



Clinical trial results:

A Multicenter, Open-Label, Long-Term Extension Of Phase III Studies (BN29552/BN29553) Of Crenezumab In Patients With Alzheimer's Disease

Summary

EudraCT number	2017-002702-12
Trial protocol	ES DE LT GB SE DK FI HU FR BE PL IT
Global end of trial date	31 May 2019

Results information

Result version number	v1
This version publication date	11 June 2020
First version publication date	11 June 2020

Trial information

Trial identification

Sponsor protocol code	BN40031
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03491150
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +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	31 May 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 May 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the long-term safety of Crenezumab

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 April 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Canada: 12
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Spain: 15
Country: Number of subjects enrolled	Finland: 3
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	Hong Kong: 1
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Korea, Republic of: 5
Country: Number of subjects enrolled	Lithuania: 1
Country: Number of subjects enrolled	Mexico: 6
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	Russian Federation: 6
Country: Number of subjects enrolled	Turkey: 1
Country: Number of subjects enrolled	United States: 85
Worldwide total number of subjects	149
EEA total number of subjects	30

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)	23
From 65 to 84 years	118
85 years and over	8

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 66 centers in 16 countries.

Pre-assignment

Screening details:

A total of 149 subjects were enrolled at 66 centers. These 149 subjects represented the Safety Analysis population and data for this population is presented here.

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	Parent Placebo

Arm description:

Subjects (who were treated with Placebo in the BN29552/BN29553 Studies) received intravenous (IV) infusion of Crenezumab every 4 weeks (Q4W).

Arm type	Placebo
Investigational medicinal product name	Crenezumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Crenezumab was administered by Intravenous (IV) infusion every 4 weeks (Q4W) at a dose of 60mg/kg.

Arm title	Parent Crenezumab
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Arm description:

Subjects (who were treated with Crenezumab in the BN29552/BN29553 Studies) received intravenous (IV) infusion of Crenezumab every 4 weeks (Q4W).

Arm type	Experimental
Investigational medicinal product name	Crenezumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Crenezumab was administered by Intravenous (IV) infusion every 4 weeks (Q4W) at a dose of 60mg/kg.

Number of subjects in period 1	Parent Placebo	Parent Crenezumab
Started	76	73
Completed	0	0
Not completed	76	73
Consent withdrawn by subject	1	2
Adverse event, non-fatal	1	-
Unknown	-	1
Study Terminated by Sponsor	74	70

Baseline characteristics

Reporting groups

Reporting group title	Parent Placebo
Reporting group description:	
Subjects (who were treated with Placebo in the BN29552/BN29553 Studies) received intravenous (IV) infusion of Crenezumab every 4 weeks (Q4W).	
Reporting group title	Parent Crenezumab
Reporting group description:	
Subjects (who were treated with Crenezumab in the BN29552/BN29553 Studies) received intravenous (IV) infusion of Crenezumab every 4 weeks (Q4W).	

Reporting group values	Parent Placebo	Parent Crenezumab	Total
Number of subjects	76	73	149
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)	0	0	0
Adults (18-64 years)	10	13	23
From 65-84 years	59	59	118
85 years and over	7	1	8
Age Continuous			
Units: Years			
arithmetic mean	73.8	72.0	
standard deviation	± 7.6	± 7.6	-
Sex: Female, Male			
Units:			
Female	37	38	75
Male	39	35	74
Race/Ethnicity, Customized			
Units: Subjects			
Hispanic or Latino	6	3	9
Not Hispanic or Latino	69	69	138
Not Stated	1	1	2
Race/Ethnicity, Customized			
Units: Subjects			
Asian	4	2	6
Black or African American	0	1	1
Unknown	0	3	3
White	72	67	139

End points

End points reporting groups

Reporting group title	Parent Placebo
Reporting group description: Subjects (who were treated with Placebo in the BN29552/BN29553 Studies) received intravenous (IV) infusion of Crenezumab every 4 weeks (Q4W).	
Reporting group title	Parent Crenezumab
Reporting group description: Subjects (who were treated with Crenezumab in the BN29552/BN29553 Studies) received intravenous (IV) infusion of Crenezumab every 4 weeks (Q4W).	

Primary: Percentage of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Percentage of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs) ^[1]
End point description: An Adverse Event is any untoward medical occurrence in a subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Preexisting conditions which worsen during a study are also considered as adverse events.	
End point type	Primary
End point timeframe: Baseline to end of study (1 year).	
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: No statistical analyses were performed as this study had only one arm.	

End point values	Parent Placebo	Parent Crenezumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	73		
Units: Percentage				
number (not applicable)				
AEs	32.9	42.5		
SAEs	3.9	5.5		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Anti-Crenezumab Antibodies

End point title	Percentage of Subjects with Anti-Crenezumab Antibodies ^[2]
End point description: Please note that for this Outcome Measure, no Subjects were evaluated at all as the existing immunogenicity data from a parent study (Study BN29552) showed a low potential of Crenezumab to induce Anti-Drug Antibodies (ADAs).	

End point type	Primary
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End point timeframe:

Baseline to end of study (1 year).

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: No statistical analyses were performed as this study had only one arm.

End point values	Parent Placebo	Parent Crenezumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[3]	0 ^[4]		
Units: Percentage				
number (not applicable)				

Notes:

[3] - ADAs were not collected in this study due to low induction potential of Crenezumab.

[4] - ADAs were not collected in this study due to low induction potential of Crenezumab.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

1 year, 1 month

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.0
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Reporting groups

Reporting group title	Parent Placebo
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Reporting group description:

Subjects (who were treated with Placebo in the BN29552/BN29553 Studies) received intravenous (IV) infusion of Crenezumab every 4 weeks (Q4W).

Reporting group title	Parent Crenezumab
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Reporting group description:

Subjects (who were treated with Crenezumab in the BN29552/BN29553 Studies) received intravenous (IV) infusion of Crenezumab every 4 weeks (Q4W).

Serious adverse events	Parent Placebo	Parent Crenezumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 76 (3.95%)	4 / 73 (5.48%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	0 / 76 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	1 / 76 (1.32%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
OPTIC ISCHAEMIC NEUROPATHY			
subjects affected / exposed	0 / 76 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders	INCARCERATED INGUINAL HERNIA			
	subjects affected / exposed	1 / 76 (1.32%)	0 / 73 (0.00%)	
	occurrences causally related to treatment / all	0 / 1	0 / 0	
	deaths causally related to treatment / all	0 / 0	0 / 0	
	RECTAL HAEMORRHAGE			
	subjects affected / exposed	1 / 76 (1.32%)	0 / 73 (0.00%)	
Infections and infestations	occurrences causally related to treatment / all	0 / 1	0 / 0	
	deaths causally related to treatment / all	0 / 0	0 / 0	
	PNEUMONIA			
	subjects affected / exposed	0 / 76 (0.00%)	1 / 73 (1.37%)	
	occurrences causally related to treatment / all	0 / 0	0 / 1	
	deaths causally related to treatment / all	0 / 0	0 / 0	
UROSEPSIS	subjects affected / exposed	0 / 76 (0.00%)	1 / 73 (1.37%)	
	occurrences causally related to treatment / all	0 / 0	0 / 1	
	deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Parent Placebo	Parent Crenezumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 76 (5.26%)	4 / 73 (5.48%)	
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	4 / 76 (5.26%)	4 / 73 (5.48%)	
occurrences (all)	5	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 August 2018	Following updates were made: [1] Improved alignment with CREAD 1 and 2 parent studies; [2] Language updated for China as China extensions activated in CREAD 1/2 studies; [3] Updating of information to align with latest Investigator's brochure; [4] Updates made to Exploratory Efficacy Objectives; [5] Number of Sites amended; [6] Recruitment period updated based on shortening of recruitment periods for CREAD 1/2 studies; [7] First Dose Window duration amended; [8] Update to Inclusion Criteria; [9] Addition of text to recognize country variability in designation of non-investigational medicinal product/investigational medicinal product status to positron emission tomography (PET) tracers; [10] Modification of physical and neurologic examination assessment; [11] Harmonisation of Vital Signs language and [12] Further updates including to Lab Samples, PD Biomarkers, Safety, Patient withdrawal, order of Clinical Assessments, timing of Brain MRI and Schedule of Activities.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported