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VACCINE NAME / COMPOUND NUMBER*:* ACC-001 – Adult (Vanutude Cridificar) / PF-05236806

PROTOCOL Numbers:
3134K1-200-EU (Pfizer: B2571004)
3134K1-2201-US (Pfizer: B2571005)
(The data from both studies was pooled).

PROTOCOL TITLE: Phase 2A, Multicenter, Randomized, Third Party Unblinded, Adjuvant and Placebo-Controlled, Multiple Ascending Dose, Safety, Tolerability, and Immunogenicity Trial of ACC-001 and QS-21 Adjuvant in Subjects with Mild to Moderate Alzheimer's Disease.

Study Center(s): Thirty study centers in total participated including 17 study centers in the European Union (EU) (France [7 centers], Germany [6 centers], and Spain [4 centers]) and 13 centers in the United States (US).

Study Initiation Date and Primary Completion or Final Completion Dates:
Study Initiation Date: 10 May 2007 in the EU and 05 November 2007 in the US.
Final Completion Date: 16 January 2013 in the EU and 21 February 2013 in the US.

The study was co-developed by Pfizer/Janssen Alzheimer Immunotherapy Alliance.

Phase of Development: Phase 2A

Study Objectives:

Safety Objective

The primary objective was to evaluate the 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 Alzheimer's disease (AD). The hypothesis was that treatment with multiple doses of ACC-001 in subjects with mild to moderate AD would be safe and well tolerated.

Immunogenicity Objective

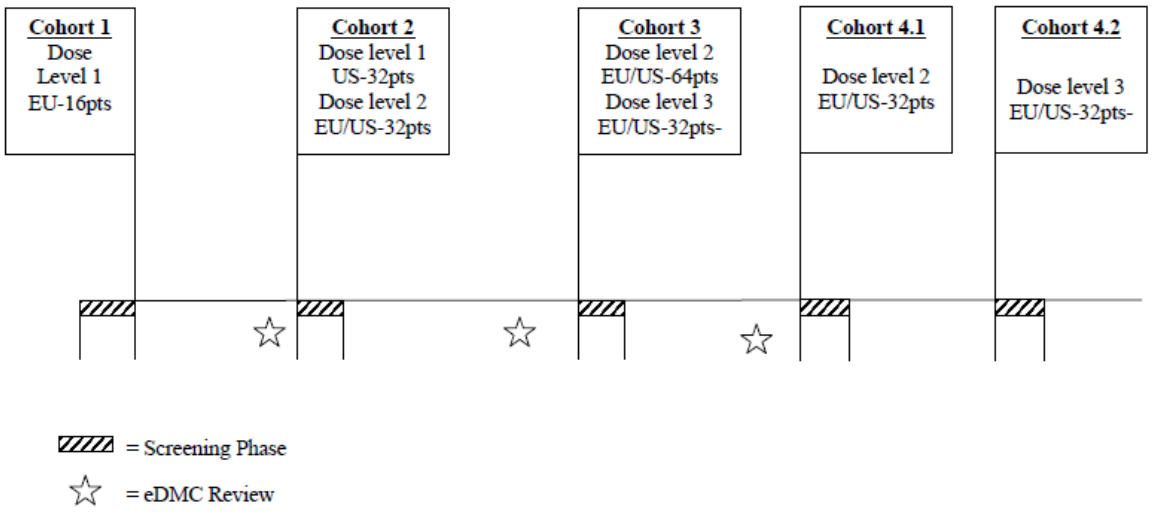
The secondary objective was to assess the immunogenicity of doses of 3, 10, and 30 µg of ACC-001 (CRM-conjugated A-beta $_{(1-7)}$ antigen, alone and in combination with QS-21 adjuvant) in subjects with mild to moderate AD.

METHODS

Study Design: These were Phase 2A, multicenter, randomized, third-party unblinded, adjuvant and placebo-controlled, multiple ascending dose, safety, tolerability, and immunogenicity studies of ACC-001 with and without QS-21 adjuvant in subjects with mild to moderate AD. Subjects were stratified by a Mini-Mental State Examination (MMSE) score of low (16-20) or high (21-26) to address mild and moderate subgroups. Germany only enrolled subjects with high MMSE score (21-26) (as requested by the Paul Ehrlich Institut; the German regulatory agency for vaccines and biomedicines).

ACC-001 with and without QS-21 adjuvant, as well as adjuvant alone were administered at 3 dose levels (3, 10, and 30 µg) in 4 cohorts of subjects. Phosphate-buffered saline (PBS) was administered as a control in the 10 and 30 µg dose cohorts. The dose of QS-21 was fixed at 50 µg. An independent external data monitoring committee (eDMC) met on a regular basis, independently of the sponsor to review combined data from both the 3134K1-200-EU and 3134K1-2205-US studies to assess the safety of the drug. Before proceeding to the next higher dose level, the eDMC met to review the safety data from the subjects randomized in the current cohort and all available aggregate safety data. Dose escalation occurred only after the sponsor and eDMC determined there were no safety issues that would preclude escalation to the next higher dose level (see Figure 1).

Figure 1 Study Flow Diagram for EU and US Studies



Abbreviations: eDMC=external data monitoring committee; EU=European Union; pts=patients; US=United States.

Dosing proceeded in 4 cohorts across the EU and US protocols. At each dose level, one third of subjects were dosed in a cohort preceding dosing of the remaining two third of the subjects. This "pioneer" strategy allowed for safety evaluation of the first set of subjects from each dose level before completing dosing of the next cohort and proceeding to the next dose level. In Cohorts 1, 2, and 3, if levels of anti-A-beta antibodies drawn 2 weeks prior to each

immunization reached 1:4000, injections of PBS diluent were substituted for ACC-001 at 3, 6, and 12 months (as per the PBS substitution rule).

Interim analyses conducted in studies 3134K1-200-EU and 3134K1-2201-US revealed that co-administration of QS-21 with ACC-001 may be required to produce an optimal serological anti-A-beta titer response and that the anti-A-beta antibody titer control PBS substitution rule may not be needed. Upon review of data from these interim analyses, the eDMC recommended the removal of the PBS substitution rule from the current Phase 2 trials. The sponsor agreed to implement removal of the titer based PBS substitution rule only for subjects randomized in Cohort 4. As a result, Cohort 4 enrolled additional subjects assigned to ACC-001+QS-21(no subjects received ACC-001 alone) without the anti-A-beta titer-based PBS substitution rule.

The studies included up to a 6-week screening period, 52 weeks of dosing, and 52 weeks for follow-up after the last dose. Subjects who completed the studies through Week 78 (Month 18) had the option to exit after Week 78 for continued treatment and follow-up under extension protocols 3134K1-2203-EU (Pfizer: B2571007) or 3134K1-2205-US (Pfizer: B2571008), if all inclusion and exclusion criteria for the extension studies were satisfied. Subjects who were not entering extension studies 3134K1-2203-EU or 3134K1-2205-US continued to be followed through Week 104.

The frequency and timing of the immunogenicity and safety measurements are displayed in Table 1.

Table 1: Schedule of Activities

PROCEDURES	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**	**V10**	**V11**	**V12**	**V13**	**V14**	**V15**	**V16**	**V17**	**V18**	**V19**	**V20**	**V21**	**V22**	**V23**	**V24**	
(Study Day, Week)	**D-42**	**D1**	**W2**	**W4**	**W6**	**W8**	**W10**	**W12**	**W14**	**W16**	**W24**	**W26**	**W28**	**W30**	**W40**	**W48**	**W50**	**W52**	**W54**	**W56**	**W66**	**W78**	**W91**	**W104**	**ET**
STUDY MONTH				**1**		**2**		**3**				**6**						**12**				**18**		**24**	
STUDY WINDOWS[a]			(±3 days)																(±7 days)						
Informed Consent	X																								
Injection of Study drug[b]		X		X				X				X						X							
Assess Injection Site		X	X	X	X			X	X			X	X					X	X						
24H T/C[c]		X		X				X				X						X							
Prior Med/Psyc Hx	X																								
Inc/Exc Criteria	X	X																							
NINCDS/ADRDA criteria	X																								
DSM-IV-TR Criteria	X																								
HAM-D_{17}, Rosen Hachinski	X																								
MMSE	X			X		X		X		X		X		X	X			X				X		X	X
ADAS-Cog, NTB, DAD		X						X				X						X				X		X	X
NPI, CDR		X						X				X						X				X		X	X
RUD Lite		X						X				X						X				X		X	X
PPQSA		X						X				X						X				X		X	X
WPAI		X						X				X						X				X		X	X
CRA		X						X				X						X				X		X	X
Brain MRI[d]	X						X				X						X					X			X
Physical Exam[e]	X	X						X				X			X			X			X	X	X	X	X
Neurological Exam	X	X						X				X			X			X			X	X	X	X	X
12-Lead ECG	X						X										X					X		X	X
Clinical Interview/Suicidality Assessment[f]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Vital Signs[g]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Table 1: Schedule of Activities

PROCEDURES	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	V13	V14	V15	V16	V17	V18	V19	V20	V21	V22	V23	V24	
(Study Day, Week)	D-42	D1	W2	W4	W6	W8	W10	W12	W14	W16	W24	W26	W28	W30	W40	W48	W50	W52	W54	W56	W66	W78	W91	W104	ET
STUDY MONTH				1		2		3				6						12				18		24	
STUDY WINDOWS[a]			(±3 days)																(±7 days)						
Clinical Labs[h]	X		X		X		X		X		X		X		X		X		X		X	X	X	X	X
Adverse Events	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant Meds	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pharmacogenomics		X										X													
Apo E4	X																								
Anti-A-beta Titers[i]	X		X	X	X	X	X		X	X	X		X	X	X		X		X	X	X	X	X	X	X
Immune Complexes and Complement	X				X					X				X						X					
Anti-Diphtheria Titers	X					X								X											
Plasma A-beta		X		X		X				X				X						X					
CSF[j]	X																X					X[k]		X[k]	X[k]
T-cell[k] Profile Assessment	X											X								X[k]					

Abbreviations: A-beta=beta-amyloid protein; ADAS-Cog=Alzheimer 's Disease Assessment Scale-Cognitive; ADRDA= Alzheimer's Disease and Related Disorders Association criteria; Apo E4=apolipoprotein E4; CDR=Clinical Dementia Rating; CRA=Caregiver Reaction Assessment; CSF=cerebrospinal fluid; D=Day; DAD=Disability Assessment for Dementia Scale; DSM-IV-TR=Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition-Text Revision; ECG=electrocardiogram; ET=early termination; exam=examination; HAM-D_{17}=Hamilton Psychiatric Rating Scale for Depression, 17 item; IgG=immunoglobulin G; IgM=immunoglobulin M; Inc/Exc=inclusion/exclusion; IVRS=interactive voice response system; Med/Psyc Hx=medical/psychiatric history; meds=medications; MMSE=Mini-Mental State Examination; MRI=magnetic resonance imaging; NINCDS=National Institute of Neurological and Communicative Disorders and Stroke; NPI=Neuropsychiatric Inventory; NTB=Neuropsychological Test Battery; PPQSA=Patient-Partner Questionnaire for Shared Activities; RUD Lite=abbreviated Resource Utilization in Dementia - Lite; tau= tubule associated unit protein; T/C=telephone call; V=Visit; W=week; WPAI=Work Productivity and Activity Impairment.

[a] Reporting of anti-A-beta titers from blood drawn at the previous visit was to be made available before injection of study drug at the 3, 6, and 12-month time-points for Cohorts 1 to 3.

[b] Clinical personnel called IVRS to confirm injection was done.

[c] Clinic personnel were to phone subjects within 24 hours of clinic visit for follow-up information.

[d] Screening MRI could be done after subject was determined to be eligible per clinical and laboratory criteria. Clinical MRI results must have been available for review prior to Day 1 injection. Post-screening MRIs could be completed on or before scheduled visit days. ET MRIs were only performed if the subject discontinued before Week 78 (Month 18).

[e] Weight was included as part of the physical examinations at screening and at Week 104 or ET. Height was recorded at screening.

[f] The suicidality assessment was performed at each clinic visit from the time of approval of Protocol Amendment 15 (EU) and 16 (Germany) of 3134K1-200-EU, and Protocol Amendment 5 of 3134K1-2201-US.

[g] Vital signs included sitting pulse and blood pressure, and temperature (oral or tympanic).

[h] Hematology, coagulation, blood chemistry, and urinalysis. Vitamin B12, folate, and thyroid panel were included in screening tests.

[i] Anti-A-beta IgG (total) and IgM were measured at all time-points; plasma A-beta concentrations and IgG subtypes could be measured at selected time-points when there was measurable IgG (total). Ig G subtypes were not assessed.

[j] A-beta, anti-A-beta, tau and phosphorylated-tau were measured in CSF samples. The lumbar puncture for the first CSF sample was scheduled just before Visit 2 if the subject was determined to be eligible per clinical, laboratory and MRI data. The CSF sample was performed at Week 104 only if Week 78 (Visit 22) was passed by the time of approval of 3134K1-200-EU Protocol Amendment 17 and 3134K1-2201-US Protocol Amendment 6. The lumbar puncture for the ET CSF sample was performed for subjects who terminated early before or after Week 50, providing the ET Visit occurred more than 12 weeks following any prior CSF collection.

[k] The blood sampling for the first T-cell assessment was scheduled just before Visit 2 if the subject was determined to be eligible per clinical, laboratory and MRI data. Week 56 assessment was applicable for 3134K1-2201-US study only.

Number of Subjects (Planned and Analyzed): Initially, 228 subjects were planned to be enrolled in the EU only, as stated in the original protocol (3134K1-200-EU, dated 03 August 2006). Further to a request from the Paul-Ehrlich-Institut, AEMPS (Spanish agency for the safety of health products), and ANSM (French agency for the safety of health products [previously known as AFSSAPS]) to reduce the number of subjects in the first dose cohort, the total number of planned subjects in study 3134K1-200-EU was limited to 56 subjects (Protocol Amendment 1) before First Subject First Visit (FSFV).

Further to this request from the EU regulatory authorities, the Food and Drug Administration (FDA) agreed that a second study could be conducted in the US (3134K1-2201-US) to make up the balance in numbers and reach a total of 228 subjects across both studies. As a result, the decision was taken to pool the data from both studies (see Amendments 5 [EU] and 6 [Germany] of the 3134K1-200-EU protocol and Amendment 1 of the 3134K1-2201-US protocol). A maximum of 240 subjects were expected to be randomized in the 2 separate multiple ascending dose protocols, with Protocol 3134K1-200-EU to contribute a maximum of 80 subjects.

A total of 245 subjects (159 in US, 42 in Germany, 27 in France, and 17 in Spain) were randomized (Table 3). Assigned vaccination is displayed in Table 2.

Diagnosis and Main Criteria for Inclusion: The studies included subjects diagnosed with mild to moderate AD, aged 50 to 85, and with an MMSE score of 16 to 26 (21 to 26 in Germany only). Subjects with a significant neurological disease, other than AD, that might affect cognition or with a major psychiatric disorder were excluded.

Study Vaccine: Each subject received 1 dose of one of the following at each of the 5 vaccination visits (Day 1 and Weeks 4, 12, 26 and 52):

- ACC-001 (3 µg)+QS-21 (50 µg);
- ACC-001 (10 µg)+QS-21 (50 µg);
- ACC-001 (30 µg)+QS-21 (50 µg);
- ACC-001 (10 µg);
- ACC-001 (30 µg);
- QS-21 (50 µg);
- PBS.

The vaccinations were administered by blinded clinical personnel, by intramuscular injection into the deltoid muscle.

Safety Evaluations:

- The incidence and severity of treatment-emergent adverse events (TEAEs);
- Clinically important changes in safety assessment results including injection site assessment, adverse events (AEs), serious adverse events (SAEs), AEs of Special Circumstance, clinical laboratory test results (including potential cases of drug-induced liver injury), vital signs, physical and neurological exams, electrocardiograms (ECGs), magnetic resonance imaging (MRI) scans, and suicidality assessments.

Clinical Efficacy, Biomarker, and Outcomes Research Endpoints: No primary or secondary clinical efficacy, biomarker, or health outcomes research endpoints were defined.

Immunogenicity Endpoints:

- Change from baseline levels of anti-A-beta immunoglobulin G (IgG) total at Weeks 2, 4, 6, 8, 10, 14, 16, 24, 28, 30, 40, 50, 54, 56, 66, 78, 91, and 104;
- Change from baseline levels of anti-A-beta immunoglobulin M (IgM) at Weeks 2, 4, 6, 8, 10, 14, 16, 24, 28, 30, 40, 50, 54, 56, 66, 78, 91, and 104;
- If applicable, change from baseline levels of IgG subtypes at visits where an IgG_{total} response was measurable.

Statistical Methods:

Immunogenicity population: The immunogenicity population included all randomized subjects with documented injection of at least one dose of study vaccine and at least one immunogenicity data point collected. Immunogenicity results were summarized according to the treatment that a subject actually received.

Safety population: All randomized subjects with documented use of at least one dose of study vaccine were included in the safety population. All safety analyses were conducted on the safety population. Safety results were summarized according to the treatment that a subject actually received.

Immunogenicity Analysis

For IgG, 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 assigned for IgG. For IgM, the LLOQ was 50 U/mL and when the assay result was below LLOQ (50 U/mL), 25 U/mL was assigned for IgM.

The immune response for each immune parameter in each treatment group at each time point was summarized as the geometric mean titer (GMT) in anti-A-beta IgG and anti-A-beta IgM.

Further to one of the interim analyses conducted for the 3134K1-200-EU and 3134K1-2201-US studies, a decision was made in 2010 not to analyze the change from baseline levels of IgG subtypes.

Safety Analysis

In general, results and changes over time were analyzed using continuous data approaches. Categorical data including potentially clinically important (PCI) events were analyzed using methods for dichotomous and ordinal response variables.

Summary statistics of study vaccine exposure and compliance were generated and no comparative statistics were produced.

RESULTS

Subject Disposition and Demography:

Subject Disposition

Of the 245 subjects who were randomized to treatment, 44 (18.0%) subjects completed 12 months of treatment with 12 months of follow-up and 149 (60.8%) subjects completed 12 months of treatment with 6 months of follow-up.

Fifty-two (21.2%) subjects discontinued from the studies. The primary reasons for discontinuation were AEs (16 [6.5%] subjects), subject request (11[4.5%] subjects), caregiver request (9 [3.7%] subjects) and "other" (9 [3.7%] subjects).

Of 245 subjects randomized, 244 (99.6%) subjects were included in the immunogenicity and safety population (1 subject was randomized but did not receive any doses of the study vaccine) (Table 2).

Table 2 Subject Disposition and Subjects Analyzed by Treatment Group (All Randomized Subjects)

	Treatment Group (as Randomized)							
Status	**ACC 3 µg+QS-21 (N[a]=36) n (%)**	**ACC 10 µg+QS-21 (N[a]=61) n (%)**	**ACC 30 µg+QS-21 (N[a]=40) n (%)**	**ACC 10 µg (N[a]=35) n (%)**	**ACC 30 µg (N[a]=12) n (%)**	**QS-21 Alone (N[a]=44) n (%)**	**PBS (N[a]=17) n (%)**	**Total (N[a]=245) n (%)**
Assigned to Study Treatment	36	61	40	35	12	44	17	245
Treated[b]	36 (100.0)	60 (98.4)	40 (100.0)	35 (100.0)	12 (100.0)	44 (100.0)	17 (100.0)	244 (99.6)
Completed 12 Months of Treatment with 12 Months of Follow-up	11 (30.6)	10 (16.4)	4 (10.0)	6 (17.1)	2 (16.7)	8 (18.2)	3 (17.6)	44 (18.0)
Completed 12 Months of Treatment with 6 months of Follow-up[c]	15 (41.7)	41 (67.2)	28 (70.0)	24 (68.6)	6 (50.0)	23 (52.3)	12 (70.6)	149 (60.8)
Discontinued from Studies	10 (27.8)	10 (16.4)	8 (20.0)	5 (14.3)	4 (33.3)	13 (29.5)	2 (11.8)	52 (21.2)
Adverse Event	2 (5.6)	3 (4.9)	3 (7.5)	2 (5.7)	2 (16.7)	3 (6.8)	1 (5.9)	16 (6.5)
Subject Request	3 (8.3)	0	1 (2.5)	1 (2.9)	1 (8.3)	4 (9.1)	1 (5.9)	11 (4.5)
Caregiver Request	2 (5.6)	2 (3.3)	2 (5.0)	0	1 (8.3)	2 (4.5)	0	9 (3.7)
Other	2 (5.6)	3 (4.9)	1 (2.5)	0	0	3 (6.8)	0	9 (3.7)
Lost to Follow-up	0	2 (3.3)	0	2 (5.7)	0	0	0	4 (1.6)
Unsatisfactory Response - Efficacy	1 (2.8)	0	0	0	0	0	0	1 (0.4)
Investigator Request	0	0	1 (2.5)	0	0	0	0	1 (0.4)
Death[d]	0	0	0	0	0	1 (2.3)	0	1 (0.4)

Table 2 Subject Disposition and Subjects Analyzed by Treatment Group (All Randomized Subjects)

	Treatment Group (as Randomized)							
Status	**ACC 3 µg+QS-21 (N[a]=36) n (%)**	**ACC 10 µg+QS-21 (N[a]=61) n (%)**	**ACC 30 µg+QS-21 (N[a]=40) n (%)**	**ACC 10 µg (N[a]=35) n (%)**	**ACC 30 µg (N[a]=12) n (%)**	**QS-21 Alone (N[a]=44) n (%)**	**PBS (N[a]=17) n (%)**	**Total (N[a]=245) n (%)**
Analyzed for Immunogenicity:								
Immunogenicity Population[e]	36 (100.0)	60 (98.4)	40 (100.0)	35 (100.0)	12 (100.0)	44 (100.0)	17 (100.0)	244 (99.6)
Analyzed for Safety[f]:								
Adverse Events	36 (100.0)	60 (98.4)	40 (100.0)	35 (100.0)	12 (100.0)	44 (100.0)	17 (100.0)	244 (99.6)
Laboratory Data	36 (100.0)	60 (98.4)	40 (100.0)	35 (100.0)	12 (100.0)	44 (100.0)	17 (100.0)	244 (99.6)

Abbreviations: N=number of subjects in group; n (%)=number (percent) of subjects in category; PBS=phosphate-buffered saline.

[a] The value was used as the denominator for percentages.

[b] Treated means subject received at least one study drug injection.

[c] Subjects in this row with intention to enter the extension studies after Week 78 (Month 18) Visit.

[d] Two subjects died during the study. However, one of the subjects was discontinued due to an adverse event, with an outcome of death.

[e] The immunogenicity population included all randomized subjects who received at least one dose of the study drug, and who had at least one immunogenicity data point collected.

[f] The safety population included all randomized subjects who received at least one dose of the study drug. The subjects were assigned to a treatment group based on the treatment they actually received.

Subject Demography

Of the 245 subjects randomized, the mean age was 69.1 (standard deviation [SD] of 8.87) years and more subjects were female (139 [56.7%] subjects), white (236 [96.3%] subjects) and from the US (159 [64.9%] subjects). In the European study (3134K1-200 EU) about half of the subjects were randomized in Germany. The mean duration of AD at baseline was 3.54 (SD of 2.637) years. Eighty five (34.7%) subjects were non-carriers, 121 (49.4%) subjects were heterozygous carriers, and 37 (15.1%) subjects were homozygous carriers of Apolipoprotein E4 (Apo E4). Mean baseline MMSE score was 21.4 (SD of 3.13) and most subjects (161 [65.7%]) were in the high MMSE stratum (baseline MMSE score=21-26). Two-hundred and thirty-three (233 [95.1%]) subjects were receiving cholinesterase inhibitor or memantine at baseline.

The groups were generally balanced with respect to age, race, country of origin, duration of AD, baseline MMSE score, and MMSE stratum (except in Germany where only subjects with high MMSE score were randomized) (Table 3).

Table 3 Demographic and Baseline Characteristics (All Randomized Subjects)

	Treatment Group (as Randomized)							
Characteristic	**ACC 3 µg+QS-21 (N[a]=36)**	**ACC 10 µg+QS-21 (N[a]=61)**	**ACC 30 µg+QS-21 (N[a]=40)**	**ACC 10 µg (N[a]=35)**	**ACC 30 µg (N[a]=12)**	**QS-21 Alone (N[a]=44)**	**PBS (N[a]=17)**	**Total (N[a]=245)**
AGE (YEARS)								
n	36	61	40	35	12	44	17	245
Mean	65.7	69.3	69.0	71.9	70.9	68.8	69.4	69.1
Standard Deviation	7.75	9.57	9.27	8.96	9.59	8.07	7.85	8.87
Median	65.0	71.0	71.0	74.0	72.0	68.0	70.0	70.0
Minimum	51	52	51	53	53	51	57	51
Maximum	81	85	81	86	83	84	82	86
SEX, n (%)								
n	36	61	40	35	12	44	17	245
Female	16 (44.4)	29 (47.5)	22 (55.0)	19 (54.3)	8 (66.7)	31 (70.5)	14 (82.4)	139 (56.7)
Male	20 (55.6)	32 (52.5)	18 (45.0)	16 (45.7)	4 (33.3)	13 (29.5)	3 (17.6)	106 (43.3)
RACE, n (%)								
n	36	61	40	35	12	44	17	245
White	33 (91.7)	60 (98.4)	38 (95.0)	34 (97.1)	11 (91.7)	43 (97.7)	17 (100)	236 (96.3)
Other	2 (5.6)	1 (1.6)	1 (2.5)	1 (2.9)	0	0	0	5 (2.0)
Black or African American	1 (2.8)	0	1 (2.5)	0	0	1 (2.3)	0	3 (1.2)
Asian	0	0	0	0	1 (8.3)	0	0	1 (0.4)

Table 3 Demographic and Baseline Characteristics (All Randomized Subjects)

	Treatment Group (as Randomized)							
Characteristic	**ACC 3 µg+QS-21 (N[a]=36)**	**ACC 10 µg+QS-21 (N[a]=61)**	**ACC 30 µg+QS-21 (N[a]=40)**	**ACC 10 µg (N[a]=35)**	**ACC 30 µg (N[a]=12)**	**QS-21 Alone (N[a]=44)**	**PBS (N[a]=17)**	**Total (N[a]=245)**
COUNTRY, n (%)								
n	36	61	40	35	12	44	17	245
USA	21 (58.3)	40 (65.6)	24 (60.0)	22 (62.9)	9 (75.0)	30 (68.2)	13 (76.5)	159 (64.9)
Germany	11 (30.6)	13 (21.3)	9 (22.5)	5 (14.3)	0	4 (9.1)	0	42 (17.1)
France	3 (8.3)	3 (4.9)	5 (12.5)	6 (17.1)	2 (16.7)	6 (13.6)	2 (11.8)	27 (11.0)
Spain	1 (2.8)	5 (8.2)	2 (5.0)	2 (5.7)	1 (8.3)	4 (9.1)	2 (11.8)	17 (6.9)
DURATION of AD (Years)								
n	36	61	40	35	12	44	17	245
Mean	4.32	3.33	3.67	3.23	3.38	3.04	4.43	3.54
Standard Deviation	2.200	2.597	2.632	2.200	1.999	2.339	4.714	2.637
Median	4.35	2.63	2.98	2.91	3.52	2.60	3.48	3.01
Minimum	0.5	0.3	0.2	0.5	0.1	0.5	0.4	0.1
Maximum	8.4	13.6	10.9	11.5	7.0	9.2	18.1	18.1
Apo E4 STATUS[b], n (%)								
n	36	61	40	35	12	43	16	243
Non-Carrier	12 (33.3)	27 (44.3)	15 (37.5)	14 (40.0)	3 (25.0)	11 (25.0)	3 (17.6)	85 (34.7)
Heterozygous	15 (41.7)	26 (42.6)	23 (57.5)	17 (48.6)	6 (50.0)	22 (50.0)	12 (70.6)	121 (49.4)
Homozygous	9 (25.0)	8 (13.1)	2 (5.0)	4 (11.4)	3 (25.0)	10 (22.7)	1 (5.9)	37 (15.1)

Table 3 Demographic and Baseline Characteristics (All Randomized Subjects)

	Treatment Group (as Randomized)							
Characteristic	**ACC 3 µg+QS-21 (N[a]=36)**	**ACC 10 µg+QS-21 (N[a]=61)**	**ACC 30 µg+QS-21 (N[a]=40)**	**ACC 10 µg (N[a]=35)**	**ACC 30 µg (N[a]=12)**	**QS-21 Alone (N[a]=44)**	**PBS (N[a]=17)**	**Total (N[a]=245)**
BASELINE MMSE SCORE[c]								
n	36	60	40	35	12	44	17	244
Mean	21.4	21.4	21.0	21.6	21.8	21.7	21.2	21.4
Standard Deviation	2.96	3.38	2.92	3.16	3.60	3.11	3.17	3.13
Median	22.0	22.0	21.0	22.0	22.5	22.5	22.0	22.0
Minimum	16	16	16	17	16	16	16	16
Maximum	26	26	26	26	26	26	26	26
BASELINE MMSE STRATUM, n (%)								
n	36	61	40	35	12	44	17	245
High (21-26)	26 (72.2)	40 (65.6)	24 (60.0)	23 (65.7)	8 (66.7)	29 (65.9)	11 (64.7)	161 (65.7)
Low (16-20)	10 (27.8)	21 (34.4)	16 (40.0)	12 (34.3)	4 (33.3)	15 (34.1)	6 (35.3)	84 (34.3)
CHOLINESTERASE INHIBITOR OR MEMANTINE USE, n (%)								
n	36	61	40	35	12	44	17	245
No	0	3 (4.9)	3 (7.5)	3 (8.6)	1 (8.3)	2 (4.5)	0	12 (4.9)
Yes	36 (100)	58 (95.1)	37 (92.5)	32 (91.4)	11 (91.7)	42 (95.5)	17 (100)	233 (95.1)

Abbreviation: AD=Alzheimer's disease; Apo E4=Apolipoprotein E4; CRF=case report form; MMSE=Mini-Mental state examination; N=number of subjects in group; n (%)=number (percent) of subjects in category; PBS=phosphate-buffered saline; USA=United States of America.

[a] The value in this row was used as the denominator for percentages.

[b] Two subjects had unknown Apo E4 results.

[c] One subject was randomized, but did not receive injection of study drug. Baseline MMSE collected in the CRF was not derived since the first dose date was missing.

Exposure and Compliance

Exposure during the two studies is summarized in Table 4.

No dose-compliance relationship was apparent.

The lowest numbers of subjects with all injections received were in the ACC 3µg+QS-21 (19 [52.8%] subjects) and QS-21 alone (28 [63.6%] subjects) groups and this was mostly due to the clinical hold in 2008.

Table 4 Summary of Exposure and Compliance (All Randomized Subjects)

	Treatment Group (as Randomized)							
Total Number of Injections	**ACC 3 µg+QS-21 (N[a]=36) n (%)**	**ACC 10 µg+QS-21 (N[a]=61) n (%)**	**ACC 30 µg+QS-21 (N[a]=40) n (%)**	**ACC 10 µg (N[a]=35) n (%)**	**ACC 30 µg (N[a]=12) n (%)**	**QS-21 Alone (N[a]=44) n (%)**	**PBS (N[a]=17) n (%)**	**Total (N[a]=245) n (%)**
1	1 (2.8)	1 (1.6)	0	0	0	0	1 (5.9)	3 (1.2)
2	1 (2.8)	0	3 (7.5)	2 (5.7)	1 (8.3)	4 (9.1)	0	11 (4.5)
3	2 (5.6)	6 (9.8)	2 (5.0)	4 (11.4)	2 (16.7)	4 (9.1)	0	20 (8.2)
4	13 (36.1)	6 (9.8)	2 (5.0)	3 (8.6)	0	8 (18.2)	1 (5.9)	33 (13.5)
5	19 (52.8)	47 (77.0)	33 (82.5)	26 (74.3)	9 (75.0)	28 (63.6)	15 (88.2)	177 (72.2)

Abbreviations: PBS=phosphate-buffered saline; N=number of subjects in group; n (%)=number (percent) of subjects in category.
[a] The value in this row was used as the denominator for percentages.

Immunogenicity Endpoint:

Anti-A-beta immunoglobulin G geometric mean titers

Anti-A-beta IgG GMTs (referred to below as anti-A-beta IgG titers) by study week for the immunogenicity population are illustrated in Figure 2 and summarized in Table 5.

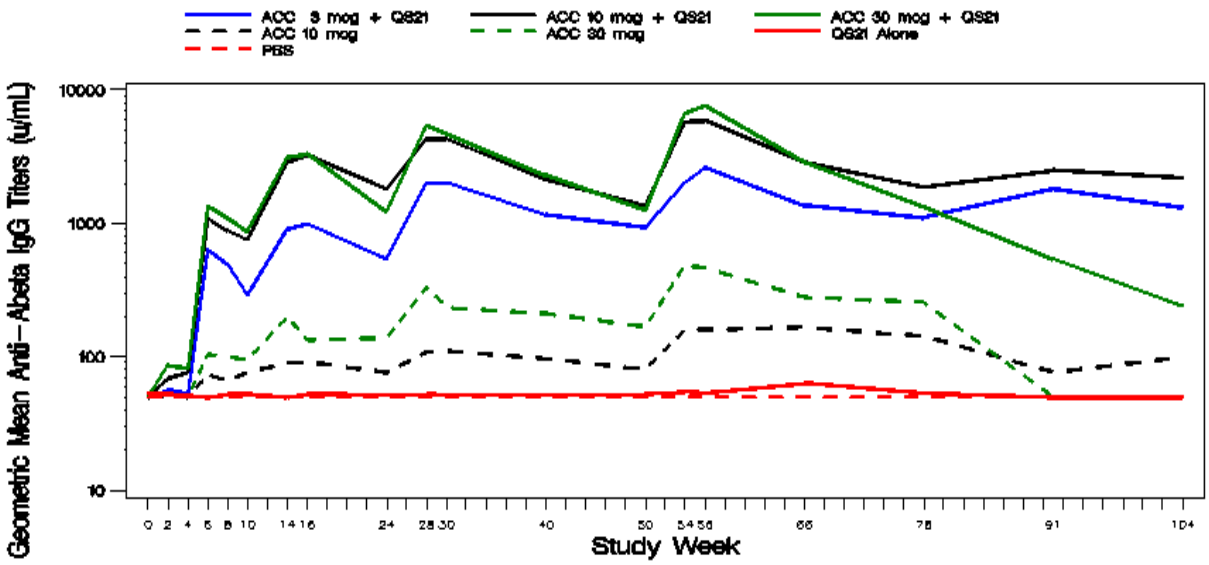
In the ACC+QS-21 vaccine groups, anti-A-beta IgG titers increased compared to baseline after each of the 5 vaccinations and a sustained increase in antibody production was observed after the second vaccination.

In the ACC alone vaccine groups, anti-A-beta IgG titers increased compared to baseline after vaccinations 2, 3, 4, and 5 and a sustained increase in antibody production was observed after the second vaccination.

Higher anti-A-beta IgG titers were observed in the ACC+QS-21 vaccine groups compared to the ACC alone vaccine groups.

Note: Following Week 78, there was a smaller number of subjects in each group due to the rollover of subjects to the extension studies at this time point; except for the ACC 3 µg+QS-21 vaccine group, who rolled over only on or after study completion.

Figure 2 Geometric Mean Anti-A-beta IgG Titers by Study Week (Immunogenicity Population)



Sample Size by Study Week

	0	2	4	6	8	10	14	16	24	28	30	40	50	54	56	66	78	91	104
ACC 3 mcg + QS21	36	35	35	36	33	34	33	33	34	31	33	32	29	27	31	31	31	15	15
ACC 10 mcg + QS21	59	60	57	58	57	59	52	59	58	51	56	54	53	51	52	54	52	9	9
ACC 30 mcg + QS21	40	39	38	37	39	40	39	38	37	33	36	33	33	30	34	34	32	3	4
ACC 10 mcg	35	35	31	33	33	33	31	34	33	29	32	33	33	29	32	31	32	8	7
ACC 30 mcg	12	12	12	12	12	12	11	12	10	8	10	9	9	9	9	9	8	2	1
QS21 Alone	44	43	43	41	41	43	33	41	40	36	38	37	36	29	34	33	32	6	6
PBS	17	16	16	16	17	17	14	16	16	16	16	15	16	14	15	15	14	2	2

Abbreviations: A-beta=beta amyloid; IgG=immunoglobulin G; PBS=phosphate-buffered saline.

Table 5 Geometric Mean Anti-A-beta IgG ELISA Titers by Study Week (Immunogenicity Population)

Parameter = Anti-A-beta IgG (U/mL)		Treatment Group (as Received)						
Study Week	**Category**	**ACC 3 µg+QS-21 (N=36)**	**ACC 10 µg+QS-21 (N=60)**	**ACC 30 µg+ QS-21 (N=40)**	**ACC 10 µg (N=35)**	**ACC 30 µg (N=12)**	**QS-21 Alone (N=44)**	**PBS (N=17)**
Baseline	n	36	59	40	35	12	44	17
	GMT	50.0	50.0	50.0	50.0	50.0	53.1	50.0
	95% CI	(50.0, 50.0)	(50.0, 50.0)	(50.0, 50.0)	(50.0, 50.0)	(50.0, 50.0)	(47.1, 59.8)	(50.0, 50.0)
2	n	35	60	39	35	12	43	16
	GMT	56.6	69.0	86.5	51.7	50.0	52.5	50.0
	95% CI	(49.1, 65.3)	(57.4, 83.0)	(65.7, 113.9)	(48.3, 55.2)	(50.0, 50.0)	(47.5, 58.1)	(50.0, 50.0)
4	n	35	57	38	31	12	43	16
	GMT	53.2	77.1	82.8	50.0	50.0	51.3	50.0
	95% CI	(48.5, 58.4)	(61.9, 96.0)	(63.0, 108.8)	(50.0, 50.0)	(50.0, 50.0)	(48.7, 53.9)	(50.0, 50.0)
6	n	36	58	37	33	12	41	16
	GMT	634.8	1089.4	1343.5	73.4	103.7	50.0	50.0
	95% CI	(322.7, 1248.5)	(646.0, 1837.2)	(716.0, 2521.1)	(50.6, 106.4)	(38.2, 281.4)	(50.0, 50.0)	(50.0, 50.0)
8	n	33	57	39	33	12	41	17
	GMT	497.4	885.2	1098.2	66.3	99.8	52.4	50.0
	95% CI	(253.5, 976.1)	(530.0, 1478.7)	(626.9, 1924.0)	(48.2, 91.1)	(38.8, 256.6)	(47.6, 57.7)	(50.0, 50.0)
10	n	34	59	40	33	12	43	17
	GMT	292.3	762.8	878.5	77.0	94.9	53.0	50.0
	95% CI	(156.5, 546.0)	(468.5, 1242.2)	(531.3, 1452.6)	(48.0, 123.3)	(39.8, 226.5)	(47.1, 59.7)	(50.0, 50.0)
14	n	33	52	39	31	11	33	14
	GMT	907.5	2892.3	3136.8	89.6	199.4	50.0	50.0
	95% CI	(474.6, 1735.6)	(1705.9, 4903.8)	(1877.6, 5240.7)	(50.8, 158.3)	(73.7, 539.8)	(50.0, 50.0)	(50.0, 50.0)

Table 5 Geometric Mean Anti-A-beta IgG ELISA Titers by Study Week (Immunogenicity Population)

Parameter = Anti-A-beta IgG (U/mL)		Treatment Group (as Received)						
Study Week	**Category**	**ACC 3 µg+QS-21 (N=36)**	**ACC 10 µg+QS-21 (N=60)**	**ACC 30 µg+ QS-21 (N=40)**	**ACC 10 µg (N=35)**	**ACC 30 µg (N=12)**	**QS-21 Alone (N=44)**	**PBS (N=17)**
16	n	33	59	38	34	12	41	16
	GMT	996.1	3273.2	3324.7	91.7	133.9	52.6	50.0
	95% CI	(487.1, 2037.1)	(2083.9, 5141.4)	(1959.4, 5641.3)	(55.2, 152.1)	(56.1, 319.9)	(47.5, 58.1)	(50.0, 50.0)
24	n	34	58	37	33	10	40	16
	GMT	547.8	1827.6	1231.3	76.1	139.1	52.3	50.0
	95% CI	(278.8, 1076.3)	(1145.3, 2916.1)	(712.2, 2128.6)	(52.1, 111.1)	(52.1, 371.3)	(47.7, 57.4)	(50.0, 50.0)
28	n	31	51	33	29	8	36	16
	GMT	2011.2	4299.6	5407.7	108.9	334.1	52.4	50.0
	95% CI	(986.9, 4098.8)	(2843.8, 6500.8)	(3676.0, 7955.3)	(61.9, 191.8)	(77.1, 1448.3)	(47.6, 57.6)	(50.0, 50.0)
30	n	33	56	36	32	10	38	16
	GMT	2028.9	4316.8	4713.0	110.4	234.5	51.8	50.0
	95% CI	(1035.8, 3973.8)	(2900.2, 6425.2)	(3076.0, 7221.2)	(64.1, 190.0)	(65.3, 842.5)	(48.2, 55.7)	(50.0, 50.0)
40	n	32	54	33	33	9	37	15
	GMT	1167.3	2147.2	2292.9	97.2	211.0	52.1	50.0
	95% CI	(609.1, 2237.1)	(1407.6, 3275.3)	(1436.6, 3659.8)	(62.4, 151.3)	(53.6, 830.7)	(47.9, 56.7)	(50.0, 50.0)
50	n	29	53	33	33	9	36	16
	GMT	937.3	1364.4	1262.3	80.7	168.4	52.8	50.0
	95% CI	(482.0, 1822.6)	(911.9, 2041.4)	(828.5, 1923.2)	(54.8, 118.9)	(52.4, 541.3)	(47.3, 58.8)	(50.0, 50.0)
54	n	27	51	30	29	9	29	14
	GMT	2031.6	5744.6	6677.3	160.6	491.6	55.0	50.0
	95% CI	(1024.2, 4029.7)	(3609.1, 9143.7)	(3678.7, 12120.1)	(69.7, 370.2)	(85.9, 2812.2)	(45.2, 66.9)	(50.0, 50.0)

Table 5 Geometric Mean Anti-A-beta IgG ELISA Titers by Study Week (Immunogenicity Population)

Parameter = Anti-A-beta IgG (U/mL)		Treatment Group (as Received)						
Study Week	**Category**	**ACC 3 µg+QS-21 (N=36)**	**ACC 10 µg+QS-21 (N=60)**	**ACC 30 µg+ QS-21 (N=40)**	**ACC 10 µg (N=35)**	**ACC 30 µg (N=12)**	**QS-21 Alone (N=44)**	**PBS (N=17)**
56	n	31	52	34	32	9	34	15
	GMT	2635.7	5906.1	7642.5	159.2	463.7	53.4	50.0
	95% CI	(1355.5, 5125.2)	(4058.8, 8594.2)	(5057.9, 11547.9)	(74.2, 341.8)	(81.1, 2650.5)	(46.7, 60.9)	(50.0, 50.0)
66	n	31	54	34	31	9	33	15
	GMT	1372.0	2867.4	2882.2	166.3	280.0	63.5	50.0
	95% CI	(717.1, 2625.1)	(1835.9, 4478.5)	(1793.1, 4632.8)	(78.8, 350.9)	(56.3, 1393.9)	(43.7, 92.3)	(50.0, 50.0)
78	n	31	52	32	32	8	32	14
	GMT	1108.4	1867.5	1338.1	142.7	256.1	53.6	50.0
	95% CI	(585.1, 2099.4)	(1197.4, 2912.5)	(827.3, 2164.4)	(71.5, 285.1)	(58.2, 1128.2)	(46.5, 61.6)	(50.0, 50.0)
91	n	15	9	3	8	2	6	2
	GMT	1824.6	2497.0	543.0	76.8	50.0	50.0	50.0
	95% CI	(1063.2, 3131.2)	(644.8, 9670.1)	(33.6, 8767.8)	(27.8, 211.9)	(50.0, 50.0)	(50.0, 50.0)	(50.0, 50.0)
104	n	15	9	4	7	1	6	2
	GMT	1326.1	2212.7	243.3	98.9	50.0	50.0	50.0
	95% CI	(785.0, 2240.2)	(406.4, 12048.4)	(28.8, 2052.4)	(30.7, 318.3)	(50.0, 50.0)	(50.0, 50.0)	(50.0, 50.0)

Abbreviations: CI=confidence interval; ELISA=Enzyme-linked immunosorbent assay; GMT=Geometric Mean Titer; IgG=immunoglobulin G; N=number of subjects in group; n=number of subjects in group with test result for that visit; PBS=phosphate-buffered saline.

Note: Results were not presented unless sample size was at least 3. CIs are back transformations of CIs based on the Student t distribution for the mean logarithm of the titer.

Anti-A-beta immunoglobulin M geometric mean titers

Anti-A-beta IgM GMTs (referred to below as anti-A-beta IgM titers) by study week for the immunogenicity population are illustrated in Figure 3 and summarized in Table 6.

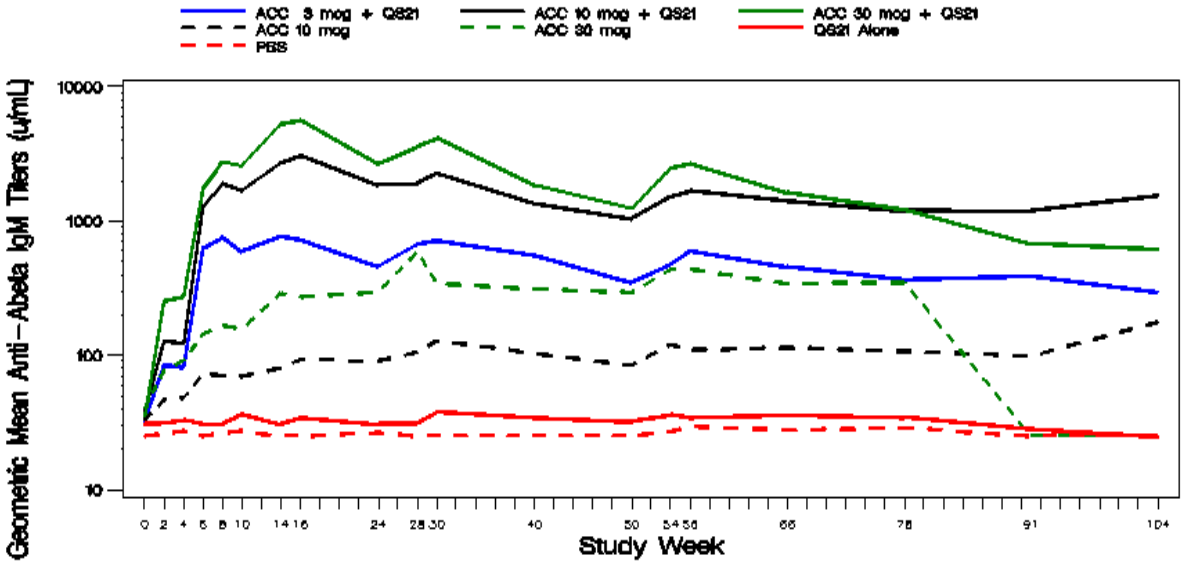
In the ACC+QS-21 vaccine groups, anti-A-beta IgM titers increased compared to baseline after each of the 5 vaccinations and a sustained increase in antibody production was observed after the second vaccination.

In the ACC alone vaccine groups, anti-A-beta IgM titers increased compared to baseline after vaccinations 2, 3, 4, and 5 and a sustained increase in antibody production was observed after the second vaccination.

Higher anti-A-beta IgM titers were observed in the ACC+QS-21 vaccine groups compared with the ACC alone vaccine groups. There seemed to be a dose-dependent relationship in the anti-A-beta IgM titers among the ACC+QS-21 vaccine groups.

Note: Following Week 78, there was a small number of subjects in each group due to the rollover of subjects to the extension studies at this time point; except for the ACC 3 µg+QS-21 vaccine group, who rolled over only on or after study completion.

Figure 3 Geometric Mean Anti-A-beta IgM Titers by Study Week (Immunogenicity Population)



Sample Size by Study Week

	0	2	4	6	8	10	14	16	24	28	30	40	50	54	56	66	78	91	104
ACC 3 mcg + QS21	36	35	35	36	33	34	33	33	34	31	33	32	29	27	31	31	31	15	15
ACC 10 mcg + QS21	59	60	57	58	57	59	52	59	58	51	56	54	53	51	52	54	52	9	9
ACC 30 mcg + QS21	40	39	38	37	39	40	39	38	37	33	36	33	33	30	34	34	32	3	4
ACC 10 mcg	35	35	31	33	33	33	31	34	33	29	32	33	33	29	32	31	32	8	7
ACC 30 mcg	12	12	12	12	12	12	11	12	10	8	10	9	9	9	9	9	8	2	1
QS21 Alone	44	43	43	41	41	43	33	41	40	36	38	37	36	29	34	33	32	6	6
PBS	17	16	16	16	17	17	14	16	16	16	16	15	16	14	15	15	14	2	2

Abbreviations: A-beta=beta amyloid; IgM=immunoglobulin M; PBS=phosphate-buffered saline.

Table 6 Geometric Mean Anti-A-beta IgM ELISA Titers by Study Week (Immunogenicity Population)

Parameter = Anti-A-beta IgM (U/mL)		Treatment Group (as Received)						
Study Week	**Category**	**ACC 3 µg+QS-21 (N=36)**	**ACC 10 µg+QS-21 (N=60)**	**ACC 30 µg+QS-21 (N=40)**	**ACC 10 µg (N=35)**	**ACC 30 µg (N=12)**	**QS-21 Alone (N=44)**	**PBS (N=17)**
Baseline	N	36	59	40	35	12	44	17
	GMT	32.3	38.2	34.2	32.9	40.3	30.8	25.0
	95% CI	(24.6, 42.4)	(30.8, 47.2)	(27.7, 42.2)	(28.1, 38.5)	(27.1, 59.9)	(26.4, 36.0)	(25.0, 25.0)
2	n	35	60	39	35	12	43	16
	GMT	85.1	127.7	254.5	46.5	76.9	31.5	26.5
	95% CI	(54.2, 133.8)	(79.5, 205.0)	(133.6, 484.9)	(32.4, 66.7)	(40.5, 146.2)	(26.6, 37.3)	(23.4, 29.9)
4	n	35	57	38	31	12	43	16
	GMT	82.3	123.4	276.6	48.2	92.0	33.2	27.3
	95% CI	(52.8, 128.4)	(75.9, 200.7)	(143.3, 533.6)	(33.2, 70.2)	(46.7, 181.1)	(28.0, 39.3)	(24.0, 30.9)
6	n	36	58	37	33	12	41	16
	GMT	626.5	1283.8	1736.6	72.3	144.1	31.1	25.0
	95% CI	(340.5, 1152.8)	(742.6, 2219.4)	(906.4, 3327.1)	(40.8, 128.2)	(55.9, 371.6)	(26.6, 36.3)	(25.0, 25.0)
8	n	33	57	39	33	12	41	17
	GMT	758.9	1903.8	2769.5	70.8	166.4	31.0	26.3
	95% CI	(388.6, 1482.4)	(1097.7, 3301.9)	(1407.2, 5450.9)	(40.8, 123.0)	(60.3, 459.3)	(26.1, 36.8)	(23.6, 29.4)
10	n	34	59	40	33	12	43	17
	GMT	595.2	1697.7	2598.1	69.9	157.1	36.6	27.3
	95% CI	(310.0, 1143.0)	(980.8, 2938.6)	(1382.6, 4882.0)	(38.3, 127.6)	(56.1, 440.1)	(28.0, 47.9)	(24.0, 31.1)
14	n	33	52	39	31	11	33	14
	GMT	770.2	2721.0	5271.3	80.8	290.7	31.0	25.0
	95% CI	(416.1, 1425.6)	(1608.3, 4603.4)	(2904.4, 9567.3)	(40.2, 162.3)	(71.8, 1177.7)	(25.5, 37.8)	(25.0, 25.0)

Table 6 Geometric Mean Anti-A-beta IgM ELISA Titers by Study Week (Immunogenicity Population)

Parameter = Anti-A-beta IgM (U/mL)		Treatment Group (as Received)						
Study Week	**Category**	**ACC 3 µg+QS-21 (N=36)**	**ACC 10 µg+QS-21 (N=60)**	**ACC 30 µg+QS-21 (N=40)**	**ACC 10 µg (N=35)**	**ACC 30 µg (N=12)**	**QS-21 Alone (N=44)**	**PBS (N=17)**
16	n	33	59	38	34	12	41	16
	GMT	727.3	3098.3	5666.4	93.4	271.8	34.5	25.0
	95% CI	(395.0, 1339.0)	(1904.1, 5041.2)	(3264.6, 9835.3)	(47.5, 183.4)	(70.5, 1047.5)	(27.6, 43.0)	(25.0, 25.0)
24	n	34	58	37	33	10	40	16
	GMT	461.3	1862.5	2672.4	90.8	296.2	30.9	26.6
	95% CI	(260.4, 817.2)	(1137.9, 3048.3)	(1553.6, 4597.0)	(48.1, 171.3)	(56.6, 1549.6)	(26.1, 36.7)	(23.3, 30.2)
28	n	31	51	33	29	8	36	16
	GMT	669.0	1915.3	3593.2	105.5	590.9	31.3	25.0
	95% CI	(388.0, 1153.6)	(1256.2, 2920.0)	(2050.4, 6296.9)	(50.2, 221.6)	(63.4, 5511.6)	(26.1, 37.5)	(25.0, 25.0)
30	n	33	56	36	32	10	38	16
	GMT	717.3	2259.4	4147.2	128.4	343.3	37.8	25.0
	95% CI	(432.6, 1189.5)	(1524.0, 3349.6)	(2423.1, 7098.1)	(63.1, 261.1)	(49.9, 2361.4)	(27.7, 51.6)	(25.0, 25.0)
40	n	32	54	33	33	9	37	15
	GMT	559.0	1351.6	1855.9	103.9	311.9	34.2	25.0
	95% CI	(350.7, 891.0)	(885.3, 2063.3)	(1074.3, 3206.1)	(54.2, 199.3)	(39.1, 2491.7)	(28.1, 41.6)	(25.0, 25.0)
50	n	29	53	33	33	9	36	16
	GMT	351.3	1049.6	1246.4	84.7	294.6	32.2	25.0
	95% CI	(210.2, 587.2)	(701.4, 1570.8)	(707.2, 2196.7)	(45.6, 157.3)	(41.2, 2104.6)	(27.1, 38.3)	(25.0, 25.0)
54	n	27	51	30	29	9	29	14
	GMT	477.7	1529.1	2479.5	121.1	436.9	36.2	27.2
	95% CI	(305.2, 747.7)	(1045.4, 2236.7)	(1373.5, 4476.4)	(52.1, 281.7)	(52.1, 3662.2)	(28.4, 46.3)	(22.7, 32.5)

Table 6 Geometric Mean Anti-A-beta IgM ELISA Titers by Study Week (Immunogenicity Population)

Parameter = Anti-A-beta IgM (U/mL)		Treatment Group (as Received)						
Study Week	**Category**	**ACC 3 µg+QS-21 (N=36)**	**ACC 10 µg+QS-21 (N=60)**	**ACC 30 µg+QS-21 (N=40)**	**ACC 10 µg (N=35)**	**ACC 30 µg (N=12)**	**QS-21 Alone (N=44)**	**PBS (N=17)**
56	n	31	52	34	32	9	34	15
	GMT	598.7	1696.1	2681.8	109.8	438.5	34.3	29.5
	95% CI	(375.1, 955.5)	(1173.6, 2451.3)	(1480.7, 4857.0)	(49.4, 244.1)	(51.5, 3734.3)	(27.2, 43.2)	(22.6, 38.6)
66	n	31	54	34	31	9	33	15
	GMT	457.6	1422.0	1637.2	114.3	342.1	36.1	27.8
	95% CI	(282.2, 742.1)	(980.7, 2061.9)	(961.9, 2786.6)	(51.6, 253.1)	(41.2, 2839.9)	(26.5, 49.1)	(23.8, 32.6)
78	n	31	52	32	32	8	32	14
	GMT	368.2	1204.4	1217.7	107.5	346.0	34.6	28.9
	95% CI	(238.4, 568.7)	(815.6, 1778.6)	(706.1, 2100.1)	(52.2, 221.4)	(31.2, 3832.0)	(27.9, 43.0)	(23.4, 35.8)
91	n	15	9	3	8	2	6	2
	GMT	391.2	1203.4	679.2	98.9	25.0	28.3	25.0
	95% CI	(205.6, 744.2)	(399.9, 3621.9)	(28.5, 16208.4)	(18.4, 530.4)	(25.0, 25.0)	(20.5, 39.1)	(25.0, 25.0)
104	n	15	9	4	7	1	6	2
	GMT	299.1	1561.8	620.3	176.7	25.0	25.0	25.0
	95% CI	(144.2, 620.8)	(438.0, 5569.0)	(78.8, 4882.2)	(26.1, 1197.0)	(25.0, 25.0)	(25.0, 25.0)	(25.0, 25.0)

Abbreviations: CI=confidence interval; ELISA=Enzyme-linked immunosorbent assay; GMT=Geometric Mean Titer; IgM=immunoglobulin M; N=Number of subjects in group; n=number of subjects in group with test result for that visit; PBS=phosphate-buffered saline.
Note: Results were not presented unless sample size was at least 3. CIs are back transformations of CIs based on the Student t distribution for the mean logarithm of the titer.

Safety Results:

Injection Site Reactions

A total of 68 (27.9%) subjects experienced injection site reactions (ISRs). A higher percentage of subjects experienced ISRs in the ACC+QS 21 group (54 [39.7%] subjects) than in the ACC alone and placebo groups (5 [10.6%] subjects and 9 (14.8%] subjects, respectively). Subjects in the ACC+QS-21 group experienced up to 5 ISRs and in the ACC alone group, subjects experienced one (1) ISR only (Table 7).

ISRs were mainly mild (82.4% of subjects) in intensity and of 1 to 7 days duration. Most subjects experienced their first ISR following the first or second injection of study vaccine. In the ACC+QS-21 groups, a dose-dependent relationship to ISR experienced after the first injection was apparent; in the 3 µg, 10 µg, and 30 µg dose groups, the percentage of subjects experiencing ISR after first injection was 21.4%, 37.5%, and 43.8%, respectively (Table 8).

The most frequent ISR symptoms were pain (42.0% of the symptoms), erythema (19.5%) and swelling (17.2%). No action was taken for the majority of the ISR symptoms (87.0%) (Table 9).

Table 7 Number of Injection Site Reactions (Safety Population)

		Number (%) Subjects with the Specified Number of Injection Site Reactions[a]			
Treatment (as Received)		1	2-3	4-5	Total
Overall	(N[b]=244)	38 (15.6)	22 (9.0)	8 (3.3)	68 (27.9)
ACC 3 µg+QS-21	(N[b]=36)	9 (25.0)	5 (13.9)	0	14 (38.9)
ACC 10 µg+QS-21	(N[b]=60)	11 (18.3)	8 (13.3)	5 (8.3)	24 (40.0)
ACC 30 µg+QS-21	(N[b]=40)	7 (17.5)	6 (15.0)	3 (7.5)	16 (40.0)
ACC 10 µg	(N[b]=35)	4 (11.4)	0	0	4 (11.4)
ACC 30 µg	(N[b]=12)	1 (8.3)	0	0	1 (8.3)
QS-21 Alone	(N[b]=44)	4 (9.1)	3 (6.8)	0	7 (15.9)
PBS	(N[b]=17)	2 (11.8)	0	0	2 (11.8)
Overall ACC+QS-21	(N[b]=136)	27 (19.9)	19 (14.0)	8 (5.9)	54 (39.7)
Overall ACC Alone	(N[b]=47)	5 (10.6)	0	0	5 (10.6)
Overall Control	(N[b]=61)	6 (9.8)	3 (4.9)	0	9 (14.8)

Abbreviations: ISR=injection site reaction; N=number subjects in group; PBS=phosphate-buffered saline.
[a] Multiple injection site reaction symptoms occurring after an injection of the study drug were counted once. Each subject was scheduled to have 5 injections of study drug per the protocols for the base studies B2571004 and B2571005; therefore, each subject could have up to 5 ISRs in the base studies.
[b] This value was used as the denominator for percentages.
Note: Overall Control group includes subjects randomized to either QS-21 alone or PBS alone group.
Note: Overall ACC+QS-21 group includes subjects randomized to either ACC 3 µg+QS-21, ACC 10 µg+QS-21 or ACC 30 µg+QS-21 group.
Note: Overall ACC alone group includes subjects randomized to either ACC 10 µg alone or ACC 30 µg alone group.

Table 8 Severity, Duration, and Timing of Injection Site Reactions (Safety Population)

	Treatment Group (as Received)							
	ACC 3 µg+QS-21 (N=36) n (%)	**ACC 10 µg+QS-21 (N=60) n (%)**	**ACC 30 µg+QS-21 (N=40) n (%)**	**ACC 10 µg (N=35) n (%)**	**ACC 30 µg (N=12) n (%)**	**QS-21 Alone (N=44) n (%)**	**PBS (N=17) n (%)**	**Total (N=244) n (%)**
Severity of ISR[ab]	**n=14**	**n=24**	**n=16**	**n=4**	**n=1**	**n=7**	**n=2**	**n=68**
Mild	8 (57.1)	21 (87.5)	13 (81.3)	4 (100)	1 (100)	7 (100)	2 (100)	56 (82.4)
Moderate	6 (42.9)	2 (8.3)	2 (12.5)	0	0	0	0	10 (14.7)
Severe	0	1 (4.2)	1 (6.3)	0	0	0	0	2 (2.9)
Life Threatening	0	0	0	0	0	0	0	0
Duration of ISR[ac]	**n=14**	**n=24**	**n=16**	**n=4**	**n=1**	**n=7**	**n=2**	**n=68**
1-3 days	7 (50.0)	13 (54.2)	7 (43.8)	3 (75.0)	1 (100)	6 (85.7)	0	37 (54.4)
4-7 days	6 (42.9)	2 (8.3)	3 (18.8)	0	0	1 (14.3)	0	12 (17.6)
>7-14 days	0	5 (20.8)	2 (12.5)	1 (25.0)	0	0	0	8 (11.8)
>14-28 days	1 (7.1)	2 (8.3)	4 (25.0)	0	0	0	2 (100)	9 (13.2)
>28 days	0	2 (8.3)	0	0	0	0	0	2 (2.9)
First ISR Occurred Following	**n=14**	**n=24**	**n=16**	**n=4**	**n=1**	**n=7**	**n=2**	**n=68**
Injection 1 - Day 1	3 (21.4)	9 (37.5)	7 (43.8)	2 (50.0)	0	3 (42.9)	0	24 (35.3)
Injection 2 - Week 4	3 (21.4)	9 (37.5)	4 (25.0)	0	1 (100)	3 (42.9)	1 (50.0)	21 (30.9)
Injection 3 - Week 12	2 (14.3)	5 (20.8)	2 (12.5)	1 (25.0)	0	0	0	10 (14.7)
Injection 4 - Week 26	4 (28.6)	1 (4.2)	2 (12.5)	1 (25.0)	0	1 (14.3)	0	9 (13.2)
Injection 5 - Week 52	2 (14.3)	0	1 (6.3)	0	0	0	1 (50.0)	4 (5.9)

Abbreviations: ISR=injection site reaction; N=number of subjects in groups; n (%)=number (percent) of subjects with ISR; PBS=phosphate-buffered saline.
[a] The values in this row were used as the denominators for percentages.
[b] Multiple ISR symptoms occurring after an injection of test product were counted once. Each subject was scheduled to have 5 injections of study medication per the protocols for the base studies B2571004 and B2571005; therefore, each subject could have up to 5 ISRs collected in the base studies; however, the most severe reaction is displayed.
[c] The longest duration was counted when there were multiple ISRs.

Table 9 Injection Site Reaction Symptoms and Actions Taken (Safety Population)

	Treatment Group (as Received)							
	ACC 3 µg+QS-21 (N = 36) n (%)	**ACC 10 µg+QS-21 (N = 60) n (%)**	**ACC 30 µg+QS-21 (N = 40) n (%)**	**ACC 10 µg (N = 35) n (%)**	**ACC 30 µg (N = 12) n (%)**	**QS-21 Alone (N = 44) n (%)**	**PBS (N = 17) n (%)**	**Total (N = 244) n (%)**
Any ISR Symptom[a]	**n = 27**	**n = 71**	**n = 52**	**n = 4**	**n = 1**	**n = 11**	**n = 3**	**n = 169**
Pain	10 (37.0)	33 (46.5)	16 (30.8)	4 (100)	1 (100)	7 (63.6)	0	71 (42.0)
Erythema	8 (29.6)	13 (18.3)	11 (21.2)	0	0	1 (9.1)	0	33 (19.5)
Swelling	2 (7.4)	11 (15.5)	15 (28.8)	0	0	0	1 (33.3)	29 (17.2)
Pruritus	1 (3.7)	5 (7.0)	3 (5.8)	0	0	0	0	9 (5.3)
Induration	0	5 (7.0)	1 (1.9)	0	0	1 (9.1)	0	7 (4.1)
Reaction	4 (14.8)	0	0	0	0	1 (9.1)	0	5 (3.0)
Bruising	1 (3.7)	0	2 (3.8)	0	0	0	1 (33.3)	4 (2.4)
Warmth	1 (3.7)	3 (4.2)	0	0	0	0	0	4 (2.4)
Inflammation	0	0	2 (3.8)	0	0	1 (9.1)	0	3 (1.8)
Haemorrhage	0	0	1 (1.9)	0	0	0	1 (33.3)	2 (1.2)
Discomfort	0	1 (1.4)	0	0	0	0	0	1 (0.6)
Vesicles	0	0	1 (1.9)	0	0	0	0	1 (0.6)
Any Action Taken[b]	**n = 27**	**n = 71**	**n = 52**	**n = 4**	**n = 1**	**n = 11**	**n = 3**	**n = 169**
No Action Taken	24 (88.9)	61 (85.9)	43 (82.7)	4 (100)	1 (100)	11 (100)	3 (100)	147 (87.0)
Primary reason for study withdrawal	0	0	0	0	0	0	0	0
Withdrawn from studies	0	0	0	0	0	0	0	0
Discontinued test article permanently	0	0	1 (1.9)	0	0	0	0	1 (0.6)
Hospitalized	0	0	0	0	0	0	0	0
Concomitant Medication	3 (11.1)	8 (11.3)	3 (5.8)	0	0	0	0	14 (8.3)
Other	0	2 (2.8)	5 (9.6)	0	0	0	0	7 (4.1)

Table 9 Injection Site Reaction Symptoms and Actions Taken (Safety Population)

	Treatment Group (as Received)							
	ACC 3 µg+QS-21 (N = 36) n (%)	**ACC 10 µg+QS-21 (N = 60) n (%)**	**ACC 30 µg+QS-21 (N = 40) n (%)**	**ACC 10 µg (N = 35) n (%)**	**ACC 30 µg (N = 12) n (%)**	**QS-21 Alone (N = 44) n (%)**	**PBS (N = 17) n (%)**	**Total (N = 244) n (%)**

Abbreviations: ISR=injection site reaction; N=number of subjects in groups; n (%)=number (percent) of a specific symptom; PBS=phosphate-buffered saline.
[a] When there are multiple symptoms occurring at a single visit for a subject, the actual number of symptoms captured is used in the count as displayed. The values in this row were used as the denominators for percentages.
[b] Multiple actions can be taken for a single injection site reaction symptom. The actual number of actions taken is used in the count as displayed.
Note: ISR symptoms correspond to descriptive treatment-emergent adverse events.

Adverse Events

Overall, TEAEs (serious or non-serious) were experienced by 226 (92.6%) subjects, 99 (40.6%) subjects experienced treatment-related TEAEs, 28 (11.5%) subjects experienced severe TEAEs, 3 (1.2%) subjects experienced life threatening TEAEs, 3 (1.2%) subjects experienced TEAEs of Special Circumstance, 68 (27.9%) subjects experienced ISRs (which included the pre-defined ISR symptoms as described in Table 9), 42 (17.2%) subjects experienced serious TEAEs, 18 (7.4%) subjects experienced AEs leading to discontinuation of study vaccine or withdrawal from the studies, and 2 (0.8%) subjects reported TEAEs that resulted in death (Table 10).

Overall, non-serious TEAEs were experienced by 212 (86.9%) subjects. The most frequent non-serious AEs by Preferred Term (PT) experienced by the safety population were: injection site pain (44 [18.0%] subjects), headache (32 [13.1%] subjects), and depression and diarrhoea (both: 30 [12.3%] subjects). All other events occurred in ≤10% of subjects (Table 11).

Non-serious treatment-related TEAEs were not separated out.

Table 10 Overview of Adverse Events (Safety Population)

	Treatment Group (as Received)							
	ACC 3 µg+QS-21 (N[a]=36) n (%)	**ACC 10 µg+QS-21 (N[a]=60) n (%)**	**ACC 30 µg+QS-21 (N[a]=40) n (%)**	**ACC 10 µg (N[a]=35) n (%)**	**ACC 30 µg (N[a]=12) n (%)**	**QS-21 Alone (N[a]=44) n (%)**	**PBS (N[a]=17) n (%)**	**Total (N[a]=244) n (%)**
Subjects with AEs	35 (97.2)	56 (93.3)	37 (92.5)	32 (91.4)	12 (100)	40 (90.9)	17 (100)	229 (93.9)
Subjects with TEAEs	35 (97.2)	56 (93.3)	36 (90.0)	32 (91.4)	10 (83.3)	40 (90.9)	17 (100)	226 (92.6)
Subjects with related TEAEs	21 (58.3)	28 (46.7)	17 (42.5)	11 (31.4)	2 (16.7)	15 (34.1)	5 (29.4)	99 (40.6)
Subjects with severe TEAEs	5 (13.9)	6 (10.0)	4 (10.0)	5 (14.3)	3 (25.0)	3 (6.8)	2 (11.8)	28 (11.5)
Subjects with life-threatening TEAEs	1 (2.8)	1 (1.7)	0	0	0	1 (2.3)	0	3 (1.2)
Subjects with TEAEs of Special Circumstance	1 (2.8)	0	1 (2.5)	1 (2.9)	0	0	0	3 (1.2)
Subjects with ISRs[c] >0	14 (38.9)	24 (40.0)	16 (40.0)	4 (11.4)	1 (8.3)	7 (15.9)	2 (11.8)	68 (27.9)
Subjects with SAEs	6 (16.7)	11 (18.3)	7 (17.5)	5 (14.3)	5 (41.7)	5 (11.4)	3 (17.6)	42 (17.2)
Subjects with serious TEAEs	6 (16.7)	11 (18.3)	7 (17.5)	5 (14.3)	5 (41.7)	5 (11.4)	3 (17.6)	42 (17.2)
Subjects with serious TEAEs assessed as related	1 (2.8)	0	1 (2.5)	3 (8.6)	0	2 (4.5)	1 (5.9)	8 (3.3)
Subjects with AEs causing discontinuation of study drug or withdrawal from studies	2 (5.6)	4 (6.7)	3 (7.5)	2 (5.7)	2 (16.7)	4 (9.1)	1 (5.9)	18 (7.4)
Subjects who died	0	1 (1.7)	0	0	0	1 (2.3)	0	2 (0.8)

Abbreviations: AE=adverse event; ISR=injection site reaction; N=number subjects in group; n (%)=number (percent) subjects in category; PBS=phosphate-buffered saline; SAE=serious adverse event; TEAE=treatment-emergent adverse event.

[a] The values was used as the denominator for percentages.

[c] ISR includes the pre-defined ISR symptoms as described in Table 9.

Table 11 Treatment-Emergent Non-serious Adverse Events (All Causalities) in ≥5% of Total Subjects by System Organ Class and Preferred Term (Safety population)

	Treatment Group (as Received)							
System Organ Class[a] Preferred Term	**ACC 3 µg+QS-21 (N[b]=36) n (%)**	**ACC 10 µg+QS-21 (N[b]=60) n (%)**	**ACC 30 µg+QS-21 (N[b]=40) n (%)**	**ACC 10 µg (N[b]=35) n (%)**	**ACC 30 µg (N[b]=12) n (%)**	**QS-21 Alone (N[b]=44) n (%)**	**PBS (N[b]=17) n (%)**	**Total (N[b]=244) n (%)**
Any Non-Serious Treatment-Emergent Adverse Event	34 (94.4)	48 (80.0)	35 (87.5)	28 (80.0)	10 (83.3)	40 (90.9)	17 (100)	212 (86.9)
General disorders and administration site conditions	**21 (58.3)**	**30 (50.0)**	**18 (45.0)**	**8 (22.9)**	**5 (41.7)**	**11 (25.0)**	**3 (17.6)**	**96 (39.3)**
Injection site pain	7 (19.4)	17 (28.3)	9 (22.5)	4 (11.4)	1 (8.3)	6 (13.6)	0	44 (18.0)
Fatigue	5 (13.9)	7 (11.7)	4 (10.0)	1 (2.9)	0	5 (11.4)	1 (5.9)	23 (9.4)
Injection site erythema	7 (19.4)	9 (15.0)	6 (15.0)	0	0	1 (2.3)	0	23 (9.4)
Injection site swelling	2 (5.6)	6 (10.0)	7 (17.5)	0	0	0	1 (5.9)	16 (6.6)
Asthenia	1 (2.8)	2 (3.3)	1 (2.5)	3 (8.6)	2 (16.7)	1 (2.3)	0	10 (4.1)
Oedema peripheral	2 (5.6)	2 (3.3)	2 (5.0)	1 (2.9)	1 (8.3)	2 (4.5)	0	10 (4.1)
Injection site pruritus	1 (2.8)	3 (5.0)	3 (7.5)	0	0	0	0	7 (2.9)
Gait disturbance	1 (2.8)	3 (5.0)	0	2 (5.7)	0	0	0	6 (2.5)
Injection site induration	0	4 (6.7)	1 (2.5)	0	0	1 (2.3)	0	6 (2.5)
Malaise	2 (5.6)	1 (1.7)	1 (2.5)	0	2 (16.7)	0	0	6 (2.5)
Injection site bruising	1 (2.8)	0	2 (5.0)	0	0	0	1 (5.9)	4 (1.6)
Injection site reaction[c]	3 (8.3)	0	0	0	0	1 (2.3)	0	4 (1.6)
Injection site warmth	1 (2.8)	3 (5.0)	0	0	0	0	0	4 (1.6)
Pyrexia	0	3 (5.0)	0	1 (2.9)	0	0	0	4 (1.6)
Injection site inflammation	0	0	2 (5.0)	0	0	1 (2.3)	0	3 (1.2)
Irritability	2 (5.6)	0	0	0	1 (8.3)	0	0	3 (1.2)
Injection site haemorrhage	0	0	1 (2.5)	0	0	0	1 (5.9)	2 (0.8)

Table 11 Treatment-Emergent Non-serious Adverse Events (All Causalities) in ≥5% of Total Subjects by System Organ Class and Preferred Term (Safety population)

	Treatment Group (as Received)							
System Organ Class[a] Preferred Term	**ACC 3 µg+QS-21 (N[b]=36) n (%)**	**ACC 10 µg+QS-21 (N[b]=60) n (%)**	**ACC 30 µg+QS-21 (N[b]=40) n (%)**	**ACC 10 µg (N[b]=35) n (%)**	**ACC 30 µg (N[b]=12) n (%)**	**QS-21 Alone (N[b]=44) n (%)**	**PBS (N[b]=17) n (%)**	**Total (N[b]=244) n (%)**
Infections and infestations	**11 (30.6)**	**17 (28.3)**	**9 (22.5)**	**11 (31.4)**	**5 (41.7)**	**14 (31.8)**	**9 (52.9)**	**76 (31.1)**
Urinary tract infection	3 (8.3)	6 (10.0)	2 (5.0)	4 (11.4)	0	2 (4.5)	4 (23.5)	21 (8.6)
Nasopharyngitis	4 (11.1)	6 (10.0)	1 (2.5)	2 (5.7)	0	4 (9.1)	1 (5.9)	18 (7.4)
Upper respiratory tract infection	3 (8.3)	3 (5.0)	5 (12.5)	3 (8.6)	1 (8.3)	1 (2.3)	1 (5.9)	17 (7.0)
Sinusitis	0	2 (3.3)	1 (2.5)	0	1 (8.3)	1 (2.3)	1 (5.9)	6 (2.5)
Bronchitis	3 (8.3)	1 (1.7)	0	0	0	1 (2.3)	0	5 (2.0)
Viral upper respiratory tract infection	1 (2.8)	2 (3.3)	0	1 (2.9)	1 (8.3)	0	0	5 (2.0)
Influenza	0	0	0	0	0	4 (9.1)	0	4 (1.6)
Oral herpes	0	2 (3.3)	0	1 (2.9)	0	0	1 (5.9)	4 (1.6)
Rhinitis	0	1 (1.7)	0	0	1 (8.3)	2 (4.5)	0	4 (1.6)
Lower respiratory tract infection	1 (2.8)	0	0	2 (5.7)	0	0	0	3 (1.2)
Tooth infection	1 (2.8)	0	0	1 (2.9)	0	0	1 (5.9)	3 (1.2)
Fungal skin infection	0	0	0	0	1 (8.3)	0	1 (5.9)	2 (0.8)
Furuncle	0	1 (1.7)	0	0	0	0	1 (5.9)	2 (0.8)
Gingivitis	0	0	0	0	1 (8.3)	1 (2.3)	0	2 (0.8)
Herpes simplex ophthalmic	0	0	0	0	0	0	1 (5.9)	1 (0.4)
Nervous system disorders	**14 (38.9)**	**24 (40.0)**	**11 (27.5)**	**7 (20.0)**	**4 (33.3)**	**11 (25.0)**	**4 (23.5)**	**75 (30.7)**
Headache	3 (8.3)	14 (23.3)	4 (10.0)	2 (5.7)	0	8 (18.2)	1 (5.9)	32 (13.1)
Dizziness	3 (8.3)	7 (11.7)	4 (10.0)	0	1 (8.3)	0	0	15 (6.1)
Cognitive disorder	1 (2.8)	3 (5.0)	1 (2.5)	1 (2.9)	0	1 (2.3)	1 (5.9)	8 (3.3)
Somnolence	1 (2.8)	2 (3.3)	0	0	1 (8.3)	1 (2.3)	1 (5.9)	6 (2.5)
Syncope	0	2 (3.3)	3 (7.5)	1 (2.9)	0	0	0	6 (2.5)

Table 11 Treatment-Emergent Non-serious Adverse Events (All Causalities) in ≥5% of Total Subjects by System Organ Class and Preferred Term (Safety population)

	Treatment Group (as Received)							
System Organ Class[a] Preferred Term	**ACC 3 µg+QS-21 (N[b]=36) n (%)**	**ACC 10 µg+QS-21 (N[b]=60) n (%)**	**ACC 30 µg+QS-21 (N[b]=40) n (%)**	**ACC 10 µg (N[b]=35) n (%)**	**ACC 30 µg (N[b]=12) n (%)**	**QS-21 Alone (N[b]=44) n (%)**	**PBS (N[b]=17) n (%)**	**Total (N[b]=244) n (%)**
Aphasia	2 (5.6)	0	0	1 (2.9)	0	1 (2.3)	0	4 (1.6)
Dementia Alzheimers type	1 (2.8)	0	1 (2.5)	1 (2.9)	0	0	1 (5.9)	4 (1.6)
Apraxia	2 (5.6)	0	0	0	0	0	1 (5.9)	3 (1.2)
Cerebral microhaemorrhage	0	1 (1.7)	0	0	0	1 (2.3)	1 (5.9)	3 (1.2)
Lethargy	3 (8.3)	0	0	0	0	0	0	3 (1.2)
Presyncope	1 (2.8)	0	2 (5.0)	0	0	0	0	3 (1.2)
Clonus	1 (2.8)	0	0	0	1 (8.3)	0	0	2 (0.8)
Extrapyramidal disorder	0	0	0	1 (2.9)	1 (8.3)	0	0	2 (0.8)
Sciatica	0	0	0	2 (5.7)	0	0	0	2 (0.8)
Amnesia	0	0	0	0	0	0	1 (5.9)	1 (0.4)
Memory impairment	0	0	0	0	1 (8.3)	0	0	1 (0.4)
Mental impairment	0	0	0	0	1 (8.3)	0	0	1 (0.4)
Migraine	0	0	0	0	1 (8.3)	0	0	1 (0.4)
Speech disorder	0	0	0	0	1 (8.3)	0	0	1 (0.4)
Unresponsive to stimuli	0	0	0	0	1 (8.3)	0	0	1 (0.4)
Psychiatric disorders	**16 (44.4)**	**11 (18.3)**	**7 (17.5)**	**16 (45.7)**	**4 (33.3)**	**11 (25.0)**	**8 (47.1)**	**73 (29.9)**
Depression	5 (13.9)	4 (6.7)	4 (10.0)	8 (22.9)	3 (25.0)	5 (11.4)	1 (5.9)	30 (12.3)
Agitation	4 (11.1)	4 (6.7)	0	5 (14.3)	2 (16.7)	4 (9.1)	2 (11.8)	21 (8.6)
Anxiety	3 (8.3)	5 (8.3)	1 (2.5)	2 (5.7)	2 (16.7)	2 (4.5)	0	15 (6.1)
Confusional state	2 (5.6)	1 (1.7)	0	2 (5.7)	0	2 (4.5)	0	7 (2.9)
Abnormal dreams	3 (8.3)	0	1 (2.5)	1 (2.9)	0	0	0	5 (2.0)
Aggression	1 (2.8)	1 (1.7)	1 (2.5)	0	0	0	2 (11.8)	5 (2.0)

Table 11 Treatment-Emergent Non-serious Adverse Events (All Causalities) in ≥5% of Total Subjects by System Organ Class and Preferred Term (Safety population)

	Treatment Group (as Received)							
System Organ Class[a] Preferred Term	**ACC 3 µg+QS-21 (N[b]=36) n (%)**	**ACC 10 µg+QS-21 (N[b]=60) n (%)**	**ACC 30 µg+QS-21 (N[b]=40) n (%)**	**ACC 10 µg (N[b]=35) n (%)**	**ACC 30 µg (N[b]=12) n (%)**	**QS-21 Alone (N[b]=44) n (%)**	**PBS (N[b]=17) n (%)**	**Total (N[b]=244) n (%)**
Delusion	1 (2.8)	1 (1.7)	0	1 (2.9)	0	0	2 (11.8)	5 (2.0)
Hallucination	0	1 (1.7)	0	1 (2.9)	0	2 (4.5)	1 (5.9)	5 (2.0)
Hallucination, visual	1 (2.8)	0	0	2 (5.7)	0	0	1 (5.9)	4 (1.6)
Paranoia	2 (5.6)	1 (1.7)	0	0	0	1 (2.3)	0	4 (1.6)
Delirium	1 (2.8)	0	1 (2.5)	0	0	0	1 (5.9)	3 (1.2)
Depressive symptom	0	0	1 (2.5)	0	0	0	2 (11.8)	3 (1.2)
Disorientation	0	1 (1.7)	0	0	1 (8.3)	0	0	2 (0.8)
Hallucination, auditory	0	0	0	0	1 (8.3)	0	0	1 (0.4)
Musculoskeletal and connective tissue disorders	**9 (25.0)**	**14 (23.3)**	**16 (40.0)**	**8 (22.9)**	**2 (16.7)**	**13 (29.5)**	**6 (35.3)**	**68 (27.9)**
Back pain	2 (5.6)	5 (8.3)	3 (7.5)	4 (11.4)	0	4 (9.1)	3 (17.6)	21 (8.6)
Arthralgia	2 (5.6)	5 (8.3)	4 (10.0)	1 (2.9)	0	2 (4.5)	2 (11.8)	16 (6.6)
Musculoskeletal pain	1 (2.8)	3 (5.0)	2 (5.0)	2 (5.7)	0	4 (9.1)	0	12 (4.9)
Pain in extremity	4 (11.1)	3 (5.0)	1 (2.5)	2 (5.7)	0	1 (2.3)	0	11 (4.5)
Osteoarthritis	1 (2.8)	2 (3.3)	4 (10.0)	0	1 (8.3)	0	0	8 (3.3)
Muscle spasms	1 (2.8)	1 (1.7)	1 (2.5)	0	0	1 (2.3)	1 (5.9)	5 (2.0)
Osteoporosis	1 (2.8)	0	1 (2.5)	0	1 (8.3)	1 (2.3)	0	4 (1.6)
Bursitis	1 (2.8)	0	2 (5.0)	0	0	0	0	3 (1.2)
Arthritis	0	0	2 (5.0)	0	0	0	0	2 (0.8)
Torticollis	0	0	0	0	1 (8.3)	0	0	1 (0.4)
Gastrointestinal disorders	**15 (41.7)**	**18 (30.0)**	**8 (20.0)**	**8 (22.9)**	**4 (33.3)**	**12 (27.3)**	**1 (5.9)**	**66 (27.0)**
Diarrhoea	10 (27.8)	6 (10.0)	4 (10.0)	4 (11.4)	2 (16.7)	3 (6.8)	1 (5.9)	30 (12.3)

Table 11 Treatment-Emergent Non-serious Adverse Events (All Causalities) in ≥5% of Total Subjects by System Organ Class and Preferred Term (Safety population)

	Treatment Group (as Received)							
System Organ Class[a] Preferred Term	**ACC 3 µg+QS-21 (N[b]=36) n (%)**	**ACC 10 µg+QS-21 (N[b]=60) n (%)**	**ACC 30 µg+QS-21 (N[b]=40) n (%)**	**ACC 10 µg (N[b]=35) n (%)**	**ACC 30 µg (N[b]=12) n (%)**	**QS-21 Alone (N[b]=44) n (%)**	**PBS (N[b]=17) n (%)**	**Total (N[b]=244) n (%)**
Nausea	5 (13.9)	9 (15.0)	1 (2.5)	2 (5.7)	0	5 (11.4)	1 (5.9)	23 (9.4)
Vomiting	5 (13.9)	4 (6.7)	1 (2.5)	0	2 (16.7)	5 (11.4)	0	17 (7.0)
Abdominal pain	0	4 (6.7)	0	2 (5.7)	1 (8.3)	2 (4.5)	0	9 (3.7)
Constipation	0	2 (3.3)	1 (2.5)	0	2 (16.7)	1 (2.3)	0	6 (2.5)
Gastrooesophageal reflux disease	0	1 (1.7)	2 (5.0)	0	2 (16.7)	0	0	5 (2.0)
Haemorrhoids	1 (2.8)	1 (1.7)	1 (2.5)	0	1 (8.3)	0	0	4 (1.6)
Functional gastrointestinal disorder	0	0	0	0	1 (8.3)	0	0	1 (0.4)
Injury, poisoning and procedural complications	**7 (19.4)**	**9 (15.0)**	**7 (17.5)**	**5 (14.3)**	**3 (25.0)**	**12 (27.3)**	**4 (23.5)**	**47 (19.3)**
Fall	3 (8.3)	3 (5.0)	3 (7.5)	4 (11.4)	1 (8.3)	9 (20.5)	0	23 (9.4)
Contusion	1 (2.8)	1 (1.7)	3 (7.5)	1 (2.9)	0	3 (6.8)	1 (5.9)	10 (4.1)
Laceration	1 (2.8)	3 (5.0)	1 (2.5)	0	1 (8.3)	1 (2.3)	0	7 (2.9)
Arthropod bite	2 (5.6)	2 (3.3)	0	0	0	1 (2.3)	1 (5.9)	6 (2.5)
Procedural pain	2 (5.6)	0	2 (5.0)	1 (2.9)	0	1 (2.3)	0	6 (2.5)
Excoriation	0	3 (5.0)	0	0	0	0	0	3 (1.2)
Wound	0	0	1 (2.5)	0	1 (8.3)	1 (2.3)	0	3 (1.2)
Thermal burn	1 (2.8)	0	0	0	0	0	1 (5.9)	2 (0.8)
Skin injury	0	0	0	0	0	0	1 (5.9)	1 (0.4)
Spinal compression fracture	0	0	0	0	1 (8.3)	0	0	1 (0.4)
Tooth fracture	0	0	0	0	0	0	1 (5.9)	1 (0.4)

Table 11 Treatment-Emergent Non-serious Adverse Events (All Causalities) in ≥5% of Total Subjects by System Organ Class and Preferred Term (Safety population)

	Treatment Group (as Received)							
System Organ Class[a] Preferred Term	**ACC 3 µg+QS-21 (N[b]=36) n (%)**	**ACC 10 µg+QS-21 (N[b]=60) n (%)**	**ACC 30 µg+QS-21 (N[b]=40) n (%)**	**ACC 10 µg (N[b]=35) n (%)**	**ACC 30 µg (N[b]=12) n (%)**	**QS-21 Alone (N[b]=44) n (%)**	**PBS (N[b]=17) n (%)**	**Total (N[b]=244) n (%)**
Respiratory, thoracic and mediastinal disorders	**8 (22.2)**	**8 (13.3)**	**3 (7.5)**	**2 (5.7)**	**2 (16.7)**	**5 (11.4)**	**3 (17.6)**	**31 (12.7)**
Cough	6 (16.7)	4 (6.7)	2 (5.0)	2 (5.7)	2 (16.7)	4 (9.1)	2 (11.8)	22 (9.0)
Oropharyngeal pain	1 (2.8)	3 (5.0)	1 (2.5)	0	0	0	0	5 (2.0)
Rhinorrhoea	2 (5.6)	0	0	0	0	1 (2.3)	0	3 (1.2)
Chronic obstructive pulmonary disease	0	1 (1.7)	0	0	0	0	1 (5.9)	2 (0.8)
Pleural effusion	0	0	0	0	0	0	1 (5.9)	1 (0.4)
Vascular disorders	**4 (11.1)**	**4 (6.7)**	**4 (10.0)**	**3 (8.6)**	**1 (8.3)**	**9 (20.5)**	**2 (11.8)**	**27 (11.1)**
Hypertension	4 (11.1)	3 (5.0)	1 (2.5)	3 (8.6)	1 (8.3)	5 (11.4)	1 (5.9)	18 (7.4)
Haematoma	0	1 (1.7)	1 (2.5)	0	0	4 (9.1)	1 (5.9)	7 (2.9)
Orthostatic hypotension	0	0	2 (5.0)	0	0	0	0	2 (0.8)
Investigations	**5 (13.9)**	**6 (10.0)**	**4 (10.0)**	**2 (5.7)**	**3 (25.0)**	**3 (6.8)**	**3 (17.6)**	**26 (10.7)**
Weight decreased	1 (2.8)	4 (6.7)	2 (5.0)	0	2 (16.7)	1 (2.3)	1 (5.9)	11 (4.5)
Weight increased	1 (2.8)	1 (1.7)	1 (2.5)	2 (5.7)	0	2 (4.5)	1 (5.9)	8 (3.3)
Blood creatine phosphokinase increased	3 (8.3)	1 (1.7)	0	0	0	0	1 (5.9)	5 (2.0)
Blood urea increased	0	0	1 (2.5)	0	0	0	1 (5.9)	2 (0.8)
Blood albumin decreased	0	0	0	0	1 (8.3)	0	0	1 (0.4)
Blood creatinine increased	0	0	0	0	0	0	1 (5.9)	1 (0.4)
Haematocrit decreased	0	0	0	0	1 (8.3)	0	0	1 (0.4)
Haemoglobin decreased	0	0	0	0	1 (8.3)	0	0	1 (0.4)
Skin and subcutaneous tissue disorders	**8 (22.2)**	**4 (6.7)**	**2 (5.0)**	**4 (11.4)**	**2 (16.7)**	**1 (2.3)**	**3 (17.6)**	**24 (9.8)**
Rash	3 (8.3)	1 (1.7)	1 (2.5)	2 (5.7)	0	1 (2.3)	0	8 (3.3)

Table 11 Treatment-Emergent Non-serious Adverse Events (All Causalities) in ≥5% of Total Subjects by System Organ Class and Preferred Term (Safety population)

	Treatment Group (as Received)							
System Organ Class[a] Preferred Term	**ACC 3 µg+QS-21 (N[b]=36) n (%)**	**ACC 10 µg+QS-21 (N[b]=60) n (%)**	**ACC 30 µg+QS-21 (N[b]=40) n (%)**	**ACC 10 µg (N[b]=35) n (%)**	**ACC 30 µg (N[b]=12) n (%)**	**QS-21 Alone (N[b]=44) n (%)**	**PBS (N[b]=17) n (%)**	**Total (N[b]=244) n (%)**
Skin lesion	4 (11.1)	3 (5.0)	0	1 (2.9)	0	0	0	8 (3.3)
Hyperhidrosis	1 (2.8)	0	1 (2.5)	1 (2.9)	0	0	1 (5.9)	4 (1.6)
Ecchymosis	0	0	0	0	1 (8.3)	0	1 (5.9)	2 (0.8)
Petechiae	1 (2.8)	0	0	0	1 (8.3)	0	0	2 (0.8)
Intertrigo	0	0	0	0	0	0	1 (5.9)	1 (0.4)
Rash pruritic	0	0	0	0	1 (8.3)	0	0	1 (0.4)
Urticaria	0	0	0	0	0	0	1 (5.9)	1 (0.4)
Renal and urinary disorders	**2 (5.6)**	**1 (1.7)**	**3 (7.5)**	**2 (5.7)**	**2 (16.7)**	**0**	**2 (11.8)**	**12 (4.9)**
Urinary incontinence	2 (5.6)	1 (1.7)	3 (7.5)	2 (5.7)	1 (8.3)	0	0	9 (3.7)
Incontinence	0	0	0	0	1 (8.3)	0	1 (5.9)	2 (0.8)
Hydronephrosis	0	0	0	0	0	0	1 (5.9)	1 (0.4)
Renal failure	0	0	0	0	0	0	1 (5.9)	1 (0.4)
Blood and lymphatic system disorders	**1 (2.8)**	**1 (1.7)**	**1 (2.5)**	**1 (2.9)**	**0**	**2 (4.5)**	**2 (11.8)**	**8 (3.3)**
Anaemia	1 (2.8)	1 (1.7)	1 (2.5)	1 (2.9)	0	2 (4.5)	1 (5.9)	7 (2.9)
Iron deficiency anaemia	0	0	0	0	0	0	1 (5.9)	1 (0.4)
Eye disorders	**0**	**3 (5.0)**	**1 (2.5)**	**1 (2.9)**	**1 (8.3)**	**0**	**0**	**6 (2.5)**
Cataract	0	3 (5.0)	1 (2.5)	1 (2.9)	1 (8.3)	0	0	6 (2.5)
Eye movement disorder	0	0	0	0	1 (8.3)	0	0	1 (0.4)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**0**	**2 (3.3)**	**0**	**3 (8.6)**	**1 (8.3)**	**0**	**0**	**6 (2.5)**
Squamous cell carcinoma	0	1 (1.7)	0	3 (8.6)	0	0	0	4 (1.6)

Table 11 Treatment-Emergent Non-serious Adverse Events (All Causalities) in ≥5% of Total Subjects by System Organ Class and Preferred Term (Safety population)

	Treatment Group (as Received)							
System Organ Class[a] Preferred Term	**ACC 3 µg+QS-21 (N[b]=36) n (%)**	**ACC 10 µg+QS-21 (N[b]=60) n (%)**	**ACC 30 µg+QS-21 (N[b]=40) n (%)**	**ACC 10 µg (N[b]=35) n (%)**	**ACC 30 µg (N[b]=12) n (%)**	**QS-21 Alone (N[b]=44) n (%)**	**PBS (N[b]=17) n (%)**	**Total (N[b]=244) n (%)**
Basal cell carcinoma	0	1 (1.7)	0	1 (2.9)	1 (8.3)	0	0	3 (1.2)
Metabolism and nutrition disorders	**0**	**0**	**0**	**1 (2.9)**	**3 (25.0)**	**0**	**0**	**4 (1.6)**
Decreased appetite	0	0	0	1 (2.9)	2 (16.7)	0	0	3 (1.2)
Hyponatraemia	0	0	0	0	1 (8.3)	0	0	1 (0.4)
Reproductive system and breast disorders	**0**	**0**	**0**	**0**	**0**	**0**	**1 (5.9)**	**1 (0.4)**
Breast swelling	0	0	0	0	0	0	1 (5.9)	1 (0.4)

Abbreviations: ISR=injection site reaction; N=number subjects in group; n (%)=number (percent) subjects in category; PBS=phosphate-buffered saline.

[a] Totals for the number of subjects at a higher level are not necessarily the sum of those at the lower levels since a subject may report two or more different adverse events within the higher level category.

[b] The value was used as the denominator for percentages.

[c] ISR includes the pre-defined ISR symptoms as described in Table 9.

Classifications of adverse events are based on the Medical Dictionary for Regulatory Activities (MedDRA 15.1).

Serious Adverse Events

Overall, serious TEAEs were experienced by 42 (17.2%) subjects.

The most frequent serious TEAEs by System Organ Class (SOC) experienced by the safety population were: nervous system disorders (13 [5.3%] subjects), neoplasms benign, malignant and unspecified (incl cysts and polyps) (8 [3.3%] subjects), and cardiac disorders (5 [2.0%] subjects).

The only serious TEAEs by PT experienced by more than 1 subject of the safety population were: dizziness, syncope, vasogenic cerebral oedema, myocardial infarction, gastroenteritis, urinary tract infection, dehydration, renal failure acute, and vertigo positional; all these events were experienced by 2 (0.8%) subjects (Table 12).

By total, 8 (3.3%) subjects experienced serious TEAEs which were assessed by the investigator as related to the study vaccine. Of these, the only event experienced by more than 1 subject of the safety population was vasogenic cerebral oedema experienced by 2 (0.8%) subjects (Table 13).

Table 12 Treatment-Emergent Serious Adverse Events (All Causalities) by System Organ Class and Preferred Term (Safety population)

	Treatment Group (as Received)							
System Organ Class[a] Preferred Term	**ACC 3 µg+QS-21 (N[b]=36) n (%)**	**ACC 10 µg+QS-21 (N[b]=60) n (%)**	**ACC 30 µg+QS-21 (N[b]=40) n (%)**	**ACC 10 µg (N[b]=35) n (%)**	**ACC 30 µg (N[b]=12) n (%)**	**QS-21 Alone (N[b]=44) n (%)**	**PBS (N[b]=17) n (%)**	**Total (N[b]=244) n (%)**
Any Serious Treatment-Emergent Adverse Event	6 (16.7)	11 (18.3)	7 (17.5)	5 (14.3)	5 (41.7)	5 (11.4)	3 (17.6)	42 (17.2)
Nervous system disorders	**2 (5.6)**	**2 (3.3)**	**3 (7.5)**	**3 (8.6)**	**1 (8.3)**	**2 (4.5)**	**0**	**13 (5.3)**
Dizziness	1 (2.8)	1 (1.7)	0	0	0	0	0	2 (0.8)
Syncope	1 (2.8)	0	1 (2.5)	0	0	0	0	2 (0.8)
Vasogenic cerebral oedema	0	0	1 (2.5)	1 (2.9)	0	0	0	2 (0.8)
Ataxia	0	0	0	0	0	1 (2.3)	0	1 (0.4)
Balance disorder	0	0	0	0	0	1 (2.3)	0	1 (0.4)
Bradykinesia	0	0	0	0	0	1 (2.3)	0	1 (0.4)
Cerebrovascular accident	0	0	0	0	1 (8.3)	0	0	1 (0.4)
Convulsion	0	0	1 (2.5)	0	0	0	0	1 (0.4)
Dementia Alzheimers type	0	0	0	1 (2.9)	0	0	0	1 (0.4)
Dystonia	0	0	0	0	0	1 (2.3)	0	1 (0.4)
Embolic stroke	0	0	0	1 (2.9)	0	0	0	1 (0.4)
Headache	0	0	0	0	0	1 (2.3)	0	1 (0.4)
Transient ischaemic attack	0	1 (1.7)	0	0	0	0	0	1 (0.4)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**0**	**3 (5.0)**	**1 (2.5)**	**1 (2.9)**	**1 (8.3)**	**1 (2.3)**	**1 (5.9)**	**8 (3.3)**
Basal cell carcinoma	0	1 (1.7)	0	0	0	0	0	1 (0.4)
Carcinoid tumour pulmonary	0	0	0	0	0	0	1 (5.9)	1 (0.4)
Lung cancer metastatic	0	0	0	0	0	1 (2.3)	0	1 (0.4)
Lung neoplasm malignant	0	0	0	0	1 (8.3)	0	0	1 (0.4)

Table 12 Treatment-Emergent Serious Adverse Events (All Causalities) by System Organ Class and Preferred Term (Safety population)

	Treatment Group (as Received)							
System Organ Class[a] Preferred Term	**ACC 3 µg+QS-21 (N[b]=36) n (%)**	**ACC 10 µg+QS-21 (N[b]=60) n (%)**	**ACC 30 µg+QS-21 (N[b]=40) n (%)**	**ACC 10 µg (N[b]=35) n (%)**	**ACC 30 µg (N[b]=12) n (%)**	**QS-21 Alone (N[b]=44) n (%)**	**PBS (N[b]=17) n (%)**	**Total (N[b]=244) n (%)**
Non-Hodgkins lymphoma	0	1 (1.7)	0	0	0	0	0	1 (0.4)
Prostate cancer	0	0	0	1 (2.9)	0	0	0	1 (0.4)
Squamous cell carcinoma	0	1 (1.7)	0	0	0	0	0	1 (0.4)
Uterine cancer	0	0	1 (2.5)	0	0	0	0	1 (0.4)
Cardiac disorders	**2 (5.6)**	**2 (3.3)**	**0**	**0**	**0**	**0**	**1 (5.9)**	**5 (2.0)**
Myocardial infarction	1 (2.8)	1 (1.7)	0	0	0	0	0	2 (0.8)
Atrial fibrillation	0	0	0	0	0	0	1 (5.9)	1 (0.4)
Cardiac arrest	0	1 (1.7)	0	0	0	0	0	1 (0.4)
Cyanosis	1 (2.8)	0	0	0	0	0	0	1 (0.4)
Infections and infestations	**1 (2.8)**	**0**	**2 (5.0)**	**0**	**0**	**0**	**1 (5.9)**	**4 (1.6)**
Gastroenteritis	1 (2.8)	0	1 (2.5)	0	0	0	0	2 (0.8)
Urinary tract infection	0	0	1 (2.5)	0	0	0	1 (5.9)	2 (0.8)
Vascular disorders	**2 (5.6)**	**0**	**1 (2.5)**	**0**	**0**	**0**	**1 (5.9)**	**4 (1.6)**
Deep vein thrombosis	0	0	0	0	0	0	1 (5.9)	1 (0.4)
Hypotension	0	0	1 (2.5)	0	0	0	0	1 (0.4)
Orthostatic hypotension	1 (2.8)	0	0	0	0	0	0	1 (0.4)
Vasculitis	1 (2.8)	0	0	0	0	0	0	1 (0.4)
General disorders and administration site conditions	**1 (2.8)**	**1 (1.7)**	**0**	**1 (2.9)**	**0**	**0**	**0**	**3 (1.2)**
Fatigue	1 (2.8)	0	0	0	0	0	0	1 (0.4)
Feeling cold	1 (2.8)	0	0	0	0	0	0	1 (0.4)
Gait disturbance	0	0	0	1 (2.9)	0	0	0	1 (0.4)

Table 12 Treatment-Emergent Serious Adverse Events (All Causalities) by System Organ Class and Preferred Term (Safety population)

	Treatment Group (as Received)							
System Organ Class[a] Preferred Term	**ACC 3 µg+QS-21 (N[b]=36) n (%)**	**ACC 10 µg+QS-21 (N[b]=60) n (%)**	**ACC 30 µg+QS-21 (N[b]=40) n (%)**	**ACC 10 µg (N[b]=35) n (%)**	**ACC 30 µg (N[b]=12) n (%)**	**QS-21 Alone (N[b]=44) n (%)**	**PBS (N[b]=17) n (%)**	**Total (N[b]=244) n (%)**
Malaise	0	1 (1.7)	0	0	0	0	0	1 (0.4)
Oedema peripheral	1 (2.8)	0	0	0	0	0	0	1 (0.4)
Metabolism and nutrition disorders	**0**	**0**	**1 (2.5)**	**0**	**1 (8.3)**	**0**	**1 (5.9)**	**3 (1.2)**
Dehydration	0	0	1 (2.5)	0	0	0	1 (5.9)	2 (0.8)
Decreased appetite	0	0	0	0	1 (8.3)	0	0	1 (0.4)
Psychiatric disorders	**0**	**0**	**0**	**0**	**1 (8.3)**	**1 (2.3)**	**1 (5.9)**	**3 (1.2)**
Agitation	0	0	0	0	1 (8.3)	0	0	1 (0.4)
Confusional state	0	0	0	0	1 (8.3)	0	0	1 (0.4)
Delusion	0	0	0	0	0	0	1 (5.9)	1 (0.4)
Hallucination	0	0	0	0	1 (8.3)	0	0	1 (0.4)
Restlessness	0	0	0	0	0	1 (2.3)	0	1 (0.4)
Renal and urinary disorders	**1 (2.8)**	**1 (1.7)**	**0**	**0**	**0**	**1 (2.3)**	**0**	**3 (1.2)**
Renal failure acute	0	1 (1.7)	0	0	0	1 (2.3)	0	2 (0.8)
Stress urinary incontinence	1 (2.8)	0	0	0	0	0	0	1 (0.4)
Ear and labyrinth disorders	**0**	**2 (3.3)**	**0**	**0**	**0**	**0**	**0**	**2 (0.8)**
Vertigo positional	0	2 (3.3)	0	0	0	0	0	2 (0.8)
Gastrointestinal disorders	**1 (2.8)**	**1 (1.7)**	**0**	**0**	**0**	**0**	**0**	**2 (0.8)**
Gastrointestinal haemorrhage	1 (2.8)	0	0	0	0	0	0	1 (0.4)
Intestinal obstruction	0	1 (1.7)	0	0	0	0	0	1 (0.4)
Hepatobiliary disorders	**0**	**0**	**0**	**0**	**1 (8.3)**	**1 (2.3)**	**0**	**2 (0.8)**
Bile duct stone	0	0	0	0	0	1 (2.3)	0	1 (0.4)
Cholelithiasis	0	0	0	0	1 (8.3)	0	0	1 (0.4)

Table 12 Treatment-Emergent Serious Adverse Events (All Causalities) by System Organ Class and Preferred Term (Safety population)

	Treatment Group (as Received)							
System Organ Class[a] Preferred Term	**ACC 3 µg+QS-21 (N[b]=36) n (%)**	**ACC 10 µg+QS-21 (N[b]=60) n (%)**	**ACC 30 µg+QS-21 (N[b]=40) n (%)**	**ACC 10 µg (N[b]=35) n (%)**	**ACC 30 µg (N[b]=12) n (%)**	**QS-21 Alone (N[b]=44) n (%)**	**PBS (N[b]=17) n (%)**	**Total (N[b]=244) n (%)**
Injury, poisoning and procedural complications	**0**	**0**	**0**	**1 (2.9)**	**0**	**0**	**1 (5.9)**	**2 (0.8)**
Clavicle fracture	0	0	0	0	0	0	1 (5.9)	1 (0.4)
Humerus fracture	0	0	0	1 (2.9)	0	0	0	1 (0.4)
Musculoskeletal and connective tissue disorders	**0**	**0**	**2 (5.0)**	**0**	**0**	**0**	**0**	**2 (0.8)**
Arthralgia	0	0	1 (2.5)	0	0	0	0	1 (0.4)
Intervertebral disc protrusion	0	0	1 (2.5)	0	0	0	0	1 (0.4)
Respiratory, thoracic and mediastinal disorders	**0**	**0**	**0**	**0**	**0**	**0**	**1 (5.9)**	**1 (0.4)**
Pulmonary embolism	0	0	0	0	0	0	1 (5.9)	1 (0.4)
Skin and subcutaneous tissue disorders	**1 (2.8)**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (0.4)**
Skin erosion	1 (2.8)	0	0	0	0	0	0	1 (0.4)

Abbreviations: N=number subjects in group; n (%)=number (percent) subjects in category; PBS=phosphate-buffered saline.

[a] Totals for the number of subjects at a higher level are not necessarily the sum of those at the lower levels since a subject may report two or more different adverse events within the higher level category.

[b] The value was used as the denominator for percentages.

Classifications of adverse events are based on the Medical Dictionary for Regulatory Activities (MedDRA 15.1).

Table 13 Treatment-Emergent Serious Adverse Events (Treatment-related) by System Organ Class and Preferred Term (Safety population)

	Treatment Group (as Received)							
System Organ Class[a] Preferred Term	**ACC 3 µg+QS-21 (N[b]=36) n (%)**	**ACC 10 µg +QS-21 (N[b]=60) n (%)**	**ACC 30 µg+QS-21 (N[b]=40) n (%)**	**ACC 10 µg (N[b]=35) n (%)**	**ACC 30 µg (N[b]=12) n (%)**	**QS-21 Alone (N[b]=44) n (%)**	**PBS (N[b]=17) n (%)**	**Total (N[b]=244) n (%)**
Any Treatment-Related serious TEAEs	1 (2.8)	0	1 (2.5)	3 (8.6)	0	2 (4.5)	1 (5.9)	8 (3.3)
Nervous system disorders	**0**	**0**	**1 (2.5)**	**3 (8.6)**	**0**	**1 (2.3)**	**0**	**5 (2.0)**
Vasogenic cerebral oedema	0	0	1 (2.5)	1 (2.9)	0	0	0	2 (0.8)
Dementia Alzheimer's type	0	0	0	1 (2.9)	0	0	0	1 (0.4)
Dystonia	0	0	0	0	0	1 (2.3)	0	1 (0.4)
Embolic stroke	0	0	0	1 (2.9)	0	0	0	1 (0.4)
Cardiac disorders	**1 (2.8)**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (0.4)**
Cyanosis	1 (2.8)	0	0	0	0	0	0	1 (0.4)
Vascular disorders	**1 (2.8)**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (0.4)**
Vasculitis	1 (2.8)	0	0	0	0	0	0	1 (0.4)
General disorders and administration site conditions	**1 (2.8)**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (0.4)**
Fatigue	1 (2.8)	0	0	0	0	0	0	1 (0.4)
Feeling cold	1 (2.8)	0	0	0	0	0	0	1 (0.4)
Oedema peripheral	1 (2.8)	0	0	0	0	0	0	1 (0.4)
Psychiatric disorders	**0**	**0**	**0**	**0**	**0**	**0**	**1 (5.9)**	**1 (0.4)**
Delusion	0	0	0	0	0	0	1 (5.9)	1 (0.4)
Renal and urinary disorders	**0**	**0**	**0**	**0**	**0**	**1 (2.3)**	**0**	**1 (0.4)**
Renal failure acute	0	0	0	0	0	1 (2.3)	0	1 (0.4)
Skin and subcutaneous tissue disorders	**1 (2.8)**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (0.4)**
Skin erosion	1 (2.8)	0	0	0	0	0	0	1 (0.4)

Table 13 Treatment-Emergent Serious Adverse Events (Treatment-related) by System Organ Class and Preferred Term (Safety population)

	Treatment Group (as Received)							
System Organ Class[a] Preferred Term	**ACC 3 µg+QS-21 (N[b]=36) n (%)**	**ACC 10 µg +QS-21 (N[b]=60) n (%)**	**ACC 30 µg+QS-21 (N[b]=40) n (%)**	**ACC 10 µg (N[b]=35) n (%)**	**ACC 30 µg (N[b]=12) n (%)**	**QS-21 Alone (N[b]=44) n (%)**	**PBS (N[b]=17) n (%)**	**Total (N[b]=244) n (%)**

Abbreviations: N=number subjects in group; n (%)=number (percent) of subjects in each category; PBS=phosphate-buffered saline; TEAE=treatment-emergent adverse event.

[a] Totals for the number of subjects at a higher level are not necessarily the sum of those at the lower levels since a subject may report two or more different adverse events within the higher level category.

[b] The value was used as the denominator for percentages.

Note: For each subject, adverse events are reported for the closest drug relationship observed.

Classifications of adverse events are based on the Medical Dictionary for Regulatory Activities (MedDRA 15.1).

Any Adverse Event Causing Discontinuation of the Study Drug or Withdrawal from the Studies

AEs leading to discontinuation of study vaccine or withdrawal from the studies were experienced by 18 (7.4%) subjects. The only AE leading to discontinuation of study vaccine or withdrawal from studies experienced by more than 1 subject of the safety population was myocardial infarction (2 [0.8%] subjects). The events of myocardial infarction were not considered as related to study vaccine by the investigator (Table 14).

Table 14 Adverse Events Leading to Discontinuation of Study Drug or Withdrawal from the Studies (Safety Population)

	Treatment Group (as Received)							
System Organ Class[a] Preferred Term	**ACC 3 µg+QS-21 (N[b]=36) n (%)**	**ACC 10 µg+QS-21 (N[b]=60) n (%)**	**ACC 30 µg+QS-21 (N[b]=40) n (%)**	**ACC 10 µg (N[b]=35) n (%)**	**ACC 30 µg (N[b]=12) n (%)**	**QS-21 Alone (N[b]=44) n (%)**	**PBS (N[b]=17) n (%)**	**Total (N[b]=244) n (%)**
Any Adverse Event Causing Discontinuation of Study Drug or Withdrawal from the Studies	2 (5.6)	4 (6.7)	3 (7.5)	2 (5.7)	2 (16.7)	4 (9.1)	1 (5.9)	18 (7.4)
Nervous system disorders	**0**	**0**	**1 (2.5)**	**2 (5.7)**	**1 (8.3)**	**2 (4.5)**	**0**	**6 (2.5)**
Ataxia	0	0	0	0	0	1 (2.3)	0	1 (0.4)
Cerebral ischaemia	0	0	0	0	0	1 (2.3)	0	1 (0.4)
Cerebrovascular accident	0	0	0	0	1 (8.3)	0	0	1 (0.4)
Embolic stroke	0	0	0	1 (2.9)	0	0	0	1 (0.4)
Lacunar infarction	0	0	1 (2.5)	0	0	0	0	1 (0.4)
Vasogenic cerebral oedema	0	0	0	1 (2.9)	0	0	0	1 (0.4)
Cardiac disorders	**1 (2.8)**	**2 (3.3)**	**0**	**0**	**0**	**0**	**1 (5.9)**	**4 (1.6)**
Myocardial infarction	1 (2.8)	1 (1.7)	0	0	0	0	0	2 (0.8)
Atrial fibrillation	0	0	0	0	0	0	1 (5.9)	1 (0.4)
Cardiac arrest	0	1 (1.7)	0	0	0	0	0	1 (0.4)
Neoplasms benign, malignant and unspecified (including cysts and polyps)	**0**	**2 (3.3)**	**0**	**0**	**1 (8.3)**	**0**	**0**	**3 (1.2)**
Lung neoplasm malignant	0	0	0	0	1 (8.3)	0	0	1 (0.4)
Meningioma	0	1 (1.7)	0	0	0	0	0	1 (0.4)
Non-Hodgkins lymphoma	0	1 (1.7)	0	0	0	0	0	1 (0.4)
Vascular disorders	**1 (2.8)**	**0**	**0**	**0**	**0**	**1 (2.3)**	**0**	**2 (0.8)**
Hypertension	0	0	0	0	0	1 (2.3)	0	1 (0.4)
Vasculitis	1 (2.8)	0	0	0	0	0	0	1 (0.4)

Table 14 Adverse Events Leading to Discontinuation of Study Drug or Withdrawal from the Studies (Safety Population)

	Treatment Group (as Received)							
System Organ Class[a] Preferred Term	**ACC 3 µg+QS-21 (N[b]=36) n (%)**	**ACC 10 µg+QS-21 (N[b]=60) n (%)**	**ACC 30 µg+QS-21 (N[b]=40) n (%)**	**ACC 10 µg (N[b]=35) n (%)**	**ACC 30 µg (N[b]=12) n (%)**	**QS-21 Alone (N[b]=44) n (%)**	**PBS (N[b]=17) n (%)**	**Total (N[b]=244) n (%)**
General disorders and administration site conditions	**0**	**0**	**1 (2.5)**	**0**	**0**	**0**	**0**	**1 (0.4)**
Injection site vesicles	0	0	1 (2.5)	0	0	0	0	1 (0.4)
Infections and infestations	**0**	**0**	**0**	**0**	**0**	**0**	**1 (5.9)**	**1 (0.4)**
Urinary tract infection	0	0	0	0	0	0	1 (5.9)	1 (0.4)
Investigations	**0**	**0**	**0**	**0**	**0**	**0**	**1 (5.9)**	**1 (0.4)**
Blood creatinine increased	0	0	0	0	0	0	1 (5.9)	1 (0.4)
Blood urea increased	0	0	0	0	0	0	1 (5.9)	1 (0.4)
Metabolism and nutrition disorders	**0**	**0**	**0**	**0**	**0**	**0**	**1 (5.9)**	**1 (0.4)**
Dehydration	0	0	0	0	0	0	1 (5.9)	1 (0.4)
Psychiatric disorders	**0**	**0**	**1 (2.5)**	**0**	**0**	**0**	**0**	**1 (0.4)**
Aggression	0	0	1 (2.5)	0	0	0	0	1 (0.4)
Alcoholism	0	0	1 (2.5)	0	0	0	0	1 (0.4)
Renal and urinary disorders	**0**	**0**	**0**	**0**	**0**	**1 (2.3)**	**0**	**1 (0.4)**
Renal failure acute	0	0	0	0	0	1 (2.3)	0	1 (0.4)

Abbreviations: N=number subjects in group; n (%)=number (percent) of subjects in each category; PBS=phosphate-buffered saline.

[a] Totals for the number of subjects at a higher level are not necessarily the sum of those at the lower levels since a subject may report two or more different adverse events within the higher level category.

[b] The value was used as the denominator for percentages.

Classifications of adverse events are based on the Medical Dictionary for Regulatory Activities (MedDRA 15.1).

Subjects with Adverse Events of Special Circumstance

Three (1.2%) subjects experienced TEAEs of Special Circumstance. The TEAEs of Special Circumstance were all assessed as related to study vaccine by the investigator. Of these, 2 [0.8%] subjects experienced vasogenic cerebral oedema (1 subject each, in the ACC 30 µg+QS-21 and ACC 10 µg groups) and 1 [0.4%] subject (in the ACC 3 µg+QS-21 group) experienced vasculitis (Table 15).

Table 15 Treatment-Emergent Adverse Events of Special Circumstance (Safety Population)

	Treatment Group (as Received)							
Preferred Term	ACC 3 µg+QS-21 (N[a]=36) n (%)	ACC 10 µg+QS-21 (N[a]=60) n (%)	ACC 30 µg+QS-21 (N[a]=40) n (%)	ACC 10 µg (N[a]=35) n (%)	ACC 30 µg (N[a]=12) n (%)	QS-21 Alone (N[a]=44) n (%)	PBS (N[a]=17) n (%)	Total (N[a]=244) n (%)
Any TEAE of Special Circumstance[b]	1 (2.8)	0	1 (2.5)	1 (2.9)	0	0	0	3 (1.2)
Vasogenic cerebral oedema	0	0	1 (2.5)	1 (2.9)	0	0	0	2 (0.8)
Vasculitis	1 (2.8)	0	0	0	0	0	0	1 (0.4)

Abbreviations: N=number subjects in group; n (%)=number (percent) of subjects in each category; PBS=phosphate-buffered saline; TEAE=treatment-emergent adverse event.
[a] The value was used as the denominator for percentages.
[b] Includes TEAEs of Special Circumstance related to study drug (vasogenic cerebral oedema, intracranial haemorrhage including cerebral haemorrhage, subdural haemorrhage, extradural haematoma, subarachnoid haemorrhage, vasculitis, and the following immune-mediated events following an injection: anaphylaxis, angioedema, urticaria, and clinical syndrome diagnostic of serum sickness).

Classifications of adverse events are based on the Medical Dictionary for Regulatory Activities (MedDRA 15.1).

Deaths

In total, 2 (0.8%) subjects died during the studies. In the ACC 10 µg+QS-21 group, 1 subject died from cardiac arrest and in the QS-21 alone group 1 subject died from metastatic lung cancer. Both events were considered as not related to study vaccine by the investigator (Table 16).

Table 16 Deaths (Safety population)

	Treatment Group (as Received)							
Preferred Term	ACC 3 µg+QS-21 (N[a]=36) n (%)	ACC 10 µg+QS-21 (N[a]=60) n (%)	ACC 30 µg+QS-21 (N[a]=40) n (%)	ACC 10 µg (N[a]=35) n (%)	ACC 30 µg (N[a]=12) n (%)	QS-21 Alone (N[a]=44) n (%)	PBS (N[a]=17) n (%)	Total (N[a]=244) n (%)
Any Adverse Event Resulting in Death	0	1 (1.7)	0	0	0	1 (2.3)	0	2 (0.8)
Cardiac arrest	0	1 (1.7)	0	0	0	0	0	1 (0.4)
Lung cancer metastatic	0	0	0	0	0	1 (2.3)	0	1 (0.4)

Abbreviations: N=number subjects in group; n (%)=number (percent) of subjects in each category; PBS=phosphate-buffered saline.
[a] The value was used as the denominator for percentages.
Classifications of adverse events are based on the Medical Dictionary for Regulatory Activities (MedDRA 15.1).

Clinical Laboratory Evaluation

At least one change from baseline of PCI in a laboratory assessment was experienced by 154 (63.1%) subjects. The most frequent findings, by total were positive urine protein/albumin (83 [34.0%] subjects), positive urine hemoglobin/blood (27 [11.1%] subjects), and increased triglycerides of ≥3.7 mmol/L (26 [10.7%] subjects). A dose dependent change from baseline in urine protein/albumin and urine blood was observed in the ACC+QS-21 vaccine groups. There were no potential cases of drug induced liver injury (Table 17).

To further evaluate this potential safety signal, a urine protein to urine creatinine ratio was obtained from the 10 µg cohort and all subsequent cohorts/subjects with urinalysis positive for protein. The total number of subjects with a urine protein/urine creatinine ratio ≥0.2 at any time after screening was 15 (6.1%) subjects. Among these subjects only 3 (2 subjects in the ACC 10µg+QS-21 group and 1 subject in the QS-21 group) had a change from baseline of serum creatinine >1.5 x upper limit of normal (ULN) and 1 subject (same subject in the QS-21 group) had a change from baseline of blood urea nitrogen (BUN) >1.5 x ULN.

Vital Signs, Physical and Neurological Examinations, Electrocardiogram, and Suicidality Assessment

There were no clinically significant safety signals in immune complex, complement, anti-diphtheria or T-cell data, vital signs, ECGs, or suicidality evaluations.

Table 17 Laboratory Test Results Change from Baseline of Potential Clinical Importance (Safety Population)

Data Analysis Interval: On-therapy[b]	Treatment Group (as Received)							
Test (unit) Criteria	ACC 3 µg+QS-21 (N[a]=36) m/n (%)	ACC 10 µg+QS-21 (N[a]=60) m/n (%)	ACC 30 µg+QS-21 (N[a]=40) m/n (%)	ACC 10 µg (N[a]=35) m/n (%)	ACC 30 µg (N[a]=12) m/n (%)	QS-21 Alone (N[a]=44) m/n (%)	PBS (N[a]=17) m/n (%)	Total (N[a]=244) m/n (%)
Any PCI result	22/36 (61.1)	33/60 (55.0)	30/40 (75.0)	22/35 (62.9)	8/12 (66.7)	32/44 (72.7)	7/17 (41.2)	154/244 (63.1)
Urine Protein/albumin positive	10/36 (27.8)	18/60 (30.0)	16/40 (40.0)	12/35 (34.3)	7/12 (58.3)	15/44 (34.1)	5/17 (29.4)	83/244 (34.0)
Urine Hemoglobin/blood positive	1/36 (2.8)	2/60 (3.3)	9/40 (22.5)	2/35 (5.7)	3/12 (25.0)	9/44 (20.5)	1/17 (5.9)	27/244 (11.1)
Triglycerides, fasting/nonfasting/unknown (≥3.7 mmol/L)	2/36 (5.6)	11/60 (18.3)	5/40 (12.5)	5/35 (14.3)	1/12 (8.3)	2/44 (4.5)	0/17	26/244 (10.7)
Hemoglobin (g/L)	3/36 (8.3)	1/60 (1.7)	8/40 (20.0)	5/35 (14.3)	1/12 (8.3)	4/44 (9.1)	0/17	22/244 (9.0)
Low (males <115 g/L; females <95 g/L)	1/36 (2.8)	0/60	3/40 (7.5)	1/35 (2.9)	1/12 (8.3)	1/44 (2.3)	0/17	7/244 (2.9)
Decreased from baseline (≥20 g/L)	3/36 (8.3)	1/60 (1.7)	6/40 (15.0)	4/35 (11.4)	1/12 (8.3)	3/44 (6.8)	0/17	18/244 (7.4)
Low + Decrease	1/36 (2.8)	0/60	1/40 (2.5)	0/35	1/12 (8.3)	0/44	0/17	3/244 (1.2)
Bicarbonate (mmol/L)	5/36 (13.9)	3/60 (5.0)	3/40 (7.5)	1/35 (2.9)	1/12 (8.3)	6/44 (13.6)	2/17 (11.8)	21/244 (8.6)
Increased from baseline ≥4 mmol/L and ONR	5/36 (13.9)	1/60 (1.7)	3/40 (7.5)	1/35 (2.9)	1/12 (8.3)	3/44 (6.8)	1/17 (5.9)	15/244 (6.1)
Decreased from baseline ≥4 mmol/L and ONR	0/36	2/60 (3.3)	0/40	0/35	0/12	3/44 (6.8)	1/17 (5.9)	6/244 (2.5)
Hematocrit (L/L)	3/36 (8.3)	3/60 (5.0)	4/40 (10.0)	5/35 (14.3)	1/12 (8.3)	2/44 (4.5)	1/17 (5.9)	19/244 (7.8)
Low (males <0.37; females <0.32)	3/36 (8.3)	3/60 (5.0)	4/40 (10.0)	4/35 (11.4)	1/12 (8.3)	2/44 (4.5)	1/17 (5.9)	18/244 (7.4)
Decreased from baseline (≥0.10)	0/36	0/60	1/40 (2.5)	1/35 (2.9)	1/12 (8.3)	0/44	0/17	3/244 (1.2)
Low + Decrease	0/36	0/60	1/40 (2.5)	0/35	1/12 (8.3)	0/44	0/17	2/244 (0.8)
Glucose, fasting/nonfasting/unknown (≥11.10 mmol/L)	2/36 (5.6)	6/60 (10.0)	3/40 (7.5)	1/35 (2.9)	0/12	5/44 (11.4)	1/17 (5.9)	18/244 (7.4)
Urine Ketones positive	2/36 (5.6)	3/60 (5.0)	4/40 (10.0)	3/35 (8.6)	0/12	2/44 (4.5)	0/17	14/244 (5.7)
Urine Glucose/sugar positive	2/36 (5.6)	3/60 (5.0)	5/40 (12.5)	0/35	0/12	2/44 (4.5)	1/17 (5.9)	13/244 (5.3)

Table 17 Laboratory Test Results Change from Baseline of Potential Clinical Importance (Safety Population)

Data Analysis Interval: On-therapy[b] Test (unit) Criteria	Treatment Group (as Received) ACC 3 µg+QS-21 (N[a]=36) m/n (%)	ACC 10 µg+QS-21 (N[a]=60) m/n (%)	ACC 30 µg+QS-21 (N[a]=40) m/n (%)	ACC 10 µg (N[a]=35) m/n (%)	ACC 30 µg (N[a]=12) m/n (%)	QS-21 Alone (N[a]=44) m/n (%)	PBS (N[a]=17) m/n (%)	Total (N[a]=244) m/n (%)
Cholesterol, fasting/nonfasting/unknown ≥7.758 mmol/L	1/36 (2.8)	2/60 (3.3)	4/40 (10.0)	0/35	0/12	4/44 (9.1)	0/17	11/244 (4.5)
Uric acid (mmol/L) (males; >0.5948 mmol/L; females >0.4758 mmol/L)	0/36	1/60 (1.7)	4/40 (10.0)	1/35 (2.9)	0/12	1/44 (2.3)	0/17	7/244 (2.9)
Total bilirubin (umol/L) ≥1.5xULN	0/36	1/60 (1.7)	1/40 (2.5)	1/35 (2.9)	0/12	1/44 (2.3)	0/17	4/244 (1.6)
Creatinine (umol/L) ≥1.5xULN	0/36	2/60 (3.3)	0/40	0/35	0/12	1/44 (2.3)	0/17	3/244 (1.2)
WBC count (10^9/L)	0/36	0/60	2/40 (5.0)	0/35	0/12	0/44	1/17 (5.9)	3/244 (1.2)
High (>16x10^9/L)	0/36	0/60	0/40	0/35	0/12	0/44	1/17 (5.9)	1/244 (0.4)
Low (<2.8x10^9/L)	0/36	0/60	2/40 (5.0)	0/35	0/12	0/44	0/17	2/244 (0.8)
Neutrophils (<1.0x10^9/L)	0/36	0/60	1/40 (2.5)	0/35	0/12	0/44	0/17	1/244 (0.4)
Albumin <25 g/L	1/36 (2.8)	0/60	0/40	0/35	1/12 (8.3)	0/44	0/17	2/244 (0.8)
BUN (mmol/L) ≥1.5xULN	0/36	0/60	0/40	0/35	0/12	2/44 (4.5)	0/17	2/244 (0.8)
ALT/SGPT (U/L) ≥3xULN	0/36	0/60	0/40	0/35	0/12	1/44 (2.3)	0/17	1/244 (0.4)
Calcium (mmol/L) [m (m/n %)] <2.046 mmol/L	1/36 (2.8)	0/60	0/40	0/35	0/12	0/44	0/17	1/244 (0.4)

Abbreviations: ALT=alanine transaminase; BUN=blood urea nitrogen; m=number of subjects meeting each PCI criteria in the corresponding treatment group; N=number subjects in group; n=number of total subjects having data available in each treatment group; ONR= utside normal range; PBS=phosphate-buffered saline, PCI=potential clinical importance; SGPT=serum glutamic-pyruvic transaminase; ULN=upper limit of normal range; WBC=white blood cell.
Note: m/n (%): percentage is based on the subjects meeting each criteria / number of total subjects with at least one data point available for each parameter.
[a] The value was used as the denominator for percentages.
[b] The mean of evaluations within a visit interval was used for purpose of post-baseline summaries.

CONCLUSIONS:

- An acceptable safety and tolerability profile was demonstrated with injection site pain, headache, depression and diarrhoea as the most frequently reported TEAEs.

- There were 1.2% of subjects who experienced TEAEs of Special Circumstance in the ACC treatment groups which were assessed as related to study vaccine, of which 0.8% of the subjects experienced vasogenic cerebral oedema

- The ACC-001+QS-21 vaccine elicited a robust immune response at the low (3 µg), mid (10 µg), and high (30 µg) dose level as demonstrated by anti-A-beta IgG and anti-A-beta IgM titers.

- The IgG and IgM levels increased compared to baseline after each of the 5 immunizations for all ACC+QS-21 treatment groups.

- Higher IgG levels were obtained in the ACC+QS-21 treatment groups compared to the ACC alone treatment groups.