



Clinical trial results:

A Phase 2b, Dose-Ranging Study of the Effect of GS-5745 on FEV1 in Adult Subjects with Cystic Fibrosis

Summary

EudraCT number	2015-002192-23
Trial protocol	DE BE ES
Global end of trial date	21 July 2017

Results information

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

Trial information

Trial identification

Sponsor protocol code	GS-US-404-1808
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02759562
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA , United States, 94404
Public contact	Gilead Clinical Study Information Center , Gilead Sciences , GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center , Gilead Sciences , GileadClinicalTrials@gilead.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	21 July 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 July 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the effect of andecaliximab (GS-5745) on pre-bronchodilator forced expiratory volume in 1 second (FEV1 % predicted) in adults with cystic fibrosis (CF) after 8 weeks of treatment.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 November 2016
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	Spain: 1
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	Australia: 1
Worldwide total number of subjects	6
EEA total number of subjects	5

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	5
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Australia and Europe. The first participant was screened on 04 November 2016. The last study visit occurred on 21 July 2017.

Pre-assignment

Screening details:

26 participants were screened.

Period 1

Period 1 title	Double-Blind Treatment Period (8 Weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Andecaliximab

Arm description:

Andecaliximab 600 mg administered via subcutaneous injection weekly for 8 weeks

Arm type	Experimental
Investigational medicinal product name	Andecaliximab
Investigational medicinal product code	
Other name	GS-5745
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

600 mg administered weekly for 8 doses

Arm title	Placebo
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Arm description:

Placebo administered via subcutaneous injection weekly for 8 doses

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered weekly for 8 doses

Number of subjects in period 1	Andecaliximab	Placebo
Started	3	3
Completed	3	3

Period 2

Period 2 title	Open-Label Treatment Period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Andecaliximab 600 mg to Andecaliximab 600 mg

Arm description:

Andecaliximab 600 mg administered via subcutaneous injection weekly for up to 16 weeks

Arm type	Experimental
Investigational medicinal product name	Andecaliximab
Investigational medicinal product code	
Other name	GS-5745
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

600 mg administered weekly for up to 16 weeks

Arm title	Placebo to Andecaliximab 600 mg
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Arm description:

Andecaliximab 600 mg administered via subcutaneous injection weekly for up to 16 weeks

Arm type	Experimental
Investigational medicinal product name	Andecaliximab
Investigational medicinal product code	
Other name	GS-5745
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

600 mg weekly for up to 16 weeks

Number of subjects in period 2 ^[1]	Andecaliximab 600 mg to Andecaliximab 600 mg	Placebo to Andecaliximab 600 mg
Started	2	2
Completed	0	0
Not completed	2	2
Withdrew Consent	1	-
Study Terminated by Sponsor	1	2

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: 2 participants completed the Double-Blind Phase, but did not enter in the Open-Label Phase.

Baseline characteristics

Reporting groups

Reporting group title	Andecaliximab
Reporting group description: Andecaliximab 600 mg administered via subcutaneous injection weekly for 8 weeks	
Reporting group title	Placebo
Reporting group description: Placebo administered via subcutaneous injection weekly for 8 doses	

Reporting group values	Andecaliximab	Placebo	Total
Number of subjects	3	3	6
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	46.0 ± 20.42	43.3 ± 10.02	-
Gender categorical Units: Subjects			
Female	2	0	2
Male	1	3	4
Ethnicity Units: Subjects			
Not Hispanic or Latino	3	3	6
Race Units: Subjects			
White	3	3	6
Pre-bronchodilator Forced expiratory volume in 1 second (FEV1) % predicted			
FEV1 % predicted is defined as FEV1 of the patient divided by the average FEV1 in the population for any person of similar age, sex, race, and body composition.			
Units: percent arithmetic mean standard deviation	49.7 ± 8.70	59.1 ± 19.26	-
Post-bronchodilator FEV1 % predicted Units: percent arithmetic mean standard deviation	52.1 ± 5.90	64.6 ± 20.58	-

End points

End points reporting groups

Reporting group title	Andecaliximab
Reporting group description: Andecaliximab 600 mg administered via subcutaneous injection weekly for 8 weeks	
Reporting group title	Placebo
Reporting group description: Placebo administered via subcutaneous injection weekly for 8 doses	
Reporting group title	Andecaliximab 600 mg to Andecaliximab 600 mg
Reporting group description: Andecaliximab 600 mg administered via subcutaneous injection weekly for up to 16 weeks	
Reporting group title	Placebo to Andecaliximab 600 mg
Reporting group description: Andecaliximab 600 mg administered via subcutaneous injection weekly for up to 16 weeks	

Primary: Absolute change in pre-bronchodilator FEV1 percent predicted from Baseline to Week 8

End point title	Absolute change in pre-bronchodilator FEV1 percent predicted from Baseline to Week 8 ^[1]
End point description: Full Analysis Set: all randomized participants who took at least 1 dose of study drug.	
End point type	Primary
End point timeframe: Baseline; Week 8	
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 comparison was performed.	

End point values	Andecaliximab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: percent				
arithmetic mean (standard deviation)	-2.10 (± 4.446)	2.90 (± 3.461)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in post-bronchodilator FEV1 percent predicted from Baseline to Week 8

End point title	Absolute change in post-bronchodilator FEV1 percent predicted from Baseline to Week 8
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End point description:	
Full Analysis Set	
End point type	Secondary
End point timeframe:	
Baseline; Week 8	

End point values	Andecaliximab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: percent				
arithmetic mean (standard deviation)	1.01 ($\pm$ 4.534)	-1.45 ($\pm$ 1.655)		

Statistical analyses

No statistical analyses for this end point

Secondary: Relative Change in Pre-bronchodilator FEV1 Percent Predicted From Baseline to Week 8

End point title	Relative Change in Pre-bronchodilator FEV1 Percent Predicted From Baseline to Week 8	
End point description:		
Full Analysis Set		
End point type	Secondary	
End point timeframe:		
Baseline; Week 8		

End point values	Andecaliximab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: percent of FEV1 % predicted				
arithmetic mean (standard deviation)	-3.85 ($\pm$ 9.009)	4.41 ($\pm$ 4.196)		

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change in post-bronchodilator FEV1 percent predicted from Baseline to Week 8

End point title	Relative change in post-bronchodilator FEV1 percent predicted from Baseline to Week 8			
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End point description:	
Full Analysis Set	
End point type	Secondary
End point timeframe:	
Baseline; Week 8	

End point values	Andecaliximab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: percent of FEV1 % predicted				
arithmetic mean (standard deviation)	2.28 (± 9.323)	-1.98 (± 1.749)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to the last dose date plus 30 days (maximum exposure: 140 days)

Adverse event reporting additional description:

Safety Analysis Set

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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Reporting groups

Reporting group title	Andecaliximab (Double-Blind)
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Reporting group description:

Andecaliximab 600 mg administered via subcutaneous injection weekly for 8 weeks

Reporting group title	Placebo
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Reporting group description:

Placebo administered via subcutaneous injection weekly for 8 doses

Reporting group title	Andecaliximab (Open-Label)
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Reporting group description:

Andecaliximab 600 mg administered via subcutaneous injection weekly for up to 16 weeks

Serious adverse events	Andecaliximab (Double-Blind)	Placebo	Andecaliximab (Open-Label)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Andecaliximab (Double-Blind)	Placebo	Andecaliximab (Open-Label)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	4 / 4 (100.00%)
Investigations			
Bacterial test positive			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Congenital, familial and genetic disorders			

Cystic fibrosis subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Nervous system disorders Seizure subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 4 (25.00%) 1
General disorders and administration site conditions Injection site pruritus subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 3 (33.33%) 1	0 / 4 (0.00%) 0
Injection site bruising subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 4 (0.00%) 0
Injection site erythema subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Injection site haematoma subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 2	0 / 4 (0.00%) 0
Injection site pain subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Injection site rash subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 4 (25.00%) 1
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Gastritis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 4 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Haemoptysis			

subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	2 / 4 (50.00%) 2
Wheezing subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 4 (0.00%) 0
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 4 (0.00%) 0
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 4 (0.00%) 0
Musculoskeletal stiffness subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 4 (0.00%) 0
Infections and infestations Oral herpes subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 4 (25.00%) 1
Rhinitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 4 (0.00%) 0
Metabolism and nutrition disorders Hypoglycaemia subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 May 2016	• Updated bilirubin exclusion criteria from 3 times the ULN to 2 times the ULN • Added additional ECG monitoring at Baseline, Week 4, 8, 16, 24, and 30-day Follow-up. • Added an active plan of soliciting symptoms on a monthly basis by increasing symptom driven PE's to be conducted monthly, including musculoskeletal symptoms. • Clarified the home health visits, timing of those visits and procedures conducted • Clarified the use of antibiotic use in the study and those that are to be excluded • Clarified pre-bronchodilator PEFR will be collected, not post • Last dose of OLE dosing clarified in schedule of assessments

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
06 June 2017	Gilead made a decision to discontinue the development of andecaliximab in cystic fibrosis. This decision was not due to any safety concerns with andecaliximab or with study procedures. As a result of the decision, this study was terminated.	-

Notes:

Limitations and caveats

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

The study was terminated after 6 subjects had been enrolled. Therefore, no inferential analyses were performed.

Notes: