# Clinical trial results:
# A Multi-center, Randomized, Double-blind, Placebo-controlled, 24 months Study in Patients with amnestic Mild Cognitive Impairment or Very Mild Alzheimer's Disease to Investigate the Safety, Tolerability and Immune Response of Repeated Subcutaneous Injections of ABvac40

## Summary

| | |
|---|---|
| EudraCT number | 2016-004352-30 |
| Trial protocol | ES SE FR IT |
| Global end of trial date | 23 March 2023 |

### Results information

| | |
|---|---|
| Result version number | v1 |
| This version publication date | 07 April 2024 |
| First version publication date | 07 April 2024 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | AB1601 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03461276 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Araclon Biotech, S.L. a Grifols company |
| Sponsor organisation address | Vía de la Hispanidad, 21, Zaragoza, Spain, 50009 |
| Public contact | Araclon Biotech, S.L. a Grifols company, Araclon Biotech, S.L. a Grifols company, info@araclon.com |
| Scientific contact | Maria Pascual Lucas, Araclon Biotech, S.L. a Grifols company, mpascual@araclon.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 | 18 August 2023 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 23 March 2023 |
| Global end of trial reached? | Yes |
| Global end of trial date | 23 March 2023 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Primary Safety Objective:
- To evaluate the safety and tolerability of repeated doses of ABvac40 in a population of patients with amnestic mild cognitive impairment (a-MCI) or very mild Alzheimer's Disease (vm-AD).

Primary Efficacy (Immunogenicity) Objective:
- To assess (quantify) the immune response produced during the study by repeated doses of ABvac40 in a population of a-MCI or vm-AD.

Protection of trial subjects:

Documented approvals to the study (including the protocol, all amendments and informed consents) were obtained for all participating centers/countries prior to study start from appropriate Institutional Review Board/Ethics Committee (IRBs/ECs), according to ICH good clinical practice (GCP) guidelines, local laws, regulations and organizations.
The procedures described in the clinical study protocol, pertaining to the conduct, evaluation, and documentation of the study were designed to ensure that the sponsor and investigator abide by ICH GCP guidelines. The study was also carried out in keeping with applicable local law(s) and regulation(s).
Written informed consent form (ICF) was obtained from the patients (or legal representatives, if applicable) and from a close relative/caregiver before any study specific procedure took place.
Subjects records and personal data were handled in strictest confidence and in accordance with local data protection laws and with the European General Data Protection Regulation (2016/679) (GDPR).
No medical waivers for protocol inclusion/exclusion criteria were allowed by the sponsor, and that in case the need for a change to the protocol was identified, it was submitted as a protocol amendment to the competent regulatory authority and/or IRBs/ECs as applicable per regulations.
Direct advertising was used in this study in order to solicit subject participation. Direct advertising included, but were not necessarily limited to: newspaper, radio, television, bulletin boards, posters that were intended for candidate subjects. Any advertisement was submitted for review and approval to the IRBs/ECs charged with this responsibility to ensure that the information contained in the advertisement was not misleading and that the procedure for recruiting subjects gave adequate protection for the rights and welfare of the subjects.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 01 December 2017 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Spain: 107 |
| Country: Number of subjects enrolled | Sweden: 3 |
| Country: Number of subjects enrolled | France: 12 |
| Country: Number of subjects enrolled | Italy: 2 |

| | |
|---|---|
| Worldwide total number of subjects | 124 |
| EEA total number of subjects | 124 |

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) | 20 |
| From 65 to 84 years | 104 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

A total of 23 centers in Spain (n=18), France (n=3), Italy (n=1) and Sweden (n=1) recruited subjects in this study.
The subjects' recruitment was competitive until the required number of subjects was completed.

### Pre-assignment

Screening details:

238 subjects were screened and assessed for eligibility. 88 subjects were screening failures and an additional 16 subjects dropped out the study before randomized. 134 subjects were randomized. Finally, 10 randomized subjects did not receive the allocated IMP. Accordingly, 124 subjects received any IMP dose, constituting the SAF analysis set.

### Period 1

| | |
|---|---|
| Period 1 title | Part A (18-24 months duration) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Carer |

Blinding implementation details:

Only the independent representative of the Sponsor and the independent statistician worked without blinding in order to label study medication and to prepare all the data safety monitoring board (DSMB) documentation, respectively.
Blinding was only to be broken for safety concerns requiring immediate medical treatment.

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Placebo arm Part A |

Arm description:

Subjects who received Placebo during Part A

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Six administrations: the first five administered once every 4 weeks (28±3 days) and the sixth at week 42 (Visit 18), 26 weeks after the fifth. Each administration consisted of 1 mL injection of ABvac40 vehicle without its active ingredient.

| | |
|---|---|
| **Arm title** | ABvac40 arm Part A |

Arm description:

Subjects who received ABvac40 during Part A

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | ABvac40 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Six administrations: the first five administered once every 4 weeks (28±3 days) and the sixth at week 42 (Visit 18), 26 weeks after the fifth. Each administration consisted of 1 mL injection of ABvac40 (containing 0.2 mg of Aβx-40).

| **Number of subjects in period 1** | Placebo arm Part A | ABvac40 arm Part A |
|---|---|---|
| Started | 62 | 62 |
| Completed | 53 | 55 |
| Not completed | 9 | 7 |
| Adverse event, serious fatal | 1 | 1 |
| Physician decision | 1 | - |
| Consent withdrawn by subject | 1 | 1 |
| Adverse event, non-fatal | 3 | 1 |
| Patient heath status | - | 1 |
| Patient/caregiver's decision | 3 | 3 |

## Period 2

| | |
|---|---|
| Period 2 title | Part B (18 months duration) |
| Is this the baseline period? | No |
| Allocation method | Non-randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer |

Blinding implementation details:

For the Part B of the study, both the sites' principal investigators and the patients remained blinded. Blinding was only to be broken for safety concerns requiring immediate medical treatment.

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Placebo arm Part A/ABvac40 arm Part B |

Arm description:

Subjects randomized to Placebo during Part A received ABvac40 during Part B

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | ABvac40 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Six administrations: the first five administered once every 4 weeks (28±3 days) and the sixth at week 42 (Visit 18B), 26 weeks after the fifth immunization. Each administration consisted of 1 mL injection of ABvac40 (containing 0.2 mg of Aβx-40).

| | |
|---|---|
| **Arm title** | ABvac40 arm Part A/Placebo+Booster arm Part B |

Arm description:

Subjects randomized to ABvac40 during Part A received Placebo+ABvac40 booster during Part B

| | |
|---|---|
| Arm type | Experimental |

| | |
|---|---|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Five administrations: the first four administered once every 4 weeks (28±3 days) and the fifth at week 42 (Visit 18B), 30 weeks after the forth. Each administration consisted of 1 mL injection of ABvac40 vehicle without its active ingredient.

| | |
|---|---|
| Investigational medicinal product name | ABvac40 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

One administration (booster) at week 16 (Visit 13B). The administration consisted of 1 mL injection of ABvac40 (containing 0.2 mg of Aβx-40).

| **Number of subjects in period 2[1]** | Placebo arm Part A/ABvac40 arm Part B | ABvac40 arm Part A/Placebo+Booster arm Part B |
|---|---|---|
| Started | 37 | 40 |
| Completed | 33 | 38 |
| Not completed | 4 | 2 |
| Patient lost follow-up | 1 | - |
| Consent withdrawn by subject | - | 1 |
| Adverse event, non-fatal | - | 1 |
| Patient/caregiver's decision | 3 | - |

Notes:

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

Justification: A total of 108 subjects completed Part A, 53 in the Placebo arm and 55 in the ABvac40 arm. Out of these, 16 subjects in the Placebo arm and 15 in the ABvac40 arm did not continue to Part B. Accordingly, a total of 77 subjects continued into Part B, 37 in treatment sequence Placebo arm Part A/ABvac40 arm Part B and 40 in treatment sequence ABvac40 arm Part A/Placebo+Booster arm Part B.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Placebo arm Part A |
| Reporting group description: | |
| Subjects who received Placebo during Part A | |
| Reporting group title | ABvac40 arm Part A |
| Reporting group description: | |
| Subjects who received ABvac40 during Part A | |

| Reporting group values | Placebo arm Part A | ABvac40 arm Part A | Total |
|---|---|---|---|
| Number of subjects | 62 | 62 | 124 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | 0 |
| Preterm newborn infants (gestational age < 37 wks) | | | 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) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 70.1 | 70.6 | |
| standard deviation | ± 5.49 | ± 5.95 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 36 | 38 | 74 |
| Male | 26 | 24 | 50 |
| Study disease | | | |
| Units: Subjects | | | |
| amnestic Mild Cognitive Impairment (a-MCI) | 42 | 38 | 80 |
| Very Mild Alzheimer’s Disease (VM-AD) | 20 | 24 | 44 |
| a-PET status | | | |
| amyloid-positron emission tomography (a-PET) status | | | |
| Units: Subjects | | | |
| Positive | 45 | 47 | 92 |
| Negative | 17 | 15 | 32 |
| ApoE status | | | |
| Apolipoprotein E (ApoE) status | | | |
| Units: Subjects | | | |
| Noncarriers: E2/E2 and E2/E3, E3/E3 | 24 | 24 | 48 |
| Carriers (Heterozygous: E2/E4, E3/E4) | 33 | 29 | 62 |

| | | | |
|---|---|---|---|
| Carriers (Homozygous: E4/E4) | 5 | 9 | 14 |

| | | | |
|---|---|---|---|
| Time from Disease Diagnosis to Informed Consent | | | |
| Units: month | | | |
| arithmetic mean | 14.48 | 14.68 | |
| standard deviation | ± 15.81 | ± 13.71 | - |

## Subject analysis sets

| | |
|---|---|
| Subject analysis set title | SAF |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

The Safety (SAF) analysis set consisted of all randomized subjects who received any amount of IMP. All safety analyses used the SAF analysis set. Subjects were analyzed according to the treatment received, regardless of the treatment assigned.

Note: Subjects S04-002 and S14-006 were randomized to the Placebo arm in Part A and inadvertently received ABvac40 on Visit 10 and Visit 7 respectively. They received ABvac40 in Part B. These 2 subjects were summarized for the SAF analysis set in ABvac40 arm for Part A and Part B.

| | |
|---|---|
| Subject analysis set title | ITT |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

The Intent-to-treat (ITT) analysis set consisted of all subjects randomized who received any IMP.
Analysis of all secondary efficacy endpoints was carried out using the ITT analysis set. Subjects were analyzed according to their randomized treatment assignment, regardless of the treatment received.

| | |
|---|---|
| Subject analysis set title | mITT |
| Subject analysis set type | Modified intention-to-treat |

Subject analysis set description:

The Modified Intent-to-treat (mITT) analysis set comprised all subjects in the ITT analysis set who had a Baseline- and at least 1 post-Baseline anti-Aβ40 antibody assessment (optical density [OD] in ELISA without pre-adsorption).
Analysis of the primary efficacy endpoint was carried out using the mITT analysis set. Subjects were analyzed according to their randomized treatment assignment, regardless of the treatment received.

| | |
|---|---|
| Subject analysis set title | PP (Part A) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

The Per protocol (PP) analysis set (Part A) comprised all subjects in the ITT analysis set who received all doses of the IMP (on V1, V4, V7, V10, V13 and V18 in Part A), attended the safety visit after Booster (V20 in Part A) and had no major protocol deviations that could have affected the efficacy analyses.
Analysis of the primary efficacy endpoint and secondary efficacy endpoints relating to the characterization of immune response and the assessment of disease biomarkers in Part A was repeated using the Part A PP analysis set. Subjects were analyzed according to their randomized treatment assignment, regardless of the treatment received.
Note: Summaries of the primary efficacy endpoint and secondary efficacy endpoints relating to the characterization of immune response and the assessment of disease biomarkers over the entire duration of the study (Parts A and B combined) were repeated using subjects who were in Part A PP analysis set and the Part B PP analysis set.

| | |
|---|---|
| Subject analysis set title | PPc (Part A) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Per protocol cognition (PPc) analysis set (Part A) comprised all subjects in the ITT analysis set who received all doses of the IMP (on V1, V4, V7, V10, V13 and V18 in Part A), attended the safety visit after Booster (V20 in Part A), had no major protocol deviations that could have affected the efficacy analyses or major protocol deviations that were classified as "Use of disallowed concomitant medication", relating to use of anti-AD medication.
Analysis of secondary efficacy endpoints relating to the assessment of cognition and quality of life in Part A was repeated using the Part A PPc analysis set.

Subjects were analyzed according to their randomized treatment assignment, regardless of the treatment received.
Note: Analysis of secondary efficacy endpoints relating to the assessment of cognition and quality of life over the entire duration of the study (Parts A and B combined), were repeated using subjects who were in Part A PPc analysis set and the Part B PPc analysis set.

| | |
|---|---|
| Subject analysis set title | PP (Part B) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

The Per protocol (PP) analysis set (Part B) comprised all subjects in the ITT analysis set who received all doses of the IMP (on V1B, V4B, V7B, V10B, V13B and V18B in Part B), attended the safety visit after Booster (V20B in Part B) and had no major protocol deviations that could have affected the summary of efficacy.
Subjects were analyzed according to their randomized treatment assignment, regardless of the treatment received
Note: Summaries of the primary efficacy endpoint and secondary efficacy endpoints relating to the characterization of immune response and the assessment of disease biomarkers over the entire duration of the study (Parts A and B combined) were repeated using subjects who were in Part A PP analysis set and the Part B PP analysis set.

| | |
|---|---|
| Subject analysis set title | PPc (Part B) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Per protocol cognition (PPc) analysis set (Part B) comprised all subjects in the ITT analysis set who received all doses of the IMP (on V1B, V4B, V7B, V10B, V13B and V18B in Part B), attended the safety visit after Booster (V20B in Part B), had no major protocol deviations that could have affected the efficacy analyses or major protocol deviations that were classified as "Use of disallowed concomitant medication", relating to use of anti-AD medication.
Subjects were analyzed according to their randomized treatment assignment, regardless of the treatment received.
Note: Analysis of secondary efficacy endpoints relating to the assessment of cognition and quality of life over the entire duration of the study (Parts A and B combined), were repeated using subjects who were in Part A PPc analysis set and the Part B PPc analysis set

| **Reporting group values** | SAF | ITT | mITT |
|---|---|---|---|
| Number of subjects | 124 | 124 | 122 |
| Age categorical<br>Units: Subjects | | | |
| In utero | | | |
| Preterm newborn infants (gestational age < 37 wks) | | | |
| Newborns (0-27 days) | | | |
| Infants and toddlers (28 days-23 months) | | | |
| Children (2-11 years) | | | |
| Adolescents (12-17 years) | | | |
| Adults (18-64 years) | | | |
| From 65-84 years | | | |
| 85 years and over | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | | 70.4 | |
| standard deviation | ± | ± 5.71 | ± |
| Gender categorical<br>Units: Subjects | | | |
| Female | | 74 | |
| Male | | 50 | |

| | | | |
|---|---|---|---|
| Study disease<br>Units: Subjects | | | |
| amnestic Mild Cognitive Impairment (a-MCI) | | 80 | |
| Very Mild Alzheimer’s Disease (VM-AD) | | 44 | |
| a-PET status | | | |
| amyloid-positron emission tomography (a-PET) status | | | |
| Units: Subjects | | | |
| Positive | | 92 | |
| Negative | | 32 | |
| ApoE status | | | |
| Apolipoprotein E (ApoE) status | | | |
| Units: Subjects | | | |
| Noncarriers: E2/E2 and E2/E3, E3/E3 | | 48 | |
| Carriers (Heterozygous: E2/E4, E3/E4) | | 62 | |
| Carriers (Homozygous: E4/E4) | | 14 | |
| Time from Disease Diagnosis to Informed Consent<br>Units: month | | | |
| arithmetic mean | | 14.58 | |
| standard deviation | ± | ± 14.74 | ± |

| **Reporting group values** | PP (Part A) | PPc (Part A) | PP (Part B) |
|---|---|---|---|
| Number of subjects | 100 | 97 | 65 |
| Age categorical<br>Units: Subjects | | | |
| In utero | | | |
| Preterm newborn infants (gestational age < 37 wks) | | | |
| Newborns (0-27 days) | | | |
| Infants and toddlers (28 days-23 months) | | | |
| Children (2-11 years) | | | |
| Adolescents (12-17 years) | | | |
| Adults (18-64 years) | | | |
| From 65-84 years | | | |
| 85 years and over | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | | | |
| standard deviation | ± | ± | ± |
| Gender categorical<br>Units: Subjects | | | |
| Female | | | |
| Male | | | |
| Study disease<br>Units: Subjects | | | |
| amnestic Mild Cognitive Impairment (a-MCI) | | | |
| Very Mild Alzheimer’s Disease (VM-AD) | | | |

| | | | |
|---|---|---|---|
| a-PET status | | | |
| amyloid-positron emission tomography (a-PET) status | | | |
| Units: Subjects | | | |
| Positive | | | |
| Negative | | | |
| ApoE status | | | |
| Apolipoprotein E (ApoE) status | | | |
| Units: Subjects | | | |
| Noncarriers: E2/E2 and E2/E3, E3/E3 | | | |
| Carriers (Heterozygous: E2/E4, E3/E4) | | | |
| Carriers (Homozygous: E4/E4) | | | |
| Time from Disease Diagnosis to Informed Consent | | | |
| Units: month | | | |
| arithmetic mean | | | |
| standard deviation | ± | ± | ± |

| **Reporting group values** | PPc (Part B) | | |
|---|---|---|---|
| Number of subjects | 63 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | |
| Preterm newborn infants (gestational age < 37 wks) | | | |
| Newborns (0-27 days) | | | |
| Infants and toddlers (28 days-23 months) | | | |
| Children (2-11 years) | | | |
| Adolescents (12-17 years) | | | |
| Adults (18-64 years) | | | |
| From 65-84 years | | | |
| 85 years and over | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | ± | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | | | |
| Male | | | |
| Study disease | | | |
| Units: Subjects | | | |
| amnestic Mild Cognitive Impairment (a-MCI) | | | |
| Very Mild Alzheimer’s Disease (VM-AD) | | | |
| a-PET status | | | |
| amyloid-positron emission tomography (a-PET) status | | | |
| Units: Subjects | | | |
| Positive | | | |
| Negative | | | |
| ApoE status | | | |

| Apolipoprotein E (ApoE) status | | | |
|---|---|---|---|
| Units: Subjects | | | |
| Noncarriers: E2/E2 and E2/E3, E3/E3<br>Carriers (Heterozygous: E2/E4, E3/E4)<br>Carriers (Homozygous: E4/E4) | | | |
| Time from Disease Diagnosis to Informed Consent<br>Units: month<br>arithmetic mean<br>standard deviation | ± | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Placebo arm Part A |
| Reporting group description: | |
| Subjects who received Placebo during Part A | |
| Reporting group title | ABvac40 arm Part A |
| Reporting group description: | |
| Subjects who received ABvac40 during Part A | |
| Reporting group title | Placebo arm Part A/ABvac40 arm Part B |
| Reporting group description: | |
| Subjects randomized to Placebo during Part A received ABvac40 during Part B | |
| Reporting group title | ABvac40 arm Part A/Placebo+Booster arm Part B |
| Reporting group description: | |
| Subjects randomized to ABvac40 during Part A received Placebo+ABvac40 booster during Part B | |
| Subject analysis set title | SAF |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

The Safety (SAF) analysis set consisted of all randomized subjects who received any amount of IMP. All safety analyses used the SAF analysis set. Subjects were analyzed according to the treatment received, regardless of the treatment assigned.

Note: Subjects S04-002 and S14-006 were randomized to the Placebo arm in Part A and inadvertently received ABvac40 on Visit 10 and Visit 7 respectively. They received ABvac40 in Part B. These 2 subjects were summarized for the SAF analysis set in ABvac40 arm for Part A and Part B.

| | |
|---|---|
| Subject analysis set title | ITT |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

The Intent-to-treat (ITT) analysis set consisted of all subjects randomized who received any IMP.
Analysis of all secondary efficacy endpoints was carried out using the ITT analysis set. Subjects were analyzed according to their randomized treatment assignment, regardless of the treatment received.

| | |
|---|---|
| Subject analysis set title | mITT |
| Subject analysis set type | Modified intention-to-treat |

Subject analysis set description:

The Modified Intent-to-treat (mITT) analysis set comprised all subjects in the ITT analysis set who had a Baseline- and at least 1 post-Baseline anti-Aβ40 antibody assessment (optical density [OD] in ELISA without pre-adsorption).
Analysis of the primary efficacy endpoint was carried out using the mITT analysis set. Subjects were analyzed according to their randomized treatment assignment, regardless of the treatment received.

| | |
|---|---|
| Subject analysis set title | PP (Part A) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

The Per protocol (PP) analysis set (Part A) comprised all subjects in the ITT analysis set who received all doses of the IMP (on V1, V4, V7, V10, V13 and V18 in Part A), attended the safety visit after Booster (V20 in Part A) and had no major protocol deviations that could have affected the efficacy analyses.
Analysis of the primary efficacy endpoint and secondary efficacy endpoints relating to the characterization of immune response and the assessment of disease biomarkers in Part A was repeated using the Part A PP analysis set. Subjects were analyzed according to their randomized treatment assignment, regardless of the treatment received.
Note: Summaries of the primary efficacy endpoint and secondary efficacy endpoints relating to the characterization of immune response and the assessment of disease biomarkers over the entire duration of the study (Parts A and B combined) were repeated using subjects who were in Part A PP analysis set and the Part B PP analysis set.

| | |
|---|---|
| Subject analysis set title | PPc (Part A) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Per protocol cognition (PPc) analysis set (Part A) comprised all subjects in the ITT analysis set who received all doses of the IMP (on V1, V4, V7, V10, V13 and V18 in Part A), attended the safety visit after Booster (V20 in Part A), had no major protocol deviations that could have affected the efficacy analyses or major protocol deviations that were classified as "Use of disallowed concomitant medication", relating to use of anti-AD medication.
Analysis of secondary efficacy endpoints relating to the assessment of cognition and quality of life in Part A was repeated using the Part A PPc analysis set.
Subjects were analyzed according to their randomized treatment assignment, regardless of the treatment received.
Note: Analysis of secondary efficacy endpoints relating to the assessment of cognition and quality of life over the entire duration of the study (Parts A and B combined), were repeated using subjects who were in Part A PPc analysis set and the Part B PPc analysis set.

| Subject analysis set title | PP (Part B) |
|---|---|
| Subject analysis set type | Per protocol |

Subject analysis set description:

The Per protocol (PP) analysis set (Part B) comprised all subjects in the ITT analysis set who received all doses of the IMP (on V1B, V4B, V7B, V10B, V13B and V18B in Part B), attended the safety visit after Booster (V20B in Part B) and had no major protocol deviations that could have affected the summary of efficacy.
Subjects were analyzed according to their randomized treatment assignment, regardless of the treatment received
Note: Summaries of the primary efficacy endpoint and secondary efficacy endpoints relating to the characterization of immune response and the assessment of disease biomarkers over the entire duration of the study (Parts A and B combined) were repeated using subjects who were in Part A PP analysis set and the Part B PP analysis set.

| Subject analysis set title | PPc (Part B) |
|---|---|
| Subject analysis set type | Per protocol |

Subject analysis set description:

Per protocol cognition (PPc) analysis set (Part B) comprised all subjects in the ITT analysis set who received all doses of the IMP (on V1B, V4B, V7B, V10B, V13B and V18B in Part B), attended the safety visit after Booster (V20B in Part B), had no major protocol deviations that could have affected the efficacy analyses or major protocol deviations that were classified as "Use of disallowed concomitant medication", relating to use of anti-AD medication.
Subjects were analyzed according to their randomized treatment assignment, regardless of the treatment received.
Note: Analysis of secondary efficacy endpoints relating to the assessment of cognition and quality of life over the entire duration of the study (Parts A and B combined), were repeated using subjects who were in Part A PPc analysis set and the Part B PPc analysis set

## Primary: MΔ of anti-Aβ40 antibody signal (OD in ELISA)

| End point title | MΔ of anti-Aβ40 antibody signal (OD in ELISA) |
|---|---|

End point description:

Average maximal increment (MΔ) of plasma anti-Aβ40 antibody signal (optical density [OD] in ELISA) in each subject with regard to Baseline visit.
For the primary efficacy analysis, the trial was considered successfully confirmatory regarding efficacy (immunogenicity) of ABvac40 since the average MΔ of anti-Aβ40 antibody signal in the ABvac40 arm was significantly greater that the average MΔ in anti-Aβ40 antibody signal in the Placebo arm.

| End point type | Primary |
|---|---|

End point timeframe:

Maximal increment (MΔ) from Baseline across all Part A post-Baseline visits

| End point values | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 60[1] | 61[2] | | |
| Units: no unit of measure since results are OD | | | | |
| arithmetic mean (standard deviation) | 0.12 (± 0.21) | 3.27 (± 0.75) | | |

Notes:

[1] - mITT analysis set

[2] - mITT analysis set

## Statistical analyses

| Statistical analysis title | t-test |
|---|---|

Statistical analysis description:

1-sided t-test to compare the ABvac40 and placebo groups

| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
|---|---|
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[3] |
| P-value | < 0.0001 [4] |
| Method | t-test, 1-sided |

Notes:

[3] - The trial was considered successfully confirmatory regarding efficacy (immunogenicity) of ABvac40 if the average MΔ of anti-Aβ40 antibody signal (OD in ELISA) in the ABvac40 group was significantly greater than the average MΔ of anti-Aβ40 antibody signal in the Placebo group. i.e.
– Null hypothesis: average MΔ anti-Aβ40 (ABvac40) ≤ average MΔ anti-Aβ40 (placebo).
– Alternative hypothesis: average MΔ anti-Aβ40 (ABvac40) > average MΔ anti-Aβ40 (placebo)

[4] - A 1-sided t-test with a significance level of 0.025 was employed

| Statistical analysis title | Mann-Whitney U test |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[5] |
| P-value | < 0.0001 [6] |
| Method | Wilcoxon (Mann-Whitney) |

Notes:

[5] - Additional test

[6] - 1-sided

| Statistical analysis title | ANCOVA model |
|---|---|

Statistical analysis description:

The average MΔ of anti-Aβ40 antibody signal between the two treatment groups was compared using an ANCOVA model, using the MΔ anti-Aβ40 antibody signal as the dependent variable, baseline anti-Aβ40 antibody signal (OD in ELISA) as covariate and treatment group and amyloid positivity as fixed effects.

| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
|---|---|
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Parameter estimate | Least squares mean differences |
| Point estimate | 3.15 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.96 |
| upper limit | 3.34 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.1 |

| **Statistical analysis title** | t-test (sensitivity hypothesis) |
|---|---|

Statistical analysis description:

1-sided t-test to compare the ABvac40 and placebo groups

| | |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[7] |
| P-value | < 0.0001 [8] |
| Method | t-test, 1-sided |

Notes:

[7] - The primary analysis (t-test) was repeated, using the mITT Analysis Set to test the hypothesis:
- Null hypothesis: average MΔ anti-Aβ40 (ABvac40) - average MΔ anti-Aβ40 (placebo) ≤ 1.778
- Alternative hypothesis: average MΔ anti-Aβ40 (ABvac40) - average MΔ anti-Aβ40 (placebo) > 1.778
The alternative hypothesis was confirmed.

[8] - A 1-sided t-test with a significance level of 0.025 was employed

| **Statistical analysis title** | MMRM |
|---|---|

Statistical analysis description:

The change in anti-Aβ40 antibody signal from baseline to each post-baseline efficacy visit was analyzed using a Mixed-Model Repeated Measures (MMRM), using the mITT Analysis Set.
Dependent variable: change from baseline in anti-Aβ40 antibody signal. Fixed effects: treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity. Covariates: baseline anti-Aβ40 antibody signal and baseline age; Repeated measure: measures within-patient at each visit.
(See chart)

| | |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 121 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.05 [9] |
| Method | Mixed models analysis |

Notes:

[9] - The MMRM showed positive differences in LS mean change from Baseline of plasma anti Aβ40 antibody signal between the ABvac40 and Placebo arms at all Part A post Baseline visits (p<0.05)

## Secondary: Subject discontinuations due to TEAEs

| End point title | Subject discontinuations due to TEAEs |
|---|---|

End point description:

Number of withdrawn subjects due to treatment-emergent adverse events (TEAEs) during the whole study.
There were 7 TEAEs leading to study withdrawal in 7 subjects (2 [2.0%] subjects in the ABvac40 (Part A)/ABvac40 (Part B) group, 4 [6.5%] subjects in the Placebo (Part A) group, and 1 [2.5%] in the Placebo (Part B)/Booster (Part B) group).

| End point type | Secondary |
|---|---|

End point timeframe:

Whole study duration (Part A+Part B; up to 42 months)

| End point values | SAF | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 124 | | | |
| Units: subjects | 7 | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with clinically significant abnormalities in physical examination

| End point title | Number of subjects with clinically significant abnormalities in physical examination |
|---|---|

End point description:

Clinically significant (CS) abnormalities in physical examination during the study.
There were a total of 14 CS abnormalities in 11 subjects:
3 subjects presented a total of 5 CS abnormalities in treatment sequence ABvac40 arm Part A/Placebo+Booster arm Part B
8 subjects presented a total of 9 CS abnormalities in treatment sequence Placebo arm Part A/ABvac40 arm Part B
No consistently recurrent or persistent CS abnormalities were observed in the physical examination, suggesting no IMP impact.

| End point type | Secondary |
|---|---|

End point timeframe:

Whole study duration (Part A+Part B; up to 42 months)

| End point values | SAF | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 124 | | | |
| Units: subjects | 11 | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with clinically significant abnormalities in neurological examination

| End point title | Number of subjects with clinically significant abnormalities in neurological examination |
|---|---|

End point description:

Clinically significant (CS) abnormalities in neurological examination during the study.
There were a total of 110 CS abnormalities in 13 subjects:
6 subjects presented a total of 67 CS abnormalities in treatment sequence ABvac40 arm Part

A/Placebo+Booster arm Part B
7 subjects presented a total of 43 CS abnormalities in treatment sequence Placebo arm Part A/ABvac40 arm Part B

The most frequently reported CS abnormalities were related to cortical functions, which may be anticipated in this study population. No other consistently recurrent or persistent CS abnormalities were observed in the neurological examination, suggesting no IMP impact.

| End point type | Secondary |
|---|---|

End point timeframe:

Whole study duration (Part A+Part B; up to 42 months)

| **End point values** | SAF | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 124 | | | |
| Units: subjects | 13 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with clinically significant abnormalities in analytical hematology

| End point title | Number of subjects with clinically significant abnormalities in analytical hematology |
|---|---|

End point description:

Clinically significant (CS) abnormalities in hematology parameters during the study.
There were a total of 60 CS abnormalities in 12 subjects:
7 subjects presented a total of 24 CS abnormalities in treatment sequence ABvac40 arm Part A/Placebo+Booster arm Part B
5 subjects presented a total of 36 CS abnormalities in treatment sequence Placebo arm Part A/ABvac40 arm Part B
No consistently recurrent or persistent clinically significant abnormalities were observed in the hematology parameters, suggesting no IMP impact.

| End point type | Secondary |
|---|---|

End point timeframe:

Whole study duration (Part A+Part B; up to 42 months)

| **End point values** | SAF | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 124 | | | |
| Units: subjects | 12 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with clinically significant abnormalities in analytical biochemistry

| End point title | Number of subjects with clinically significant abnormalities in analytical biochemistry |
|---|---|

End point description:

Clinically significant (CS) abnormalities in biochemistry parameters during the study.
There were a total of 91 CS abnormalities in 24 subjects:
9 subjects presented a total of 24 CS abnormalities in treatment sequence ABvac40 arm Part A/Placebo+Booster arm Part B
15 subjects presented a total of 67 CS abnormalities in treatment sequence Placebo arm Part A/ABvac40 arm Part B
No consistently recurrent or persistent clinically significant abnormalities were observed in the biochemistry parameters, suggesting no IMP impact.

| End point type | Secondary |
|---|---|

End point timeframe:

Whole study duration (Part A+Part B; up to 42 months)

| **End point values** | SAF | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 124 | | | |
| Units: subjects | 24 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with clinically significant abnormalities in coagulation

| End point title | Number of subjects with clinically significant abnormalities in coagulation |
|---|---|

End point description:

Clinically significant (CS) abnormalities in coagulation parameters during the study.
There were a total of 16 CS abnormalities in 8 subjects:
3 subjects presented a total of 7 CS abnormalities in treatment sequence ABvac40 arm Part A/Placebo+Booster arm Part B
5 subjects presented a total of 9 CS abnormalities in treatment sequence Placebo arm Part A/ABvac40 arm Part B
No consistently recurrent or persistent clinically significant abnormalities were observed in the coagulation parameters, suggesting no IMP impact.

| End point type | Secondary |
|---|---|

End point timeframe:

Whole study duration (Part A+Part B; up to 42 months)

| End point values | SAF | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 124 | | | |
| Units: subjects | 8 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Level of anti-Aβ40 antibodies in CSF

| End point title | Level of anti-Aβ40 antibodies in CSF |
|---|---|

End point description:

The change in levels of anti-Aβ40 antibodies in cerebrospinal fluid (CSF) from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were differences ($p<0.05$) between groups at Week 50A and Week 104A.

The MMRM included the recorded outcome value as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline age as covariates; and measures within-patient at each visit as a repeated measure. An unstructured variance-covariance matrix was used.

| End point type | Secondary |
|---|---|

End point timeframe:

Part A

| End point values | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: ng/mL | | | | |
| least squares mean (standard error) | | | | |
| Week 50A | 0.1654 (± 3.86502) | 30.1826 (± 3.90756) | | |
| Week 104A | 0.2014 (± 0.36753) | 1.2437 (± 0.41902) | | |

### Statistical analyses

| Statistical analysis title | MMRM - Week 50A |
|---|---|
| Comparison groups | ABvac40 arm Part A v Placebo arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.047 |
| Method | Mixed models analysis |

## Secondary: Level of anti-Aβ40 antibodies in plasma

| End point title | Level of anti-Aβ40 antibodies in plasma |
|---|---|

End point description:

The change in levels of anti-Aβ40 antibodies in plasma from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were differences ($p<0.05$) between groups at each Part A visit (except at Week 2A, Week 77A and Week 104A).

The MMRM included the recorded outcome value as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline age as covariates; and measures within-patient at each visit as a repeated measure. A compound symmetric variance-covariance matrix was used.

| End point type | Secondary |
|---|---|

End point timeframe:

Part A

| End point values | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: µg/mL | | | | |
| least squares mean (standard error) | | | | |
| Week 2A | 1.5580 (± 4.22100) | 1.5112 (± 4.40221) | | |
| Week 6A | 1.5580 (± 4.22100) | 13.7052 (± 4.44801) | | |
| Week 10A | 1.6172 (± 4.24276) | 44.3187 (± 4.41509) | | |
| Week 14A | 1.5479 (± 4.24276) | 62.1946 (± 4.43781) | | |
| Week 18A | 1.5789 (± 4.30746) | 69.8861 (± 4.43781) | | |
| Week 24A | 1.5926 (± 4.26432) | 39.9483 (± 4.44151) | | |
| Week 40A | 1.6027 (± 4.33264) | 14.6139 (± 4.48526) | | |
| Week 44A | 1.5463 (± 4.35267) | 57.5771 (± 4.48568) | | |

| | | | | |
|---|---|---|---|---|
| Week 50A | 1.5993 (± 4.35363) | 33.5366 (± 4.51418) | | |
| Week 77A | 1.5232 (± 4.37735) | 10.8197 (± 4.57100) | | |
| Week 104A | 1.7400 (± 5.57743) | 10.8365 (± 5.82224) | | |

**Statistical analyses**

| **Statistical analysis title** | MMRM - Week 2A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.9936 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 6A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0391 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 10A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.0001 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 14A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.0001 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 18A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.0001 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 24A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.0001 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 40A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0299 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 44A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.0001 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |

| | |
|---|---|
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.0001 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 77A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.1267 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2477 |
| Method | Mixed models analysis |

## Secondary: Level of antibody-secreting cells

| End point title | Level of antibody-secreting cells |
|---|---|

End point description:

The change in levels of antibody-secreting cells from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were differences ($p<0.05$) between groups at each Part A visit (except at Week 2A and Week 104A).

The MMRM included the recorded outcome value as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline age as covariates; and measures within-patient at each visit as a repeated measure. An unstructured variance-covariance matrix was used. The following factor was significantly associated with the response measure ($p < 0.15$) and was included in the model: clinical subgroup – mild cognitive impairment or very mild Alzheimer Disease.

| End point type | Secondary |
|---|---|

End point timeframe:

Part A

| End point values | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: SFU/0.5x10^6 PBMCs | | | | |
| least squares mean (standard error) | | | | |
| Week 2A | -0.4365 (± 0.37501) | 0.1868 (± 0.34352) | | |
| Week 6A | -0.0906 (± 0.72718) | 2.3144 (± 0.67867) | | |
| Week 10A | 0.3092 (± 0.79081) | 4.0397 (± 0.73611) | | |
| Week 14A | -0.1484 (± 1.44968) | 7.5119 (± 1.36804) | | |
| Week 18A | 0.2873 (± 1.02944) | 6.8827 (± 0.93624) | | |
| Week 24A | 0.4827 (± 0.74628) | 3.6323 (± 0.68609) | | |
| Week 40A | -0.5201 (± 0.41447) | 1.2117 (± 0.37194) | | |
| Week 44A | -1.1915 (± 2.45820) | 10.3597 (± 2.23485) | | |
| Week 50A | -0.3489 (± 1.07737) | 4.5496 (± 1.00962) | | |
| Week 77A | -0.3969 (± 0.52153) | 1.8382 (± 0.47244) | | |
| Week 104A | 0.1732 (± 0.40914) | 0.3638 (± 0.40349) | | |

**Statistical analyses**

| Statistical analysis title | MMRM - Week 2A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2151 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 6A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0169 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 10A |
|---|---|

| | |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0008 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 14A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0002 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 18A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.0001 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 24A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0023 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 40A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0021 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 44A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0007 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0012 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 77A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0018 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.738 |
| Method | Mixed models analysis |

## Secondary: Level of Aβ40 peptides in plasma – ABtest-IA

| End point title | Level of Aβ40 peptides in plasma – ABtest-IA |
|---|---|

End point description:

The change in levels of anti-Aβ40 peptides in plasma (ABtest-IA) from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were differences ($p<0.05$) between groups at each Part A visit (except at Week 2A, Week 6A and Week 10A).

The MMRM included change from baseline in the efficacy parameter as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at

each visit as a repeated measure. An unstructured variance-covariance matrix was used. The following factors were significantly associated with the response measure ($p < 0.15$) and were included in the model: baseline use of Alzheimer Disease symptomatic medication and clinical subgroup – mild cognitive impairment or very mild Alzheimer Disease.

| End point type | Secondary |
|---|---|
| End point timeframe: | |
| Part A | |

| **End point values** | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: pg/mL | | | | |
| least squares mean (standard error) | | | | |
| Week 2A | 2.5948 (± 2.22120) | 3.4620 (± 2.16724) | | |
| Week 6A | 3.2541 (± 2.66184) | 8.3468 (± 2.60510) | | |
| Week 10A | 4.2669 (± 3.43764) | -3.3200 (± 3.38626) | | |
| Week 14A | 4.7946 (± 4.75127) | -10.5837 (± 4.71154) | | |
| Week 18A | 7.7216 (± 4.68637) | -13.4213 (± 4.61987) | | |
| Week 24A | 6.3608 (± 4.06529) | -30.6595 (± 4.00199) | | |
| Week 40A | 4.7336 (± 4.73069) | -43.2898 (± 4.62000) | | |
| Week 44A | 7.4722 (± 5.45150) | -36.7343 (± 5.32882) | | |
| Week 50A | 6.5136 (± 5.56714) | -36.9475 (± 5.43416) | | |
| Week 77A | 9.9852 (± 5.15517) | -31.8000 (± 5.04184) | | |
| Week 104A | 7.9352 (± 7.65221) | -16.5218 (± 7.67117) | | |

**Statistical analyses**

| **Statistical analysis title** | MMRM - Week 2A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.7623 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 6A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |

| | |
|---|---|
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.1506 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 10A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.1071 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 14A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0212 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 18A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0014 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 24A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.0001 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 40A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.0001 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 44A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.0001 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.0001 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 77A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.0001 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0251 |
| Method | Mixed models analysis |

## Secondary: Level of Aβ42 peptides in plasma – ABtest-IA

| End point title | Level of Aβ42 peptides in plasma – ABtest-IA |
|---|---|

End point description:

The change in levels of anti-Aβ42 peptides in plasma (ABtest-IA) from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were differences ($p<0.05$) between groups only at Week 40A and Week 44A.

The MMRM included change from baseline in the efficacy parameter as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at each visit as a repeated measure. An unstructured variance-covariance matrix was used. The following factor was significantly associated with the response measure ($p < 0.15$) and was included in the model: baseline use of Alzheimer Disease symptomatic medication.

| End point type | Secondary |
|---|---|

End point timeframe:

Part A

| End point values | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: pg/mL | | | | |
| least squares mean (standard error) | | | | |
| Week 2A | 0.6745 (± 0.47690) | 0.3868 (± 0.47126) | | |
| Week 6A | 1.2776 (± 0.77358) | 1.6248 (± 0.76131) | | |
| Week 10A | 1.2091 (± 0.88576) | 2.1331 (± 0.87167) | | |
| Week 14A | 1.6433 (± 0.73975) | 1.0209 (± 0.72987) | | |
| Week 18A | 1.9821 (± 0.55465) | 1.2815 (± 0.54507) | | |
| Week 24A | 2.8599 (± 0.72452) | 1.6125 (± 0.71101) | | |
| Week 40A | 2.0361 (± 0.84268) | -1.2781 (± 0.81992) | | |
| Week 44A | 1.7850 (± 1.00896) | -0.9785 (± 0.98520) | | |
| Week 50A | 2.6958 (± 1.24460) | 0.5563 (± 1.21767) | | |
| Week 77A | 2.9304 (± 1.15392) | 0.9045 (± 1.13274) | | |
| Week 104A | 0.8402 (± 1.36427) | 0.5027 (± 1.34946) | | |

### Statistical analyses

| **Statistical analysis title** | MMRM - Week 2A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.6515 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 6A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.7447 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 10A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.4518 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 14A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.5416 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 18A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.3504 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 24A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2109 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 40A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0049 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 44A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0498 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2181 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 77A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |

| | |
|---|---|
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2087 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.8599 |
| Method | Mixed models analysis |

## Secondary: Level of Aβ40 peptides in plasma – ABtest-MS

| End point title | Level of Aβ40 peptides in plasma – ABtest-MS |
|---|---|

End point description:

The change in levels of anti-Aβ40 peptides in plasma (ABtest-MS) from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were differences ($p<0.05$) between groups at each Part A visit between Week 14A and Week 50A.

The MMRM included change from baseline in the efficacy parameter as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at each visit as a repeated measure. A compound symmetric variance-covariance matrix was used.

| End point type | Secondary |
|---|---|

End point timeframe:

Part A

| **End point values** | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: pg/mL | | | | |
| least squares mean (standard error) | | | | |
| Week 2A | 15.0554 (± 86.19364) | 7.2235 (± 87.23687) | | |
| Week 6A | 12.9981 (± 86.19364) | 26.8351 (± 87.24290) | | |
| Week 10A | 10.8314 (± 86.57079) | 123.0016 (± 87.42725) | | |
| Week 14A | 10.1449 (± 86.57079) | 277.9974 (± 87.75818) | | |
| Week 18A | 10.1987 (± 87.66045) | 397.6406 (± 88.10607) | | |
| Week 24A | 31.0861 (± 86.93514) | 453.1893 (± 88.16061) | | |

| | | | | |
|---|---|---|---|---|
| Week 40A | -26.9761 (± 88.54373) | 377.7762 (± 88.44661) | | |
| Week 44A | -28.4349 (± 88.50690) | 846.1633 (± 88.82717) | | |
| Week 50A | -34.2153 (± 88.91637) | 628.9483 (± 88.88059) | | |
| Week 77A | -30.9656 (± 89.32946) | 155.5480 (± 89.69327) | | |
| Week 104A | -37.3585 (± 110.48329) | 85.9804 (± 113.05734) | | |

**Statistical analyses**

| **Statistical analysis title** | MMRM - Week 2A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.9469 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 6A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.9063 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 10A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.3418 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 14A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |

| | |
|---|---|
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0236 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 18A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0012 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 24A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0004 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 40A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0008 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 44A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.0001 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.0001 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 77A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.1255 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.4232 |
| Method | Mixed models analysis |

## Secondary: Level of Aβ42 peptides in plasma – ABtest-MS

| End point title | Level of Aβ42 peptides in plasma – ABtest-MS |
|---|---|

End point description:

The change in levels of anti-Aβ42 peptides in plasma (ABtest-MS) from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were no differences of note between groups at applicable Part A visits (referring to MMRM p-values).

The MMRM included change from baseline in the efficacy parameter as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at each visit as a repeated measure. An unstructured variance-covariance matrix was used. The following factors were significantly associated with the response measure ($p < 0.15$) and were included in the model: ApoE carrier status and clinical subgroup – mild cognitive impairment or very mild Alzheimer Disease.

| End point type | Secondary |
|---|---|

End point timeframe:

Part A

| End point values | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: pg/mL | | | | |
| least squares mean (standard error) | | | | |
| Week 2A | -0.1364 (± 1.23360) | 0.0301 (± 1.23242) | | |
| Week 6A | -0.1492 (± 1.32406) | 1.8092 (± 1.32222) | | |
| Week 10A | -1.0248 (± 1.33166) | 0.8740 (± 1.32527) | | |
| Week 14A | 0.1680 (± 1.15553) | 0.4841 (± 1.15690) | | |
| Week 18A | 0.6469 (± 1.51683) | -0.9551 (± 1.49962) | | |
| Week 24A | -0.0526 (± 1.38574) | -1.6059 (± 1.38522) | | |
| Week 40A | 2.9633 (± 1.71207) | 3.3472 (± 1.68092) | | |
| Week 44A | 1.6060 (± 1.52120) | 1.9498 (± 1.49737) | | |
| Week 50A | 0.2069 (± 1.49045) | 2.7196 (± 1.46044) | | |
| Week 77A | 1.4766 (± 1.61328) | 4.7243 (± 1.58567) | | |
| Week 104A | 4.7604 (± 2.18825) | 2.6870 (± 2.19551) | | |

**Statistical analyses**

| Statistical analysis title | MMRM - Week 2A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.9211 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 6A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2817 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 10A |
|---|---|

| | |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2984 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 14A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.8402 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 18A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.4428 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 24A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.4156 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 40A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.8706 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 44A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.8691 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2188 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 77A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.1448 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.5004 |
| Method | Mixed models analysis |

## Secondary: Cortical fibrillary amyloid deposition assessed by a-PET scans

| End point title | Cortical fibrillary amyloid deposition assessed by a-PET scans |
|---|---|

End point description:

The change in amyloid-PET (a-PET) standard centiloid global cortical area (reference Pons) from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were no differences between groups at either Week 50A (P=0.1058) or Week 104A.

The MMRM included change from baseline in the efficacy parameter as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at

each visit as a repeated measure. An unstructured variance-covariance matrix was used. The following factor was significantly associated with the response measure ($p < 0.15$) and was included in the model: baseline use of Alzheimer Disease symptomatic medication.

| End point type | Secondary |
|---|---|

End point timeframe:

Part A

| **End point values** | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: Centiloids | | | | |
| least squares mean (standard error) | | | | |
| Week 50A | 1.411 (± 1.1203) | 3.561 (± 1.0918) | | |
| Week 104A | 4.461 (± 1.3841) | 1.241 (± 1.5403) | | |

**Statistical analyses**

| **Statistical analysis title** | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.1058 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0922 |
| Method | Mixed models analysis |

**Secondary: Percentage of change in brain volume**

| End point title | Percentage of change in brain volume |
|---|---|

End point description:

The percent change in brain volume from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were no differences of note between groups at applicable Part A visits (referring to MMRM p-values).

The MMRM included change from baseline in the efficacy parameter as the dependent variable;

treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at each visit as a repeated measure. An unstructured variance-covariance matrix was used.

| End point type | Secondary |
|---|---|

End point timeframe:

Part A

| **End point values** | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: percent | | | | |
| least squares mean (standard error) | | | | |
| Week 24A | -1.39 (± 0.157) | -1.40 (± 0.165) | | |
| Week 50A | -2.05 (± 0.175) | -1.75 (± 0.187) | | |
| Week 104A | -4.16 (± 0.470) | -3.11 (± 0.412) | | |

**Statistical analyses**

| **Statistical analysis title** | MMRM - Week 24A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.9313 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2243 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |

| | |
|---|---|
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0952 |
| Method | Mixed models analysis |

## Secondary: Percentage of change in hippocampal volume

| | |
|---|---|
| End point title | Percentage of change in hippocampal volume |

End point description:

The percent change in right and left hippocampal volume from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were no differences of note between groups at applicable Part A visits (referring to MMRM p-values).

The MMRM included change from baseline in the efficacy parameter as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at each visit as a repeated measure. An unstructured variance-covariance matrix was used. The following factor was significantly associated with the response measure ($p < 0.15$) and was included in the model (only for left hippocampus): clinical subgroup – mild cognitive impairment or very mild Alzheimer Disease.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Part A

| End point values | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: percent | | | | |
| least squares mean (standard error) | | | | |
| Week 24A - left | -1.60 (± 0.454) | -2.14 (± 0.450) | | |
| Week 50A - left | -4.13 (± 0.588) | -4.24 (± 0.571) | | |
| Week 104A - left | -7.13 (± 1.060) | -8.15 (± 0.965) | | |
| Week 24A - right | -1.37 (± 0.442) | -1.44 (± 0.439) | | |
| Week 50A - right | -3.34 (± 0.513) | -3.23 (± 0.506) | | |
| Week 104A - right | -6.37 (± 1.001) | -6.49 (± 0.901) | | |

### Statistical analyses

| Statistical analysis title | MMRM - Week 24A - left |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |

| | |
|---|---|
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.3599 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 50A - left |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.8913 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 104A - left |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.4736 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 24A - right |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.9095 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 50A - right |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.8744 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 104A - right |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.9307 |
| Method | Mixed models analysis |

## Secondary: Percentage of change in ventricular volume

| End point title | Percentage of change in ventricular volume |
|---|---|

End point description:

The percent change in ventricular volume from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were no differences of note between groups at applicable Part A visits (referring to MMRM p-values).

The MMRM included change from baseline in the efficacy parameter as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at each visit as a repeated measure. An unstructured variance-covariance matrix was used.
The following factor was significantly associated with the response measure ($p < 0.15$) and was included in the model: baseline use of Alzheimer Disease symptomatic medication.

| End point type | Secondary |
|---|---|

End point timeframe:

Part A

| End point values | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: percent | | | | |
| least squares mean (standard error) | | | | |
| Week 24A | 5.30 (± 0.584) | 5.94 (± 0.573) | | |
| Week 50A | 10.63 (± 0.809) | 10.21 (± 0.819) | | |
| Week 104A | 22.51 (± 1.887) | 21.26 (± 1.848) | | |

## Statistical analyses

| Statistical analysis title | MMRM - Week 24A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |

| | |
|---|---|
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.3982 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.7035 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.6334 |
| Method | Mixed models analysis |

## Secondary: Level of Aβ42 Peptides in CSF

| End point title | Level of Aβ42 Peptides in CSF |
|---|---|

End point description:

The change in levels of Aβ42 peptides in cerebrospinal fluid (CSF) from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were no differences of note between groups at applicable Part A visits (referring to MMRM p-values).

The MMRM included change from baseline in the efficacy parameter as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at each visit as a repeated measure. An unstructured variance-covariance matrix was used.

| End point type | Secondary |
|---|---|

End point timeframe:

Part A

| End point values | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: pg/mL | | | | |
| least squares mean (standard error) | | | | |
| Week 50A | 29.0 (± 19.40) | -2.0 (± 19.79) | | |
| Week 104A | -15.3 (± 22.51) | 4.0 (± 25.82) | | |

## Statistical analyses

| Statistical analysis title | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2193 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.5543 |
| Method | Mixed models analysis |

## Secondary: Level of Aβ40 peptides in CSF

| End point title | Level of Aβ40 peptides in CSF |
|---|---|

End point description:

The change in levels of Aβ40 peptides in cerebrospinal fluid (CSF) from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were no differences of note between groups at applicable Part A visits (referring to MMRM p-values).

The MMRM included change from baseline in the efficacy parameter as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at each visit as a repeated measure. An unstructured variance-covariance matrix was used.

| End point type | Secondary |
|---|---|

End point timeframe:

Part A

| End point values | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: pg/mL | | | | |
| least squares mean (standard error) | | | | |
| Week 50A | -62.3 (± 173.57) | -141.8 (± 180.07) | | |
| Week 104A | -652.4 (± 227.08) | -192.5 (± 260.67) | | |

## Statistical analyses

| Statistical analysis title | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.7324 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.1719 |
| Method | Mixed models analysis |

## Secondary: Aβ42/Aβ40 ratio in CSF

| End point title | Aβ42/Aβ40 ratio in CSF |
|---|---|

End point description:

The change in Aβ42/Aβ40 ratio in cerebrospinal fluid (CSF) from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were no differences of note between groups at applicable Part A visits (referring to MMRM p-values).

The MMRM included change from baseline in the efficacy parameter as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at each visit as a repeated measure. An unstructured variance-covariance matrix was used. The following factor was significantly associated with the response measure ($p < 0.15$) and was included in the model: baseline use of Alzheimer Disease symptomatic medication.

| End point type | Secondary |
|---|---|

End point timeframe:

Part A

| End point values | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: n/a | | | | |
| least squares mean (standard error) | | | | |
| Week 50A | 0.0005 (± 0.00135) | 0.0009 (± 0.00129) | | |
| Week 104A | 0.0016 (± 0.00183) | 0.0020 (± 0.00205) | | |

**Statistical analyses**

| Statistical analysis title | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.7977 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.8828 |
| Method | Mixed models analysis |

**Secondary: Level of total Tau in CSF**

| End point title | Level of total Tau in CSF |
|---|---|

End point description:

The change in levels of total Tau in cerebrospinal fluid (CSF) from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were no differences of note between groups at applicable Part A visits (referring to MMRM p-values).

The MMRM included change from baseline in the efficacy parameter as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at each visit as a repeated measure. An unstructured variance-covariance matrix was used. The following factor was significantly associated with the response measure ($p < 0.15$) and was included in the model: baseline use of Alzheimer Disease symptomatic medication.

| End point type | Secondary |
|---|---|

| End point timeframe: |
|---|
| Part A |

| End point values | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: pg/mL | | | | |
| least squares mean (standard error) | | | | |
| Week 50A | 23.4 (± 12.20) | 27.6 (± 12.39) | | |
| Week 104A | 25.9 (± 14.20) | 14.7 (± 16.38) | | |

**Statistical analyses**

| Statistical analysis title | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.7954 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.5895 |
| Method | Mixed models analysis |

**Secondary: Level of p-Tau 181 in CSF**

| End point title | Level of p-Tau 181 in CSF |
|---|---|

End point description:

The change in levels of p-Tau 181 in cerebrospinal fluid (CSF) from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were no differences of note between groups at applicable Part A visits (referring to MMRM p-values).

The MMRM included change from baseline in the efficacy parameter as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at each visit as a repeated measure. An unstructured variance-covariance matrix was used. The following factor was significantly associated with the response measure ($p < 0.15$) and was included in the model: baseline use of Alzheimer Disease symptomatic medication.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Part A

| End point values | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: pg/mL | | | | |
| least squares mean (standard error) | | | | |
| Week 50A | 2.43 (± 1.684) | 3.15 (± 1.697) | | |
| Week 104A | 1.55 (± 2.387) | 0.82 (± 2.634) | | |

**Statistical analyses**

| Statistical analysis title | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.743 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.832 |
| Method | Mixed models analysis |

## Secondary: Level of neurofilament light in CSF

| End point title | Level of neurofilament light in CSF |
|---|---|

End point description:

The change in levels of neurofilament light in cerebrospinal fluid (CSF) from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were no differences of note between groups at applicable Part A visits (referring to MMRM p-values).

The MMRM included change from baseline in the efficacy parameter as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at each visit as a repeated measure. An unstructured variance-covariance matrix was used.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Part A

| End point values | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: pg/mL | | | | |
| least squares mean (standard error) | | | | |
| Week 50A | 59.36 (± 76.513) | 181.20 (± 78.606) | | |
| Week 104A | 317.11 (± 190.948) | 276.14 (± 216.781) | | |

**Statistical analyses**

| Statistical analysis title | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2283 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.886 |
| Method | Mixed models analysis |

**Secondary: Level of neurogranin in CSF**

| End point title | Level of neurogranin in CSF |
|---|---|

End point description:

The change in levels of neurogranin in cerebrospinal fluid (CSF) from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were no differences of note between groups at applicable Part A visits (referring to MMRM p-values).

The MMRM included change from baseline in the efficacy parameter as the dependent variable; treatment, protocol-specified visits, and treatment-by-visit interaction as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at each visit as a repeated measure. An unstructured variance-covariance matrix was used.

| End point type | Secondary |
|---|---|

End point timeframe:

Part A

| End point values | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: pg/mL | | | | |
| least squares mean (standard error) | | | | |
| Week 50A | -4.69 (± 8.023) | -5.93 (± 8.328) | | |
| Week 104A | -34.97 (± 13.533) | -31.13 (± 15.571) | | |

**Statistical analyses**

| Statistical analysis title | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.909 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.8498 |
| Method | Mixed models analysis |

## Secondary: Mini Mental State Examination Score

| End point title | Mini Mental State Examination Score |
|---|---|

End point description:

The change in Mini Mental State Examination (MMSE) score from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were no differences of note between groups at applicable Part A visits (referring to MMRM p-values).

The MMRM included change from baseline in the efficacy parameter as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at

each visit as a repeated measure. An unstructured variance-covariance matrix was used. The following factor was significantly associated with the response measure ($p < 0.15$) and was included in the model: baseline use of Alzheimer Disease symptomatic medication.

| End point type | Secondary |
|---|---|
| End point timeframe: | |
| Part A | |

| **End point values** | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | | | | |
| Week 24A | -2.15 (± 0.422) | -2.24 (± 0.420) | | |
| Week 50A | -3.64 (± 0.465) | -2.65 (± 0.460) | | |
| Week 77A | -4.58 (± 0.628) | -4.15 (± 0.621) | | |
| Week 104A | -5.98 (± 0.816) | -4.97 (± 0.816) | | |

**Statistical analyses**

| **Statistical analysis title** | MMRM - Week 24A |
|---|---|
| Comparison groups | ABvac40 arm Part A v Placebo arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.8711 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.1098 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 77A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |

| | |
|---|---|
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.6179 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.3715 |
| Method | Mixed models analysis |

## Secondary: Clinical Dementia Rating-Sum of Boxes score

| End point title | Clinical Dementia Rating-Sum of Boxes score |
|---|---|

End point description:

The change in clinical dementia rating-sum of boxes (CDR-SB) score from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were no differences of note between groups at applicable Part A visits (referring to MMRM p-values).

The MMRM included change from baseline in the efficacy parameter as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at each visit as a repeated measure. An unstructured variance-covariance matrix was used. The following factor was significantly associated with the response measure ($p < 0.15$) and was included in the model: ApoE carrier status.

| End point type | Secondary |
|---|---|

End point timeframe:

Part A

| **End point values** | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | | | | |
| Week 24A | 0.75 (± 0.152) | 0.73 (± 0.156) | | |
| Week 50A | 1.41 (± 0.222) | 1.36 (± 0.221) | | |
| Week 77A | 2.12 (± 0.328) | 2.05 (± 0.325) | | |
| Week 104A | 3.21 (± 0.463) | 2.90 (± 0.462) | | |

**Statistical analyses**

| **Statistical analysis title** | MMRM - Week 24A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.8949 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.8712 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 77A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.8748 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.6402 |
| Method | Mixed models analysis |

**Secondary: Repeatable Battery for the Assessment of Neuropsychological Status score**

| End point title | Repeatable Battery for the Assessment of Neuropsychological Status score |
|---|---|

End point description:

The change in Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) total score from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were no differences of note between groups at applicable Part A visits (referring to MMRM p-values).

The MMRM included change from baseline in the efficacy parameter as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at each visit as a repeated measure. An unstructured variance-covariance matrix was used.

| End point type | Secondary |
|---|---|

End point timeframe:

Part A

| **End point values** | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | | | | |
| Week 24A | -1.30 (± 1.009) | -2.10 (± 1.022) | | |
| Week 50A | -5.45 (± 1.076) | -5.56 (± 1.077) | | |
| Week 77A | -4.71 (± 1.273) | -2.66 (± 1.255) | | |
| Week 104A | -3.17 (± 1.798) | -1.33 (± 1.793) | | |

**Statistical analyses**

| **Statistical analysis title** | MMRM - Week 24A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.552 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.9371 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 77A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |

| | |
|---|---|
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2354 |
| Method | Mixed models analysis |

| | |
|---|---|
| **Statistical analysis title** | MMRM - Week 104A |
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.4608 |
| Method | Mixed models analysis |

## Secondary: Alzheimer's Disease Cooperative Study - Activities of Daily Living, Mild Cognitive Impairment score

| | |
|---|---|
| End point title | Alzheimer's Disease Cooperative Study - Activities of Daily Living, Mild Cognitive Impairment score |

End point description:

The change in Alzheimer’s Disease Cooperative Study – Activities of Daily Living, Mild Cognitive Impairment (ADCS-ADL MCI) total score from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were no differences of note between groups at applicable Part A visits (referring to MMRM p-values).

The MMRM included change from baseline in the efficacy parameter as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at each visit as a repeated measure. An unstructured variance-covariance matrix was used.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Part A

| **End point values** | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | | | | |
| Week 24A | -0.99 (± 0.834) | -2.08 (± 0.844) | | |
| Week 50A | -4.15 (± 1.124) | -3.78 (± 1.112) | | |
| Week 77A | -6.33 (± 1.399) | -6.54 (± 1.380) | | |
| Week 104A | -9.87 (± 2.002) | -10.02 (± 1.982) | | |

**Statistical analyses**

| **Statistical analysis title** | MMRM - Week 24A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.3246 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.8047 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 77A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.916 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.9582 |
| Method | Mixed models analysis |

**Secondary: Trail Making Test scores**

| End point title | Trail Making Test scores |
|---|---|

End point description:

The change in Trail Making Test (TMT) scores (Trail A and Trail B) from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were no differences of note between groups at applicable Part A visits for either TMT score, except at Week 77A for Trail A (referring to MMRM p-values).

The MMRM included change from baseline in the efficacy parameter as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at each visit as a repeated measure. An unstructured variance-covariance matrix was used. The following factor was significantly associated with the response measure ($p < 0.15$) and was included in the model: ApoE carrier status (only for Trail A).

| End point type | Secondary |
|---|---|

End point timeframe:

Part A

| **End point values** | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: seconds | | | | |
| least squares mean (standard error) | | | | |
| Week 24A - Trail A | 0.54 (± 2.960) | -0.59 (± 2.939) | | |
| Week 50A - Trail A | 11.34 (± 4.186) | 3.59 (± 4.023) | | |
| Week 77A - Trail A | 17.42 (± 4.669) | 2.79 (± 4.425) | | |
| Week 104A - Trail A | 20.09 (± 7.253) | 9.24 (± 6.967) | | |
| Week 24A - Trail B | 5.43 (± 8.102) | -8.47 (± 8.464) | | |
| Week 50A - Trail B | 18.83 (± 8.503) | 18.43 (± 9.122) | | |
| Week 77A - Trail B | 17.13 (± 8.680) | 2.38 (± 9.762) | | |
| Week 104A - Trail B | 20.81 (± 10.715) | -4.64 (± 11.206) | | |

## Statistical analyses

| **Statistical analysis title** | MMRM - Week 24A - Trail A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.777 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 50A - Trail A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.1727 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 77A - Trail A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0218 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 104A - Trail A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2789 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 24A - Trail B |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2261 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 50A - Trail B |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.9743 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 77A - Trail B |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2556 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 104A - Trail B |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.1008 |
| Method | Mixed models analysis |

## Secondary: Investigator Global Evaluation score

| End point title | Investigator Global Evaluation score |
|---|---|

End point description:

The change in Investigator Global Evaluation (IGE) score from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were no differences of note between groups at applicable Part A visits (referring to MMRM p-values).

The MMRM included IGE after baseline as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at each visit as a repeated measure. An unstructured variance-covariance matrix was used. The following factor was significantly associated with the response measure ($p < 0.15$) and was included in the model: ApoE carrier status.

| End point type | Secondary |
|---|---|

End point timeframe:

Part A

| End point values | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | | | | |
| Week 24A | 4.02 (± 0.075) | 4.07 (± 0.077) | | |
| Week 50A | 4.26 (± 0.101) | 4.21 (± 0.101) | | |
| Week 104A | 4.55 (± 0.180) | 4.45 (± 0.184) | | |

**Statistical analyses**

| **Statistical analysis title** | MMRM - Week 24A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.6189 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.6937 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.6981 |
| Method | Mixed models analysis |

| **Secondary: Columbia Suicide Severity Rating Scale** | |
|---|---|
| End point title | Columbia Suicide Severity Rating Scale |
| End point description:<br>Summary statistics of subjects with suicidal ideation or suicidal behavior since last visit. | |
| End point type | Secondary |
| End point timeframe:<br>Part A | |

| End point values | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 57[10] | 58[11] | | |
| Units: subjects | | | | |
| Week 24A - suicidal ideation | 1 | 1 | | |
| Week 24A - suicidal behavior | 0 | 0 | | |
| Week 50A - suicidal ideation | 1 | 2 | | |
| Week 50A - suicidal behavior | 0 | 0 | | |
| Week 77A - suicidal ideation | 1 | 4 | | |
| Week 77A - suicidal behavior | 0 | 0 | | |
| Week 104A - suicidal ideation | 0 | 0 | | |
| Week 104A - suicidal behavior | 0 | 0 | | |

Notes:

[10] - At Week 24A, n=57; at Week 50A, n=56; at Week 77A, n=54; at Week 104A, n=26

[11] - At Week 24A, n=58; at Week 50A, n=58; at Week 77A, n=56; at Week 104A, n=25

### Statistical analyses

No statistical analyses for this end point

## Secondary: EuroQol 5 Dimensions 5 Levels Overall Severity Index Score

| End point title | EuroQol 5 Dimensions 5 Levels Overall Severity Index Score |
|---|---|

End point description:

The change in Euroqol 5 Dimensions 5 levels (EQ-5D-5L) - overall severity index score from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were no differences of note between groups at applicable Part A visits (referring to MMRM p-values).

The MMRM included change from baseline in the efficacy parameter as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at each visit as a repeated measure. An unstructured variance-covariance matrix was used.

| End point type | Secondary |
|---|---|

End point timeframe:

Part A

| End point values | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | | | | |
| Week 50A | -0.99 (± 1.204) | -2.71 (± 1.196) | | |
| Week 104A | -3.06 (± 1.740) | -0.92 (± 1.725) | | |

### Statistical analyses

| Statistical analysis title | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2863 |
| Method | Mixed models analysis |

| Statistical analysis title | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.3703 |
| Method | Mixed models analysis |

## Secondary: EuroQol 5 Dimensions 5 Levels - Visual Analogue Scale Score

| End point title | EuroQol 5 Dimensions 5 Levels - Visual Analogue Scale Score |
|---|---|

End point description:

The change in Euroqol 5 Dimensions 5 levels (EQ-5D-5L) - visual analogue scale (VAS) score from baseline to each applicable post-baseline efficacy visit (Part A) was analyzed using a Mixed-Model Repeated Measures (MMRM), and the ITT analysis set. There were no differences of note between groups at applicable Part A visits (referring to MMRM p-values).

The MMRM included change from baseline in the efficacy parameter as the dependent variable; treatment, protocol-specified visits, treatment-by-visit interaction, and amyloid positivity as the fixed effects; baseline efficacy parameter and baseline age as covariates; and measures within-patient at each visit as a repeated measure. An unstructured variance-covariance matrix was used. The following factor was significantly associated with the response measure ($p < 0.15$) and was included in the model: ApoE carrier status and clinical subgroup – mild cognitive impairment or very mild Alzheimer Disease.

| End point type | Secondary |
|---|---|

End point timeframe:

Part A

| End point values | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 62 | | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | | | | |
| Week 50A | -5.20 (± 2.335) | -5.07 (± 2.289) | | |
| Week 104A | -5.55 (± 3.109) | -1.84 (± 3.111) | | |

**Statistical analyses**

| **Statistical analysis title** | MMRM - Week 50A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.9663 |
| Method | Mixed models analysis |

| **Statistical analysis title** | MMRM - Week 104A |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 124 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.3843 |
| Method | Mixed models analysis |

| **Other pre-specified: MΔ of anti-Aβ40 antibody signal (OD in ELISA) - Sensitivity** | |
|---|---|
| End point title | MΔ of anti-Aβ40 antibody signal (OD in ELISA) - Sensitivity |

End point description:

Average maximal increment (MΔ) of plasma anti-Aβ40 antibody signal (optical density [OD] in ELISA) in each subject with regard to Baseline visit.
Sensitivity analyses in the PP (Part A) analysis set.
Results were aligned with primary analysis in the mITT analysis set.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Maximal increment (MΔ) from Baseline across all Part A post-Baseline visits

| **End point values** | Placebo arm Part A | ABvac40 arm Part A | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 45[12] | 54[13] | | |
| Units: no unit of measure since results are OD | | | | |
| arithmetic mean (standard deviation) | 0.10 (± 0.13) | 3.29 (± 0.67) | | |

Notes:

[12] - PP analysis set.

[13] - PP analysis set.

## Statistical analyses

| **Statistical analysis title** | t-test |
|---|---|

Statistical analysis description:

1-sided t-test to compare the ABvac40 and placebo groups

| | |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[14] |
| P-value | < 0.0001 [15] |
| Method | t-test, 1-sided |

Notes:

[14] - The trial was considered successfully confirmatory regarding efficacy (immunogenicity) of ABvac40 if the average MΔ of anti-Aβ40 antibody signal (OD in ELISA) in the ABvac40 group was significantly greater than the average MΔ of anti-Aβ40 antibody signal in the Placebo group. i.e.
– Null hypothesis: average MΔ anti-Aβ40 (ABvac40) ≤ average MΔ anti-Aβ40 (placebo).
– Alternative hypothesis: average MΔ anti-Aβ40 (ABvac40) > average MΔ anti-Aβ40 (placebo)

[15] - A 1-sided t-test with a significance level of 0.025 was employed

| **Statistical analysis title** | Mann-Whitney U test |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[16] |
| P-value | < 0.0001 [17] |
| Method | Wilcoxon (Mann-Whitney) |

Notes:

[16] - Additional test

[17] - 1-sided

| **Statistical analysis title** | ANCOVA model |
|---|---|

Statistical analysis description:

The average MΔ of anti-Aβ40 antibody signal between the two treatment groups was compared using an ANCOVA model, using the MΔ anti-Aβ40 antibody signal as the dependent variable, baseline anti-Aβ40 antibody signal (OD in ELISA) as covariate and treatment group and amyloid positivity as fixed effects.

| | |
|---|---|
| Comparison groups | Placebo arm Part A v ABvac40 arm Part A |
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Parameter estimate | Least squares mean differences |
| Point estimate | 3.21 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.02 |
| upper limit | 3.4 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.09 |

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| Whole study duration (Part A+Part B; up to 42 months) | |
| Adverse event reporting additional description: | |
| Only treatment-emergent adverse events are reported. | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 20.0 |

| Reporting groups | |
|---|---|
| Reporting group title | ABvac40 (Part A) ABvac40 (Part B) |
| Reporting group description: | |
| All subjects in the ABvac40 arm Part A/Placebo+Booster arm Part B treatment sequence who took ABvac40 in Part A, and all subjects in the Placebo arm Part A/ABvac40 arm Part B treatment sequence who took ABvac40 in Part B were included in summary group 'ABvac40 (part A) ABvac40 (part B)' | |
| Reporting group title | Placebo (Part A) |
| Reporting group description: | |
| All subjects who took Placebo in Part A of the study were included in summary group 'Placebo (Part A)' | |
| Reporting group title | Placebo (Part B) Booster (Part B) |
| Reporting group description: | |
| All subjects in the ABvac40 arm Part A/Placebo+Booster arm Part B treatment sequence who took either Placebo or ABvac40 booster in Part B of the study were included in summary group 'Placebo (Part B) Booster (Part B)' | |

| Serious adverse events | ABvac40 (Part A) ABvac40 (Part B) | Placebo (Part A) | Placebo (Part B) Booster (Part B) |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 23 / 99 (23.23%) | 16 / 62 (25.81%) | 2 / 40 (5.00%) |
| number of deaths (all causes) | 1 | 1 | 0 |
| number of deaths resulting from adverse events | 1 | 1 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Rectal cancer | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 0 / 62 (0.00%) | 0 / 40 (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 |
| Invasive lobular breast carcinoma | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 62 (1.61%) | 0 / 40 (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 |
| Nasal cavity cancer | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 62 (1.61%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatic neoplasm | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 62 (1.61%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Femur fracture | | | |
| subjects affected / exposed | 2 / 99 (2.02%) | 0 / 62 (0.00%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Humerus fracture | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 0 / 62 (0.00%) | 0 / 40 (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 |
| Pelvic fracture | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 0 / 62 (0.00%) | 0 / 40 (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 | 0 / 99 (0.00%) | 1 / 62 (1.61%) | 0 / 40 (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 |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 62 (1.61%) | 0 / 40 (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 |
| Vascular disorders | | | |
| Peripheral artery stenosis | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 0 / 62 (0.00%) | 0 / 40 (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 |

| | | | |
|---|---|---|---|
| Venous thrombosis limb | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 0 / 62 (0.00%) | 0 / 40 (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 |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 0 / 62 (0.00%) | 0 / 40 (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 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 1 / 62 (1.61%) | 0 / 40 (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 |
| Atrioventricular block complete | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 0 / 62 (0.00%) | 0 / 40 (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 |
| Nervous system disorders | | | |
| Amyloid related imaging abnormalities | Additional description: All ARIA events were classified as ARIA-H per study protocol and conservatively interpreted. | | |
| subjects affected / exposed | 9 / 99 (9.09%) | 9 / 62 (14.52%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 4 / 10 | 10 / 13 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebellar infarction | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 0 / 62 (0.00%) | 0 / 40 (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 |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 62 (1.61%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral infarction | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 62 (1.61%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Lacunar infarction | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 62 (0.00%) | 1 / 40 (2.50%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 0 / 62 (0.00%) | 0 / 40 (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 |
| General physical health deterioration | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 0 / 62 (0.00%) | 0 / 40 (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 |
| Gastrointestinal disorders | | | |
| Pancreatitis acute | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 0 / 62 (0.00%) | 0 / 40 (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 |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 62 (1.61%) | 0 / 40 (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 |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 99 (1.01%) | 0 / 62 (0.00%) | 0 / 40 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 3 / 99 (3.03%) | 0 / 62 (0.00%) | 0 / 40 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Agitation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 62 (1.61%) | 0 / 40 (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 |
| Infections and infestations | | | |
| Coronavirus infection | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 62 (0.00%) | 1 / 40 (2.50%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 62 (1.61%) | 0 / 40 (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 |

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

| **Non-serious adverse events** | ABvac40 (Part A)<br>ABvac40 (Part B) | Placebo (Part A) | Placebo (Part B)<br>Booster (Part B) |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 85 / 99 (85.86%) | 54 / 62 (87.10%) | 30 / 40 (75.00%) |
| Investigations | | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 62 (0.00%) | 2 / 40 (5.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 9 / 99 (9.09%) | 4 / 62 (6.45%) | 4 / 40 (10.00%) |
| occurrences (all) | 9 | 4 | 4 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 3 / 99 (3.03%) | 6 / 62 (9.68%) | 0 / 40 (0.00%) |
| occurrences (all) | 3 | 6 | 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 8 / 99 (8.08%) | 7 / 62 (11.29%) | 3 / 40 (7.50%) |
| occurrences (all) | 8 | 7 | 3 |
| Dizziness | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 99 (3.03%) | 2 / 62 (3.23%) | 2 / 40 (5.00%) |
| occurrences (all) | 3 | 2 | 2 |
| Loss of consciousness | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 62 (0.00%) | 2 / 40 (5.00%) |
| occurrences (all) | 0 | 0 | 2 |
| General disorders and administration site conditions | | | |
| Injection site erythema | | | |
| subjects affected / exposed | 9 / 99 (9.09%) | 4 / 62 (6.45%) | 1 / 40 (2.50%) |
| occurrences (all) | 9 | 4 | 1 |
| Injection site reaction | | | |
| subjects affected / exposed | 8 / 99 (8.08%) | 4 / 62 (6.45%) | 3 / 40 (7.50%) |
| occurrences (all) | 8 | 4 | 3 |
| Injection site swelling | | | |
| subjects affected / exposed | 7 / 99 (7.07%) | 1 / 62 (1.61%) | 1 / 40 (2.50%) |
| occurrences (all) | 7 | 1 | 1 |
| Fatigue | | | |
| subjects affected / exposed | 5 / 99 (5.05%) | 4 / 62 (6.45%) | 2 / 40 (5.00%) |
| occurrences (all) | 5 | 4 | 2 |
| Peripheral swelling | | | |
| subjects affected / exposed | 5 / 99 (5.05%) | 1 / 62 (1.61%) | 1 / 40 (2.50%) |
| occurrences (all) | 5 | 1 | 1 |
| Inflammation | | | |
| subjects affected / exposed | 4 / 99 (4.04%) | 0 / 62 (0.00%) | 2 / 40 (5.00%) |
| occurrences (all) | 4 | 0 | 2 |
| Injection site induration | | | |
| subjects affected / exposed | 4 / 99 (4.04%) | 1 / 62 (1.61%) | 3 / 40 (7.50%) |
| occurrences (all) | 4 | 1 | 3 |
| Injection site pain | | | |
| subjects affected / exposed | 3 / 99 (3.03%) | 1 / 62 (1.61%) | 3 / 40 (7.50%) |
| occurrences (all) | 3 | 1 | 3 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 4 / 62 (6.45%) | 0 / 40 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|---|---|---|
| Erythema | | | |
| subjects affected / exposed | 13 / 99 (13.13%) | 7 / 62 (11.29%) | 0 / 40 (0.00%) |
| occurrences (all) | 13 | 7 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 5 / 99 (5.05%) | 1 / 62 (1.61%) | 0 / 40 (0.00%) |
| occurrences (all) | 5 | 1 | 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 5 / 99 (5.05%) | 2 / 62 (3.23%) | 1 / 40 (2.50%) |
| occurrences (all) | 5 | 2 | 1 |
| Irritability | | | |
| subjects affected / exposed | 3 / 99 (3.03%) | 1 / 62 (1.61%) | 2 / 40 (5.00%) |
| occurrences (all) | 3 | 1 | 2 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 4 / 99 (4.04%) | 3 / 62 (4.84%) | 2 / 40 (5.00%) |
| occurrences (all) | 4 | 3 | 2 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 4 / 99 (4.04%) | 2 / 62 (3.23%) | 2 / 40 (5.00%) |
| occurrences (all) | 4 | 2 | 2 |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 16 / 99 (16.16%) | 3 / 62 (4.84%) | 4 / 40 (10.00%) |
| occurrences (all) | 16 | 3 | 4 |
| Coronavirus infection | | | |
| subjects affected / exposed | 10 / 99 (10.10%) | 1 / 62 (1.61%) | 9 / 40 (22.50%) |
| occurrences (all) | 10 | 1 | 9 |
| Periodontitis | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 0 / 62 (0.00%) | 2 / 40 (5.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 4 / 62 (6.45%) | 1 / 40 (2.50%) |
| occurrences (all) | 0 | 4 | 1 |
| Metabolism and nutrition disorders | | | |
| Iron deficiency | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 99 (1.01%) | 0 / 62 (0.00%) | 2 / 40 (5.00%) |
| occurrences (all) | 1 | 0 | 2 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 99 (0.00%) | 1 / 62 (1.61%) | 2 / 40 (5.00%) |
| occurrences (all) | 0 | 1 | 2 |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 04 August 2017 | After an exhaustive review by the sponsor and the principal investigator, the protocol was amended to avoid any misinterpretation. Additionally, some modifications were issued due to the French and Swedish competent authorities' review. This protocol amendment was issued on 04 Aug 2017, prior to the start of the study in any site but after the approval of the study in Spain. The following main changes were performed:<br>– Expansion of the screening period from 28 to 60 days.<br>– Amendment of the number of sites.<br>– Inclusion of the new potential reasons for withdrawal of subjects from this study.<br>– Clarification of the urine analysis (urine test strips) and assessment of AD biomarkers.<br>– Inclusion of neurofilament light as an additional disease biomarker.<br>– Amendment of the IMP packaging text.<br>– Clarification of the allowed concomitant medications and special safety procedures. |
| 23 July 2018 | After approximately 1 year of recruitment, it was observed that there was a low prevalence of a-PET-negative subjects among the eligible population. Accordingly, the recruitment stratification on a-PET was eliminated. This protocol amendment was issued on 23 Jul 2018 (Spain), 16 Aug 2018 (France and Sweden) and 28 Sep 2018 (Italy). The following main changes were performed:<br>– Redefinition of secondary objectives 2 and 3.<br>– A DSMB and an additional interim analysis were added.<br>– The exclusion criterion 20 was modified and a new exclusion criterion 27 was added.<br>– Clarification of the previous, concomitant, prohibited and restricted medicines.<br>– Clarification of the statistical methods.<br>– Modification of procedures and study visit windows in the schedule of assessments.<br>– Amendment of the number of sites.<br>– Simplification of the AEs causality evaluation.<br>– Other minor changes. |

| | |
|---|---|
| 22 May 2020 | The main reason for the amendment was the addition of an 18-month, open label, cross-over extension of the study (Part B), aiming to assess the effects of a delayed start with ABvac40 and of a second ABvac40 booster. This amendment was triggered after the pre-planned first interim analysis conducted in July 2019, after the first 36 subjects had completed their 24 week visit (the results showed that ABvac40 has a favorable profile concerning futility criteria, safety and immunogenicity data). Additionally, the requirement of subjects being COVID-19 free to receive the IMP was added. This protocol amendment was issued on 22 May 2020 (Spain), 19 Jun 2020 (France) and 22 Jun 2020 (Italy and Sweden).<br>The following main changes were performed:<br>– Introduction of an 18-month, open label, cross-over extension of the study (Part B).<br>– Requirement of subjects being COVID-19 free to receive the IMP.<br>– Amendment of the planned study duration.<br>– Deletion of the stratification based on a PET positivity.<br>– Cancellation of the third interim analysis planned (after the 50-week visit).*<br>– Adjustment of the number of participant sites.<br>– Clarification of exclusion criterion number 26. The definition of childbearing potential woman was added.<br>– Amendment in the study administrative structure; the members of the DSMB and medical expert were included.<br>– Clarification of the study hypothesis. The original study hypothesis was broken down into 2 parts, including a confirmatory and satisfactory analysis.<br>– Amendment of the reporting and follow up of Amyloid Imaging Related Abnormalities (ARIA) findings.<br>– Clarification of the reporting of the previous concomitant medication for any disease and for Alzheimer’s disease.<br>– Clarification in the wording of the main efficacy variable.<br>– Clarification of the DSMB activities and procedures.<br>– Clarification of the subject replacement |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported