjects	10	10	20
Age categorical Units: Subjects			
Age Continuous | Units: years			
arithmetic mean	12.6	15.8	
standard deviation	± 0.7	± 0.9	-
Gender, Male/Female Units: Participants			
Female	3	3	6
Male	7	7	14

Subject analysis sets

Subject analysis set title	Tralokinumab 300 mg (Participants aged 12-14 years) - Cohort 1
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants aged 12 to 14 years and 15 to 17 years will receive a single dose of tralokinumab (CAT-354) 300 mg, subcutaneously on Day 1.

Subject analysis set title	Tralokinumab 300mg (Participants aged 15-17 years) - Cohort 2
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants aged 15 to 17 years received a single dose of tralokinumab (CAT-354) 300 mg, subcutaneously on Day 1.

Subject analysis set title	Tralokinumab 300 mg
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants aged 12 to 14 years and 15 to 17 years will receive a single dose of tralokinumab (CAT-354) 300 mg, subcutaneously on Day 1.

Reporting group values	Tralokinumab 300 mg (Participants aged 12-14 years) - Cohort 1	Tralokinumab 300mg (Participants aged 15-17 years) - Cohort 2	Tralokinumab 300 mg
Number of subjects	10	10	20
Age categorical Units: Subjects			
Age Continuous | Units: years			
arithmetic mean	12.6	15.8	14.2
standard deviation	± 0.7	± 0.9	± 1.8
Gender, Male/Female Units: Participants			
Female	3	3	6
Male	7	7	14

End points

End points reporting groups

Reporting group title	Tralokinumab 300 mg (Participants aged 12-14 years) - Cohort 1
Reporting group description:	
Participants aged 12 to 14 years received a single dose of tralokinumab (CAT-354) 300 milligram (mg), subcutaneously on Day 1.	
Reporting group title	Tralokinumab 300 mg (Participants aged 15-17 years) - Cohort 2
Reporting group description:	
Participants aged 15 to 17 years received a single dose of tralokinumab (CAT-354) 300 mg, subcutaneously on Day 1.	
Subject analysis set title	Tralokinumab 300 mg (Participants aged 12-14 years) - Cohort 1
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants aged 12 to 14 years and 15 to 17 years will receive a single dose of tralokinumab (CAT-354) 300 mg, subcutaneously on Day 1.	
Subject analysis set title	Tralokinumab 300mg (Participants aged 15-17 years) - Cohort 2
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants aged 15 to 17 years received a single dose of tralokinumab (CAT-354) 300 mg, subcutaneously on Day 1.	
Subject analysis set title	Tralokinumab 300 mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants aged 12 to 14 years and 15 to 17 years will receive a single dose of tralokinumab (CAT-354) 300 mg, subcutaneously on Day 1.	

Primary: Time to Reach Maximum Observed Serum Concentration (Tmax)

End point title	Time to Reach Maximum Observed Serum Concentration (Tmax)[1][2]
End point description:	
End point type	Primary
End point timeframe:	
0 (predose), 3, 8 and 24 hours postdose on Day 1; Day 4, 6, 8, 10, 15, 22, 36 and 57	

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 data was not planned to be reported for this endpoint.

[2] - 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: Statistical data was not planned to be reported for this endpoint.

End point values	Tralokinumab 300 mg (Participants aged 12-14 years) - Cohort 1	Tralokinumab 300mg (Participants aged 15-17 years) - Cohort 2		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	10	10		
Units: days				

median (full range (min-max))	5.2 (3 to 9.1)	6.1 (2.9 to 9)		

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Serum Concentration (Cmax)

End point title	Maximum Observed Serum Concentration (Cmax)[3][4]

End point description:

End point type	Primary

End point timeframe:

0 (predose), 3, 8 and 24 hours postdose on Day 1; Day 4, 6, 8, 10, 15, 22, 36 and 57

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 data was not planned to be reported for this endpoint.

[4] - 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: Statistical data was not planned to be reported for this endpoint.

End point values	Tralokinumab 300 mg (Participants aged 12-14 years) - Cohort 1	Tralokinumab 300mg (Participants aged 15-17 years) - Cohort 2		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	10	10		
Units: microgram per milliliter (mcg/mL)				
arithmetic mean (standard deviation)	57 (± 21.7)	50.6 (± 16.2)		

Statistical analyses

No statistical analyses for this end point

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])[5][6]

End point description:

AUC (0 - infinity) = Area under the serum concentration versus time curve (AUC) from time zero (predose) to extrapolated infinite time (0 - infinity). It is obtained from AUC (0 - t) plus AUC (t - infinity).

End point type	Primary

End point timeframe:

0 (predose), 3, 8 and 24 hours postdose on Day 1; Day 4, 6, 8, 10, 15, 22, 36 and 57

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 data was not planned to be reported for this endpoint.

[6] - 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: Statistical data was not planned to be reported for this endpoint.

End point values	Tralokinumab 300 mg (Participants aged 12-14 years) - Cohort 1	Tralokinumab 300mg (Participants aged 15-17 years) - Cohort 2		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	10	10		
Units: (microgram*day)/milliliter (mcg*day/mL)				
arithmetic mean (standard deviation)	1916 (± 806.3)	1721.1 (± 568.5)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Area Under the Concentration-Time Curve From Zero to Last Measurable Concentration (AUC [0-t])[7][8]

End point description:

End point type	Primary

End point timeframe:

0 (predose), 3, 8 and 24 hours postdose on Day 1; Day 4, 6, 8, 10, 15, 22, 36 and 57

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 data was not planned to be reported for this endpoint.

[8] - 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: Statistical data was not planned to be reported for this endpoint.

End point values	Tralokinumab 300 mg (Participants aged 12-14 years) - Cohort 1	Tralokinumab 300mg (Participants aged 15-17 years) - Cohort 2		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	10	10		
Units: mcg*day/mL				
arithmetic mean (standard deviation)	1561.4 (± 614.9)	1384.6 (± 421.6)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Terminal Phase Elimination Half Life (t1/2)[9][10]

End point description:

Terminal phase elimination half-life is the time measured for the serum concentration to decrease by one half.

End point type	Primary

End point timeframe:

0 (predose), 3, 8 and 24 hours postdose on Day 1; Day 4, 6, 8, 10, 15, 22, 36 and 57

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 data was not planned to be reported for this endpoint.

[10] - 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: Statistical data was not planned to be reported for this endpoint.

End point values	Tralokinumab 300 mg (Participants aged 12-14 years) - Cohort 1	Tralokinumab 300mg (Participants aged 15-17 years) - Cohort 2		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	10	10		
Units: days				
arithmetic mean (standard deviation)	21.4 (± 5.5)	22.1 (± 3.5)		

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 (TESAEs)

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

End point description:

An adverse event (AE) was any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. A serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent are events between administration of

study drug and up to Day 57 that were absent before treatment or that worsened relative to pre-treatment state. Adverse events were summarized together for all participants.

End point type	Secondary

End point timeframe:

Day 1 to Day 57

End point values	Tralokinumab 300 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: participants				
TEAEs	6			
TESAEs	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Exhibiting Anti-Drug Antibodies for Tralokinumab at any Visit

End point title	Number of Participants Exhibiting Anti-Drug Antibodies for Tralokinumab at any Visit

End point description:

Immunogenicity assessment included determination of anti-drug antibodies to tralokinumab (CAT-354) antibodies in serum samples. Immunogenicity results were summarized together for all participants.

End point type	Secondary

End point timeframe:

Day 1 and Day 57

End point values	Tralokinumab 300 mg (Participants aged 12-14 years) - Cohort 1			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 1 to Day 57	
Adverse event reporting additional description:	
Adverse events were summarized together for all participants.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups	
Reporting group title	Tralokinumab 300 mg
Reporting group description:	
Participants aged 12 to 14 years and 15 to 17 years will receive a single dose of tralokinumab (CAT-354) 300 mg, subcutaneously on Day 1.	

Serious adverse events	Tralokinumab 300 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (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	Tralokinumab 300 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 20 (30.00%)		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
General disorders and administration site conditions			
Injection site pruritus			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Gastrointestinal disorders			

Diarrhoea subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Skin and subcutaneous tissue disorders Urticaria subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Pharyngitis subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 4 1 / 20 (5.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Dose-normalized AUC(0-infinity) and dose-normalized Cmax were not evaluated as they were not relevant for single-dose study. Apparent volume of distribution at steady state (Vss/F) was replaced by Vz/F as it was more relevant for subcutaneous dose.

Notes: