



## Clinical trial results:

### A Phase 3b/4 Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Verify the Clinical Benefit of Aducanumab (BIIB037) in Participants With Alzheimer's Disease Summary

|                          |                      |
|--------------------------|----------------------|
| EudraCT number           | 2022-001671-14       |
| Trial protocol           | DE ES FI PT BE IT PL |
| Global end of trial date | 12 August 2024       |

#### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1            |
| This version publication date  | 16 March 2025 |
| First version publication date | 16 March 2025 |

#### Trial information

##### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | 221AD305 |
|-----------------------|----------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT05310071 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                   |
|------------------------------|-------------------------------------------------------------------|
| Sponsor organisation name    | Biogen                                                            |
| Sponsor organisation address | 225 Binney Street, Cambridge, Massachusetts, United States, 02142 |
| Public contact               | Biogen Study Medical Director, Biogen, clinicaltrials@biogen.com  |
| Scientific contact           | Biogen Study Medical Director, Biogen, clinicaltrials@biogen.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                       | 12 August 2024 |
| Is this the analysis of the primary completion data? | No             |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 12 August 2024 |
| Was the trial ended prematurely?                     | Yes            |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study is to verify the clinical benefit of monthly doses of aducanumab in slowing cognitive and functional impairment as measured by changes in the Clinical Dementia Rating Scale Sum of Boxes (CDR-SB) score as compared with placebo in participants with early Alzheimer's disease.

Protection of trial subjects:

Written informed consent was obtained from each subject's legally authorized representative or (e.g., legal guardian), as applicable prior to evaluations being performed for eligibility. Subjects or the subject's legally authorized representative were given adequate time to review the information in the informed consent/assent and were allowed to ask, and have answered questions concerning all portions of the conduct of the study.

Background therapy: -

Evidence for comparator: -

|                                                           |              |
|-----------------------------------------------------------|--------------|
| Actual start date of recruitment                          | 02 June 2022 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | Yes          |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Australia: 21          |
| Country: Number of subjects enrolled | Belgium: 5             |
| Country: Number of subjects enrolled | Brazil: 2              |
| Country: Number of subjects enrolled | Canada: 53             |
| Country: Number of subjects enrolled | Finland: 17            |
| Country: Number of subjects enrolled | France: 74             |
| Country: Number of subjects enrolled | Germany: 59            |
| Country: Number of subjects enrolled | Italy: 65              |
| Country: Number of subjects enrolled | Japan: 86              |
| Country: Number of subjects enrolled | Korea, Republic of: 19 |
| Country: Number of subjects enrolled | Mexico: 5              |
| Country: Number of subjects enrolled | Poland: 110            |
| Country: Number of subjects enrolled | Spain: 133             |
| Country: Number of subjects enrolled | Sweden: 8              |
| Country: Number of subjects enrolled | United Kingdom: 40     |
| Country: Number of subjects enrolled | United States: 327     |

|                                    |      |
|------------------------------------|------|
| Worldwide total number of subjects | 1024 |
| EEA total number of subjects       | 471  |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|-------------------------------------------|-----|
| 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)                      | 124 |
| From 65 to 84 years                       | 894 |
| 85 years and over                         | 6   |

## Subject disposition

### Recruitment

Recruitment details:

Participants took part in the study at the investigative sites in Australia, Belgium, Brazil, Canada, Finland, France, Germany, Italy, Japan, Mexico, Poland, South Korea, Spain, Sweden, United Kingdom, and United States from 02 Jun 2022 to 12 Aug 2024.

### Pre-assignment

Screening details:

A total of 1027 participants with Alzheimer's Disease (AD) were enrolled and randomised in this study. Of these, 1024 participants were dosed to receive placebo or aducanumab. None of the participants completed the study due to early termination of the study. [Change in Treatment (CIT)].

### Period 1

|                              |                                        |
|------------------------------|----------------------------------------|
| Period 1 title               | Overall Study (overall period)         |
| Is this the baseline period? | Yes                                    |
| Allocation method            | Randomised - controlled                |
| Blinding used                | Double blind                           |
| Roles blinded                | Subject, Investigator, Carer, Assessor |

### Arms

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes     |
| <b>Arm title</b>             | Placebo |

Arm description:

Participants received placebo, once every four weeks (Q4W), administered as an intravenous (IV) infusion.

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

Dosage and administration details:

Administered as specified in the treatment arm.

|                  |            |
|------------------|------------|
| <b>Arm title</b> | Aducanumab |
|------------------|------------|

Arm description:

Participants received aducanumab, up to 10 milligrams per kilogram (mg/kg) of body weight, Q4W, administered as an IV infusion.

|                                        |                                       |
|----------------------------------------|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | Aducanumab                            |
| Investigational medicinal product code | BIIB037                               |
| Other name                             | ADUHELM                               |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

Dosage and administration details:

Administered as specified in the treatment arm.

| <b>Number of subjects in period 1</b>              | Placebo | Aducanumab |
|----------------------------------------------------|---------|------------|
| Started                                            | 344     | 680        |
| Completed                                          | 0       | 0          |
| Not completed                                      | 344     | 680        |
| Adverse event, serious fatal                       | -       | 3          |
| Reason Not Specified                               | 1       | 3          |
| Withdrawal by Participant - Relocation             | 1       | 3          |
| Site Terminated by Sponsor                         | -       | 2          |
| Study Terminated by Sponsor                        | 282     | 559        |
| Failure to Meet Continuation Criteria              | 2       | -          |
| Adverse event, non-fatal                           | 4       | 31         |
| Failure to Meet Randomization Criteria             | 1       | 2          |
| Lack of Efficacy - Based on Participant Perception | -       | 2          |
| Withdrawal by Participant - Other                  | 25      | 30         |
| Randomised by Mistake                              | -       | 1          |
| Withdrawal by Participant - Concern About Study    | 2       | 6          |
| Lost to follow-up                                  | 2       | 4          |
| Withdrawal by Participant - Scheduling Conflicts   | 14      | 17         |
| Withdrawal by Participant - Desire for CIT         | 8       | 17         |
| Protocol deviation                                 | 2       | -          |

## Baseline characteristics

### Subject analysis sets

|                            |               |
|----------------------------|---------------|
| Subject analysis set title | Placebo       |
| Subject analysis set type  | Full analysis |

Subject analysis set description:

Participants received placebo, once every four weeks (Q4W), administered as an intravenous (IV) infusion.

|                            |               |
|----------------------------|---------------|
| Subject analysis set title | Aducanumab    |
| Subject analysis set type  | Full analysis |

Subject analysis set description:

Participants received aducanumab, up to 10 milligrams per kilogram (mg/kg) of body weight, Q4W, administered as an IV infusion.

| Reporting group values | Placebo | Aducanumab |  |
|------------------------|---------|------------|--|
| Number of subjects     | 344     | 680        |  |
| Age Categorical        |         |            |  |
| Units: Subjects        |         |            |  |

|                                                                                                                                           |        |        |  |
|-------------------------------------------------------------------------------------------------------------------------------------------|--------|--------|--|
| Age continuous                                                                                                                            |        |        |  |
| Full Analysis Set (FAS) included all randomised participants who had received at least 1 dose of study treatment (aducanumab or placebo). |        |        |  |
| Units: years                                                                                                                              |        |        |  |
| arithmetic mean                                                                                                                           | 72.4   | 72.2   |  |
| standard deviation                                                                                                                        | ± 6.18 | ± 5.81 |  |
| Gender categorical                                                                                                                        |        |        |  |
| Units: Subjects                                                                                                                           |        |        |  |
| Male                                                                                                                                      | 157    | 327    |  |
| Female                                                                                                                                    | 187    | 353    |  |
| Race                                                                                                                                      |        |        |  |
| Units: Subjects                                                                                                                           |        |        |  |
| American Indian or Alaska Native                                                                                                          | 1      | 0      |  |
| Asian                                                                                                                                     | 39     | 73     |  |
| Black or African American                                                                                                                 | 3      | 9      |  |
| Native Hawaiian or Other Pacific Islander                                                                                                 | 1      | 0      |  |
| White                                                                                                                                     | 273    | 533    |  |
| Not Reported Due to Confidentiality Regulations                                                                                           | 26     | 57     |  |
| Other                                                                                                                                     | 0      | 3      |  |
| American Indian or Alaska Native and White                                                                                                | 0      | 1      |  |
| Unknown                                                                                                                                   | 1      | 4      |  |
| Ethnicity                                                                                                                                 |        |        |  |
| Units: Subjects                                                                                                                           |        |        |  |
| Hispanic or Latino                                                                                                                        | 27     | 51     |  |
| Not Hispanic or Latino                                                                                                                    | 293    | 585    |  |
| Not Reported Due to Confidentiality Regulations                                                                                           | 24     | 43     |  |

|         |   |   |  |
|---------|---|---|--|
| Unknown | 0 | 1 |  |
|---------|---|---|--|

|  |
|--|
|  |
|  |

## End points

### End points reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Participants received placebo, once every four weeks (Q4W), administered as an intravenous (IV) infusion.

|                       |            |
|-----------------------|------------|
| Reporting group title | Aducanumab |
|-----------------------|------------|

Reporting group description:

Participants received aducanumab, up to 10 milligrams per kilogram (mg/kg) of body weight, Q4W, administered as an IV infusion.

|                            |         |
|----------------------------|---------|
| Subject analysis set title | Placebo |
|----------------------------|---------|

|                           |               |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

Participants received placebo, once every four weeks (Q4W), administered as an intravenous (IV) infusion.

|                            |            |
|----------------------------|------------|
| Subject analysis set title | Aducanumab |
|----------------------------|------------|

|                           |               |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

Participants received aducanumab, up to 10 milligrams per kilogram (mg/kg) of body weight, Q4W, administered as an IV infusion.

### Primary: Change From Baseline in Clinical Dementia Rating Scale - Sum of Boxes (CDR-SB) Score at Week 78

|                 |                                                                                                                |
|-----------------|----------------------------------------------------------------------------------------------------------------|
| End point title | Change From Baseline in Clinical Dementia Rating Scale - Sum of Boxes (CDR-SB) Score at Week 78 <sup>[1]</sup> |
|-----------------|----------------------------------------------------------------------------------------------------------------|

End point description:

The Clinical Dementia Rating Scale integrates assessments from 3 domains of cognition (memory, orientation, judgment/problem-solving) and 3 domains of function (community affairs, home/hobbies, personal care). Following the caregiver interview and systematic participant examination, the rater assigns a score describing the participant's current performance level in each of these domains of life functioning. The "Sum of boxes" scoring methodology sums the score for each of the 6 domains and provides a value ranging from 0 to 18. Higher scores indicate greater impairment. A positive change from baseline indicates greater impairment. FAS included all randomised participants who had received at least 1 dose of study treatment (aducanumab or placebo). Here, 'overall number of participants analysed' signifies the number of participants available for outcome measure analysis.

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

End point timeframe:

Baseline, Week 78

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistical data were planned for this endpoint.

| End point values                     | Placebo         | Aducanumab      |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 6               | 8               |  |  |
| Units: score on a scale              |                 |                 |  |  |
| arithmetic mean (standard deviation) | 0.67 (± 0.408)  | 1.56 (± 1.635)  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Integrated Alzheimer's Disease Rating Scale (iADRS) Score at Week 78

|                 |                                                                                              |
|-----------------|----------------------------------------------------------------------------------------------|
| End point title | Change From Baseline in Integrated Alzheimer's Disease Rating Scale (iADRS) Score at Week 78 |
|-----------------|----------------------------------------------------------------------------------------------|

End point description:

The iADRS composite captures a decline in both cognition and daily function. It is a simple linear combination of Alzheimer's disease assessment scale, cognitive subscale (ADAS-Cog13), and Alzheimer's disease cooperative study scale for activities of daily living in mild cognitive impairment (ADCS-ADL-MCI). ADAS-Cog13 scale ranges from 0 to 85 (higher scores indicate worse performance) and ADCS-ADL-MCI scale ranges from 0 to 53 (higher scores indicate greater independent, healthy functioning). Total score for iADRS scale ranges from 0 to 138, where higher scores indicate better performance. A negative change from baseline indicates worse performance. FAS. Here, 'overall number of participants analysed' signifies number of participants available for outcome measure analysis. Assessment was also planned for Week 106 for this outcome measure, but no assessments were conducted at Week 106 due to early termination.

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

End point timeframe:

Baseline, Week 78

| End point values                     | Placebo                 | Aducanumab             |  |  |
|--------------------------------------|-------------------------|------------------------|--|--|
| Subject group type                   | Reporting group         | Reporting group        |  |  |
| Number of subjects analysed          | 3                       | 5                      |  |  |
| Units: score on a scale              |                         |                        |  |  |
| arithmetic mean (standard deviation) | -14.667 ( $\pm$ 4.4869) | -7.796 ( $\pm$ 6.7805) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Alzheimer's Disease Cooperative Study for Activities of Daily Living in Mild Cognitive Impairment (ADCS-ADL-MCI) Scale Score at Weeks 78

|                 |                                                                                                                                                                  |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Change From Baseline in Alzheimer's Disease Cooperative Study for Activities of Daily Living in Mild Cognitive Impairment (ADCS-ADL-MCI) Scale Score at Weeks 78 |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

The ADCS-ADL-MCI scale consists of 17 instrumental items (e.g., shopping, preparing meals, using household appliances.etc.) and 1 basic item (getting dressed). Ratings reflect caregiver observations about the participant's actual functioning over the previous month and provide an assessment of change in the functional state of the participant over time. The total score ranges from 0 to 53. Higher scores indicate greater independent, healthy functioning. A positive change from baseline indicates healthy functioning while a negative change from baseline indicates a decline in independent functioning. FAS included all randomised participants who had received at least 1 dose of study treatment (aducanumab or placebo). Here 'overall number of participants analysed' signifies the number of participants available for outcome measure analysis. Assessment was also planned for Week 106 for this outcome measure, but no assessments were conducted at Week 106 due to early termination.

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

End point timeframe:

Baseline, Week 78

| End point values                     | Placebo            | Aducanumab         |  |  |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type                   | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed          | 3                  | 5                  |  |  |
| Units: score on a scale              |                    |                    |  |  |
| arithmetic mean (standard deviation) | -5.0 ( $\pm$ 3.61) | -0.4 ( $\pm$ 7.60) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Alzheimer's Disease Assessment Scale, Cognitive Subscale (ADAS-Cog13) at Week 78

|                 |                                                                                                          |
|-----------------|----------------------------------------------------------------------------------------------------------|
| End point title | Change From Baseline in Alzheimer's Disease Assessment Scale, Cognitive Subscale (ADAS-Cog13) at Week 78 |
|-----------------|----------------------------------------------------------------------------------------------------------|

End point description:

ADAS-Cog13 comprises both cognitive tasks and clinical ratings of cognitive performance. The cognitive subscale items capture word recall, ability to follow commands, the ability to correctly copy or draw an image, naming, the ability to interact with everyday objects, orientation, word recognition, memory, comprehension of spoken language, word-finding, and language ability, with a measure for delayed word recall and concentration/distractibility. The total score ranges from 0 to 85. Higher scores indicate worse performance. A positive change from baseline indicates decline in cognitive performance. FAS included all randomised participants who had received at least 1 dose of study treatment (aducanumab or placebo). Here, 'overall number of participants analysed' signifies the number of participants available for outcome measure analysis. Assessment was also planned for Week 106 for this outcome measure, but no assessments were conducted at Week 106 due to early termination.

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

End point timeframe:

Baseline, Week 78

| End point values                     | Placebo               | Aducanumab            |  |  |
|--------------------------------------|-----------------------|-----------------------|--|--|
| Subject group type                   | Reporting group       | Reporting group       |  |  |
| Number of subjects analysed          | 3                     | 5                     |  |  |
| Units: score on a scale              |                       |                       |  |  |
| arithmetic mean (standard deviation) | 9.667 ( $\pm$ 0.8844) | 7.396 ( $\pm$ 2.3262) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Mini-Mental State Examination (MMSE) Scale

## Score at Week 78

|                 |                                                                                     |
|-----------------|-------------------------------------------------------------------------------------|
| End point title | Change From Baseline in Mini-Mental State Examination (MMSE) Scale Score at Week 78 |
|-----------------|-------------------------------------------------------------------------------------|

### End point description:

The MMSE scale is a performance-based test of global cognitive status. It consists of 11 tasks that assess orientation, word recall, attention and calculation, language abilities, and visuospatial functions. The scores from the 11 tests are combined to obtain the total score, which ranges from 0 to 30. Higher scores indicate better performance. A negative change from baseline indicates decline in cognitive performance. FAS included all randomised participants who had received at least 1 dose of study treatment (aducanumab or placebo). Here, 'overall number of participants analysed' signifies the number of participants available for outcome measure analysis. Assessment was also planned for Week 106 for this outcome measure, but no assessments were conducted at Week 106 due to early termination.

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

### End point timeframe:

Baseline, Week 78

| End point values                     | Placebo            | Aducanumab         |  |  |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type                   | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed          | 3                  | 5                  |  |  |
| Units: score on a scale              |                    |                    |  |  |
| arithmetic mean (standard deviation) | -6.0 ( $\pm$ 1.00) | -1.2 ( $\pm$ 1.48) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Tau PET Signal at Weeks 38

|                 |                                                    |
|-----------------|----------------------------------------------------|
| End point title | Change From Baseline in Tau PET Signal at Weeks 38 |
|-----------------|----------------------------------------------------|

### End point description:

The cerebral tau level was measured by tau PET imaging. Tau PET imaging was conducted using radiotracer. SUVR is a ratio of PET uptake measured in brain region of interest and a disease-free reference region. A higher SUVR is an indication of increased PET radiotracer uptake and worsening disease. FAS included all randomised participants who had received at least 1 dose of study treatment (aducanumab or placebo). 9999 indicates that standard deviation was not estimable as there was only 1 participant analysed. Here, 'overall number of participants analysed' signifies the number of participants available for outcome measure analysis. Assessment was planned for Weeks 78 and 104 for this outcome measure but was not performed due to early termination (ET). The analysis was performed at week 38, hence data for week 38 is reported here.

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

### End point timeframe:

Baseline, Week 38

| End point values                                  | Placebo         | Aducanumab       |  |  |
|---------------------------------------------------|-----------------|------------------|--|--|
| Subject group type                                | Reporting group | Reporting group  |  |  |
| Number of subjects analysed                       | 1               | 0 <sup>[2]</sup> |  |  |
| Units: SUVR                                       |                 |                  |  |  |
| arithmetic mean (standard deviation)              |                 |                  |  |  |
| Total Anterior Cingulate Cortex:Early Termination | 1.130 (± 9999)  | ()               |  |  |
| Total Braak 1 and 2: Early Termination            | 1.320 (± 9999)  | ()               |  |  |
| Total Braak 3 and 4: Early Termination            | 1.270 (± 9999)  | ()               |  |  |
| Total Braak 5 and 6: Early Termination            | 1.150 (± 9999)  | ()               |  |  |
| Total Frontal Cortex: Early Termination           | 1.190 (± 9999)  | ()               |  |  |
| Total Inferior Temporal Cortex:Early Termination  | 1.420 (± 9999)  | ()               |  |  |
| Total Lateral Temporal Cortex: Early Termination  | 1.320 (± 9999)  | ()               |  |  |
| Total Medial Temporal Lobe Gray Matter: ET        | 1.480 (± 9999)  | ()               |  |  |
| Total Occipital Cortex: Early Termination         | 1.220 (± 9999)  | ()               |  |  |
| Total Parietal Cortex: Early Termination          | 1.110 (± 9999)  | ()               |  |  |
| Total Post Cingulate Cortex: Early Termination    | 1.100 (± 9999)  | ()               |  |  |
| Total Temporal Cortex: Early Termination          | 1.360 (± 9999)  | ()               |  |  |

Notes:

[2] - 'Overall number of participants analysed' = number of participants available for analysis.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Neuropsychiatric Inventory-10 (NPI-10) Score at Week 78

|                 |                                                                                 |
|-----------------|---------------------------------------------------------------------------------|
| End point title | Change From Baseline in Neuropsychiatric Inventory-10 (NPI-10) Score at Week 78 |
|-----------------|---------------------------------------------------------------------------------|

End point description:

The NPI-10 is a questionnaire administered to the informant, designed to obtain information on the presence of neuropsychiatric symptoms and behaviors in a participant with Alzheimer's disease. Ten areas are assessed: delusions, hallucinations, agitation/aggression, depression, anxiety, elation/euphoria, apathy/indifference, disinhibition, irritability and aberrant motor behavior. The NPI total score ranges from 0 to 120. Higher scores indicate greater impairment. A negative change from baseline indicates improvement (symptom reduction). FAS included all randomised participants who had received at least 1 dose of study treatment (aducanumab or placebo). Here, 'overall number of participants analysed' signifies the number of participants available for outcome measure analysis. Assessment was also planned for Week 106 for this outcome measure, but no assessments were conducted at Week 106 due to early termination.

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

End point timeframe:

Baseline, Week 78

| End point values                     | Placebo         | Aducanumab      |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 3               | 5               |  |  |
| Units: score on a scale              |                 |                 |  |  |
| arithmetic mean (standard deviation) | -8.3 (± 16.20)  | -1.8 (± 6.94)   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Amyloid Positron Emission Tomography (PET) Signal at Week 78

|                 |                                                                                      |
|-----------------|--------------------------------------------------------------------------------------|
| End point title | Change From Baseline in Amyloid Positron Emission Tomography (PET) Signal at Week 78 |
|-----------------|--------------------------------------------------------------------------------------|

End point description:

Amyloid PET scan assesses cerebral amyloid load using radiotracers which is standardized into centiloids. Centiloid values on centiloid scale is based on mean composite standardized uptake value ratio (SUVR). FAS included all randomised participants who had received at least 1 dose of study treatment (aducanumab or placebo). 9999 indicates that standard deviation was not estimable as there was only 1 participant analysed. Here, 'overall number of participants analysed' signifies the number of participants available for outcome measure analysis. Assessment was also planned for Week 104 for this outcome measure, but no assessments were conducted at Week 104 due to early termination.

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

End point timeframe:

Baseline, Week 78

| End point values                     | Placebo          | Aducanumab      |  |  |
|--------------------------------------|------------------|-----------------|--|--|
| Subject group type                   | Reporting group  | Reporting group |  |  |
| Number of subjects analysed          | 0 <sup>[3]</sup> | 1               |  |  |
| Units: SUVR                          |                  |                 |  |  |
| arithmetic mean (standard deviation) | ()               | -2.360 (± 9999) |  |  |

Notes:

[3] - 'Overall number of participants analysed' = number of participants available for analysis.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in CDR-SB Score at Week 106

|                 |                                                  |
|-----------------|--------------------------------------------------|
| End point title | Change From Baseline in CDR-SB Score at Week 106 |
|-----------------|--------------------------------------------------|

End point description:

The CDR integrates assessments from 3 domains of cognition (memory, orientation, judgment/problem-solving) and 3 domains of function (community affairs, home/hobbies, personal care). Following caregiver interview and systematic participant examination, the rater assigns a score describing the participant's current performance level in each of these domains of life functioning. The CDR-SB sums the score for each of the 6 domains and provides a value ranging from 0 to 18. Higher scores indicate greater impairment. Positive change from baseline indicates greater impairment. Assessment was planned for Week 106 for this outcome measure, but no assessments were conducted at Week 106 due

to early termination.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Baseline, Week 106   |           |

| End point values                     | Placebo          | Aducanumab       |  |  |
|--------------------------------------|------------------|------------------|--|--|
| Subject group type                   | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed          | 0 <sup>[4]</sup> | 0 <sup>[5]</sup> |  |  |
| Units: score on a scale              |                  |                  |  |  |
| arithmetic mean (standard deviation) | ( )              | ( )              |  |  |

Notes:

[4] - Data is not reported for week 106 as no assessments were conducted due to the ET of the study.

[5] - Data is not reported for week 106 as no assessments were conducted due to the ET of the study.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Global Statistical Test (GST) Composite Z-Score at Week 78

|                 |                                                                                       |
|-----------------|---------------------------------------------------------------------------------------|
| End point title | Change From Baseline in Global Statistical Test (GST)<br>Composite Z-Score at Week 78 |
|-----------------|---------------------------------------------------------------------------------------|

End point description:

GST is composite z-score defined as average of standardized z-scores of CDR-SB, ADAS-Cog13, and ADCS-ADL-MCI. CDR-SB assess 3 cognitive (memory, orientation, judgment/problem-solving) and 3 functional (community affairs, home/hobbies, personal care) domains, with scores based on caregiver interviews and participant exams. "SB" method combines scores across 6 domains, ranging from 0-18 (Higher score = greater impairment). ADAS-Cog13 evaluates cognitive tasks like word recall, naming, orientation, and memory, with a total score from 0-85 (Higher score = worse performance). ADCS-ADL-MCI rates 17 instrumental tasks (e.g., shopping, preparing meal) and 1 basic task (dressing), with scores from 0-53 (Higher score = greater independent, healthy functioning). A positive change from baseline indicates improvement. FAS. Overall number of participants analysed = number of participants available for outcome measure analysis. Assessment was also planned for Week 106, but no assessments were conducted due to early termination.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Baseline, Week 78    |           |

| End point values                     | Placebo         | Aducanumab      |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 3               | 4               |  |  |
| Units: z-score                       |                 |                 |  |  |
| arithmetic mean (standard deviation) | 0.88 (± 0.116)  | 0.48 (± 0.515)  |  |  |

## Statistical analyses



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug up to last follow-up visit (up to approximately 2 years 2 months)

Adverse event reporting additional description:

Safety analysis set included all randomised participants who had received at least 1 dose of study treatment (aducanumab or placebo). One participant in the placebo arm received drug. This participant was considered in Aducanumab group for safety analysis.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 26.1 |
|--------------------|------|

### Reporting groups

|                       |            |
|-----------------------|------------|
| Reporting group title | Aducanumab |
|-----------------------|------------|

Reporting group description:

Participants received aducanumab, up to 10 mg/kg of body weight, Q4W, administered as IV infusion.

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Participants received placebo, Q4W, administered as IV infusion.

| Serious adverse events                                              | Aducanumab       | Placebo          |  |
|---------------------------------------------------------------------|------------------|------------------|--|
| Total subjects affected by serious adverse events                   |                  |                  |  |
| subjects affected / exposed                                         | 59 / 681 (8.66%) | 23 / 343 (6.71%) |  |
| number of deaths (all causes)                                       | 3                | 0                |  |
| number of deaths resulting from adverse events                      | 3                | 0                |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                  |                  |  |
| Breast cancer                                                       |                  |                  |  |
| subjects affected / exposed                                         | 0 / 681 (0.00%)  | 1 / 343 (0.29%)  |  |
| occurrences causally related to treatment / all                     | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 0            |  |
| Breast cancer stage i                                               |                  |                  |  |
| subjects affected / exposed                                         | 1 / 681 (0.15%)  | 0 / 343 (0.00%)  |  |
| occurrences causally related to treatment / all                     | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 0            |  |
| Intraductal proliferative breast lesion                             |                  |                  |  |
| subjects affected / exposed                                         | 1 / 681 (0.15%)  | 0 / 343 (0.00%)  |  |
| occurrences causally related to treatment / all                     | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 0            |  |

|                                                               |                 |                 |  |
|---------------------------------------------------------------|-----------------|-----------------|--|
| Non-small cell lung cancer<br>subjects affected / exposed     | 0 / 681 (0.00%) | 1 / 343 (0.29%) |  |
| occurrences causally related to<br>treatment / all            | 0 / 0           | 0 / 1           |  |
| deaths causally related to<br>treatment / all                 | 0 / 0           | 0 / 0           |  |
| Pleural mesothelioma malignant<br>subjects affected / exposed | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to<br>treatment / all            | 0 / 1           | 0 / 0           |  |
| deaths causally related to<br>treatment / all                 | 0 / 0           | 0 / 0           |  |
| Squamous cell carcinoma<br>subjects affected / exposed        | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to<br>treatment / all            | 0 / 1           | 0 / 0           |  |
| deaths causally related to<br>treatment / all                 | 0 / 0           | 0 / 0           |  |
| Vascular disorders                                            |                 |                 |  |
| Hypertensive emergency<br>subjects affected / exposed         | 0 / 681 (0.00%) | 1 / 343 (0.29%) |  |
| occurrences causally related to<br>treatment / all            | 0 / 0           | 0 / 1           |  |
| deaths causally related to<br>treatment / all                 | 0 / 0           | 0 / 0           |  |
| Deep vein thrombosis<br>subjects affected / exposed           | 2 / 681 (0.29%) | 1 / 343 (0.29%) |  |
| occurrences causally related to<br>treatment / all            | 0 / 2           | 0 / 1           |  |
| deaths causally related to<br>treatment / all                 | 0 / 0           | 0 / 0           |  |
| Aortic aneurysm<br>subjects affected / exposed                | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to<br>treatment / all            | 0 / 1           | 0 / 0           |  |
| deaths causally related to<br>treatment / all                 | 0 / 0           | 0 / 0           |  |
| Orthostatic hypotension<br>subjects affected / exposed        | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to<br>treatment / all            | 0 / 1           | 0 / 0           |  |
| deaths causally related to<br>treatment / all                 | 0 / 0           | 0 / 0           |  |
| General disorders and administration<br>site conditions       |                 |                 |  |
| Asthenia<br>subjects affected / exposed                       | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to<br>treatment / all            | 0 / 1           | 0 / 0           |  |
| deaths causally related to<br>treatment / all                 | 0 / 0           | 0 / 0           |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| Fatigue                                         |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gait disturbance                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory, thoracic and mediastinal disorders |                 |                 |  |
| Pulmonary embolism                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Acute respiratory failure                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Psychiatric disorders                           |                 |                 |  |
| Suicide attempt                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Completed suicide                               |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Investigations                                  |                 |                 |  |
| Blood pressure increased                        |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Troponin increased                              |                 |                 |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Injury, poisoning and procedural complications  |                 |                 |  |
| Procedural pneumothorax                         |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Clavicle fracture                               |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Craniocerebral injury                           |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Fall                                            |                 |                 |  |
| subjects affected / exposed                     | 7 / 681 (1.03%) | 3 / 343 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 7           | 0 / 3           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Femoral neck fracture                           |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Femur fracture                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Fractured sacrum                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 681 (0.00%) | 1 / 343 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hip fracture                                    |                 |                 |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                     | 2 / 681 (0.29%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Poisoning                                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Humerus fracture                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Skin laceration                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 681 (0.00%) | 1 / 343 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Spinal compression fracture                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 681 (0.00%) | 1 / 343 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Subdural haematoma                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Tendon rupture                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 681 (0.00%) | 1 / 343 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Upper limb fracture                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 681 (0.00%) | 1 / 343 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiac disorders                               |                 |                 |  |
| Bradycardia                                     |                 |                 |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 681 (0.15%) | 1 / 343 (0.29%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Atrial flutter                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 681 (0.00%) | 1 / 343 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Atrial fibrillation                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 681 (0.00%) | 2 / 343 (0.58%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Acute myocardial infarction                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Tachycardia                                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Myocardial infarction                           |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Ischaemic cardiomyopathy                        |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Coronary artery disease                         |                 |                 |  |
| subjects affected / exposed                     | 0 / 681 (0.00%) | 1 / 343 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiac arrest                                  |                 |                 |  |

|                                                                                 |                 |                 |  |
|---------------------------------------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                                                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all                                 | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all                                      | 0 / 1           | 0 / 0           |  |
| Nervous system disorders                                                        |                 |                 |  |
| Amyloid related imaging abnormality-microhaemorrhages and haemosiderin deposits |                 |                 |  |
| subjects affected / exposed                                                     | 2 / 681 (0.29%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all                                 | 2 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0           |  |
| Seizure                                                                         |                 |                 |  |
| subjects affected / exposed                                                     | 3 / 681 (0.44%) | 1 / 343 (0.29%) |  |
| occurrences causally related to treatment / all                                 | 2 / 3           | 0 / 1           |  |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0           |  |
| Normal pressure hydrocephalus                                                   |                 |                 |  |
| subjects affected / exposed                                                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all                                 | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0           |  |
| Neurological symptom                                                            |                 |                 |  |
| subjects affected / exposed                                                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all                                 | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0           |  |
| Lacunar stroke                                                                  |                 |                 |  |
| subjects affected / exposed                                                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all                                 | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0           |  |
| Ischaemic stroke                                                                |                 |                 |  |
| subjects affected / exposed                                                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all                                 | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0           |  |
| Headache                                                                        |                 |                 |  |
| subjects affected / exposed                                                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all                                 | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0           |  |
| Embolic cerebral infarction                                                     |                 |                 |  |

|                                                     |                 |                 |  |
|-----------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                         | 0 / 681 (0.00%) | 1 / 343 (0.29%) |  |
| occurrences causally related to treatment / all     | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           |  |
| Dizziness                                           |                 |                 |  |
| subjects affected / exposed                         | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all     | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           |  |
| Cerebral haemorrhage                                |                 |                 |  |
| subjects affected / exposed                         | 1 / 681 (0.15%) | 1 / 343 (0.29%) |  |
| occurrences causally related to treatment / all     | 1 / 1           | 1 / 1           |  |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           |  |
| Carotid artery stenosis                             |                 |                 |  |
| subjects affected / exposed                         | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all     | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           |  |
| Aphasia                                             |                 |                 |  |
| subjects affected / exposed                         | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all     | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           |  |
| Amyloid related imaging abnormality-oedema/effusion |                 |                 |  |
| subjects affected / exposed                         | 7 / 681 (1.03%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all     | 7 / 7           | 0 / 0           |  |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           |  |
| Subarachnoid haemorrhage                            |                 |                 |  |
| subjects affected / exposed                         | 2 / 681 (0.29%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all     | 2 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           |  |
| Tremor                                              |                 |                 |  |
| subjects affected / exposed                         | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all     | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           |  |
| Transient ischaemic attack                          |                 |                 |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Syncope                                         |                 |                 |  |
| subjects affected / exposed                     | 6 / 681 (0.88%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 7           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Superficial siderosis of central nervous system |                 |                 |  |
| subjects affected / exposed                     | 2 / 681 (0.29%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastrointestinal disorders                      |                 |                 |  |
| Intestinal obstruction                          |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Nausea                                          |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Obstructive pancreatitis                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 681 (0.00%) | 1 / 343 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hepatobiliary disorders                         |                 |                 |  |
| Cholecystitis acute                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 681 (0.00%) | 1 / 343 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Renal and urinary disorders                     |                 |                 |  |
| Acute kidney injury                             |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| Musculoskeletal and connective tissue disorders |                 |                 |  |
| Back pain                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 681 (0.00%) | 1 / 343 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Osteoarthritis                                  |                 |                 |  |
| subjects affected / exposed                     | 3 / 681 (0.44%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infections and infestations                     |                 |                 |  |
| Bronchitis                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 681 (0.00%) | 1 / 343 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Clostridium difficile colitis                   |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cellulitis                                      |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Covid-19                                        |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia                                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Sepsis                                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 681 (0.00%) | 1 / 343 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| Urinary tract infection                         |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 2 / 343 (0.58%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Erysipelas                                      |                 |                 |  |
| subjects affected / exposed                     | 1 / 681 (0.15%) | 0 / 343 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Metabolism and nutrition disorders              |                 |                 |  |
| Hyponatraemia                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 681 (0.00%) | 1 / 343 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

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

| <b>Non-serious adverse events</b>                     | Aducanumab         | Placebo            |  |
|-------------------------------------------------------|--------------------|--------------------|--|
| Total subjects affected by non-serious adverse events |                    |                    |  |
| subjects affected / exposed                           | 359 / 681 (52.72%) | 127 / 343 (37.03%) |  |
| Injury, poisoning and procedural complications        |                    |                    |  |
| Fall                                                  |                    |                    |  |
| subjects affected / exposed                           | 55 / 681 (8.08%)   | 32 / 343 (9.33%)   |  |
| occurrences (all)                                     | 66                 | 36                 |  |
| Nervous system disorders                              |                    |                    |  |
| Superficial siderosis of central nervous system       |                    |                    |  |
| subjects affected / exposed                           | 69 / 681 (10.13%)  | 5 / 343 (1.46%)    |  |
| occurrences (all)                                     | 87                 | 5                  |  |
| Amyloid related imaging abnormality-oedema/effusion   |                    |                    |  |
| subjects affected / exposed                           | 159 / 681 (23.35%) | 8 / 343 (2.33%)    |  |
| occurrences (all)                                     | 228                | 8                  |  |
| Dizziness                                             |                    |                    |  |
| subjects affected / exposed                           | 42 / 681 (6.17%)   | 17 / 343 (4.96%)   |  |
| occurrences (all)                                     | 59                 | 19                 |  |
| Headache                                              |                    |                    |  |

|                                                                                                                                                                                                                |                                                                          |                                                                     |  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|---------------------------------------------------------------------|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Amyloid related imaging abnormality-microhaemorrhages and haemosiderin deposits</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>81 / 681 (11.89%)</p> <p>123</p> <p>167 / 681 (24.52%)</p> <p>238</p> | <p>33 / 343 (9.62%)</p> <p>48</p> <p>34 / 343 (9.91%)</p> <p>40</p> |  |
| <p>Infections and infestations</p> <p>Covid-19</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nasopharyngitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>              | <p>49 / 681 (7.20%)</p> <p>50</p> <p>42 / 681 (6.17%)</p> <p>45</p>      | <p>19 / 343 (5.54%)</p> <p>21</p> <p>26 / 343 (7.58%)</p> <p>27</p> |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date          | Amendment                                                          |
|---------------|--------------------------------------------------------------------|
| 15 April 2022 | Typographical errors were corrected in the Schedule of Assessment. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

|                                                                       |
|-----------------------------------------------------------------------|
| The study was terminated prematurely based on the sponsor's decision. |
|-----------------------------------------------------------------------|

Notes: