



Clinical trial results:

Long-Term Safety and Tolerability of ABT-126 in Subjects with Mild-to-Moderate Alzheimer's Disease: An Open-Label Extension Study for Subjects Completing Study M10-985

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2011-004780-75 |
| Trial protocol | GB |
| Global end of trial date | 12 March 2014 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 |
| This version publication date | 20 April 2016 |
| First version publication date | 10 July 2015 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | M11-427 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01676935 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Abbvie Deutschland GmbH & Co.KG |
| Sponsor organisation address | Abbott House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6 4XE |
| Public contact | Global Medical Information, AbbVie, 001 800-633-9110, |
| Scientific contact | Laura Gault MD PhD, AbbVie, laura.gault@abbvie.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 March 2014 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 12 March 2014 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The objective of this study is to evaluate the long-term safety and tolerability of ABT-126 in subjects with mild-to-moderate Alzheimer's disease (AD) in 28-week open-label extension of study 2011-002004-32 (M10-985).

Protection of trial subjects:

Participant and/or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 28 August 2012 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------------|
| Country: Number of subjects enrolled | Russian Federation: 124 |
| Country: Number of subjects enrolled | Ukraine: 46 |
| Country: Number of subjects enrolled | United States: 26 |
| Country: Number of subjects enrolled | South Africa: 85 |
| Country: Number of subjects enrolled | Poland: 27 |
| Country: Number of subjects enrolled | United Kingdom: 41 |
| Worldwide total number of subjects | 349 |
| EEA total number of subjects | 68 |

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) | 52 |
| From 65 to 84 years | 264 |
| 85 years and over | 33 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Only subjects randomized into Study 2011-002004-32 who completed dosing through Week 24 of that study were eligible for Study 2011-004780-75. Each subject had routine safety procedures/clinical laboratory tests performed either on Day -1 or as part of the 2011-002004-32 Week 24 visit. Subjects who met the selection criteria were entered into study.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------|---------|
| Arm title | ABT-126 |
|------------------|---------|

Arm description:

ABT-126 25 mg hard gelatin capsule administered orally beginning at 75 mg once daily (QD), which could have been adjusted downward in 25 mg increments with the permission of the AbbVie medical monitor for safety or tolerability issues.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | ABT-126 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

The allowable total daily dose of ABT-126 was 25 mg to 75 mg.

| Number of subjects in period 1 | ABT-126 |
|--------------------------------|---------|
| Started | 349 |
| Completed | 183 |
| Not completed | 166 |
| Consent withdrawn by subject | 19 |
| Study terminated prematurely | 129 |
| Not specified | 3 |
| Adverse event | 13 |
| Lost to follow-up | 2 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | ABT-126 |
|-----------------------|---------|

Reporting group description:

ABT-126 25 mg hard gelatin capsule administered orally beginning at 75 mg once daily (QD), which could have been adjusted downward in 25 mg increments with the permission of the AbbVie medical monitor for safety or tolerability issues.

| Reporting group values | ABT-126 | Total | |
|------------------------|---------|-------|--|
| Number of subjects | 349 | 349 | |
| Age categorical | | | |
| Units: Subjects | | | |
| < 75 years | 167 | 167 | |
| ≥ 75 years | 182 | 182 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 74.1 | | |
| standard deviation | ± 7.88 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 210 | 210 | |
| Male | 139 | 139 | |

End points

End points reporting groups

| | |
|---|---------|
| Reporting group title | ABT-126 |
| Reporting group description: ABT-126 25 mg hard gelatin capsule administered orally beginning at 75 mg once daily (QD), which could have been adjusted downward in 25 mg increments with the permission of the AbbVie medical monitor for safety or tolerability issues. | |

Primary: Number of Subjects With Treatment Emergent Adverse Events

| | |
|--|--|
| End point title | Number of Subjects With Treatment Emergent Adverse |
| End point description: A treatment-emergent adverse event (TEAE) was defined as any adverse event that began or worsened in severity on or after the first day of ABT-126 dosing in Study M11-427 and no more than 30 days after the last study drug dose date. | |
| End point type | Primary |
| End point timeframe: Day -1 through Week 28 (or premature discontinuation) of treatment plus 30 days. Mean (SD) number of treatment exposure days was 163.1 (48.15). | |

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: Safety data was summarized using descriptive statistics. No statistical testing was performed.

| End point values | ABT-126 | | | |
|--|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 349 | | | |
| Units: subjects | | | | |
| Any adverse event (AE) | 167 | | | |
| AE w/reasonable possibility of relatedness to drug | 66 | | | |
| Any severe AE | 18 | | | |
| Any serious AE | 17 | | | |
| AE leading to discontinuation of study drug | 17 | | | |
| Any fatal AE | 4 | | | |
| All deaths | 4 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Meeting Criteria for Potentially Clinically Significant Hematology Values

| | |
|-----------------|---|
| End point title | Number of Subjects Meeting Criteria for Potentially Clinically Significant Hematology Values ^[2] |
|-----------------|---|

End point description:

F=female, M=male

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

End point timeframe:

Day -1 through Week 28 (or premature discontinuation).

Notes:

[2] - 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: Safety data was summarized using descriptive statistics. No statistical testing was performed.

| End point values | ABT-126 | | | |
|--|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 349 ^[3] | | | |
| Units: subjects | | | | |
| Hemoglobin < 90 g/L (F) or < 100 g/L (M); n=345 | 1 | | | |
| Platelet count < $95 \times 10^9/L$; n=344 | 1 | | | |
| White blood cell count < $2.8 \times 10^9/L$; n=345 | 15 | | | |
| White blood cell count > $18 \times 10^9/L$; n=345 | 2 | | | |
| Neutrophils < $1.2 \times 10^9/L$; n=345 | 13 | | | |
| Lymphocytes < $0.75 \times 10^9/L$; n=345 | 19 | | | |

Notes:

[3] - n=subjects with post-baseline values for each parameter

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Meeting Criteria for Potentially Clinically Significant Chemistry Values

| | |
|-----------------|--|
| End point title | Number of Subjects Meeting Criteria for Potentially Clinically Significant Chemistry Values ^[4] |
|-----------------|--|

End point description:

ULN=upper limit of normal, F=female, M=male

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

End point timeframe:

Day -1 through Week 28 (or premature discontinuation).

Notes:

[4] - 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: Safety data was summarized using descriptive statistics. No statistical testing was performed.

| End point values | ABT-126 | | | |
|------------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 345 ^[5] | | | |
| Units: subjects | | | | |
| Alanine aminotransferase > 3*ULN | 3 | | | |
| Aspartate aminotransferase > 3*ULN | 2 | | | |
| Total bilirubin > 29 µmol/L | 2 | | | |

| | | | | |
|---|---|--|--|--|
| Creatinine > 159 (F) or > 180 (M) $\mu\text{mol/L}$ | 4 | | | |
| Uric acid > 500 (F) or > 590 (M) $\mu\text{mol/L}$ | 7 | | | |
| Calcium < 1.75 mmol/L | 5 | | | |
| Sodium < 126 mmol/L | 7 | | | |
| Sodium > 156 mmol/L | 1 | | | |
| Potassium < 3 mmol/L | 2 | | | |
| Potassium > 6 mmol/L | 3 | | | |
| Glucose < 2.75 mmol/L | 3 | | | |
| Glucose > 16.5 mmol/L | 2 | | | |

Notes:

[5] - subjects with post-baseline values for each parameter

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Meeting Criteria for Potentially Clinically Significant Vital Sign and Weight Values

| | |
|--|--|
| End point title | Number of Subjects Meeting Criteria for Potentially Clinically Significant Vital Sign and Weight Values ^[6] |
| End point description: | |
| SBP=systolic blood pressure | |
| End point type | Primary |
| End point timeframe: | |
| Day -1 through Week 28 (or premature discontinuation). | |

Notes:

[6] - 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: Safety data was summarized using descriptive statistics. No statistical testing was performed.

| | | | | |
|---|--------------------|--|--|--|
| End point values | ABT-126 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 345 ^[7] | | | |
| Units: subjects | | | | |
| SBP \geq 180 mmHg; \geq 40 mmHg increase | 2 | | | |
| Weight \geq 7% decrease | 25 | | | |
| Weight \geq 7% increase | 23 | | | |
| Temperature \geq 1.1° C decrease | 3 | | | |
| Temperature > 38.5° C or \geq 1.1° C increase | 5 | | | |

Notes:

[7] - subjects with post-baseline values for each parameter

Statistical analyses

No statistical analyses for this end point

Primary: Columbia-Suicide Severity Rating Scale (C-SSRS) Summary

| | |
|-----------------|--|
| End point title | Columbia-Suicide Severity Rating Scale (C-SSRS) Summary ^[8] |
|-----------------|--|

End point description:

The C-SSRS is a systematically administered instrument developed to track suicidal adverse events across a treatment study. The instrument is designed to assess suicidal behavior and ideation, track and assess all suicidal events, as well as the lethality of attempts. The C-SSRS was administered to the subject and an assessment completed using information gathered from the subject and caregiver. Summary data presents the number of subjects with suicidal ideation or behavior at any time during the study.

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

End point timeframe:

Day -1 through Week 28 (or premature discontinuation) plus 30 days follow-up

Notes:

[8] - 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: Safety data was summarized using descriptive statistics. No statistical testing was performed.

| End point values | ABT-126 | | | |
|--|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 349 | | | |
| Units: subjects | | | | |
| Ideation: wish to be dead | 14 | | | |
| Ideation: non-specific active suicidal thoughts | 2 | | | |
| Ideation: active thoughts without intent to act | 1 | | | |
| Ideation: active thoughts with some intent/no plan | 0 | | | |
| Ideation: active thoughts with plan and intent | 0 | | | |
| Behavior: actual attempt | 0 | | | |
| Behavior: interrupted attempt | 0 | | | |
| Behavior: aborted attempt | 0 | | | |
| Behavior: preparatory acts or behavior | 0 | | | |
| Behavior: suicidal behavior | 1 | | | |
| Behavior: completed suicide | 0 | | | |
| Subjects with suicidal ideations | 14 | | | |
| Subjects with suicidal ideations only | 14 | | | |
| Subjects with suicidal behaviors | 1 | | | |
| Subjects with suicidal behaviors or ideations | 15 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change from Baseline in Cornell Scale for Depression in Dementia (CSDD)

| | |
|-----------------|---|
| End point title | Mean Change from Baseline in Cornell Scale for Depression in Dementia (CSDD) ^[9] |
|-----------------|---|

End point description:

The CSDD is a 19-item interviewer-rated scale for assessing the signs and symptoms of major depression in patients with dementia. Information is obtained from two semi-structured interviews: an interview with the subject and an interview with the caregiver. Each item is ranked on a severity scale of 0 to 2 (0 = absent; 1 = mild or intermittent; 2 = severe). The individual item scores are summed for a

total score. The CSDD scores range from 0 to 38, with higher scores indicative of greater depression. Scores above 10 indicate a probable major depression.

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

End point timeframe:

Baseline (Day -1), Final Evaluation (up to Week 28)

Notes:

[9] - 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: Safety data was summarized using descriptive statistics. No statistical testing was performed.

| | | | | |
|--------------------------------------|---------------------|--|--|--|
| End point values | ABT-126 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 220 ^[10] | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | 0.36 (± 2.42) | | | |

Notes:

[10] - subjects with baseline and post-baseline values

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Meeting Criteria for Potentially Clinically Significant Electrocardiogram Values

| | |
|-----------------|---|
| End point title | Number of Subjects Meeting Criteria for Potentially Clinically Significant Electrocardiogram Values ^[11] |
|-----------------|---|

End point description:

Measurements include heart rate, RR interval, PR interval, QRS duration and QT intervals.

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

End point timeframe:

Day -1 through Week 28 (or premature discontinuation).

Notes:

[11] - 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: Safety data was summarized using descriptive statistics. No statistical testing was performed.

| | | | | |
|--|---------------------|--|--|--|
| End point values | ABT-126 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 344 ^[12] | | | |
| Units: subjects | | | | |
| Bazett QTC interval > 500 msec | 7 | | | |
| Bazett QTC interval > 60 msec increase | 7 | | | |
| Fredericia QTC interval > 500 msec | 3 | | | |

Notes:

[12] - subjects with post-baseline values for the respective parameter

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day -1 through Week 28 (or premature discontinuation) of treatment plus 30 days. Mean (SD) number of treatment exposure days was 163.1 (48.15).

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 17.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | ABT-126 |
|-----------------------|---------|

Reporting group description:

ABT-126 25 mg hard gelatin capsule administered orally beginning at 75 mg once daily (QD), which could have been adjusted downward in 25 mg increments with the permission of the AbbVie medical monitor for safety or tolerability issues.

| Serious adverse events | ABT-126 | | |
|--|------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 17 / 349 (4.87%) | | |
| number of deaths (all causes) | 4 | | |
| number of deaths resulting from adverse events | | | |
| Vascular disorders | | | |
| Arterial thrombosis | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Death | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary oedema | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Psychiatric disorders | | | |
| Agitation | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| anxiety | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Confusional state | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Delusion | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| Body temperature increased | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 2 / 349 (0.57%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Cardiac disorders | | | |
| Aortic valve disease | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Mitral valve disease | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial fibrosis | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Brain oedema | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Brain stem syndrome | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Cerebral infarction | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |

| | | | |
|---|-----------------|--|--|
| Convulsion | | | |
| subjects affected / exposed | 3 / 349 (0.86%) | | |
| occurrences causally related to treatment / all | 1 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ear and labyrinth disorders | | | |
| Hearing impaired | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Gastrointestinal necrosis | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Cholangitis | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Urinary incontinence | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Mobility decreased | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Respiratory tract infection bacterial | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 349 (0.29%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | ABT-126 | | |
|---|-------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 54 / 349 (15.47%) | | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 15 / 349 (4.30%) | | |
| occurrences (all) | 22 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 11 / 349 (3.15%) | | |
| occurrences (all) | 12 | | |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 17 / 349 (4.87%) | | |
| occurrences (all) | 17 | | |
| Nausea | | | |

| | | | |
|---|----------------------|--|--|
| subjects affected / exposed occurrences (all) | 7 / 349 (2.01%) 7 | | |
| Psychiatric disorders Aggression subjects affected / exposed occurrences (all) | 6 / 349 (1.72%) 8 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|---|
| 09 July 2013 | <p>The purpose of this amendment was to make the following changes:</p> <ul style="list-style-type: none">• Add additional contact information to Title Page, Section 6.5, and Section 7.0 for AbbVie Medical Monitor.• Delete reference from Table 1 (Study Activities) stating study drug dispensed at Day -1 visit may be re-dispensed at Day 14 and Week 4, in order to align the Study Activities Table with text in Section 5.5.2.1 as study drug product was not to be re-dispensed.• Add rating scales to assess apathy symptoms associated with Alzheimer's disease (AD) measured by Dementia in Apathy Interview and Rating (DAIR) and the Apathy Evaluation Scale (AES).• Add rating scales to assess impairment of executive function associated with Alzheimer's disease measured by change in behavioral symptoms (Everyday Cognition (eCOG), Frontal Systems Behavior Scale (FrSBe), as well cognitive performance tests (such as Controlled Oral Word Association Test (COWAT), Categorical Verbal Fluency Test (CFT), Trails Making Test A (TMT-A) and Trails Making Test B (TMT-B), Digit Symbol Substitution Test (DSST), Letter Number Sequencing (LNS), Spatial Span (SS) Test, and Digit Span Backward (DSB).• Update language in Section 5.3.1.1 (12-Lead ECG) regarding the timing of the ECGs relative to blood sample collection. Delete reference to blinded study drug assignment, in order to clarify that ECGs should be obtained prior to any blood collections, only if these procedures are scheduled within approximately 30 minutes of each other.• Delete the 14 day follow-up visit from the text in Section 5.4.1, in order to ensure consistency within the protocol.• Correction in Section 8.1.3.1 (Cumulative Data Set) regarding the baseline for those subjects who received ABT-126 in Study M10-985 and who had a gap of 7 days or less between studies.• Other changes to the protocol were for administrative purposes, to correct typographical errors or ensure consistency throughout the protocol. |

Notes:

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.

This extension study was terminated on 15 January 2014 due to the insufficient efficacy of ABT-126 in the double-blind phase 2 study 2011-002004-32 (M10-985) to support further clinical development.

Notes: