



Clinical trial results:

An Open-Label Safety Study of Patients with Severe Eosinophilic Asthma Who Were Previously Enrolled in the Reslizumab Open Label Extension Study C38072/3085

Summary

EudraCT number	2014-002659-25
Trial protocol	FR
Global end of trial date	06 March 2017

Results information

Result version number	v1 (current)
This version publication date	21 October 2018
First version publication date	21 October 2018

Trial information

Trial identification

Sponsor protocol code	C38072-AS-30024
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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., 1 888-483-8279, info.era-clinical@teva.de
Scientific contact	Director, Clinical Research, Teva Branded Pharmaceutical Products R&D, Inc., 1 888-483-8279, info.era-clinical@teva.de

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	06 March 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 March 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this open-label study is to obtain additional long-term safety data for reslizumab in patients with eosinophilic asthma who enrolled in open-label extension study C38072/3085. These data include adverse events, vital signs, and concomitant medications.

Protection of trial subjects:

This study was conducted in full accordance with the International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Consolidated Guideline (E6) and any applicable national and local laws and regulations (eg, EU Directive 2001/20/EC on the approximation of the laws, regulations, and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 November 2014
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	France: 7
Worldwide total number of subjects	7
EEA total number of subjects	7

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)	0
Adults (18-64 years)	4
From 65 to 84 years	3

85 years and over	0
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Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Eligible patients must have completed the Study C38072/3085 end-of-treatment visit or early termination visit. In all cases, the screening/baseline visit must have been scheduled at least 21 days after the subject's last dose of reslizumab in the previous study.

Period 1

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

Arms

Arm title	Reslizumab
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Arm description:

Reslizumab (3.0 mg/kg), administered by intravenous (IV) infusion every 4 weeks (28 days $\pm$ 7 days) for up to 104 weeks.

Arm type	Experimental
Investigational medicinal product name	reslizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The reslizumab dose was calculated based on baseline body weight.

Number of subjects in period 1	Reslizumab
Started	7
Completed	7

Baseline characteristics

Reporting groups

Reporting group title	Overall Study
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Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	7	7	
Age categorical			
Units: Subjects			
<65 years	4	4	
>=65 years	3	3	
Age continuous			
Units: years			
arithmetic mean	59.1		
standard deviation	± 13.78	-	
Gender categorical			
Units: Subjects			
Female	5	5	
Male	2	2	
Race			
Units: Subjects			
White	7	7	
Ethnicity			
Units: Subjects			
Not Hispanic or Latino	6	6	
Hispanic or Latino	1	1	

End points

End points reporting groups

Reporting group title	Reslizumab
Reporting group description:	
Reslizumab (3.0 mg/kg), administered by intravenous (IV) infusion every 4 weeks (28 days±7 days) for up to 104 weeks.	

Primary: Number of Subjects with Treatment Emergent Adverse Events (AEs) and Serious AEs (SAEs)

End point title	Number of Subjects with Treatment Emergent Adverse Events (AEs) and Serious AEs (SAEs) ^[1]
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End point description:

An AE was defined as any untoward medical occurrence in a patient administered a pharmaceutical product, regardless of whether it had a causal relationship with this treatment. An SAE was defined as an AE occurring at any dose that resulted in any of the following outcomes or actions: death; a life-threatening AE; inpatient hospitalization or prolongation of existing hospitalization; persistent or significant disability or incapacity; a congenital anomaly or birth defect; an important medical event that may have resulted in death, was not life-threatening, or did not require hospitalization, but may have jeopardized the patient and required medical intervention to prevent 1 of the outcomes listed in this definition. AEs summarized are those that began or worsened after treatment with reslizumab.

End point type	Primary
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End point timeframe:

Day 1 up to Day 757.

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: There is no analysis because the study has a single arm

End point values	Reslizumab			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: subjects				
Any AEs	7			
Severe AEs	2			
Treatment-related AEs	1			
Deaths	0			
Other SAEs	2			
Discontinuations from treatment due to AEs	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Rate of Clinical Asthma Exacerbations (CAEs)

End point title	Annualized Rate of Clinical Asthma Exacerbations (CAEs)
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End point description:

Rate of yearly asthma exacerbation is defined as number of exacerbations/(duration of treatment phase

(days)/365.25).

CAEs were recorded on the electronic case report form. A worsening of asthma was recorded in the adverse event electronic case report form (eCRF) as a clinical asthma exacerbation if it met 1 or more of the following criteria:

1. use of systemic corticosteroids (or at least a doubling of the maintenance dose of systemic corticosteroids) for 3 days or more,
2. an emergency department visit because of asthma that required systemic corticosteroids for 3 days or more, or
3. hospitalization because of asthma.

Additional adverse events other than "clinical asthma exacerbations" that were reported by the investigator as associated to asthma and had a concomitant requirement for a systemic corticosteroid or resulted in hospitalization were adjudicated as asthma exacerbation and were also counted, if applicable.

End point type	Secondary
End point timeframe:	
Day 1 up to Day 757.	

End point values	Reslizumab			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: CAEs/year/subject				
arithmetic mean (standard deviation)	1.350 ($\pm$ 0.6799)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 up to Day 757.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Reporting groups

Reporting group title	Reslizumab
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Reporting group description:

Reslizumab (3.0 mg/kg), administered by intravenous (IV) infusion every 4 weeks (28 days $\pm$ 7 days) for up to 104 weeks.

Serious adverse events	Reslizumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 7 (28.57%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Reslizumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Angiolipoma			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Dolichocolon			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Vascular disorders			
Thrombophlebitis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Cardiac disorders			
Supraventricular extrasystoles			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Immune system disorders			
Drug hypersensitivity			

subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	7 / 7 (100.00%) 20 2 / 7 (28.57%) 2		
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Polymyalgia rheumatica subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all) Limb discomfort subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2 2 / 7 (28.57%) 3 1 / 7 (14.29%) 1 1 / 7 (14.29%) 1 1 / 7 (14.29%) 1		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Acute sinusitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Conjunctivitis	4 / 7 (57.14%) 11 3 / 7 (42.86%) 5 2 / 7 (28.57%) 8		

subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
Respiratory tract infection viral			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Tooth abscess			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Bacterial disease carrier			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Urinary tract infection staphylococcal			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	3		
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Dehydration			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Hyponatraemia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 July 2014	The following major procedural changes were made to the protocol: - change to the planned study period in response to a request from the investigator - changes to the stopping rules and discontinuation in response to a request from the investigator
05 September 2016	The following major procedural changes were made to the protocol: - update in information on reslizumab safety, including relevant clinical results and risk/benefit assessment included in the updated Investigator's Brochure - extension of the observation period after reslizumab injection from at least 30 minutes to at least 60 minutes after the final saline flush - clarification that birth control should be used for 5 months after the last dose of reslizumab - newly identified protocol-defined adverse events for expedited reporting for reslizumab - new section to describe the capturing of specific adverse events on the eCRF

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported