Clinical trial results:
A Phase II Open-Label Extension Study to Evaluate the Long-Term Safety of Etrolizumab in Patients with Moderate to Severe Ulcerative Colitis

Summary

EudraCT number	2011-003409-36
Trial protocol	BE DE CZ ES GB
Global end of trial date	08 August 2016

Results information

Result version number	v1 (current)
This version publication date	10 August 2017
First version publication date	10 August 2017

Trial information

Trial identification

Sponsor protocol code	GA27927

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01461317
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Genentech, Inc.
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline, Genentech, Inc., +41 616878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, Genentech, Inc., +41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 August 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 August 2016
Global end of trial reached?	Yes
Global end of trial date	08 August 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to assess the long-term safety and tolerability of etrolizumab over an extended treatment period of up to 240 weeks.

Protection of trial subjects:

All subjects were required to sign an informed consent form prior to study participation.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 November 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 11
Country: Number of subjects enrolled	United States: 11
Country: Number of subjects enrolled	Belgium: 30
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Czech Republic: 11
Country: Number of subjects enrolled	Hungary: 6
Country: Number of subjects enrolled	Israel: 11
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	New Zealand: 6
Worldwide total number of subjects	108
EEA total number of subjects	64

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)	103
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 124 subjects at 40 sites were enrolled in the parent Study ABS4986g, and 118 were potentially eligible for inclusion in this extension study. Of these, 115 subjects were enrolled, and 108 received study drug.

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	Etrolizumab

Arm description:

Etrolizumab 300 milligrams (mg), subcutaneous (SC) administration (dose lowered to 100 mg at 15 - 16 weeks after first dose) every 4 weeks during the treatment period, up to 240 weeks.

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

Dosage and administration details:

Etrolizumab 300 milligrams (mg), subcutaneous (SC) administration (dose lowered to 100 mg at 15 - 16 weeks after first dose) every 4 weeks during the treatment period, up to 240 weeks.

Number of subjects in period 1	Etrolizumab
Started	108
Completed	24
Not completed	84
Physician decision	1
Pregnancy	1
Other adverse event	4
Reason not specified	2
Lost to follow-up	1
Lack of efficacy	48
Withdrawal by subject	12
Ulcerative colitis	15

Baseline characteristics

Reporting groups	
Reporting group title	Etrolizumab
Reporting group description:	
Etrolizumab 300 milligrams (mg), subcutaneous (SC) administration (dose lowered to 100 mg at 15 - 16 weeks after first dose) every 4 weeks during the treatment period, up to 240 weeks.	

Reporting group values	Etrolizumab	Total	
Number of subjects	108	108	
Age Categorical Units: Subjects			
Adults (18-64 years)	103	103	
From 65-84 years	5	5	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	40.3		
standard deviation	± 13.7	-	
Gender Categorical Units: Subjects			
Female	47	47	
Male	61	61	

End points

End points reporting groups

Reporting group title	Etrolizumab

Reporting group description:

Etrolizumab 300 milligrams (mg), subcutaneous (SC) administration (dose lowered to 100 mg at 15 - 16 weeks after first dose) every 4 weeks during the treatment period, up to 240 weeks.

Primary: Percentage of Subjects With Adverse Events (AEs)

End point title	Percentage of Subjects With Adverse Events (AEs)[1]

End point description:

An AE is any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medical treatment or procedure that may or may not be considered related to the medical treatment or procedure. The treated subjects population included any subject who received at least one dose of open-label study drug.

End point type	Primary

End point timeframe:

From first dose of study drug to 12 weeks following last dose of study drug

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: Descriptive statistics only

End point values	Etrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	108			
Units: percentage of subjects				
number (not applicable)	83.3			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Anti-Therapeutic Antibodies (ATAs) to Etrolizumab

End point title	Number of Subjects With Anti-Therapeutic Antibodies (ATAs) to Etrolizumab[2]

End point description:

A positive ATA antibody sample was defined as one in which the presence of detectable ATAs could be confirmed by competitive binding with etrolizumab. Treatment-induced ATAs = a subject with a negative baseline result followed by a positive post-dose result. Treatment-enhanced ATAs = a subject with a positive baseline result followed by positive post dose result(s) of at least 0.6 titer units greater than the baseline titer. The treated subjects population included any subject who received at least one dose of open-label study drug.

End point type	Primary

End point timeframe:

From first dose of study drug to 12 weeks following last dose of study drug (assessed at baseline, Week 4, Week 8, Week 12, every 12 weeks thereafter up to last dose and safety follow-up)

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: Descriptive statistics only

End point values	Etrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	108			
Units: subjects				
number (not applicable)				
Subjects positive for ATAs	6			
Treatment-induced ATAs	5			
Treatment-enhanced ATAs	1			
Subjects negative for ATAs	102			
Treatment unaffected	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentrations of Etrolizumab

End point title	Serum Concentrations of Etrolizumab

End point description:

Minimum serum concentration among available samples collected with 35 days of at least 3 consecutive doses of either 300 mg or 100 mg of study drug. The treated subjects population included any subject who received at least one dose of open-label study drug.

End point type	Secondary

End point timeframe:

From first dose of study drug to 12 weeks following last dose of study drug (assessed at baseline, Week 4, Week 8, Week 12, every 12 weeks thereafter up to last dose and safety follow-up)

End point values	Etrolizumab			
Subject group type	Reporting group			
Number of subjects analysed	108			
Units: micrograms per milliliter				
median (full range (min-max))				
After 3 doses of 300 mg (n=92)	14.8 (2.46 to 53.2)			
After 3 doses of 100 mg (n=41)	3.86 (0.236 to 11.5)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug to 12 weeks following last dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Etrolizumab

Reporting group description:

Etrolizumab 300 milligrams (mg), subcutaneous (SC) administration (dose lowered to 100 mg at 15 - 16 weeks after first dose) every 4 weeks during the treatment period, up to 240 weeks.

Serious adverse events	Etrolizumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 108 (24.07%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral haematoma			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intracranial venous sinus thrombosis			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colitis ulcerative				
subjects affected / exposed	13 / 108 (12.04%)			
occurrences causally related to treatment / all	0 / 13			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Ureterolithiasis				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthralgia				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Extraskeletal ossification				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vertebral foraminal stenosis				
subjects affected / exposed	1 / 108 (0.93%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Infections and infestations			
Anal abscess			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Campylobacter infection			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cytomegalovirus infection			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	3 / 108 (2.78%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Infected dermal cyst			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Liver abscess			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pilonidal cyst			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			

Dehydration			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Etrolizumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	80 / 108 (74.07%)		
Nervous system disorders			
Headache			
subjects affected / exposed	14 / 108 (12.96%)		
occurrences (all)	25		
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	6 / 108 (5.56%)		
occurrences (all)	6		
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	9 / 108 (8.33%)		
occurrences (all)	14		
Pyrexia			
subjects affected / exposed	7 / 108 (6.48%)		
occurrences (all)	7		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	9 / 108 (8.33%)		
occurrences (all)	15		
Abdominal pain upper			
subjects affected / exposed	7 / 108 (6.48%)		
occurrences (all)	8		
Colitis ulcerative			
subjects affected / exposed	27 / 108 (25.00%)		
occurrences (all)	34		
Diarrhoea			

subjects affected / exposed	9 / 108 (8.33%)		
occurrences (all)	15		
Nausea			
subjects affected / exposed	10 / 108 (9.26%)		
occurrences (all)	11		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 108 (9.26%)		
occurrences (all)	13		
Nasal congestion			
subjects affected / exposed	7 / 108 (6.48%)		
occurrences (all)	7		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	6 / 108 (5.56%)		
occurrences (all)	7		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	14 / 108 (12.96%)		
occurrences (all)	17		
Back pain			
subjects affected / exposed	8 / 108 (7.41%)		
occurrences (all)	10		
Infections and infestations			
Bronchitis			
subjects affected / exposed	11 / 108 (10.19%)		
occurrences (all)	15		
Gastroenteritis			
subjects affected / exposed	11 / 108 (10.19%)		
occurrences (all)	15		
Influenza			
subjects affected / exposed	6 / 108 (5.56%)		
occurrences (all)	7		
Nasopharyngitis			
subjects affected / exposed	28 / 108 (25.93%)		
occurrences (all)	47		

Pharyngitis subjects affected / exposed occurrences (all)	8 / 108 (7.41%) 10		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	16 / 108 (14.81%) 26		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 February 2013	The dose of etrolizumab was lowered from 300 mg to 100 mg (subcutaneously) every 4 weeks.
04 October 2013	The dosing period was extended from 104 weeks to 180 weeks.
27 June 2015	The dosing period was extended from up to 180 weeks to up to Week 240. Added the option of transferring subjects within Study GA27927 to Study GA28951 for continued access to open-label etrolizumab.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported