Clinical trial results:
A phase II a , Multicenter, Randomized , Third -party Unblinded , Long-term Extension study to Determine Safety, Tolerability and Immunogenicity of ACC-001 with and without QS21 Adjuvant in Subjects with Mild to Moderate Alzheimzer's Disease

Summary

EudraCT number	2009-010922-21
Trial protocol	DE FR ES
Global end of trial date	17 December 2013

Results information

Result version number	v1 (current)
This version publication date	23 May 2016
First version publication date	05 July 2015

Trial information

Trial identification

Sponsor protocol code	3134K1-2203-EU

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00955409
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd St, New York, United States,
Public contact	Pfizer ClinicalTrials.gov Call Center , Pfizer, Inc., 1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center , Pfizer, Inc., 1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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	03 October 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 December 2013
Global end of trial reached?	Yes
Global end of trial date	17 December 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the long-term safety and tolerability of doses of 3, 10, and 30 µg of ACC-001 (CRM-conjugated A-beta [1-7] antigen alone and in combination with QS-21 adjuvant) in subjects with mild to moderate AD. The Basic Results disclose pooled data from the extension studies 3134K1-2203-EU (B2571007) and 3434K1-2205-US (B2571008).

Protection of trial subjects:

These studies were conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonisation Good Clinical Practice guidelines. Pfizer/Janssen Alzheimer's Immunotherapy (AI) data monitoring committee (DMC) and external DMC were involved for the ongoing monitoring of participants' safety. The table 'Number of subjects enrolled per age group' below reflects the number of enrolled subjects in the extension study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 November 2009
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	United States: 110
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	France: 15
Country: Number of subjects enrolled	Germany: 26
Worldwide total number of subjects	160
EEA total number of subjects	50

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)	40
From 65 to 84 years	117
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Planned duration was approximately 2 years (including 18 months of treatment + 6 months of follow-up). Participants who completed the lead-in 3134K1-200-EU (B2571004) study through Week 78 (Week 104 for Cohort 1 and 2) had the option to stay in the lead-in study or to roll-over into the extension protocol 3134K1-2203-EU (B2571007).

Pre-assignment

Screening details:

This extension study enrolled participants who completed lead-in study 3134K1-200-EU. All participants received active treatment in this extension study (ACC-001 with QS-21 adjuvant). Basic Results disclose pooled data from extension studies 3134K1-2203-EU (B2571007) and 3134K1-2205-US (B2571008). The row 'completed'=completed study in below table.

Period 1

Period 1 title	Including treatment and follow up period (overall period)
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	ACC 3 µg+QS-21 /ACC 3 µg+QS-21

Arm description:

Participants received 3 µg of ACC-001 and 50 µg of QS-21 in the lead-in study and in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Arm type	Experimental
Investigational medicinal product name	ACC-001 + QS-21 Adjuvant
Investigational medicinal product code	ACC-001 + QS-21 Adjuvant
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Lead-in study and extension study: ACC-001 3 µg and QS-21 50 µg. Intramuscular use.

Arm title	QS-21 / ACC 3 µg+QS-21

Arm description:

Participants received 50 µg of QS-21 in the lead-in study and 3 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Arm type	Experimental
Investigational medicinal product name	ACC-001 + QS-21 Adjuvant
Investigational medicinal product code	ACC-001 + QS-21 Adjuvant
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Lead-in study: QS-21 - 50 µg. Extension study: ACC-001 - 3 µg and QS-21 - 50 µg. Intramuscular use.

Arm title	ACC 10 µg+QS-21 /ACC 10 µg+QS-21

Arm description:

Participants received 10 µg of ACC-001 and 50 µg of QS-21 in the lead-in study and in the extension

study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Arm type	Experimental
Investigational medicinal product name	ACC-001 + QS-21 Adjuvant
Investigational medicinal product code	ACC-001 + QS-21 Adjuvant
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

In both lead-in study and extension study: ACC-001 - 10 µg and QS-21 - 50 µg. Intramuscular use.

Arm title	ACC 10 µg / ACC 10 µg+QS-21

Arm description:

Participants received 10 µg of ACC-001 in the lead-in study and 10 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Arm type	Experimental
Investigational medicinal product name	ACC-001 + QS-21 Adjuvant
Investigational medicinal product code	ACC-001 + QS-21 Adjuvant
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Lead-in study: ACC-001 - 10 µg. Extension study: 10 µg ACC-001 and 50 µg QS-21. Intramuscular use.

Arm title	QS-21 / ACC 10 µg+QS-21

Arm description:

Participants received 50 µg of QS-21 in the lead-in study and 10 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Arm type	Experimental
Investigational medicinal product name	ACC-001 + QS-21 Adjuvant
Investigational medicinal product code	ACC-001 + QS-21 Adjuvant
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Lead-in study: 50 µg QS-21. Extension study: 10 µg ACC-001 and 50 µg QS-21 . Intramuscular use.

Arm title	PBS / ACC 10 µg+QS-21

Arm description:

Participants received Phosphate buffered Saline (PBS) in the lead-in study and 10 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Arm type	Experimental
Investigational medicinal product name	ACC-001 + QS-21 Adjuvant
Investigational medicinal product code	ACC-001 + QS-21 Adjuvant
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Lead-in study: PBS. Extension study: 10 µg ACC-001 and 50 µg QS-21 . Intramuscular use.

Arm title	ACC 30 µg+QS-21/ACC 30 µg+QS-21

Arm description:

Participants received 30 µg of ACC-001 and 50 µg of QS-21 in the lead-in study and in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18

months.

Arm type	Experimental
Investigational medicinal product name	ACC-001 + QS-21 Adjuvant
Investigational medicinal product code	ACC-001 + QS-21 Adjuvant
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Lead-in study and in extension study: 30 µg ACC-001 and 50 µg QS-21. Intramuscular use.

Arm title	ACC 30 µg / ACC 30 µg+QS-21

Arm description:

Participants received 30 µg of ACC-001 in the lead-in study and 30 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Arm type	Experimental
Investigational medicinal product name	ACC-001 + QS-21 Adjuvant
Investigational medicinal product code	ACC-001 + QS-21 Adjuvant
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Lead-in study: 30 µg ACC-001. Extension study: 30 µg ACC-001 and 50 µg QS-21. Intramuscular use.

Arm title	QS-21 / ACC 30 µg+QS-21

Arm description:

Participants received 50 µg of QS-21 in the lead-in study and 30 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Arm type	Experimental
Investigational medicinal product name	ACC-001 + QS-21 Adjuvant
Investigational medicinal product code	ACC-001 + QS-21 Adjuvant
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Lead-in study: 50 µg QS-21. Extension study: 30 µg ACC-001 and 50 µg QS-21. Intramuscular use.

Arm title	PBS / ACC 30 µg+QS-21

Arm description:

Participants received PBS in the lead-in study and 30 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Arm type	Experimental
Investigational medicinal product name	ACC-001 + QS-21 Adjuvant
Investigational medicinal product code	ACC-001 + QS-21 Adjuvant
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Lead-in study: PBS. Extension study: 30 µg ACC-001 and 50 µg QS-21 . Intramuscular use.

Number of subjects in period 1	ACC 3 µg+QS-21 /ACC 3 µg+QS-21	QS-21 / ACC 3 µg+QS-21	ACC 10 µg+QS-21 /ACC 10 µg+QS-21
Started	21	6	41
Completed Treatment	12	5	15
Completed	11	5	15
Not completed	10	1	26
Consent withdrawn by subject	1	-	5
Physician decision	-	-	1
Adverse Event	2	-	-
Discontinuation of Study by Sponsor	-	-	-
Caregiver Request	2	-	6
Lost to follow-up	2	-	1
Retrieval subjects; impacted by sponsor disc.	2	1	13
Lack of efficacy	1	-	-

Number of subjects in period 1	ACC 10 µg / ACC 10 µg+QS-21	QS-21 / ACC 10 µg+QS-21	PBS / ACC 10 µg+QS-21
Started	25	5	9
Completed Treatment	17	3	7
Completed	17	3	6
Not completed	8	2	3
Consent withdrawn by subject	2	-	-
Physician decision	-	-	-
Adverse Event	-	-	1
Discontinuation of Study by Sponsor	-	-	-
Caregiver Request	5	-	2
Lost to follow-up	-	-	-
Retrieval subjects; impacted by sponsor disc.	1	2	-
Lack of efficacy	-	-	-

Number of subjects in period 1	ACC 30 µg+QS-21/ACC 30 µg+QS-21	ACC 30 µg / ACC 30 µg+QS-21	QS-21 / ACC 30 µg+QS-21
Started	27	6	16
Completed Treatment	4	3	2
Completed	3	2	2
Not completed	24	4	14
Consent withdrawn by subject	2	-	1
Physician decision	-	-	-
Adverse Event	2	-	2
Discontinuation of Study by Sponsor	-	1	-
Caregiver Request	3	1	3
Lost to follow-up	1	2	-

Retrieval subjects; impacted by sponsor disc.	16	-	8
Lack of efficacy	-	-	-

Number of subjects in period 1	PBS / ACC 30 µg+QS-21
Started	4
Completed Treatment	4
Completed	3
Not completed	1
Consent withdrawn by subject	-
Physician decision	-
Adverse Event	-
Discontinuation of Study by Sponsor	-
Caregiver Request	-
Lost to follow-up	-
Retrieval subjects; impacted by sponsor disc.	1
Lack of efficacy	-

Baseline characteristics

Reporting groups

Reporting group title	ACC 3 µg+QS-21 /ACC 3 µg+QS-21

Reporting group description:

Participants received 3 µg of ACC-001 and 50 µg of QS-21 in the lead-in study and in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Reporting group title	QS-21 / ACC 3 µg+QS-21

Reporting group description:

Participants received 50 µg of QS-21 in the lead-in study and 3 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Reporting group title	ACC 10 µg+QS-21 /ACC 10 µg+QS-21

Reporting group description:

Participants received 10 µg of ACC-001 and 50 µg of QS-21 in the lead-in study and in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Reporting group title	ACC 10 µg / ACC 10 µg+QS-21

Reporting group description:

Participants received 10 µg of ACC-001 in the lead-in study and 10 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Reporting group title	QS-21 / ACC 10 µg+QS-21

Reporting group description:

Participants received 50 µg of QS-21 in the lead-in study and 10 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Reporting group title	PBS / ACC 10 µg+QS-21

Reporting group description:

Participants received Phosphate buffered Saline (PBS) in the lead-in study and 10 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Reporting group title	ACC 30 µg+QS-21/ACC 30 µg+QS-21

Reporting group description:

Participants received 30 µg of ACC-001 and 50 µg of QS-21 in the lead-in study and in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Reporting group title	ACC 30 µg / ACC 30 µg+QS-21

Reporting group description:

Participants received 30 µg of ACC-001 in the lead-in study and 30 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Reporting group title	QS-21 / ACC 30 µg+QS-21

Reporting group description:

Participants received 50 µg of QS-21 in the lead-in study and 30 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Reporting group title	PBS / ACC 30 µg+QS-21

Reporting group description:

Participants received PBS in the lead-in study and 30 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Reporting group values	ACC 3 µg+QS-21 /ACC 3 µg+QS-21	QS-21 / ACC 3 µg+QS-21	ACC 10 µg+QS-21 /ACC 10 µg+QS-21
Number of subjects	21	6	41
Age categorical Units: Subjects			
50 - 64 Years	4	2	14
≥ 65 years	17	4	27
Age continuous Units: years			
arithmetic mean	68.7	67.7	69.7
standard deviation	± 6.94	± 9.52	± 9.29
Gender categorical Units: Subjects			
Female	11	4	21
Male	10	2	20
Race/Ethnicity Units: Subjects			
Asian	0	0	0
Black or African American	0	0	1
Other	1	0	0
White	20	6	40
MMSE Ranges Units: Subjects			
MMSE score >26	0	0	5
MMSE score 21-26	5	2	9
MMSE score 16-20	5	2	12
MMSE score 10-15	10	2	15
MMSE score <10	1	0	0
MMSE Score Units: Score			
arithmetic mean	16.7	18.3	18.4
standard deviation	± 4.64	± 5.61	± 5.92

Reporting group values	ACC 10 µg / ACC 10 µg+QS-21	QS-21 / ACC 10 µg+QS-21	PBS / ACC 10 µg+QS-21
Number of subjects	25	5	9
Age categorical Units: Subjects			
50 - 64 Years	5	1	3
≥ 65 years	20	4	6
Age continuous Units: years			
arithmetic mean	72.4	75.2	69.6
standard deviation	± 9.12	± 8.23	± 7.94
Gender categorical Units: Subjects			
Female	12	3	8
Male	13	2	1
Race/Ethnicity Units: Subjects			
Asian	0	0	0
Black or African American	0	1	0

Other	0	0	0
White	25	4	9
MMSE Ranges Units: Subjects			
MMSE score >26	3	1	1
MMSE score 21-26	7	2	3
MMSE score 16-20	10	2	3
MMSE score 10-15	5	0	2
MMSE score <10	0	0	0
MMSE Score Units: Score			
arithmetic mean	19.6	21.8	20
standard deviation	± 5.45	± 4.21	± 6.14

Reporting group values	ACC 30 µg+QS-21/ACC 30 µg+QS-21	ACC 30 µg / ACC 30 µg+QS-21	QS-21 / ACC 30 µg+QS-21
Number of subjects	27	6	16
Age categorical Units: Subjects			
50 - 64 Years	6	2	3
≥ 65 years	21	4	13
Age continuous Units: years			
arithmetic mean	71.3	66.3	69.5
standard deviation	± 9.2	± 9.42	± 6.95
Gender categorical Units: Subjects			
Female	16	3	14
Male	11	3	2
Race/Ethnicity Units: Subjects			
Asian	0	0	0
Black or African American	1	0	0
Other	0	0	0
White	26	6	16
MMSE Ranges Units: Subjects			
MMSE score >26	1	0	1
MMSE score 21-26	8	3	6
MMSE score 16-20	11	2	6
MMSE score 10-15	7	1	3
MMSE score <10	0	0	0
MMSE Score Units: Score			
arithmetic mean	18.7	20.5	19.1
standard deviation	± 4.98	± 4.76	± 4.84

Reporting group values	PBS / ACC 30 µg+QS-21	Total	
Number of subjects	4	160	

Age categorical Units: Subjects			
50 - 64 Years	0	40	
≥ 65 years	4	120	
Age continuous Units: years			
arithmetic mean	75.8		
standard deviation	± 7.89	-	
Gender categorical Units: Subjects			
Female	2	94	
Male	2	66	
Race/Ethnicity Units: Subjects			
Asian	0	0	
Black or African American	0	3	
Other	0	1	
White	4	156	
MMSE Ranges Units: Subjects			
MMSE score >26	0	12	
MMSE score 21-26	3	48	
MMSE score 16-20	0	53	
MMSE score 10-15	1	46	
MMSE score <10	0	1	
MMSE Score Units: Score			
arithmetic mean	20		
standard deviation	± 4.69	-	

End points

End points reporting groups

Reporting group title	ACC 3 µg+QS-21 /ACC 3 µg+QS-21
Reporting group description:	
Participants received 3 µg of ACC-001 and 50 µg of QS-21 in the lead-in study and in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.	
Reporting group title	QS-21 / ACC 3 µg+QS-21
Reporting group description:	
Participants received 50 µg of QS-21 in the lead-in study and 3 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.	
Reporting group title	ACC 10 µg+QS-21 /ACC 10 µg+QS-21
Reporting group description:	
Participants received 10 µg of ACC-001 and 50 µg of QS-21 in the lead-in study and in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.	
Reporting group title	ACC 10 µg / ACC 10 µg+QS-21
Reporting group description:	
Participants received 10 µg of ACC-001 in the lead-in study and 10 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.	
Reporting group title	QS-21 / ACC 10 µg+QS-21
Reporting group description:	
Participants received 50 µg of QS-21 in the lead-in study and 10 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.	
Reporting group title	PBS / ACC 10 µg+QS-21
Reporting group description:	
Participants received Phosphate buffered Saline (PBS) in the lead-in study and 10 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.	
Reporting group title	ACC 30 µg+QS-21/ACC 30 µg+QS-21
Reporting group description:	
Participants received 30 µg of ACC-001 and 50 µg of QS-21 in the lead-in study and in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.	
Reporting group title	ACC 30 µg / ACC 30 µg+QS-21
Reporting group description:	
Participants received 30 µg of ACC-001 in the lead-in study and 30 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.	
Reporting group title	QS-21 / ACC 30 µg+QS-21
Reporting group description:	
Participants received 50 µg of QS-21 in the lead-in study and 30 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.	
Reporting group title	PBS / ACC 30 µg+QS-21
Reporting group description:	
Participants received PBS in the lead-in study and 30 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.	
Subject analysis set title	ACC 3 µg+QS-21 / ACC 3 µg+QS-21
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who received at least one dose of the study drug were included in the safety population. Subjects in this group received 3 µg of ACC-001 and 50 µg of QS-21 in the lead-in study and in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Subject analysis set title	QS-21 / ACC 3 µg+QS-21
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who received at least one dose of the study drug were included in the safety population. Subjects in this group received 50 µg of QS-21 in the lead-in study and 3 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Subject analysis set title	Active / ACC 10 µg+QS-21
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who received at least one dose of the study drug were included in the safety population. Subjects in this group received 10 µg of ACC-001 and 50 µg of QS-21 or 10 µg of ACC-001 alone in the lead-in study and 10 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Subject analysis set title	Control / ACC 10 µg+QS-21
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who received at least one dose of the study drug were included in the safety population. Subjects received 50 µg of QS-21 or PBS in the lead-in study and 10 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Subject analysis set title	Active / ACC 30 µg+QS-21
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who received at least one dose of the study drug were included in the safety population. Subjects received 30 µg of ACC-001 and 50 µg of QS-21 or 30 µg of ACC-001 alone in the lead-in study and 30 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Subject analysis set title	Control / ACC 30 µg+QS-21
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who received at least one dose of the study drug were included in the safety population. Subjects in this group received 50 µg of QS-21 or PBS in the lead-in study and 30 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Primary: Percentage of Participants With Treatment-emergent adverse events (AEs) or serious adverse events (SAEs)

End point title	Percentage of Participants With Treatment-emergent adverse events (AEs) or serious adverse events (SAEs)[1]

End point description:

An AE was any untoward, undesired, or unplanned clinical event in the form of signs, symptoms, disease, or laboratory or physiologic observations occurring in a person given study drug or in a sponsor's clinical study. The event did not need to be causally related to the study drug or the clinical studies. A treatment emergent AE was defined as an event that emerged during the treatment period that was absent before treatment, or worsened during the treatment period relative to the pretreatment state. An SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly.

End point type	Primary

End point timeframe:

24 months

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 analysis was performed for this endpoint.

End point values	ACC 3 µg+QS-21 / ACC 3 µg+QS-21	QS-21 / ACC 3 µg+QS-21	Active / ACC 10 µg+QS-21	Control / ACC 10 µg+QS-21
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	21	6	65	14
Units: Percentage of participants				
number (not applicable)				
With TEAEs	100	100	93.8	92.9
With serious TEAEs	28.6	0	24.6	14.3

End point values	Active / ACC 30 µg+QS-21	Control / ACC 30 µg+QS-21		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	20		
Units: Percentage of participants				
number (not applicable)				
With TEAEs	78.8	90		
With serious TEAEs	12.1	20		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Geometric Mean Titers (GMTs) of Anti-A-beta Immunoglobulin G (IgG) Total Using an Enzyme-linked Immunosorbent Assay (ELISA) at Weeks 0, 4, 12, 24, 30, 36, 50, 56, 66, 76, 82, and 104

End point title	Geometric Mean Titers (GMTs) of Anti-A-beta Immunoglobulin G (IgG) Total Using an Enzyme-linked Immunosorbent Assay (ELISA) at Weeks 0, 4, 12, 24, 30, 36, 50, 56, 66, 76, 82, and 104

End point description:

The lower limit of quantification (LLOQ) was 100 U/mL and when the assay result was below LLOQ (100 U/mL), 50 U/mL was imputed for IgG.

End point type	Other pre-specified

End point timeframe:

Weeks 0, 4, 12, 24, 30, 36, 50, 56, 66, 76, 82, and 104

End point values	ACC 3 µg+QS-21 /ACC 3 µg+QS-21	QS-21 / ACC 3 µg+QS-21	ACC 10 µg+QS-21 /ACC 10 µg+QS-21	ACC 10 µg / ACC 10 µg+QS-21
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	6	41	24
Units: U/ml				
geometric mean (confidence interval 95%)				
Screening Lead-in (N:21,6,41,24,5,9,27,6,16,4)	50 (-99999 to 99999)	50 (-99999 to 99999)	50 (-99999 to 99999)	50 (575.1 to 3808.2)
Screening Extension (N:21,6,41,24,5,9,27,6,16,4)	836.5 (362.2 to 1932.3)	50 (-99999 to 99999)	1623.4 (1015.3 to 2595.7)	180.2 (-99999 to 99999)
Week 4 (N:21,6,41,24,5,9,27,5,16,4)	4523.7 (2070.2 to 9885)	50 (-99999 to 99999)	6219.3 (3853.2 to 10038.2)	517.9 (76.4 to 425.3)
Week 12 (N:21,6,41,23,4,9,27,5,16,4)	2540.3 (1060.5 to 6084.8)	50 (-99999 to 99999)	4251 (2709.7 to 6669.2)	425.4 (166.8 to 1607.6)
Week 24 (N:21,6,39,24,4,9,27,5,15,3)	1466.6 (607.2 to 3542.4)	50 (-99999 to 99999)	3058.1 (1887.1 to 4955.9)	280.3 (137 to 1320.6)
Week 30 (N:18,6,38,20,4,6,24,5,14,3)	3780.6 (1941.7 to 7360.9)	477.1 (85.4 to 2664.5)	8682 (5670.1 to 13293.8)	1574.5 (100.2 to 784.4)
Week 36 (N:18,6,36,20,4,9,25,5,14,3)	2927.8 (1368.7 to 6262.8)	267.1 (53.6 to 1331.2)	5946.6 (3807.1 to 9288.6)	1029.4 (568.2 to 4363.1)
Week 50 (N:17,6,37,20,4,8,20,5,13,3)	1843.8 (776.1 to 4380)	141.3 (24.5 to 813.2)	3146.6 (1945.8 to 5088.4)	512.4 (346.4 to 3059.1)
Week 56 (N:17,6,32,19,4,8,12,4,5,3)	4958.8 (2257.8 to 10891)	1441.4 (159.3 to 13045.1)	10412.4 (6365.4 to 17032.7)	4562.2 (176.5 to 1487.4)
Week 66 (N:17,6,30,19,4,7,8,5,3,3)	2765 (1190.8 to 6420.3)	701.5 (86 to 5719.3)	6627.7 (3946.1 to 11131.5)	2049.2 (2233.3 to 9319.8)
Week 76 (N:14,5,23,19,4,7,5,5,3,3)	2802.1 (1334.8 to 5882.6)	842.5 (107.7 to 6592.3)	3373.8 (1763.5 to 6454.6)	1479.9 (852.2 to 4927.5)
Week 82 (N:13,5,16,18,3,7,4,4,2,3)	6831.1 (3436.2 to 13579.9)	5104.3 (540.8 to 48180.8)	12261.1 (6635.8 to 22655.2)	5771.4 (587.2 to 4172.5)
Week 104 (N:12,5,14,17,2,5,5,2,2,3)	2951.6 (1259.3 to 6918.3)	1061 (77.8 to 14476)	6644.4 (2583.6 to 17088.1)	1565.2 (3264.4 to 10203.5)

End point values	QS-21 / ACC 10 µg+QS-21	PBS / ACC 10 µg+QS-21	ACC 30 µg+QS-21/ACC 30 µg+QS-21	ACC 30 µg / ACC 30 µg+QS-21
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	9	27	6
Units: U/ml				
geometric mean (confidence interval 95%)				
Screening Lead-in (N:21,6,41,24,5,9,27,6,16,4)	50 (-99999 to 99999)	50 (-99999 to 99999)	50 (-99999 to 99999)	50 (-99999 to 99999)

Screening Extension (N:21,6,41,24,5,9,27,6,16,4)	50 (-99999 to 99999)	50 (-99999 to 99999)	1718.3 (1101.2 to 2681.3)	424.2 (70.9 to 2539.4)
Week 4 (N:21,6,41,24,5,9,27,5,16,4)	50 (-99999 to 99999)	60.6 (38.9 to 94.4)	8436.2 (5569.8 to 12778)	4223 (185 to 96408.3)
Week 12 (N:21,6,41,23,4,9,27,5,16,4)	50 (-99999 to 99999)	62 (37.8 to 101.7)	3604.3 (2009.6 to 6464.5)	761.6 (33.2 to 17472.9)
Week 24 (N:21,6,39,24,4,9,27,5,15,3)	50 (-99999 to 99999)	57.5 (41.7 to 79.2)	2146.4 (1309 to 3519.7)	541.1 (31.3 to 9362.1)
Week 30 (N:18,6,38,20,4,6,24,5,14,3)	552.2 (37.8 to 8075.8)	317 (27.5 to 3654.9)	12939.5 (8634.4 to 19391.2)	1374.9 (54.4 to 34722.9)
Week 36 (N:18,6,36,20,4,9,25,5,14,3)	282.9 (43.5 to 1838.7)	428 (83.8 to 2186.8)	6228.9 (3794.3 to 10225.7)	706.7 (33.6 to 14852.3)
Week 50 (N:17,6,37,20,4,8,20,5,13,3)	169.6 (35.8 to 804.5)	333.6 (63 to 1767)	2439 (1369.5 to 4343.8)	527.7 (33.4 to 8348.8)
Week 56 (N:17,6,32,19,4,8,12,4,5,3)	1720 (108.1 to 27356.9)	3451 (478.9 to 24871.3)	5241.2 (2459.3 to 11170.1)	2216.1 (38 to 129086.9)
Week 66 (N:17,6,30,19,4,7,8,5,3,3)	891 (32.6 to 24385.5)	1989.2 (152.1 to 26014.2)	4341.1 (1677.8 to 11232.1)	1315.8 (117.1 to 14780.6)
Week 76 (N:14,5,23,19,4,7,5,5,3,3)	628.5 (26.6 to 1478.7)	1235.3 (116.5 to 13096.6)	2030.7 (576.9 to 7147.4)	875 (94.7 to 8083.3)
Week 82 (N:13,5,16,18,3,7,4,4,2,3)	2768.5 (79 to 97040.9)	4779.6 (706.4 to 32339.3)	1902 (35 to 103340.7)	3736.1 (594.2 to 23491.3)
Week 104 (N:12,5,14,17,2,5,5,2,2,3)	1128.4 (0.1 to 25253974)	832.4 (56.5 to 12268.2)	1447.6 (548.5 to 3820.9)	3654.5 (11.3 to 1181935)

End point values	QS-21 / ACC 30 µg+QS-21	PBS / ACC 30 µg+QS-21		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	4		
Units: U/ml				
geometric mean (confidence interval 95%)				
Screening Lead-in (N:21,6,41,24,5,9,27,6,16,4)	58.8 (41.6 to 83.3)	50 (-99999 to 99999)		
Screening Extension (N:21,6,41,24,5,9,27,6,16,4)	59.5 (41 to 86.3)	50 (-99999 to 99999)		
Week 4 (N:21,6,41,24,5,9,27,5,16,4)	144.7 (67.9 to 308)	100.1 (11 to 912.6)		
Week 12 (N:21,6,41,23,4,9,27,5,16,4)	89.3 (43.7 to 182.5)	87.9 (14.6 to 529.8)		
Week 24 (N:21,6,39,24,4,9,27,5,15,3)	78.9 (42.6 to 146.1)	50 (-99999 to 99999)		
Week 30 (N:18,6,38,20,4,6,24,5,14,3)	1889.4 (570.8 to 6254.5)	4360.1 (30.3 to 627361.8)		
Week 36 (N:18,6,36,20,4,9,25,5,14,3)	1018.5 (297.8 to 3483.6)	1164.2 (23.4 to 57811.5)		
Week 50 (N:17,6,37,20,4,8,20,5,13,3)	651.3 (189.9 to 2233.5)	401.4 (4.5 to 35461.1)		
Week 56 (N:17,6,32,19,4,8,12,4,5,3)	578.3 (26.6 to 12559.5)	8033.5 (584.5 to 110404.7)		
Week 66 (N:17,6,30,19,4,7,8,5,3,3)	968.4 (43 to 21784.1)	5403.5 (171.1 to 170698.5)		

Week 76 (N:14,5,23,19,4,7,5,5,3,3)	494.1 (1.2 to 198416.2)	2042.8 (107.4 to 38841.8)		
Week 82 (N:13,5,16,18,3,7,4,4,2,3)	1617.1 (3 to 868223.9)	9922.5 (2059.8 to 47798.6)		
Week 104 (N:12,5,14,17,2,5,5,2,2,3)	321.9 (0 to 12636639)	1340.5 (421.5 to 4263.3)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Approximately 24 months, starting from Day 1, inclusive 18 months of dosing and 6 months of follow-up after the last dose.

Adverse event reporting additional description:

Treatment emergent SAEs and non-SAEs are presented. Same event may appear as both an AE and SAE. However, what is presented are distinct events. An event may be categorized as serious in 1 participant and as nonserious in another participant, or 1 participant may have experienced both a serious and nonserious event during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	ACC 3 µg+QS-21 / ACC 3 µg+QS-21

Reporting group description:

Participants received 3 µg of ACC-001 and 50 µg of QS-21 in the lead-in study and in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Reporting group title	QS-21 / ACC 3 µg+QS-21

Reporting group description:

Participants received 50 µg of QS-21 in the lead-in study and 3 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Reporting group title	Active / ACC 10 µg+QS-21

Reporting group description:

Participants received 10 µg of ACC-001 and 50 µg of QS-21 or 10 µg of ACC-001 alone in the lead-in study and 10 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Reporting group title	Control / ACC 10µg+QS-21

Reporting group description:

Participants received 50 µg of QS-21 or PBS in the lead-in study and 10 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Reporting group title	Active / ACC 30 µg+QS-21

Reporting group description:

Participants received 30 µg of ACC-001 and 50 µg of QS-21 or 30 µg of ACC-001 alone in the lead-in study and 30 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Reporting group title	Control / ACC 30 µg+QS-21

Reporting group description:

Participants received 50 µg of QS-21 or PBS in the lead-in study and 30 µg of ACC-001 and 50 µg of QS-21 in the extension study. Test article was given by intramuscular injection into the deltoid muscle at 0, 6, 12, and 18 months.

Serious adverse events	ACC 3 µg+QS-21 / ACC 3 µg+QS-21	QS-21 / ACC 3 µg+QS-21	Active / ACC 10 µg+QS-21
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 21 (28.57%)	0 / 6 (0.00%)	16 / 65 (24.62%)
number of deaths (all causes)	2	0	1

number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gallbladder cancer metastatic			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral vascular disorder			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Raynaud's phenomenon			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device dislocation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic mass			

subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agitated depression			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agitation			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Investigations			
Liver function test abnormal			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Forearm fracture			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Road traffic accident			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradyarrhythmia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cyanosis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve prolapse			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			

subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral haemosiderin deposition			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dementia Alzheimer's type			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Dysarthria			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Partial seizures			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			

subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasogenic cerebral oedema			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary colic			

subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Petechiae			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin exfoliation			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin fissures			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin haemorrhage			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Dehydration			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Control / ACC 10µg+QS-21	Active / ACC 30 µg+QS-21	Control / ACC 30 µg+QS-21
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 14 (14.29%)	4 / 33 (12.12%)	4 / 20 (20.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gallbladder cancer metastatic			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 33 (3.03%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral vascular disorder			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Raynaud's phenomenon			

subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device dislocation			
subjects affected / exposed	0 / 14 (0.00%)	1 / 33 (3.03%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic mass			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 14 (0.00%)	1 / 33 (3.03%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Abnormal behaviour			

subjects affected / exposed	1 / 14 (7.14%)	1 / 33 (3.03%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agitated depression			
subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agitation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Liver function test abnormal			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Forearm fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hand fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradyarrhythmia			

subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cyanosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve prolapse			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral haemosiderin deposition			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dementia Alzheimer's type			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysarthria			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			

subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Partial seizures			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 14 (7.14%)	2 / 33 (6.06%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasogenic cerebral oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Petechiae			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin exfoliation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin fissures			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Skin haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	0 / 14 (0.00%)	1 / 33 (3.03%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	ACC 3 µg+QS-21 / ACC 3 µg+QS-21	QS-21 / ACC 3 µg+QS-21	Active / ACC 10 µg+QS-21
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 21 (90.48%)	6 / 6 (100.00%)	55 / 65 (84.62%)
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences (all)	1	0	3
Haemorrhage			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	1	0	0

Hypertension			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	3 / 65 (4.62%)
occurrences (all)	1	0	3
Hypotension			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	5 / 65 (7.69%)
occurrences (all)	0	0	5
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 21 (14.29%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	3	0	0
Face oedema			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	2 / 21 (9.52%)	1 / 6 (16.67%)	4 / 65 (6.15%)
occurrences (all)	2	1	7
Induration			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Inflammation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Injection site bruising			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences (all)	1	0	2
Injection site erythema			
subjects affected / exposed	4 / 21 (19.05%)	0 / 6 (0.00%)	5 / 65 (7.69%)
occurrences (all)	8	0	5
Injection site haemorrhage			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	1	0	0
Injection site hypersensitivity			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Injection site induration			

subjects affected / exposed	3 / 21 (14.29%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences (all)	4	0	1
Injection site inflammation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	2 / 65 (3.08%)
occurrences (all)	0	0	3
Injection site pain			
subjects affected / exposed	4 / 21 (19.05%)	0 / 6 (0.00%)	11 / 65 (16.92%)
occurrences (all)	7	0	15
Injection site pruritus			
subjects affected / exposed	1 / 21 (4.76%)	4 / 6 (66.67%)	0 / 65 (0.00%)
occurrences (all)	1	4	0
Injection site swelling			
subjects affected / exposed	3 / 21 (14.29%)	0 / 6 (0.00%)	5 / 65 (7.69%)
occurrences (all)	3	0	6
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	2 / 21 (9.52%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	2	0	0
Reproductive system and breast disorders			
Testicular pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 21 (9.52%)	1 / 6 (16.67%)	3 / 65 (4.62%)
occurrences (all)	3	1	3
Hiccups			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0

Aggression			
subjects affected / exposed	1 / 21 (4.76%)	1 / 6 (16.67%)	2 / 65 (3.08%)
occurrences (all)	1	1	5
Agitation			
subjects affected / exposed	3 / 21 (14.29%)	4 / 6 (66.67%)	5 / 65 (7.69%)
occurrences (all)	5	4	7
Anxiety			
subjects affected / exposed	2 / 21 (9.52%)	0 / 6 (0.00%)	4 / 65 (6.15%)
occurrences (all)	2	0	5
Confusional state			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	4 / 65 (6.15%)
occurrences (all)	1	0	4
Delirium			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Delusional perception			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	3 / 21 (14.29%)	0 / 6 (0.00%)	3 / 65 (4.62%)
occurrences (all)	3	0	3
Irritability			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	1 / 65 (1.54%)
occurrences (all)	0	1	1
Nightmare			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 65 (0.00%)
occurrences (all)	0	3	0
Investigations			
Bartonella test positive			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Urine output decreased			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Vitamin B1 decreased			

subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	3 / 21 (14.29%)	1 / 6 (16.67%)	2 / 65 (3.08%)
occurrences (all)	4	1	2
Corneal abrasion			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Eye contusion			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	4 / 21 (19.05%)	1 / 6 (16.67%)	7 / 65 (10.77%)
occurrences (all)	6	1	8
Hip fracture			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	3 / 65 (4.62%)
occurrences (all)	0	0	3
Limb injury			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	1	0	0
Periorbital contusion			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			

Bradycardia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Nervous system disorders			
Balance disorder			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	1	0	0
Cognitive disorder			
subjects affected / exposed	1 / 21 (4.76%)	1 / 6 (16.67%)	0 / 65 (0.00%)
occurrences (all)	1	1	0
Dementia Alzheimer's type			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	1 / 65 (1.54%)
occurrences (all)	0	1	1
Dizziness			
subjects affected / exposed	2 / 21 (9.52%)	0 / 6 (0.00%)	5 / 65 (7.69%)
occurrences (all)	2	0	6
Headache			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	6 / 65 (9.23%)
occurrences (all)	1	0	9
Hyperreflexia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Hypoaesthesia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Myoclonus			
subjects affected / exposed	1 / 21 (4.76%)	1 / 6 (16.67%)	2 / 65 (3.08%)
occurrences (all)	1	1	2
Syncope			
subjects affected / exposed	2 / 21 (9.52%)	0 / 6 (0.00%)	2 / 65 (3.08%)
occurrences (all)	2	0	2
Tremor			

subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Hearing impaired			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Glaucoma			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Heterophoria			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Retinal degeneration			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	2 / 65 (3.08%)
occurrences (all)	0	0	2
Dental caries			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	4 / 21 (19.05%)	1 / 6 (16.67%)	3 / 65 (4.62%)
occurrences (all)	5	1	3
Faeces soft			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Inguinal hernia			

subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	3 / 65 (4.62%)
occurrences (all)	2	0	3
Periodontal disease			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	3 / 21 (14.29%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences (all)	4	0	1
Skin and subcutaneous tissue disorders			
Ecchymosis			
subjects affected / exposed	2 / 21 (9.52%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	2	0	0
Erythema			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	2 / 65 (3.08%)
occurrences (all)	0	0	2
Pruritus			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	3 / 65 (4.62%)
occurrences (all)	1	0	4
Rash			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	4 / 65 (6.15%)
occurrences (all)	1	0	5
Rosacea			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	2 / 21 (9.52%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences (all)	2	0	1
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	4 / 65 (6.15%)
occurrences (all)	0	0	6
Back pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	4 / 65 (6.15%)
occurrences (all)	0	0	5
Muscle spasms			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	4 / 65 (6.15%)
occurrences (all)	0	1	4
Musculoskeletal pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences (all)	1	0	1
Neck pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	4 / 65 (6.15%)
occurrences (all)	0	0	4
Pain in extremity			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	3 / 65 (4.62%)
occurrences (all)	1	0	3
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 21 (14.29%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences (all)	3	0	1
Conjunctivitis			
subjects affected / exposed	0 / 21 (0.00%)	2 / 6 (33.33%)	0 / 65 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal infection			
subjects affected / exposed	1 / 21 (4.76%)	1 / 6 (16.67%)	2 / 65 (3.08%)
occurrences (all)	2	1	2
Infected bites			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Localised infection			

subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Lyme disease			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	2 / 21 (9.52%)	1 / 6 (16.67%)	6 / 65 (9.23%)
occurrences (all)	4	1	9
Onychomycosis			
subjects affected / exposed	1 / 21 (4.76%)	1 / 6 (16.67%)	0 / 65 (0.00%)
occurrences (all)	2	1	0
Pneumonia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	2 / 65 (3.08%)
occurrences (all)	0	0	3
Sinusitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences (all)	4	0	1
Subcutaneous abscess			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 21 (4.76%)	0 / 6 (0.00%)	3 / 65 (4.62%)
occurrences (all)	1	0	3
Urinary tract infection			
subjects affected / exposed	1 / 21 (4.76%)	4 / 6 (66.67%)	9 / 65 (13.85%)
occurrences (all)	2	4	10
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Wound infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			

Diabetes mellitus			
subjects affected / exposed	0 / 21 (0.00%)	0 / 6 (0.00%)	1 / 65 (1.54%)
occurrences (all)	0	0	1
Glucose tolerance impaired			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	0 / 65 (0.00%)
occurrences (all)	0	1	0
Vitamin D deficiency			
subjects affected / exposed	0 / 21 (0.00%)	1 / 6 (16.67%)	3 / 65 (4.62%)
occurrences (all)	0	1	3

Non-serious adverse events	Control / ACC 10µg+QS-21	Active / ACC 30 µg+QS-21	Control / ACC 30 µg+QS-21
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 14 (92.86%)	23 / 33 (69.70%)	17 / 20 (85.00%)
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	0 / 14 (0.00%)	2 / 33 (6.06%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Hypotension			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	0 / 14 (0.00%)	1 / 33 (3.03%)	0 / 20 (0.00%)
occurrences (all)	0	1	0

Induration			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Inflammation			
subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Injection site bruising			
subjects affected / exposed	0 / 14 (0.00%)	2 / 33 (6.06%)	1 / 20 (5.00%)
occurrences (all)	0	2	1
Injection site erythema			
subjects affected / exposed	1 / 14 (7.14%)	5 / 33 (15.15%)	4 / 20 (20.00%)
occurrences (all)	1	9	6
Injection site haemorrhage			
subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	3 / 20 (15.00%)
occurrences (all)	1	0	4
Injection site hypersensitivity			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Injection site induration			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Injection site inflammation			
subjects affected / exposed	0 / 14 (0.00%)	1 / 33 (3.03%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Injection site pain			
subjects affected / exposed	2 / 14 (14.29%)	5 / 33 (15.15%)	6 / 20 (30.00%)
occurrences (all)	2	9	8
Injection site pruritus			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Injection site swelling			
subjects affected / exposed	0 / 14 (0.00%)	4 / 33 (12.12%)	1 / 20 (5.00%)
occurrences (all)	0	7	1
Immune system disorders			
Seasonal allergy			

subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Testicular pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 14 (0.00%)	1 / 33 (3.03%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Hiccups			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Aggression			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Agitation			
subjects affected / exposed	2 / 14 (14.29%)	3 / 33 (9.09%)	1 / 20 (5.00%)
occurrences (all)	2	3	1
Anxiety			
subjects affected / exposed	1 / 14 (7.14%)	1 / 33 (3.03%)	0 / 20 (0.00%)
occurrences (all)	1	3	0
Confusional state			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Delirium			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Delusional perception			

subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	3 / 14 (21.43%)	2 / 33 (6.06%)	0 / 20 (0.00%)
occurrences (all)	3	2	0
Irritability			
subjects affected / exposed	0 / 14 (0.00%)	1 / 33 (3.03%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Nightmare			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Investigations			
Bartonella test positive			
subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Urine output decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vitamin B1 decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Contusion			
subjects affected / exposed	1 / 14 (7.14%)	2 / 33 (6.06%)	1 / 20 (5.00%)
occurrences (all)	1	2	1
Corneal abrasion			
subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Eye contusion			

subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	2 / 14 (14.29%)	2 / 33 (6.06%)	2 / 20 (10.00%)
occurrences (all)	2	2	6
Hip fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Laceration			
subjects affected / exposed	1 / 14 (7.14%)	2 / 33 (6.06%)	1 / 20 (5.00%)
occurrences (all)	1	2	1
Limb injury			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Periorbital contusion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Cognitive disorder			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Dementia Alzheimer's type			
subjects affected / exposed	0 / 14 (0.00%)	1 / 33 (3.03%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	2 / 14 (14.29%)	2 / 33 (6.06%)	2 / 20 (10.00%)
occurrences (all)	2	2	2
Headache			

subjects affected / exposed	1 / 14 (7.14%)	3 / 33 (9.09%)	1 / 20 (5.00%)
occurrences (all)	1	4	1
Hyperreflexia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Hypoaesthesia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Lethargy			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Myoclonus			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Hearing impaired			
subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Glaucoma			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Heterophoria			

subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Retinal degeneration			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 14 (0.00%)	2 / 33 (6.06%)	2 / 20 (10.00%)
occurrences (all)	0	2	2
Dental caries			
subjects affected / exposed	0 / 14 (0.00%)	1 / 33 (3.03%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Diarrhoea			
subjects affected / exposed	1 / 14 (7.14%)	2 / 33 (6.06%)	0 / 20 (0.00%)
occurrences (all)	1	2	0
Faeces soft			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Inguinal hernia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	3 / 20 (15.00%)
occurrences (all)	0	0	3
Periodontal disease			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	1 / 14 (7.14%)	1 / 33 (3.03%)	1 / 20 (5.00%)
occurrences (all)	1	1	4
Skin and subcutaneous tissue disorders			
Ecchymosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Erythema			

subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	0 / 14 (0.00%)	1 / 33 (3.03%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Rash			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rosacea			
subjects affected / exposed	1 / 14 (7.14%)	1 / 33 (3.03%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Skin lesion			
subjects affected / exposed	2 / 14 (14.29%)	1 / 33 (3.03%)	1 / 20 (5.00%)
occurrences (all)	2	1	1
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 14 (7.14%)	1 / 33 (3.03%)	0 / 20 (0.00%)
occurrences (all)	1	2	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 33 (3.03%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Back pain			
subjects affected / exposed	1 / 14 (7.14%)	1 / 33 (3.03%)	2 / 20 (10.00%)
occurrences (all)	2	1	2
Muscle spasms			
subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 14 (7.14%)	1 / 33 (3.03%)	1 / 20 (5.00%)
occurrences (all)	1	1	1
Neck pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			

subjects affected / exposed	1 / 14 (7.14%)	1 / 33 (3.03%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Infected bites			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Localised infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lyme disease			
subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 33 (3.03%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Onychomycosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 33 (3.03%)	1 / 20 (5.00%)
occurrences (all)	0	1	1

Sinusitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Subcutaneous abscess			
subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 14 (14.29%)	1 / 33 (3.03%)	0 / 20 (0.00%)
occurrences (all)	2	1	0
Urinary tract infection			
subjects affected / exposed	1 / 14 (7.14%)	2 / 33 (6.06%)	1 / 20 (5.00%)
occurrences (all)	1	2	3
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Wound infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Glucose tolerance impaired			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 February 2010	The following major changes were made in protocol amendment 1: - Study design was revised to clarify the study population, inclusion/exclusion criteria, concomitant medications, and procedures. - Protocol inconsistencies, omissions and errors were corrected.
30 June 2010	The following major changes were made in protocol amendment 2: - Study design was revised to clarify the study population, inclusion/exclusion criteria, concomitant medications, and procedures. - Protocol inconsistencies, omissions and errors were corrected.
13 January 2012	Protocol amendment 3 was made to update: - Exclusion criteria, inclusion of suicidality assessment, addition of direct and indirect bilirubin testing, and to update information and instructions pertaining to retrieval subjects, CSF sample collection, AEs/SAEs, discontinuation of investigational product due to injection site reactions, and reporting of safety issues.
14 June 2012	Protocol amendment 4 was made to update: - Adverse events, adverse events of special interest, concomitant treatments, and to add cerebral hemorrhage as an adverse drug reaction.
17 December 2013	The following major changes were made in protocol amendment 5: - CSF assays for anti-A-beta antibodies and IgG subtype analysis were listed as exploratory objectives and it was clarified that the analysis will not be conducted. - Specific protocol section was revised to clarify the inconsistency with the Investigator Brochure regarding the adverse events of special circumstance.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
12 July 2013	This study was prematurely terminated. In July 2013 the Alliance made a decision that ACC-001 would not be further developed in mild to moderate AD. Consequently, on 12 July 2013, dosing in the long-term extension studies was terminated and all remaining subjects were followed for safety for up to 6 months following their last administration of investigational product in accordance with the study protocols.	-

Notes:

Limitations and caveats

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

The following endpoints are not presented as these were not analyzed: GMTs of Anti-A-beta IgM and IgG Subtypes (where an IgG total response was measurable) using ELISA at Weeks 0, 4, 12, 24, 30, 36, 50, 56, 66, 76, 82, and 104.

Notes: