Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of ABT 126 in Subjects with Mild-to-Moderate Alzheimer's Disease on Stable Doses of Acetylcholinesterase Inhibitors

Summary

EudraCT number	2011-004849-40
Trial protocol	GR DE GB
Global end of trial date	24 October 2013

Results information

Result version number	v1 (current)
This version publication date	20 April 2016
First version publication date	10 July 2015

Trial information

Trial identification

Sponsor protocol code	M11-793

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01549834
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, 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	24 October 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 October 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study is to evaluate the efficacy and safety of 2 doses of ABT-126 in subjects with mild-to-moderate Alzheimer's disease (AD) taking stable doses of acetylcholinesterase inhibitors (AChEIs).

Protection of trial subjects:

Subject 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	09 March 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 56
Country: Number of subjects enrolled	France: 49
Country: Number of subjects enrolled	Germany: 40
Country: Number of subjects enrolled	Greece: 79
Country: Number of subjects enrolled	South Africa: 44
Country: Number of subjects enrolled	Canada: 57
Country: Number of subjects enrolled	United States: 109
Worldwide total number of subjects	434
EEA total number of subjects	224

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)	43
From 65 to 84 years	346
85 years and over	45

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study included a Screening period of up to 28 days. A total of 565 subjects were screened.

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, Monitor, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Three placebo capsules once daily in the morning for 24 weeks beginning on Day 1.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo administered orally as capsules

Arm title	ABT-126 25 mg QD

Arm description:

One ABT-126 25 mg capsule and 2 placebo capsules once daily in the morning for 24 weeks beginning on Day 1.

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:

ABT-126 administered orally as capsules

Arm title	ABT-126 75 mg QD

Arm description:

Three ABT-126 25 mg capsules once daily in the morning for 24 weeks beginning on Day 1.

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:
ABT-126 administered orally as capsules

Number of subjects in period 1	Placebo	ABT-126 25 mg QD	ABT-126 75 mg QD
Started	146	143	145
Completed	129	126	122
Not completed	17	17	23
Consent withdrawn by subject	5	2	4
Adverse event	9	7	11
Other (not specified)	1	5	3
Lost to follow-up	1	1	2
Lack of efficacy	1	-	-
Noncompliance	-	2	3

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Three placebo capsules once daily in the morning for 24 weeks beginning on Day 1.	
Reporting group title	ABT-126 25 mg QD
Reporting group description:	
One ABT-126 25 mg capsule and 2 placebo capsules once daily in the morning for 24 weeks beginning on Day 1.	
Reporting group title	ABT-126 75 mg QD
Reporting group description:	
Three ABT-126 25 mg capsules once daily in the morning for 24 weeks beginning on Day 1.	

Reporting group values	Placebo	ABT-126 25 mg QD	ABT-126 75 mg QD
Number of subjects	146	143	145
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	75.1	74.6	75.6
standard deviation	± 6.86	± 8.39	± 7.65
Gender categorical Units: Subjects			
Female	72	78	87
Male	74	65	58

Reporting group values	Total		
Number of subjects	434		
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	237		
Male	197		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Three placebo capsules once daily in the morning for 24 weeks beginning on Day 1.	
Reporting group title	ABT-126 25 mg QD
Reporting group description:	
One ABT-126 25 mg capsule and 2 placebo capsules once daily in the morning for 24 weeks beginning on Day 1.	
Reporting group title	ABT-126 75 mg QD
Reporting group description:	
Three ABT-126 25 mg capsules once daily in the morning for 24 weeks beginning on Day 1.	

Primary: Alzheimer's Disease Assessment Scale – Cognitive Scale (ADAS-Cog) 11-item Total Score: Change from Baseline to Week 24

End point title	Alzheimer's Disease Assessment Scale – Cognitive Scale (ADAS-Cog) 11-item Total Score: Change from Baseline to Week 24
End point description:	
From repeated measures analysis. The ADAS-Cog 11-item total score is the sum of the following 11 items: Word Recall, Commands, Constructional Praxis, Naming Objects and Fingers, Ideational Praxis, Orientation, Word Recognition, Remembering Test Instructions, Comprehension of Spoken Language, Spoken Language Ability, and Word Finding Difficulty. The ADAS-Cog 11-item total score ranges from 0 to 70 with a lower score desirable. A decrease in the total score indicates improvement, with a higher score indicating greater cognitive impairment.	
End point type	Primary
End point timeframe:	
Baseline through Week 24	

End point values	Placebo	ABT-126 25 mg QD	ABT-126 75 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	128[1]	124[2]	121[3]	
Units: units on a scale				
least squares mean (standard error)	1.37 (± 0.42)	0.57 (± 0.43)	1.25 (± 0.43)	

Notes:

[1] - Subjects with a baseline and at least one post baseline assessment

[2] - Subjects with a baseline and at least one post baseline assessment

[3] - Subjects with a baseline and at least one post baseline assessment

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
One-sided P value from repeated measures model with fixed effects of treatment, site, visit, and baseline score; interactions of treatment by visit and baseline score by visit; covariance structure is unstructured.	
Comparison groups	ABT-126 25 mg QD v Placebo

Number of subjects included in analysis	252
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.087
Method	mixed-effects model for repeated measure
Parameter estimate	LS mean of difference
Point estimate	-0.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.77
upper limit	0.17
Variability estimate	Standard error of the mean
Dispersion value	0.59

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

One-sided P value from repeated measures model with fixed effects of treatment, site, visit, and baseline score; interactions of treatment by visit and baseline score by visit; covariance structure is unstructured.

Comparison groups	Placebo v ABT-126 75 mg QD
Number of subjects included in analysis	249
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.416
Method	mixed-effects model for repeated measure
Parameter estimate	LS mean of difference
Point estimate	-0.13
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.1
upper limit	0.85
Variability estimate	Standard error of the mean
Dispersion value	0.59

Secondary: ADAS-Cog 13-item Total Score: Change from Baseline to Week 24

End point title	ADAS-Cog 13-item Total Score: Change from Baseline to Week 24

End point description:

From repeated measures analysis. The ADAS-Cog 13-item total score is the sum of the following 13 items: Word Recall, Commands, Constructional Praxis, Naming Objects and Fingers, Ideational Praxis, Orientation, Word Recognition, Remembering Test Instructions, Comprehension of Spoken Language, Spoken Language Ability, Word Finding Difficulty, and Delayed Word Recall, and Number Cancellation Test. The ADAS-Cog 13-item total score ranges from 0 to 85 with a lower score desirable. A decrease in the total score indicates improvement, with a higher score indicating greater cognitive impairment.

End point type	Secondary

End point timeframe:

Baseline through Week 24

End point values	Placebo	ABT-126 25 mg QD	ABT-126 75 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125[4]	123[5]	119[6]	
Units: units on a scale				
least squares mean (standard error)	1.18 (± 0.48)	0.44 (± 0.48)	1.23 (± 0.49)	

Notes:

[4] - Subjects with a baseline and at least one post baseline assessment

[5] - Subjects with a baseline and at least one post baseline assessment

[6] - Subjects with a baseline and at least one post baseline assessment

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

One-sided P value from repeated measures model with treatment, site, visit, baseline score, interactions of treatment and visit; baseline score and visit; covariance structure is unstructured.

Comparison groups	Placebo v ABT-126 25 mg QD
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.135
Method	mixed-effects model for repeated measure
Parameter estimate	LS mean of difference
Point estimate	-0.74
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.85
upper limit	0.37
Variability estimate	Standard error of the mean
Dispersion value	0.67

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

One-sided P value from repeated measures model with treatment, site, visit, baseline score, interactions of treatment and visit; baseline score and visit; covariance structure is unstructured.

Comparison groups	Placebo v ABT-126 75 mg QD
Number of subjects included in analysis	244
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.525
Method	mixed-effects model for repeated measure
Parameter estimate	LS mean of difference
Point estimate	0.04

Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.07
upper limit	1.16
Variability estimate	Standard error of the mean
Dispersion value	0.68

Secondary: Mini-Mental Status Exam (MMSE) Score: Change from Baseline to Week 24

End point title	Mini-Mental Status Exam (MMSE) Score: Change from Baseline to Week 24

End point description:

From repeated measures analysis. The MMSE is a brief questionnaire administered by a trained rater that provides a quantitative measure of cognitive status in adults used to estimate the severity of cognitive impairment. The MMSE score ranges from 0 to 30 points, with a lower score indicating greater cognitive impairment and an increase from baseline indicating improvement.

End point type	Secondary

End point timeframe:

Baseline through Week 24

End point values	Placebo	ABT-126 25 mg QD	ABT-126 75 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	129[7]	125[8]	122[9]	
Units: units on a scale				
least squares mean (standard error)	-0.27 (± 0.27)	-0.49 (± 0.27)	-0.45 (± 0.27)	

Notes:

[7] - Subjects with a baseline and at least one post baseline assessment

[8] - Subjects with a baseline and at least one post baseline assessment

[9] - Subjects with a baseline and at least one post baseline assessment

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

One-sided P value from repeated measures model with treatment, site, visit, baseline score, interactions of treatment and visit; baseline score and visit; covariance structure is unstructured.

Comparison groups	Placebo v ABT-126 25 mg QD
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.721
Method	mixed-effects model for repeated measure
Parameter estimate	LS mean of difference
Point estimate	-0.22

Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.84
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.38

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

One-sided P value from repeated measures model with treatment, site, visit, baseline score, interactions of treatment and visit; baseline score and visit; covariance structure is unstructured.

Comparison groups	Placebo v ABT-126 75 mg QD
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.679
Method	mixed-effects model for repeated measure
Parameter estimate	LS mean of difference
Point estimate	-0.18
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.8
upper limit	0.45
Variability estimate	Standard error of the mean
Dispersion value	0.38

Secondary: Alzheimer's Disease Cooperative Study - Activities of Daily Living (ADCS-ADL) Score: Change from Baseline to Week 24

End point title	Alzheimer's Disease Cooperative Study - Activities of Daily Living (ADCS-ADL) Score: Change from Baseline to Week 24

End point description:

From repeated measures analysis. The ADCS-ADL is a 23-item (question) caregiver-based assessment of activities of daily living designed specifically for AD patients. The scale assesses functional activities such as eating, bathing, grooming, cooking, household chores, shopping, keeping appointments, social interactions, and hobbies. Items are assessed according to whether they were performed in the past 4 weeks and, if so, some items are further assessed as to whether they were performed independently, with supervision, or with physical help. Scores range from 0 to 78, with lower scores indicating more severe impairment and an increase from baseline indicating improvement.

End point type	Secondary

End point timeframe:

Baseline through Week 24

End point values	Placebo	ABT-126 25 mg QD	ABT-126 75 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	130[10]	124[11]	123[12]	
Units: units on a scale				
least squares mean (standard error)	-2.58 (± 0.63)	-3 (± 0.64)	-3.7 (± 0.64)	

Notes:

[10] - Subjects with a baseline and at least one post baseline assessment

[11] - Subjects with a baseline and at least one post baseline assessment

[12] - Subjects with a baseline and at least one post baseline assessment

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

One-sided P value from repeated measures model with treatment, site, visit, baseline score, interactions of treatment and visit; baseline score and visit; covariance structure is unstructured.

Comparison groups	Placebo v ABT-126 25 mg QD
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.68
Method	mixed-effects model for repeated measure
Parameter estimate	LS mean of difference
Point estimate	-0.41
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.87
upper limit	1.04
Variability estimate	Standard error of the mean
Dispersion value	0.88

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

One-sided P value from repeated measures model with treatment, site, visit, baseline score, interactions of treatment and visit; baseline score and visit; covariance structure is unstructured.

Comparison groups	Placebo v ABT-126 75 mg QD
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.895
Method	mixed-effects model for repeated measure
Parameter estimate	LS mean of difference
Point estimate	-1.11
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.57
upper limit	0.35

Variability estimate	Standard error of the mean
Dispersion value	0.89

Secondary: DEMentia Quality of Life (DEMQOL) Subject Total Score: Change from Baseline to Week 24

End point title	DEMentia Quality of Life (DEMQOL) Subject Total Score: Change from Baseline to Week 24

End point description:

From repeated measures analysis. The DEMQOL measures of health-related quality of life in dementia are appropriate for use in mild-to-moderate stages of dementia severity. The DEMQOL contains 28 items and covers 4 domains: daily activities and looking after oneself, health and well-being, cognitive functioning, and social relationships. The recall period is 1 week. Items are scored on a 4-point Likert scale, resulting in a global score ranging from 28 to 112. Higher scores indicate better health-related quality of life.

End point type	Secondary

End point timeframe:

Baseline through Week 24

End point values	Placebo	ABT-126 25 mg QD	ABT-126 75 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	130[13]	122[14]	121[15]	
Units: units on a scale				
least squares mean (standard error)	1.6 (± 0.81)	1.46 (± 0.83)	1.24 (± 0.84)	

Notes:

[13] - Subjects with a baseline and at least one post baseline assessment

[14] - Subjects with a baseline and at least one post baseline assessment

[15] - Subjects with a baseline and at least one post baseline assessment

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

One-sided P value from repeated measures model with treatment, site, visit, baseline score, interactions of treatment and visit; baseline score and visit; covariance structure is unstructured.

Comparison groups	Placebo v ABT-126 25 mg QD
Number of subjects included in analysis	252
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.547
Method	mixed-effects model for repeated measure
Parameter estimate	LS mean of difference
Point estimate	-0.13
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.01
upper limit	1.74

Variability estimate	Standard error of the mean
Dispersion value	1.14

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

One-sided P value from repeated measures model with treatment, site, visit, baseline score, interactions of treatment and visit; baseline score and visit; covariance structure is unstructured.

Comparison groups	ABT-126 75 mg QD v Placebo
Number of subjects included in analysis	251
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.625
Method	mixed-effects model for repeated measure
Parameter estimate	LS mean of difference
Point estimate	-0.36
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.25
upper limit	1.52
Variability estimate	Standard error of the mean
Dispersion value	1.14

Secondary: Clinician Interview-Based Impression of Change-Plus (CIBIC-plus): Change from Baseline to Week 24

End point title	Clinician Interview-Based Impression of Change-Plus (CIBIC-plus): Change from Baseline to Week 24

End point description:

From repeated measures analysis. The CIBIC-plus captures a global impression of change in severity of dementia using 4 major areas of assessment: general functioning, cognitive functioning, behavioral functioning, and activities of daily living. A 7-point scale is used to score the CIBIC-plus in which 1 of the following is selected: 1=markedly improved, 2=moderately improved, 3=minimally improved, 4=no change, 5=minimally worse, 6=moderately worse, or 7=markedly worse. The Clinician Interview-Based Impression of Severity (CIBIS) Score was administered on Day -1 (baseline). Missing data were imputed by Last Observation Carried Forward (LOCF).

End point type	Secondary

End point timeframe:

Baseline through Week 24

End point values	Placebo	ABT-126 25 mg QD	ABT-126 75 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	129[16]	124[17]	121[18]	
Units: units on a scale				
least squares mean (standard error)	4.28 (± 0.07)	4.48 (± 0.07)	4.45 (± 0.07)	

Notes:

[16] - Subjects with a baseline and at least one post baseline assessment

[17] - Subjects with a baseline and at least one post baseline assessment

[18] - Subjects with a baseline and at least one post baseline assessment

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

One-sided P value from repeated measures model with fixed effects of treatment, site, visit, and baseline score; interactions of treatment by visit and baseline score by visit; covariance structure is unstructured.

Comparison groups	Placebo v ABT-126 25 mg QD
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.976
Method	mixed-effects model for repeated measure
Parameter estimate	LS mean of difference
Point estimate	0.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.03
upper limit	0.36
Variability estimate	Standard error of the mean
Dispersion value	0.1

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

One-sided P value from repeated measures model with fixed effects of treatment, site, visit, and baseline score; interactions of treatment by visit and baseline score by visit; covariance structure is unstructured.

Comparison groups	Placebo v ABT-126 75 mg QD
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.957
Method	mixed-effects model for repeated measure
Parameter estimate	LS mean of difference
Point estimate	0.17
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.01
upper limit	0.33
Variability estimate	Standard error of the mean
Dispersion value	0.1

Secondary: Neuropsychiatry Inventory (NPI) 12-Item Total Score: Change from Baseline to Week 24

End point title	Neuropsychiatry Inventory (NPI) 12-Item Total Score: Change from Baseline to Week 24

End point description:

From repeated measures analysis. The NPI assesses 10 behavioral domains and 2 neurovegetative domains on the dimensions of frequency and severity. Frequency is rated on a scale where 0=absent, 1=occasionally, 2=often, 3=frequently, and 4=very frequently. Severity is rated on a scale where 0=absent, 1=mild, 2=moderate, and 3=marked. Distress is rated on a scale where 0 = not at all, 1=minimally, 2=mildly, 3=moderately, 4=severely, and 5=very severely or extremely. For each of the behavioral domains, 4 scores were obtained: frequency, severity, distress, and total (product of frequency and severity; range from 0 to 12). The 12-item NPI total score is the sum of the 10 behavioral domains and the 2 neurovegetative domains (scores range from 0 to 144 with a lower score desirable).

End point type	Secondary

End point timeframe:

Baseline through Week 24

End point values	Placebo	ABT-126 25 mg QD	ABT-126 75 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	130[19]	125[20]	123[21]	
Units: units on a scale				
least squares mean (standard error)	1.37 (± 0.85)	1.22 (± 0.86)	1.87 (± 0.87)	

Notes:

[19] - Subjects with a baseline and at least one post baseline assessment

[20] - Subjects with a baseline and at least one post baseline assessment

[21] - Subjects with a baseline and at least one post baseline assessment

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

One-sided P value from repeated measures model with fixed effects of treatment, site, visit, and baseline score; interactions of treatment by visit and baseline score by visit; covariance structure is unstructured.

Comparison groups	Placebo v ABT-126 25 mg QD
Number of subjects included in analysis	255
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.451
Method	mixed-effects model for repeated measure
Parameter estimate	LS mean of difference
Point estimate	-0.15
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.12
upper limit	1.83

Variability estimate	Standard error of the mean
Dispersion value	1.2

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

One-sided P value from repeated measures model with fixed effects of treatment, site, visit, and baseline score; interactions of treatment by visit and baseline score by visit; covariance structure is unstructured.

Comparison groups	Placebo v ABT-126 75 mg QD
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.662
Method	mixed-effects model for repeated measure
Parameter estimate	LS mean of difference
Point estimate	0.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.48
upper limit	2.49
Variability estimate	Standard error of the mean
Dispersion value	1.2

Secondary: Partner-Patient Questionnaire for Shared Activities (PPQSA) Average Score: Change from Baseline to Week 24

End point title	Partner-Patient Questionnaire for Shared Activities (PPQSA) Average Score: Change from Baseline to Week 24

End point description:

From repeated measures analysis. The PPQSA is a caregiver-completed assessment to measure the extent to which the AD patient's mood and mental state interferes with the patient-partner (i.e., patient-caregiver, patient-spouse, or patient-non-spouse partner) relationship. The scale consists of 17 shared activity items, a global interference item, and a ranking of the 5 most important activities. The scale is scored by taking a simple average of the items. Scores range from 0 to 5 with a higher score desirable.

End point type	Secondary

End point timeframe:

Baseline through Week 24

End point values	Placebo	ABT-126 25 mg QD	ABT-126 75 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	129[22]	125[23]	123[24]	
Units: units on a scale				
least squares mean (standard error)	-0.02 (± 0.06)	-0.07 (± 0.06)	-0.02 (± 0.06)	

Notes:

[22] - Subjects with a baseline and at least one post baseline assessment

[23] - Subjects with a baseline and at least one post baseline assessment

[24] - Subjects with a baseline and at least one post baseline assessment

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

One-sided P value from repeated measures model with fixed effects of treatment, site, visit, and baseline score; interactions of treatment by visit and baseline score by visit; covariance structure is unstructured.

Comparison groups	Placebo v ABT-126 25 mg QD
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.721
Method	mixed-effects model for repeated measure
Parameter estimate	LS mean of difference
Point estimate	-0.05
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.19
upper limit	0.09
Variability estimate	Standard error of the mean
Dispersion value	0.08

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

One-sided P value from repeated measures model with fixed effects of treatment, site, visit, and baseline score; interactions of treatment by visit and baseline score by visit; covariance structure is unstructured.

Comparison groups	Placebo v ABT-126 75 mg QD
Number of subjects included in analysis	252
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.493
Method	mixed-effects model for repeated measure
Parameter estimate	LS mean of difference
Point estimate	0
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.14
upper limit	0.14
Variability estimate	Standard error of the mean
Dispersion value	0.08

Secondary: Resource Use in Dementia (RUD-Lite) Caregiver Time Score: Change from Baseline to Final Evaluation (up to Week 24)

End point title	Resource Use in Dementia (RUD-Lite) Caregiver Time Score: Change from Baseline to Final Evaluation (up to Week 24)

End point description:

The RUD-Lite is a brief measure of resource utilization developed for use in clinical trials of AD and is completed by non-professional caregivers in the study. The caregiver time scores range from 0 to 1440 with a lower score desirable.

End point type	Secondary

End point timeframe:

Baseline through Final Evaluation (up to Week 24)

End point values	Placebo	ABT-126 25 mg QD	ABT-126 75 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	123[25]	120[26]	114[27]	
Units: units on a scale				
least squares mean (standard error)	38.01 (± 14.14)	32.33 (± 14.27)	38.02 (± 14.6)	

Notes:

[25] - Subjects with a baseline and at least one post baseline assessment

[26] - Subjects with a baseline and at least one post baseline assessment

[27] - Subjects with a baseline and at least one post baseline assessment

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

ANCOVA model with change from baseline to the final visit as the response, treatment and study site as the main effects, and the baseline value as the covariate.

Comparison groups	Placebo v ABT-126 25 mg QD
Number of subjects included in analysis	243
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.384
Method	ANCOVA
Parameter estimate	LS mean of difference
Point estimate	-5.68
Confidence interval	
level	90 %
sides	2-sided
lower limit	-37.53
upper limit	26.17
Variability estimate	Standard error of the mean
Dispersion value	19.31

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

ANCOVA model with change from baseline to the final visit as the response, treatment and study site as the main effects, and the baseline value as the covariate.

Comparison groups	Placebo v ABT-126 75 mg QD
Number of subjects included in analysis	237
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5
Method	ANCOVA
Parameter estimate	LS mean of difference
Point estimate	0.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	-32.29
upper limit	32.3
Variability estimate	Standard error of the mean
Dispersion value	19.58

Secondary: EuroQol-5 Dimension Questionnaire (EQ-5D-5L) Index Score: Change from Baseline to Final Evaluation (up to Week 24)

End point title	EuroQol-5 Dimension Questionnaire (EQ-5D-5L) Index Score: Change from Baseline to Final Evaluation (up to Week 24)

End point description:

The EQ-5D-5L is a 5-dimensional tool capturing subjects' mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. Subjects rate each dimension using a scale with 5 levels: no problem, slight problem, moderate problem, severe problem, and extreme problem. Subjects also rate their perception of their overall health on a visual analogue scale (VAS). EQ-5D-5L scores are derived by converting raw scores based on the Administration and Scoring Manual. The EQ-5D-5L Index Score ranges from -0.11 to 1 with a higher score desirable. The higher the score, the better the subject's health condition.

End point type	Secondary

End point timeframe:

Baseline through Final Evaluation (up to Week 24)

End point values	Placebo	ABT-126 25 mg QD	ABT-126 75 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	133[28]	126[29]	125[30]	
Units: units on a scale				
least squares mean (standard error)	0 (± 0.01)	0 (± 0.01)	0 (± 0.01)	

Notes:

[28] - Subjects with a baseline and at least one post baseline assessment

[29] - Subjects with a baseline and at least one post baseline assessment

[30] - Subjects with a baseline and at least one post baseline assessment

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
ANCOVA model with change from baseline to the final visit as the response, treatment and study site as the main effects, and the baseline value as the covariate.	
Comparison groups	ABT-126 25 mg QD v Placebo
Number of subjects included in analysis	259
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.534
Method	ANCOVA
Parameter estimate	LS mean of difference
Point estimate	0
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.02
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.01

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
ANCOVA model with change from baseline to the final visit as the response, treatment and study site as the main effects, and the baseline value as the covariate.	
Comparison groups	Placebo v ABT-126 75 mg QD
Number of subjects included in analysis	258
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.72
Method	ANCOVA
Parameter estimate	LS mean of difference
Point estimate	-0.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.02
upper limit	0.01
Variability estimate	Standard error of the mean
Dispersion value	0.01

Secondary: EuroQol-3 Dimension Questionnaire (EQ-5D-3L) Proxy Index Score: Change from Baseline to Final Evaluation (up to Week 24)

End point title	EuroQol-3 Dimension Questionnaire (EQ-5D-3L) Proxy Index Score: Change from Baseline to Final Evaluation (up to Week 24)

End point description:

The EQ-5D-3L is a 5-dimensional tool capturing subjects' mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. Proxies (e.g., caregivers) rate ach dimension using a scale with 3 levels, where 3 represents no problem, 2 represents some problem, and 1 represents extreme problem, based on how he or she (the caregiver) believes that the subject would rate their own health-related quality of life if they were able to communicate it. Proxies also rate the overall health of the subject on a visual analogue scale (VAS). EQ-5D-3L scores are derived by converting raw scores based on the Administration and Scoring Manual. The EQ-5D-3L Index Score ranges from -0.11 to 1 with a higher score desirable. The higher the score, the better the subject's health condition.

End point type	Secondary

End point timeframe:

Baseline through Final Evaluation (up to Week 24

End point values	Placebo	ABT-126 25 mg QD	ABT-126 75 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134[31]	128[32]	126[33]	
Units: units on a scale				
least squares mean (standard error)	-0.02 (± 0.01)	0.01 (± 0.01)	-0.02 (± 0.01)	

Notes:

[31] - Subjects with a baseline and at least one post baseline assessment

[32] - Subjects with a baseline and at least one post baseline assessment

[33] - Subjects with a baseline and at least one post baseline assessment

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

ANCOVA model with change from baseline to the final visit as the response, treatment and study site as the main effects, and the baseline value as the covariate.

Comparison groups	Placebo v ABT-126 25 mg QD
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.071
Method	ANCOVA
Parameter estimate	LS mean of difference
Point estimate	0.02
Confidence interval	
level	90 %
sides	2-sided
lower limit	0
upper limit	0.05

Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

ANCOVA model with change from baseline to the final visit as the response, treatment and study site as the main effects, and the baseline value as the covariate.

Comparison groups	Placebo v ABT-126 75 mg QD
Number of subjects included in analysis	260
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.605
Method	ANCOVA
Parameter estimate	LS mean of difference
Point estimate	0
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.03
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.02

Secondary: Wechsler Memory Scale-III (WMS-III) Working Memory Index: Change from Baseline through Week 18

End point title	Wechsler Memory Scale-III (WMS-III) Working Memory Index: Change from Baseline through Week 18

End point description:

The WMS-III Working Memory Index Score includes the Letter Number Sequencing (LNS) and Spatial Span (SS) tests. The LNS is a memory test in which the subjects are read a combination of letters and numbers and are asked to repeat them, saying the numbers in ascending order followed by the letters in alphabetical order. The LNS score ranges from 0 to 21 points. The SS is a measure of nonverbal working memory, with scores that range from 0 to 32. Raw scores from both LNS and SS are converted to scaled scores using the WMS-III Administration and Scoring Manual and the overall Working Memory Index is derived from these scaled scores. The WMS-III Working Memory Index ranges from 49 to 155. Higher scores and higher Working Memory Index are desirable.

End point type	Secondary

End point timeframe:

Baseline through Week 18

End point values	Placebo	ABT-126 25 mg QD	ABT-126 75 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	130[34]	131[35]	124[36]	
Units: units on a scale				
least squares mean (standard error)	-2.05 (± 0.79)	-1.7 (± 0.8)	-1.8 (± 0.81)	

Notes:

[34] - Subjects with a baseline and at least one post baseline assessment

[35] - Subjects with a baseline and at least one post baseline assessment

[36] - Subjects with a baseline and at least one post baseline assessment

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
One-sided P value from repeated measures model with treatment, site, visit, baseline score, interactions of treatment and visit; baseline score and visit; covariance structure is unstructured.	
Comparison groups	Placebo v ABT-126 25 mg QD
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.376
Method	mixed-effects model for repeated measure
Parameter estimate	LS mean of difference
Point estimate	0.35
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.47
upper limit	2.17
Variability estimate	Standard error of the mean
Dispersion value	1.1

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
One-sided P value from repeated measures model with treatment, site, visit, baseline score, interactions of treatment and visit; baseline score and visit; covariance structure is unstructured.	
Comparison groups	Placebo v ABT-126 75 mg QD
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.412
Method	mixed-effects model for repeated measure
Parameter estimate	LS mean of difference
Point estimate	0.25
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.59
upper limit	2.08
Variability estimate	Standard error of the mean
Dispersion value	1.11

Secondary: Wechsler Memory Scale-III (WMS-III) Letter Number Sequencing (LNS) Scaled Score: Change from Baseline through Week 18

End point title	Wechsler Memory Scale-III (WMS-III) Letter Number Sequencing (LNS) Scaled Score: Change from Baseline through Week 18

End point description:

From repeated measures analysis. The WMS-III Letter Number Sequencing (LNS) test is a memory test in which the subjects are read a combination of letters and numbers and are asked to repeat them, saying the numbers in ascending order followed by the letters in alphabetical order. Raw scores from LNS are converted to scaled scores using the WMS-III Administration and Scoring Manual. The WMS-III LNS Scaled Score ranges from 1 to 19 with a higher score desirable.

End point type	Secondary

End point timeframe:

Baseline through Week 18

End point values	Placebo	ABT-126 25 mg QD	ABT-126 75 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	130[37]	131[38]	124[39]	
Units: units on a scale				
least squares mean (standard error)	-0.24 (± 0.2)	-0.37 (± 0.21)	-0.05 (± 0.21)	

Notes:

[37] - Subjects with a baseline and at least one post baseline assessment

[38] - Subjects with a baseline and at least one post baseline assessment

[39] - Subjects with a baseline and at least one post baseline assessment

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

One-sided P value from repeated measures model with treatment, site, visit, baseline score, interactions of treatment and visit; baseline score and visit; covariance structure is unstructured.

Comparison groups	Placebo v ABT-126 25 mg QD
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.677
Method	mixed-effects model for repeated measure
Parameter estimate	LS mean of difference
Point estimate	-0.13
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.6
upper limit	0.34
Variability estimate	Standard error of the mean
Dispersion value	0.28

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

One-sided P value from repeated measures model with treatment, site, visit, baseline score, interactions of treatment and visit; baseline score and visit; covariance structure is unstructured.

Comparison groups	Placebo v ABT-126 75 mg QD
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.252
Method	mixed-effects model for repeated measure
Parameter estimate	LS mean of difference
Point estimate	0.19
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.28
upper limit	0.66
Variability estimate	Standard error of the mean
Dispersion value	0.29

Secondary: Wechsler Memory Scale-III (WMS-III) Spatial Span (SS) Scaled Score: Change from Baseline through Week 18

End point title	Wechsler Memory Scale-III (WMS-III) Spatial Span (SS) Scaled Score: Change from Baseline through Week 18

End point description:

From repeated measures analysis. The WMS-III Spatial Span (SS) test is a measure of nonverbal working memory. Raw scores from SS are converted to scaled scores using the WMS-III Administration and Scoring Manual. The WMS-III SS Scaled Score ranges from 1 to 19 with a higher score desirable.

End point type	Secondary

End point timeframe:

Baseline through Week 18

End point values	Placebo	ABT-126 25 mg QD	ABT-126 75 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	131[40]	133[41]	125[42]	
Units: units on a scale				
least squares mean (standard error)	-0.6 (± 0.2)	-0.16 (± 0.2)	-0.62 (± 0.21)	

Notes:

[40] - Subjects with a baseline and at least one post baseline assessment

[41] - Subjects with a baseline and at least one post baseline assessment

[42] - Subjects with a baseline and at least one post baseline assessment

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

One-sided P value from repeated measures model with treatment, site, visit, baseline score, interactions of treatment and visit; baseline score and visit; covariance structure is unstructured.

Comparison groups	Placebo v ABT-126 25 mg QD
Number of subjects included in analysis	264
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.057
Method	mixed-effects model for repeated measure
Parameter estimate	LS mean of difference
Point estimate	0.45
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.02
upper limit	0.91
Variability estimate	Standard error of the mean
Dispersion value	0.28

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

One-sided P value from repeated measures model with treatment, site, visit, baseline score, interactions of treatment and visit; baseline score and visit; covariance structure is unstructured.

Comparison groups	Placebo v ABT-126 75 mg QD
Number of subjects included in analysis	256
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.526
Method	mixed-effects model for repeated measure
Parameter estimate	LS mean of difference
Point estimate	-0.02
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.49
upper limit	0.45
Variability estimate	Standard error of the mean
Dispersion value	0.29

Secondary: Cornell Scale for Depression in Dementia (CSDD): Change from Baseline to Final Evaluation (up to Week 24)

End point title	Cornell Scale for Depression in Dementia (CSDD): Change from Baseline to Final Evaluation (up to Week 24)

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 2 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. Subjects with scores of above 10 at Screening Visit 1 were excluded from the study.

End point type	Secondary

End point timeframe:

Baseline through Final Evaluation (up to Week 24)

End point values	Placebo	ABT-126 25 mg QD	ABT-126 75 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	133[43]	127[44]	125[45]	
Units: units on a scale				
least squares mean (standard error)	-0.35 (± 0.21)	-0.31 (± 0.22)	-0.23 (± 0.22)	

Notes:

[43] - Subjects with a baseline and at least one post baseline assessment

[44] - Subjects with a baseline and at least one post baseline assessment

[45] - Subjects with a baseline and at least one post baseline assessment

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

ANCOVA model with change from baseline to the final visit as the response, treatment and study site as the main effects, and the baseline value as the covariate.

Comparison groups	Placebo v ABT-126 25 mg QD
Number of subjects included in analysis	260
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.552
Method	ANCOVA
Parameter estimate	LS mean of difference
Point estimate	0.04
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.45
upper limit	0.53
Variability estimate	Standard error of the mean
Dispersion value	0.29

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

ANCOVA model with change from baseline to the final visit as the response, treatment and study site as the main effects, and the baseline value as the covariate.

Comparison groups	Placebo v ABT-126 75 mg QD

Number of subjects included in analysis	258
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.655
Method	ANCOVA
Parameter estimate	LS mean of difference
Point estimate	0.12
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.37
upper limit	0.61
Variability estimate	Standard error of the mean
Dispersion value	0.3

Secondary: Number of Subjects in Each Category of the Clinician Interview-Based Impression of Change-Plus (CIBIC-plus) at Week 24

End point title	Number of Subjects in Each Category of the Clinician Interview-Based Impression of Change-Plus (CIBIC-plus) at Week 24

End point description:

The CIBIC-plus is designed to capture a global impression of change in severity of dementia using 4 major areas of assessment: general functioning, cognitive functioning, behavioral functioning, and activities of daily living. The CIBIC-plus and the CIBIS were performed by a trained rater who did not have access to the results of other study assessments or medical records for the subject and who did not participate in the care or management of the subject. A 7-point scale is used to score the CIBIC-plus in which 1 of the following is selected: 1=markedly improved, 2=moderately improved, 3=minimally improved, 4=no change, 5=minimally worse, 6 = moderately worse, or 7 = markedly worse. CIBIC-plus scores were stratified by Clinician Interview-Based Impression of Severity (CIBIS) Score at baseline. Subjects who did not reach Week 24 were excluded from the analysis.

End point type	Secondary

End point timeframe:

Week 24

End point values	Placebo	ABT-126 25 mg QD	ABT-126 75 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	142	137	137	
Units: subjects				
Markedly improved	0	0	0	
Moderately improved	3	0	2	
Minimally improved	21	11	14	
No change	66	64	57	
Minimally worse	39	50	52	
Moderately worse	12	11	12	
Markedly worse	1	1	0	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-126 25 mg QD
Number of subjects included in analysis	279
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.066
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-126 75 mg QD
Number of subjects included in analysis	279
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.089
Method	Cochran-Mantel-Haenszel

Secondary: EuroQol-5 Dimension Questionnaire (EQ-5D-5L) Health State Score: Change from Baseline to Final Evaluation (up to Week 24)

End point title	EuroQol-5 Dimension Questionnaire (EQ-5D-5L) Health State Score: Change from Baseline to Final Evaluation (up to Week 24)

End point description:

The EQ-5D-5L is a 5-dimensional tool capturing subjects' mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. Subjects rate each dimension using a scale with 5 levels: no problem, slight problem, moderate problem, severe problem, and extreme problem. Subjects also rate their perception of their overall health on a visual analogue scale (VAS). EQ-5D-5L scores are derived by converting raw scores based on the Administration and Scoring Manual. The EQ-5D-5L Health State Score ranges from 0 to 100 with a higher score desirable. The higher the score, the better the subject's health condition.

End point type	Secondary

End point timeframe:

Baseline through Final Evaluation (up to Week 24)

End point values	Placebo	ABT-126 25 mg QD	ABT-126 75 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	133[46]	124[47]	125[48]	
Units: units on a scale				
least squares mean (standard error)	-2.51 (± 1.22)	-1.87 (± 1.27)	0.6 (± 1.27)	

Notes:

[46] - Subjects with a baseline and at least one post baseline assessment

[47] - Subjects with a baseline and at least one post baseline assessment

[48] - Subjects with a baseline and at least one post baseline assessment

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

ANCOVA model with change from baseline to the final visit as the response, treatment and study site as the main effects, and the baseline value as the covariate.

Comparison groups	ABT-126 25 mg QD v Placebo
Number of subjects included in analysis	257
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.354
Method	ANCOVA
Parameter estimate	LS mean of difference
Point estimate	0.64
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.18
upper limit	3.47
Variability estimate	Standard error of the mean
Dispersion value	1.71

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

ANCOVA model with change from baseline to the final visit as the response, treatment and study site as the main effects, and the baseline value as the covariate.

Comparison groups	Placebo v ABT-126 75 mg QD
Number of subjects included in analysis	258
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.035
Method	ANCOVA
Parameter estimate	LS mean of difference
Point estimate	3.11
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.29
upper limit	5.93
Variability estimate	Standard error of the mean
Dispersion value	1.71

Secondary: EuroQol-3 Dimension Questionnaire (EQ-5D-3L) Proxy Health State Score: Change from Baseline to Final Evaluation (up to Week 24)

End point title	EuroQol-3 Dimension Questionnaire (EQ-5D-3L) Proxy Health State Score: Change from Baseline to Final Evaluation (up to Week 24)

End point description:

The EQ-5D-3L is a 5-dimensional tool capturing subjects' mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. Proxies (e.g., caregivers) rate ach dimension using a scale with 3 levels, where 3 represents no problem, 2 represents some problem, and 1 represents extreme problem, based on how he or she (the caregiver) believes that the subject would rate their own health-related quality of life if they were able to communicate it. Proxies also rate the overall health of the subject on a visual analogue scale (VAS). EQ-5D-3L scores are derived by converting raw scores based on the Administration and Scoring Manual. The EQ-5D-3L Health State Score ranges from 0 to 100 with a higher score desirable. The higher the score, the better the subject's health condition.

End point type	Secondary

End point timeframe:

Baseline through Final Evaluation (up to Week 24

End point values	Placebo	ABT-126 25 mg QD	ABT-126 75 mg QD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	133[49]	128[50]	126[51]	
Units: units on a scale				
least squares mean (standard error)	-0.49 (± 1.34)	-2.23 (± 1.36)	-2.01 (± 1.38)	

Notes:

[49] - Subjects with a baseline and at least one post baseline assessment

[50] - Subjects with a baseline and at least one post baseline assessment

[51] - Subjects with a baseline and at least one post baseline assessment

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

ANCOVA model with change from baseline to the final visit as the response, treatment and study site as the main effects, and the baseline value as the covariate.

Comparison groups	Placebo v ABT-126 25 mg QD
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.824
Method	ANCOVA
Parameter estimate	LS mean of difference
Point estimate	-1.74
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.81
upper limit	1.34
Variability estimate	Standard error of the mean
Dispersion value	1.86

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

ANCOVA model with change from baseline to the final visit as the response, treatment and study site as

the main effects, and the baseline value as the covariate.

Comparison groups	Placebo v ABT-126 75 mg QD
Number of subjects included in analysis	259
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.792
Method	ANCOVA
Parameter estimate	LS mean of difference
Point estimate	-1.52
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.6
upper limit	1.56
Variability estimate	Standard error of the mean
Dispersion value	1.87

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
AEs were collected from study drug administration until 30 days following last dose (28 weeks); SAEs were collected from when informed consent was obtained (32 weeks).	
Adverse event reporting additional description:	
All AEs were collected whether solicited or spontaneously reported by the subject	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Three placebo capsules once daily in the morning for 24 weeks beginning on Day 1.	
Reporting group title	ABT-126 25 mg QD
Reporting group description:	
One ABT-126 25 mg capsule and 2 placebo capsules once daily in the morning for 24 weeks beginning on Day 1.	
Reporting group title	ABT-126 75 mg QD
Reporting group description:	
Three ABT-126 25 mg capsules once daily in the morning for 24 weeks beginning on Day 1.	

Serious adverse events	Placebo	ABT-126 25 mg QD	ABT-126 75 mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 146 (8.90%)	9 / 143 (6.29%)	10 / 145 (6.90%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 146 (0.68%)	0 / 143 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Angiopathy			
subjects affected / exposed	1 / 146 (0.68%)	0 / 143 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			

subjects affected / exposed	0 / 146 (0.00%)	0 / 143 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 146 (0.00%)	1 / 143 (0.70%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Allergy to arthropod sting			
subjects affected / exposed	1 / 146 (0.68%)	0 / 143 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	0 / 146 (0.00%)	1 / 143 (0.70%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary artery thrombosis			
subjects affected / exposed	1 / 146 (0.68%)	0 / 143 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 146 (0.00%)	1 / 143 (0.70%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 146 (0.00%)	0 / 143 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination, visual			

subjects affected / exposed	0 / 146 (0.00%)	1 / 143 (0.70%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 146 (0.68%)	0 / 143 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial bones fracture			
subjects affected / exposed	1 / 146 (0.68%)	0 / 143 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 146 (0.68%)	1 / 143 (0.70%)	2 / 145 (1.38%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 146 (0.00%)	1 / 143 (0.70%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	1 / 146 (0.68%)	0 / 143 (0.00%)	2 / 145 (1.38%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 146 (0.00%)	0 / 143 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 146 (0.00%)	1 / 143 (0.70%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Atrial fibrillation			
subjects affected / exposed	0 / 146 (0.00%)	1 / 143 (0.70%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	1 / 146 (0.68%)	0 / 143 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 146 (0.68%)	0 / 143 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	1 / 146 (0.68%)	0 / 143 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 146 (0.00%)	0 / 143 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 146 (0.00%)	1 / 143 (0.70%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 146 (0.68%)	0 / 143 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Anal fissure			

subjects affected / exposed	0 / 146 (0.00%)	0 / 143 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			
subjects affected / exposed	1 / 146 (0.68%)	0 / 143 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 146 (0.00%)	0 / 143 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faecaloma			
subjects affected / exposed	0 / 146 (0.00%)	0 / 143 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 146 (0.00%)	0 / 143 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 146 (0.00%)	1 / 143 (0.70%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 146 (0.00%)	0 / 143 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Swelling face			
subjects affected / exposed	1 / 146 (0.68%)	0 / 143 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Urinary retention			
subjects affected / exposed	0 / 146 (0.00%)	0 / 143 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 146 (0.68%)	0 / 143 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tenosynovitis			
subjects affected / exposed	0 / 146 (0.00%)	0 / 143 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 146 (0.00%)	1 / 143 (0.70%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	1 / 146 (0.68%)	0 / 143 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parotitis			
subjects affected / exposed	0 / 146 (0.00%)	0 / 143 (0.00%)	1 / 145 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 146 (0.00%)	1 / 143 (0.70%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia streptococcal			
subjects affected / exposed	1 / 146 (0.68%)	0 / 143 (0.00%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Sepsis			
subjects affected / exposed	0 / 146 (0.00%)	1 / 143 (0.70%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 146 (0.00%)	0 / 143 (0.00%)	3 / 145 (2.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 146 (0.00%)	1 / 143 (0.70%)	0 / 145 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	ABT-126 25 mg QD	ABT-126 75 mg QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 146 (25.34%)	38 / 143 (26.57%)	52 / 145 (35.86%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	11 / 146 (7.53%)	9 / 143 (6.29%)	13 / 145 (8.97%)
occurrences (all)	12	14	15
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 146 (2.05%)	5 / 143 (3.50%)	8 / 145 (5.52%)
occurrences (all)	3	6	10
Headache			
subjects affected / exposed	4 / 146 (2.74%)	10 / 143 (6.99%)	9 / 145 (6.21%)
occurrences (all)	4	11	10
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	2 / 146 (1.37%)	7 / 143 (4.90%)	12 / 145 (8.28%)
occurrences (all)	3	8	16
Diarrhoea			

subjects affected / exposed	7 / 146 (4.79%)	11 / 143 (7.69%)	6 / 145 (4.14%)
occurrences (all)	7	11	6
Nausea			
subjects affected / exposed	2 / 146 (1.37%)	3 / 143 (2.10%)	11 / 145 (7.59%)
occurrences (all)	2	6	12
Psychiatric disorders			
Agitation			
subjects affected / exposed	6 / 146 (4.11%)	5 / 143 (3.50%)	9 / 145 (6.21%)
occurrences (all)	8	5	9
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	9 / 146 (6.16%)	0 / 143 (0.00%)	3 / 145 (2.07%)
occurrences (all)	9	0	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported