



Clinical trial results:

A Single-Dose, Open-Label, Parallel Group Study to Characterize the Pharmacokinetics, Pharmacodynamics, Immunogenicity, Safety, and Tolerability of Reslizumab Following Subcutaneous Administration in Children with Asthma (6 to Less Than 12 Years of Age)

Summary

EudraCT number	2017-002060-40
Trial protocol	Outside EU/EEA
Global end of trial date	15 February 2017

Results information

Result version number	v1 (current)
This version publication date	19 July 2018
First version publication date	19 July 2018

Trial information

Trial identification

Sponsor protocol code	C38072-AS-10069
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Teva Branded Pharmaceutical Products R&D, Inc
Sponsor organisation address	41 Moores Road, Frazer, Pennsylvania, United States, 19355
Public contact	Director, Clinical Research, Teva Branded Pharmaceutical Products, R&D Inc., 001 215-591-3000, info.era-clinical@teva.de
Scientific contact	Director, Clinical Research, Teva Branded Pharmaceutical Products, R&D Inc., 001 215-591-3000, info.era-clinical@teva.de

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-001202-PIP02-13
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	07 August 2017
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	15 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the pharmacokinetics and pharmacodynamics of reslizumab in pediatric patients with asthma 6 to less than 12 years of age following administration of a single subcutaneous (sc) dose.

Protection of trial subjects:

This study was conducted in full accordance with the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Consolidated Guideline (E6) and any applicable national and local laws and regulations (eg, Code of Federal Regulations [CFR] Title 21, Parts 50, 54, 56, 312, and 314).

The investigator, or a qualified person designated by the investigator, fully informed the patient and parent or other legally acceptable representative of all pertinent aspects of the study, including the written information approved by the IRB. All written and/or oral information about the study was provided in a language as nontechnical as practical and understood by the parent or legally acceptable representative, and the patient as far as is practical. The patient and parent/legal representative were given ample time and opportunity to inquire about details of the study and to decide whether or not to participate in the study. The above was detailed in the source documentation.

A personally signed and dated informed consent form was obtained from each parent/legal representative and a signed and dated assent form was obtained from each patient (if the patient was able) before any study-specific procedures or assessments were done and after the aims, methods, anticipated benefits, and potential hazards were explained; according to local IRB requirements. The forms were also signed and dated by the person who conducted the informed consent discussion. The investigator will keep the original consent and assent forms, and copies were given to the parent(s)/guardian(s) of the patients. It was also explained to the patients (and parent/legal representative) that they were free to refuse entry into the study and free to withdraw from the study at any time without prejudice to future treatment.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 August 2016
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: 37
Worldwide total number of subjects	37
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)	37
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:

A total of 56 patients with asthma were screened for enrollment into this study. Of the 56 patients screened, 37 patients at 6 centers in the US were randomized into the study.

Pre-assignment

Screening details:

Of the 19 patients who were not randomized, 14 patients were excluded on the basis of inclusion/exclusion/randomization criteria, and 5 patients withdrew consent. Randomized patients were assigned 1:1:1 to one of the three treatment regimens (reslizumab 33, 110, and 165 mg sc).

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Note that the study was randomised but not controlled.

Arms

Are arms mutually exclusive?	Yes
Arm title	Reslizumab 33 mg

Arm description:

A single 33-mg subcutaneous (sc) injection of reslizumab in the upper arm on Day 1.

Arm type	Experimental
Investigational medicinal product name	reslizumab
Investigational medicinal product code	
Other name	CEP-38072, Cinqair, Cinqaero
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Drug was supplied in pre-filled syringes containing either 33, 55, or 110 mg. Injections were made in the upper arm the morning of Day 1. Patients in the 165 mg treatment arm were given two sequential injections (55 mg and 110 mg) in the same upper arm at least 1 inch away from each other.

Arm title	Reslizumab 110 mg
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Arm description:

A single 110-mg subcutaneous (sc) injection of reslizumab in the upper arm on Day 1.

Arm type	Experimental
Investigational medicinal product name	reslizumab
Investigational medicinal product code	
Other name	CEP-38072, Cinqair, Cinqaero
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Drug was supplied in pre-filled syringes containing either 33, 55, or 110 mg. Injections were made in the upper arm the morning of Day 1. Patients in the 165 mg treatment arm were given two sequential injections (55 mg and 110 mg) in the same upper arm at least 1 inch away from each other.

Arm title	Reslizumab 165 mg
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Arm description:

Patients in the 165 mg treatment arm were given two sequential injections (55 mg and 110 mg) in the same upper arm at least 1 inch away from each other on the morning of Day 1.

Arm type	Experimental
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Investigational medicinal product name	reslizumab
Investigational medicinal product code	
Other name	CEP-38072, Cinqair, Cinqaero
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Drug was supplied in pre-filled syringes containing either 33, 55, or 110 mg. Injections were made in the upper arm the morning of Day 1. Patients in the 165 mg treatment arm were given two sequential injections (55 mg and 110 mg) in the same upper arm at least 1 inch away from each other.

Number of subjects in period 1	Reslizumab 33 mg	Reslizumab 110 mg	Reslizumab 165 mg
Started	12	12	13
Safety and Pharmacodynamics analysis set	12	12	12
Pharmacokinetics analysis set	12	12	11 ^[1]
Completed	12	12	12
Not completed	0	0	1
Randomized in error but not dosed	-	-	1

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: One patient (reslizumab 165 mg) was excluded from the pharmacokinetic analysis set because

pharmacokinetic samples were not collected at critical time points (48, 648, 1320, and 1992 hours [days 3, 28, 56, and 84]); therefore, 35 of the 36 dosed patients were included in the pharmacokinetic analysis set.

Baseline characteristics

Reporting groups

Reporting group title	Reslizumab 33 mg
Reporting group description: A single 33-mg subcutaneous (sc) injection of reslizumab in the upper arm on Day 1.	
Reporting group title	Reslizumab 110 mg
Reporting group description: A single 110-mg subcutaneous (sc) injection of reslizumab in the upper arm on Day 1.	
Reporting group title	Reslizumab 165 mg
Reporting group description: Patients in the 165 mg treatment arm were given two sequential injections (55 mg and 110 mg) in the same upper arm at least 1 inch away from each other on the morning of Day 1.	

Reporting group values	Reslizumab 33 mg	Reslizumab 110 mg	Reslizumab 165 mg
Number of subjects	12	12	13
Age categorical Units: Subjects			
>=6 to <=8 years	4	4	6
>=9 to < 12 years	8	8	7
Age continuous Units: years			
arithmetic mean	8.7	8.6	8.8
standard deviation	± 1.92	± 1.56	± 1.57
Gender categorical Units: Subjects			
Female	7	8	6
Male	5	4	7
Race Units: Subjects			
White	6	5	6
Black	6	7	7
Ethnicity Units: Subjects			
Not Hispanic or Latino	10	9	12
Hispanic or Latino	2	3	1
Weight Units: kg			
arithmetic mean	31.58	33.63	34.15
standard deviation	± 8.328	± 9.906	± 7.745
Height Units: cm			
arithmetic mean	134.60	135.21	135.88
standard deviation	± 12.468	± 9.996	± 11.235
Body Mass Index Units: kg/m ²			
arithmetic mean	17.20	18.03	18.63
standard deviation	± 2.415	± 3.430	± 5.060

Reporting group values	Total		
Number of subjects	37		
Age categorical			
Units: Subjects			
>=6 to <=8 years	14		
>=9 to < 12 years	23		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	21		
Male	16		
Race			
Units: Subjects			
White	17		
Black	20		
Ethnicity			
Units: Subjects			
Not Hispanic or Latino	31		
Hispanic or Latino	6		
Weight			
Units: kg			
arithmetic mean			
standard deviation	-		
Height			
Units: cm			
arithmetic mean			
standard deviation	-		
Body Mass Index			
Units: kg/m^2			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Reslizumab 33 mg
Reporting group description: A single 33-mg subcutaneous (sc) injection of reslizumab in the upper arm on Day 1.	
Reporting group title	Reslizumab 110 mg
Reporting group description: A single 110-mg subcutaneous (sc) injection of reslizumab in the upper arm on Day 1.	
Reporting group title	Reslizumab 165 mg
Reporting group description: Patients in the 165 mg treatment arm were given two sequential injections (55 mg and 110 mg) in the same upper arm at least 1 inch away from each other on the morning of Day 1.	

Primary: Maximum Observed Serum Drug Concentration (Cmax)

End point title	Maximum Observed Serum Drug Concentration (Cmax)
End point description: Maximum observed serum drug concentration, obtained directly from the observed concentration-time data.	
End point type	Primary
End point timeframe: PK sampling times: prior to study drug administration (day 1), and on days 3, 7, 14, 28, 56 and 84	

End point values	Reslizumab 33 mg	Reslizumab 110 mg	Reslizumab 165 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12 ^[1]	12 ^[2]	11 ^[3]	
Units: ng/mL				
arithmetic mean (standard deviation)	8730.96 (± 4388.43)	24050.81 (± 7448.04)	34917.06 (± 12762.89)	

Notes:

[1] - PK analysis set

[2] - PK analysis set

[3] - PK analysis set

Statistical analyses

Statistical analysis title	Dose Proportionality of Reslizumab: Cmax
Statistical analysis description: A power model was fit separately to describe the linear relationship between Cmax and dose (33 mg, 110 mg, and 165 mg) using the least-squares linear regression model as follows: $\ln(C_{\max}) = \alpha + \beta \ln(\text{dose}) + \epsilon$ This linear model was used to provide a 90% confidence interval (CI) for β (slope). Dose proportionality was concluded if the 90% CI of the slope β lies entirely within the limits (0.861 to 1.139). However, the study was not powered to statistically demonstrate dose proportionality	
Comparison groups	Reslizumab 33 mg v Reslizumab 110 mg v Reslizumab 165 mg

Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	other ^[4]
Parameter estimate	Slope
Point estimate	0.882
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.729
upper limit	1.035
Variability estimate	Standard error of the mean
Dispersion value	0.09

Notes:

[4] - dose proportionality. This analysis is without weight as a covariate.

Statistical analysis title	Dose Proportionality (Covariate Weight): Cmax
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Statistical analysis description:

The power model, $\ln(\text{parameter}) = a + b \cdot \ln(\text{dose}) + c \cdot \text{Weight} + \text{error}$, was used to estimate the slope and corresponding 90% confidence interval. Dose proportionality was to have been concluded if the 90% confidence interval of the slope lay entirely within 0.861 to 1.139 over the dose range of 33 mg to 165 mg. However, the study was not powered to statistically demonstrate dose proportionality.

Comparison groups	Reslizumab 33 mg v Reslizumab 110 mg v Reslizumab 165 mg
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	other ^[5]
Parameter estimate	Slope
Point estimate	0.931
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.827
upper limit	1.035
Variability estimate	Standard error of the mean
Dispersion value	0.061

Notes:

[5] - Dose proportionality. This analysis is with weight as a covariate.

Statistical analysis title	Dose Proportionality (Co- Weight, Sex, Age): Cmax
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Statistical analysis description:

The power model, $\ln(\text{parameter}) = a + b \cdot \ln(\text{dose}) + c \cdot \text{Weight} + d \cdot \text{Sex} + e \cdot \text{Age} + \text{error}$, was used to estimate the slope and corresponding 90% confidence interval. Dose proportionality was to have been concluded if the 90% confidence interval of the slope lay entirely within 0.861 to 1.139 over the dose range of 33 mg to 165 mg. However, the study was not powered to statistically demonstrate dose proportionality.

Comparison groups	Reslizumab 33 mg v Reslizumab 110 mg v Reslizumab 165 mg
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	other ^[6]
Parameter estimate	Slope
Point estimate	0.93

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.825
upper limit	1.034
Variability estimate	Standard error of the mean
Dispersion value	0.062

Notes:

[6] - Dose proportionality

Primary: Area Under the Serum Concentration-Time Curve from Time 0 to the Time of the Last Quantifiable Drug Concentration (AUC 0-t)

End point title	Area Under the Serum Concentration-Time Curve from Time 0 to the Time of the Last Quantifiable Drug Concentration (AUC 0-t)
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End point description:

Area under the serum concentration-time curve (AUC) from time 0 to the time of the last quantifiable drug concentration; calculated by the linear trapezoidal method.

End point type	Primary
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End point timeframe:

PK sampling times: prior to study drug administration (day 1), and on days 3, 7, 14, 28, 56 and 84

End point values	Reslizumab 33 mg	Reslizumab 110 mg	Reslizumab 165 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12 ^[7]	12 ^[8]	11 ^[9]	
Units: h*µg/mL				
arithmetic mean (standard deviation)	5661 (± 1996)	17414 (± 4182)	27299 (± 9937)	

Notes:

[7] - PK analysis set

[8] - PK analysis set

[9] - PK analysis set

Statistical analyses

Statistical analysis title	Dose Proportionality of Reslizumab: AUC0-t
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Statistical analysis description:

A power model was fit separately to describe the linear relationship between AUC0-t and dose using the least-squares linear regression model as follows: $\ln(\text{AUC0-t}) = \alpha + \beta \ln(\text{dose}) + \varepsilon$

This linear model was used to provide a 90% confidence interval (CI) for β (slope). Dose proportionality was concluded if the 90% CI of the slope β lies entirely within the limits (0.861 to 1.139). However, the study was not powered to statistically demonstrate dose proportionality.

Comparison groups	Reslizumab 33 mg v Reslizumab 110 mg v Reslizumab 165 mg
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Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	other ^[10]
Parameter estimate	Slope
Point estimate	0.982
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.833
upper limit	1.131
Variability estimate	Standard error of the mean
Dispersion value	0.088

Notes:

[10] - dose proportionality

Statistical analysis title	Dose Proportionality (Covariate Weight): AUC0-t
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Statistical analysis description:

The power model, $\ln(\text{parameter}) = a + b \cdot \ln(\text{dose}) + c \cdot \text{Weight} + \text{error}$, was used to estimate the slope and corresponding 90% confidence interval. Dose proportionality was to have been concluded if the 90% confidence interval of the slope lay entirely within 0.861 to 1.139 over the dose range of 33 mg to 165 mg. However, the study was not powered to statistically demonstrate dose proportionality.

Comparison groups	Reslizumab 33 mg v Reslizumab 110 mg v Reslizumab 165 mg
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	other ^[11]
Parameter estimate	Slope
Point estimate	1.016
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.886
upper limit	1.145
Variability estimate	Standard error of the mean
Dispersion value	0.077

Notes:

[11] - dose proportionality

Statistical analysis title	Dose Proportionality(Co- Weight, Sex, Age): AUC0-t
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Statistical analysis description:

The power model, $\ln(\text{parameter}) = a + b \cdot \ln(\text{dose}) + c \cdot \text{Weight} + d \cdot \text{Sex} + e \cdot \text{Age} + \text{error}$, was used to estimate the slope and corresponding 90% confidence interval. Dose proportionality was to have been concluded if the 90% confidence interval of the slope lay entirely within 0.861 to 1.139 over the dose range of 33 mg to 165 mg. However, the study was not powered to statistically demonstrate dose proportionality.

Comparison groups	Reslizumab 33 mg v Reslizumab 110 mg v Reslizumab 165 mg
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Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	other ^[12]
Parameter estimate	Slope
Point estimate	1.025
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.9
upper limit	1.151
Variability estimate	Standard error of the mean
Dispersion value	0.074

Notes:

[12] - dose proportionality

Primary: Area Under the Serum Concentration-Time Curve from Time 0 Extrapolated to Infinity (AUC0-∞)

End point title	Area Under the Serum Concentration-Time Curve from Time 0 Extrapolated to Infinity (AUC0-∞)
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End point description:

AUC from time 0 extrapolated to infinity; calculated as $[AUC_t + (C_t/\lambda_z)]$ where C_t is the last quantifiable serum drug concentration.

End point type	Primary
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End point timeframe:

PK sampling times: prior to study drug administration (day 1), and on days 3, 7, 14, 28, 56 and 84

End point values	Reslizumab 33 mg	Reslizumab 110 mg	Reslizumab 165 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12 ^[13]	12 ^[14]	11 ^[15]	
Units: h*µg/mL				
arithmetic mean (standard deviation)	6233 (± 2259)	18766 (± 4265)	29683 (± 11150)	

Notes:

[13] - PK analysis set

[14] - PK analysis set

[15] - PK analysis set

Statistical analyses

Statistical analysis title	Dose Proportionality of Reslizumab: AUC0-∞
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Statistical analysis description:

A power model was fit separately to describe the linear relationship between AUC0-∞ and dose (33, 110, and 165 mg) using the least-squares linear regression model as follows: $\ln(AUC0-\infty) = \alpha + \beta \ln(dose) + \epsilon$

This linear model was used to provide a 90% confidence interval (CI) for β (slope). Dose proportionality was concluded if the 90% CI of the slope β lies entirely within the limits (0.861 to 1.139). However, the study was not powered to statistically demonstrate dose proportionality.

Comparison groups	Reslizumab 110 mg v Reslizumab 165 mg v Reslizumab 33 mg
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Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	other ^[16]
Parameter estimate	Slope
Point estimate	0.975
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.822
upper limit	1.127
Variability estimate	Standard error of the mean
Dispersion value	0.09

Notes:

[16] - dose proportionality

Statistical analysis title	Dose Proportionality (Covariate Weight): AUC0-∞
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Statistical analysis description:

The power model, $\ln(\text{parameter}) = a + b \cdot \ln(\text{dose}) + c \cdot \text{Weight} + \text{error}$, was used to estimate the slope and corresponding 90% confidence interval. Dose proportionality was to have been concluded if the 90% confidence interval of the slope lay entirely within 0.861 to 1.139 over the dose range of 33 mg to 165 mg. However, the study was not powered to statistically demonstrate dose proportionality.

Comparison groups	Reslizumab 33 mg v Reslizumab 110 mg v Reslizumab 165 mg
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	other ^[17]
Parameter estimate	Slope
Point estimate	1.006
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.868
upper limit	1.143
Variability estimate	Standard error of the mean
Dispersion value	0.081

Notes:

[17] - dose proportionality

Statistical analysis title	Dose Proportionality(Co- Weight, Sex, Age): AUC0-∞
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Statistical analysis description:

The power model, $\ln(\text{parameter}) = a + b \cdot \ln(\text{dose}) + c \cdot \text{Weight} + d \cdot \text{Sex} + e \cdot \text{Age} + \text{error}$, was used to estimate the slope and corresponding 90% confidence interval. Dose proportionality was to have been concluded if the 90% confidence interval of the slope lay entirely within 0.861 to 1.139 over the dose range of 33 mg to 165 mg. However, the study was not powered to statistically demonstrate dose proportionality.

Comparison groups	Reslizumab 33 mg v Reslizumab 110 mg v Reslizumab 165 mg
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Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	other ^[18]
Parameter estimate	Slope
Point estimate	1.016
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.881
upper limit	1.151
Variability estimate	Standard error of the mean
Dispersion value	0.079

Notes:

[18] - dose proportionality

Primary: Time to Maximum Observed Serum Drug Concentration (tmax)

End point title	Time to Maximum Observed Serum Drug Concentration
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End point description:

Time to maximum observed serum drug concentration was obtained directly from the observed concentration-time data.

End point type	Primary
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End point timeframe:

PK sampling times: prior to study drug administration (day 1), and on days 3, 7, 14, 28, 56 and 84

Notes:

[19] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Reslizumab 33 mg	Reslizumab 110 mg	Reslizumab 165 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12 ^[20]	12 ^[21]	11 ^[22]	
Units: hours				
median (full range (min-max))	122 (47 to 297)	121 (23 to 154)	72 (24 to 169)	

Notes:

[20] - PK analysis set

[21] - PK analysis set

[22] - PK analysis set

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Terminal Elimination Half-life (t_{1/2})

End point title	Apparent Terminal Elimination Half-life (t _{1/2}) ^[23]
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End point description:

Apparent terminal elimination half-life was calculated as $[(\ln 2)/\lambda_z]$.

End point type	Primary
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End point timeframe:

PK sampling times: prior to study drug administration (day 1), and on days 3, 7, 14, 28, 56 and 84

Notes:

[23] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Reslizumab 33 mg	Reslizumab 110 mg	Reslizumab 165 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12 ^[24]	12 ^[25]	11 ^[26]	
Units: hours				
arithmetic mean (standard deviation)	526 (± 124)	507 (± 90)	523 (± 92)	

Notes:

[24] - PK analysis set

[25] - PK analysis set

[26] - PK analysis set

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Total Body Clearance (CL/F)

End point title	Apparent Total Body Clearance (CL/F) ^[27]
End point description:	
Apparent total body clearance was calculated as dose/AUC _{0-∞} .	
End point type	Primary

End point timeframe:

PK sampling times: prior to study drug administration (day 1), and on days 3, 7, 14, 28, 56 and 84

Notes:

[27] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Reslizumab 33 mg	Reslizumab 110 mg	Reslizumab 165 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12 ^[28]	12 ^[29]	11 ^[30]	
Units: mL/h				
arithmetic mean (standard deviation)	6.5 (± 4.1)	6.2 (± 1.5)	6.3 (± 2.4)	

Notes:

[28] - PK analysis set

[29] - PK analysis set

[30] - PK analysis set

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Volume of Distribution (V_z/F)

End point title	Apparent Volume of Distribution (V _z /F) ^[31]
End point description:	
Apparent volume of distribution during the terminal phase was calculated as dose/(AUC _{0-∞} × λ _z).	
End point type	Primary

End point timeframe:

PK sampling times: prior to study drug administration (day 1), and on days 3, 7, 14, 28, 56 and 84

Notes:

[31] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Reslizumab 33 mg	Reslizumab 110 mg	Reslizumab 165 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12 ^[32]	12 ^[33]	11 ^[34]	
Units: liters				
arithmetic mean (standard deviation)	4.4 (± 1.5)	4.6 (± 1.7)	4.7 (± 1.7)	

Notes:

[32] - PK analysis set

[33] - PK analysis set

[34] - PK analysis set

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Serum Terminal Elimination Rate Constant (λ_z)

End point title	Apparent Serum Terminal Elimination Rate Constant (λ_z) ^[35]
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End point description:

Apparent serum terminal elimination rate constant was estimated by linear regression of the terminal portion of the log-concentration by time curve in serum; a minimum of 3 non-BLQ data points in the elimination phase (not including C_{max}) were used for the calculation. The λ_z would not be estimated if r-squared is less than 0.8.

End point type	Primary
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End point timeframe:

PK sampling times: prior to study drug administration (day 1), and on days 3, 7, 14, 28, 56 and 84

Notes:

[35] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Reslizumab 33 mg	Reslizumab 110 mg	Reslizumab 165 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12 ^[36]	12 ^[37]	11 ^[38]	
Units: 1/hour				
arithmetic mean (standard deviation)	0.00140 (± 0.00040)	0.00141 (± 0.00025)	0.00136 (± 0.00025)	

Notes:

[36] - PK analysis set

[37] - PK analysis set

[38] - PK analysis set

Statistical analyses

No statistical analyses for this end point

Primary: Blood Eosinophil Counts from Baseline to Day 28

End point title	Blood Eosinophil Counts from Baseline to Day 28 ^[39]
End point description: Blood samples for eosinophil measurement were collected prior to reslizumab administration (baseline) and 48, 144, 312 and 648 hours postdose. The blood eosinophil counts are the pharmacodynamic outcome.	
End point type	Primary
End point timeframe: prior to study drug administration (day 1), and on days 3, 7, 14, 28	

Notes:

[39] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Reslizumab 33 mg	Reslizumab 110 mg	Reslizumab 165 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12 ^[40]	12 ^[41]	12 ^[42]	
Units: 10 ⁹ /L				
arithmetic mean (full range (min-max))				
Baseline	0.531 (0.11 to 1.71)	0.490 (0.09 to 1.47)	0.595 (0.17 to 1.06)	
48 hours postdose	0.163 (0.04 to 0.52)	0.168 (0.03 to 0.41)	0.135 (0.11 to 0.17)	
144 hours postdose	0.113 (0.03 to 0.23)	0.108 (0.02 to 0.20)	0.102 (0.06 to 0.20)	
312 hours postdose	0.104 (0.03 to 0.21)	0.106 (0.03 to 0.20)	0.086 (0.04 to 0.20)	
648 hours postdose	0.104 (0.03 to 0.20)	0.071 (0.02 to 0.21)	0.077 (0.01 to 0.15)	

Notes:

[40] - Pharmacodynamic analysis set

[41] - Pharmacodynamic analysis set

[42] - Pharmacodynamic analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Participants with a Positive Anti-Drug Antibody (ADA) Result by Visit

End point title	Participants with a Positive Anti-Drug Antibody (ADA) Result by Visit
End point description: Blood samples to test for the presence of ADAs were collected prior to reslizumab administration and at Day 14, 28, 56 and 84. The ADA analysis in human serum employed a validated homogeneous ELISA, and it was performed in a 3-tier approach consisting of screening, confirmatory, and titer assays. Data represent the count of participants with a positive ADA status at each visit.	
End point type	Secondary
End point timeframe: Day 1 predose, Days 14, 28, 56 and 84	

End point values	Reslizumab 33 mg	Reslizumab 110 mg	Reslizumab 165 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12 ^[43]	12 ^[44]	12 ^[45]	
Units: participants				
Day 1, Predose (n=12, 12, 12)	0	0	0	
Day 14 (n=12, 12, 12)	0	1	1	
Day 28 (n=12, 12, 11)	0	0	0	
Day 56 (n=12, 12, 11)	2	0	0	
Day 84 (n=12, 12, 11)	1	0	0	

Notes:

[43] - Safety analysis set

[44] - Safety analysis set

[45] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Drug Antibody Titer Result by Visit

End point title	Anti-Drug Antibody Titer Result by Visit
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End point description:

Blood samples to test for the presence of ADAs were collected prior to reslizumab administration and at Day 14, 28, 56 and 84. The ADA analysis in human serum employed a validated homogeneous ELISA, and it was performed in a 3-tier approach consisting of screening, confirmatory, and titer assays.

Titer results are offered for patients with positive ADA tests at visits when blood samples for ADA tests were collected. The number of patients with positive ADA tests is reported in the previous outcome and repeated here in this outcome as the 'n' following the visit day. Values of 0 indicate that all patients had negative ADA analyses for that visit.

End point type	Secondary
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End point timeframe:

Day 1 predose and Days 14, 28, 56 and 84

End point values	Reslizumab 33 mg	Reslizumab 110 mg	Reslizumab 165 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12 ^[46]	12 ^[47]	12 ^[48]	
Units: titer				
arithmetic mean (full range (min-max))				
Day 1 Predose (n=0, 0, 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	
Day 14 (n=0, 1, 1)	0 (0 to 0)	4.640 (4.64 to 4.64)	5.580 (5.58 to 5.58)	
Day 28 (n=0, 0, 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	
Day 56 (n=2, 0, 0)	5.220 (3.11 to 7.33)	0 (0 to 0)	0 (0 to 0)	
Day 84 (n=1, 0, 0)	5.950 (5.95 to 5.95)	0 (0 to 0)	0 (0 to 0)	

Notes:

[46] - Safety analysis set

[47] - Safety analysis set

[48] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Participants with Adverse Events

End point title	Participants with Adverse Events
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End point description:

An adverse event was defined as any untoward medical occurrence that develops or worsens in severity during the conduct of a clinical study and does not necessarily have a causal relationship to the study drug. Severity was rated by the investigator on a scale of mild, moderate and severe, with severe= an AE which prevents normal daily activities. Relation of AE to treatment was determined by the investigator and includes possibly, probably and definitely related categories. Serious AEs (SAE) include death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, a congenital anomaly or birth defect, OR an important medical event that jeopardized the patient and required medical intervention to prevent the previously listed serious outcomes.

End point type	Secondary
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End point timeframe:

Day 1 to Day 84

End point values	Reslizumab 33 mg	Reslizumab 110 mg	Reslizumab 165 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12 ^[49]	12 ^[50]	12 ^[51]	
Units: participants				
Any adverse event	4	6	2	
Severe adverse event	0	0	0	
Treatment-related AE	1	3	1	
Deaths	0	0	0	
Other serious AE	0	0	0	
Withdrawn from study due to AE	0	0	0	

Notes:

[49] - Safety analysis set

[50] - Safety analysis set

[51] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 to Day 84

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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Reporting groups

Reporting group title	Reslizumab 33 mg
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Reporting group description:

A single 33-mg subcutaneous (sc) injection of reslizumab in the upper arm on Day 1.

Reporting group title	Reslizumab 110 mg
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Reporting group description:

A single 110-mg subcutaneous (sc) injection of reslizumab in the upper arm on Day 1.

Reporting group title	Reslizumab 165 mg
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Reporting group description:

Patients in the 165 mg treatment arm were given two sequential injections (55 mg and 110 mg) in the same upper arm at least 1 inch away from each other on the morning of Day 1.

Serious adverse events	Reslizumab 33 mg	Reslizumab 110 mg	Reslizumab 165 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

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

Non-serious adverse events	Reslizumab 33 mg	Reslizumab 110 mg	Reslizumab 165 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 12 (33.33%)	6 / 12 (50.00%)	2 / 12 (16.67%)
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Scratch			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0

General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Pyrexia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Injection site reaction			
subjects affected / exposed	0 / 12 (0.00%)	3 / 12 (25.00%)	0 / 12 (0.00%)
occurrences (all)	0	3	0
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Asthma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Bronchitis			

subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Ear lobe infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	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

None reported