Clinical trial results:
A Randomized, Double-Blind, Placebo- and Active-Controlled Phase 2 Dose-Ranging Study to Evaluate the Efficacy and Safety of ABT-126 in Subjects with Mild to Moderate Alzheimer's Disease

Summary

EudraCT number	2011-002004-32
Trial protocol	GB PL
Global end of trial date	10 December 2013

Results information

Result version number	v2 (current)
This version publication date	18 May 2016
First version publication date	11 July 2015
Version creation reason	• Correction of full data set new version being created so writer can re-gain access to the published study to re-confirm that study has no errors.

Trial information

Trial identification

Sponsor protocol code	M10-985

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01527916
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	10 December 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 December 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the dose-response relationship with respect to the efficacy of symptomatic treatment and safety of three doses of ABT-126 in subjects with mild to moderate Alzheimer's disease (AD). The primary efficacy measure is the Alzheimer's Disease Assessment Scale – cognitive subscale (ADAS-Cog).

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	08 February 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	7 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 39
Country: Number of subjects enrolled	United Kingdom: 65
Country: Number of subjects enrolled	Russian Federation: 153
Country: Number of subjects enrolled	Ukraine: 50
Country: Number of subjects enrolled	South Africa: 95
Country: Number of subjects enrolled	United States: 36
Worldwide total number of subjects	438
EEA total number of subjects	104

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)	62
From 65 to 84 years	336
85 years and over	40

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects were to undergo screening procedures within 28 days prior to enrollment.

Pre-assignment period milestones

Number of subjects started	438
Number of subjects completed	436

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Randomized but not treated: 2

Period 1

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

Blinding implementation details:

The study was designed to have 2 parts with different randomization schemes for each part. In Part 1, 350 subjects were randomized to 5 treatment groups using a Bayesian response adaptive randomization scheme. In Part 2 of the study, approximately 80 subjects were randomized in equal ratio to placebo and an ABT-126 dose (50 mg) selected by an independent data monitoring committee based on an interim evaluation of the data from Part 1. The treatment duration for Parts 1 and 2 was 24 weeks.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Three placebo capsules taken orally 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:

All investigational products were made to appear identical in order to maintain the blind.

Arm title	ABT-126 25 mg

Arm description:

One ABT-126 25 mg capsule and 2 placebo capsules taken orally 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:

All investigational products were made to appear identical in order to maintain the blind.

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

Dosage and administration details:

All investigational products were made to appear identical in order to maintain the blind.

Arm title	ABT-126 50 mg

Arm description:

Two ABT-126 25 mg capsules and 1 placebo capsule taken orally 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:

All investigational products were made to appear identical in order to maintain the blind.

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

Dosage and administration details:

All investigational products were made to appear identical in order to maintain the blind.

Arm title	ABT-126 75 mg

Arm description:

Three ABT-126 25 mg capsules taken orally 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:

All investigational products were made to appear identical in order to maintain the blind.

Arm title	Donepezil

Arm description:

One 5 mg donepezil capsule and 2 placebo capsules taken orally once daily in the morning for 4 weeks beginning on Day 1, and one 10 mg donepezil capsule and 2 placebo capsules taken orally once daily in the morning for 20 weeks thereafter.

Arm type	Active comparator

Investigational medicinal product name	Donepezil
Investigational medicinal product code	
Other name	Aricept®
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

All investigational products were made to appear identical in order to maintain the blind.

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

Dosage and administration details:

All investigational products were made to appear identical in order to maintain the blind.

Number of subjects in period 1[1]	Placebo	ABT-126 25 mg	ABT-126 50 mg
Started	104	77	107
Completed	89	64	92
Not completed	15	13	15
Consent withdrawn by subject	9	4	9
Not specified	2	2	1
Adverse event	3	5	3
Lost to follow-up	-	-	-
Noncompliance	1	2	1
Lack of efficacy	-	-	1

Number of subjects in period 1[1]	ABT-126 75 mg	Donepezil
Started	73	75
Completed	62	60
Not completed	11	15
Consent withdrawn by subject	8	5
Not specified	1	1
Adverse event	2	7
Lost to follow-up	-	1
Noncompliance	-	1
Lack of efficacy	-	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Two subjects were randomized but not treated, and are not included in the baseline period.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Three placebo capsules taken orally once daily in the morning for 24 weeks beginning on Day 1.	
Reporting group title	ABT-126 25 mg
Reporting group description:	
One ABT-126 25 mg capsule and 2 placebo capsules taken orally once daily in the morning for 24 weeks beginning on Day 1.	
Reporting group title	ABT-126 50 mg
Reporting group description:	
Two ABT-126 25 mg capsules and 1 placebo capsule taken orally once daily in the morning for 24 weeks beginning on Day 1.	
Reporting group title	ABT-126 75 mg
Reporting group description:	
Three ABT-126 25 mg capsules taken orally once daily in the morning for 24 weeks beginning on Day 1.	
Reporting group title	Donepezil
Reporting group description:	
One 5 mg donepezil capsule and 2 placebo capsules taken orally once daily in the morning for 4 weeks beginning on Day 1, and one 10 mg donepezil capsule and 2 placebo capsules taken orally once daily in the morning for 20 weeks thereafter.	

Reporting group values	Placebo	ABT-126 25 mg	ABT-126 50 mg
Number of subjects	104	77	107
Age categorical			
Data are provided for the Intent-to-treat population (subjects who received at least 1 dose of study drug).			
Units: Subjects			
< 75 years	59	37	50
≥ 75 years	45	40	57
Age continuous			
Data are provided for the Intent-to-treat population (subjects who received at least 1 dose of study drug).			
Units: years			
arithmetic mean	73.2	73	73.9
standard deviation	± 7.39	± 7.62	± 8.26
Gender categorical			
Data are provided for the Intent-to-treat population (subjects who received at least 1 dose of study drug).			
Units: Subjects			
Female	65	40	68
Male	39	37	39

Reporting group values	ABT-126 75 mg	Donepezil	Total
Number of subjects	73	75	436
Age categorical			
Data are provided for the Intent-to-treat population (subjects who received at least 1 dose of study drug).			
Units: Subjects			
< 75 years	30	30	206

≥ 75 years	43	45	230

Age continuous			
Data are provided for the Intent-to-treat population (subjects who received at least 1 dose of study drug).			
Units: years			
arithmetic mean	76.2	75.1	
standard deviation	± 8.14	± 7.75	-
Gender categorical			
Data are provided for the Intent-to-treat population (subjects who received at least 1 dose of study drug).			
Units: Subjects			
Female	52	40	265
Male	21	35	171

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Three placebo capsules taken orally once daily in the morning for 24 weeks beginning on Day 1.	
Reporting group title	ABT-126 25 mg
Reporting group description:	
One ABT-126 25 mg capsule and 2 placebo capsules taken orally once daily in the morning for 24 weeks beginning on Day 1.	
Reporting group title	ABT-126 50 mg
Reporting group description:	
Two ABT-126 25 mg capsules and 1 placebo capsule taken orally once daily in the morning for 24 weeks beginning on Day 1.	
Reporting group title	ABT-126 75 mg
Reporting group description:	
Three ABT-126 25 mg capsules taken orally once daily in the morning for 24 weeks beginning on Day 1.	
Reporting group title	Donepezil
Reporting group description:	
One 5 mg donepezil capsule and 2 placebo capsules taken orally once daily in the morning for 4 weeks beginning on Day 1, and one 10 mg donepezil capsule and 2 placebo capsules taken orally once daily in the morning for 20 weeks thereafter.	

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

End point title	Alzheimer's Disease Assessment Scale – Cognitive Subscale (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 being 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	ABT-126 50 mg	ABT-126 75 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88[1]	63[2]	90[3]	62[4]
Units: units on a scale				
least squares mean (standard error)	-0.31 (± 0.61)	-0.77 (± 0.73)	-1.18 (± 0.61)	-1.38 (± 0.73)

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

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

End point values	Donepezil			
Subject group type	Reporting group			
Number of subjects analysed	59[5]			
Units: units on a scale				
least squares mean (standard error)	-2.6 (± 0.76)			

Notes:

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

Statistical analyses

Statistical analysis title	ABT-126 25 mg v. Placebo
Comparison groups	Placebo v ABT-126 25 mg
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.309 [6]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-0.47
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.02
upper limit	1.08
Variability estimate	Standard error of the mean
Dispersion value	0.94

Notes:

[6] - 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.

Statistical analysis title	ABT-126 50 mg v. Placebo
Comparison groups	Placebo v ABT-126 50 mg
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.153 [7]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-0.87
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.27
upper limit	0.53
Variability estimate	Standard error of the mean
Dispersion value	0.85

Notes:

[7] - 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.

Statistical analysis title	ABT-126 75 mg v. Placebo
Comparison groups	Placebo v ABT-126 75 mg
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.127 [8]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-1.08
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.63
upper limit	0.48
Variability estimate	Standard error of the mean
Dispersion value	0.94

Notes:

[8] - 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.

Statistical analysis title	Donepezil v. Placebo
Comparison groups	Placebo v Donepezil
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008 [9]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-2.29
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.87
upper limit	-0.72
Variability estimate	Standard error of the mean
Dispersion value	0.95

Notes:

[9] - 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. Statistically significant at the P = 0.05 level.

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:

The ADAS-Cog 13-item total score differs from the primary efficacy measure (ADAS-Cog 11-item total score) by 2 additional items of Delayed Word Recall and Number Cancellation Test. The ADAS-Cog 13-item total score ranges from 0 to 85. 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	ABT-126 50 mg	ABT-126 75 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88[10]	63[11]	87[12]	61[13]
Units: units on a scale				
least squares mean (standard error)	-0.67 (± 0.71)	-1.14 (± 0.84)	-1.7 (± 0.71)	-1.87 (± 0.84)

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

End point values	Donepezil			
Subject group type	Reporting group			
Number of subjects analysed	59[14]			
Units: units on a scale				
least squares mean (standard error)	-3.54 (± 0.87)			

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

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	ABT-126 25 mg v Placebo
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.333 [15]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-0.47
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.25
upper limit	1.31
Variability estimate	Standard error of the mean
Dispersion value	1.08

Notes:
[15] - 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.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-126 50 mg

Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.149 [16]
Method	mixed-effects model for repeated measure
Parameter estimate	Least Squares Mean of Difference
Point estimate	-1.03
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.65
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.98

Notes:

[16] - 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.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-126 75 mg
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.137 [17]
Method	mixed-effects model for repeated measure
Parameter estimate	Least Squares Mean of Difference
Point estimate	-1.19
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.98
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	1.09

Notes:

[17] - 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.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Donepezil
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005 [18]
Method	mixed-effects model for repeated measure
Parameter estimate	Least Squares Mean of Difference
Point estimate	-2.86
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.67
upper limit	-1.05

Variability estimate	Standard error of the mean
Dispersion value	1.1

Notes:

[18] - 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. Statistically significant at the P = 0.01 level.

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

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

End point description:

The MMSE is a brief questionnaire that provides a quantitative measure of cognitive status and was used to estimate the severity of cognitive impairment. The MMSE total score ranges from 0 to 30 with a higher score being desirable. An increase in the total score indicates improvement, with a lower score indicating greater cognitive impairment.

End point type	Secondary

End point timeframe:

Baseline through Week 24

End point values	Placebo	ABT-126 25 mg	ABT-126 50 mg	ABT-126 75 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[19]	64[20]	92[21]	62[22]
Units: units on a scale				
least squares mean (standard error)	0.39 (± 0.32)	-0.16 (± 0.38)	0.78 (± 0.32)	0.53 (± 0.38)

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

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

End point values	Donepezil			
Subject group type	Reporting group			
Number of subjects analysed	59[23]			
Units: units on a scale				
least squares mean (standard error)	1.19 (± 0.39)			

Notes:

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

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-126 25 mg
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.866 [24]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-0.55

Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.36
upper limit	0.27
Variability estimate	Standard error of the mean
Dispersion value	0.49

Notes:

[24] - 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.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-126 50 mg
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.191 [25]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	0.39
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.34
upper limit	1.12
Variability estimate	Standard error of the mean
Dispersion value	0.44

Notes:

[25] - 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.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-126 75 mg
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.39 [26]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	0.14
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.68
upper limit	0.95
Variability estimate	Standard error of the mean
Dispersion value	0.49

Notes:

[26] - 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.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Donepezil

Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.055 [27]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	0.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.02
upper limit	1.62
Variability estimate	Standard error of the mean
Dispersion value	0.5

Notes:

[27] - 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. Statistically significant at the P = 0.10 level.

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

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

End point description:

The NPI is used to assess changes in the subject's behavior that have occurred in a defined period of time. 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; ranges from 0 to 12). A 12-item NPI total score was calculated by also including the domain total scores for the 2 neurovegetative domains (ranges 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	ABT-126 50 mg	ABT-126 75 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[28]	64[29]	93[30]	62[31]
Units: units on a scale				
least squares mean (standard error)	-0.11 (± 0.95)	-0.92 (± 1.11)	0.05 (± 0.94)	-0.54 (± 1.12)

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

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

End point values	Donepezil			
Subject group type	Reporting group			
Number of subjects analysed	59[32]			

Units: units on a scale				
least squares mean (standard error)	-2.67 (± 1.15)			

Notes:

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

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-126 25 mg
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.287 [33]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-0.81
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.17
upper limit	1.56
Variability estimate	Standard error of the mean
Dispersion value	1.44

Notes:

[33] - 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.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-126 50 mg
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.549 [34]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	0.16
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.98
upper limit	2.3
Variability estimate	Standard error of the mean
Dispersion value	1.3

Notes:

[34] - 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.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-126 75 mg

Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.383 [35]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-0.43
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.82
upper limit	1.96
Variability estimate	Standard error of the mean
Dispersion value	1.45

Notes:

[35] - 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.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Donepezil
Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.041 [36]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-2.55
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.96
upper limit	-0.15
Variability estimate	Standard error of the mean
Dispersion value	1.46

Notes:

[36] - 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. Statistically significant at the P = 0.10 level.

Secondary: Neuropsychiatric Inventory (NPI) 10-item Total Score: Change from Baseline to Week 24

End point title	Neuropsychiatric Inventory (NPI) 10-item Total Score: Change from Baseline to Week 24

End point description:

The NPI is used to assess changes in the subject's behavior that have occurred in a defined period of time. 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; ranges from 0 to 12). A 10-item NPI total score was calculated by summing the domain total scores for the 10 behavioral domains (ranges from 0 to 120 with a lower score desirable).

End point type	Secondary

End point timeframe:
Baseline through Week 24

End point values	Placebo	ABT-126 25 mg	ABT-126 50 mg	ABT-126 75 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[37]	64[38]	93[39]	62[40]
Units: units on a scale				
least squares mean (standard error)	-0.26 (± 0.82)	-1.09 (± 0.96)	-0.5 (± 0.81)	-0.13 (± 0.96)

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

End point values	Donepezil			
Subject group type	Reporting group			
Number of subjects analysed	59[41]			
Units: units on a scale				
least squares mean (standard error)	-2.72 (± 0.99)			

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

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-126 25 mg
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.252 [42]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-0.82
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.86
upper limit	1.21
Variability estimate	Standard error of the mean
Dispersion value	1.23

Notes:
[42] - 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.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-126 50 mg

Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.416 [43]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-0.24
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.07
upper limit	1.6
Variability estimate	Standard error of the mean
Dispersion value	1.11

Notes:

[43] - 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.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-126 75 mg
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.544 [44]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	0.14
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.92
upper limit	2.19
Variability estimate	Standard error of the mean
Dispersion value	1.25

Notes:

[44] - 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.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Donepezil
Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.026 [45]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-2.45
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.53
upper limit	-0.38

Variability estimate	Standard error of the mean
Dispersion value	1.26

Notes:

[45] - 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. Statistically significant at the P = 0.10 level.

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

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

End point description:

The ADCS-ADL is a 23-item, caregiver-based assessment of activities of daily living designed specifically for AD patients and is completed by a trained rater. 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. The ADCS-ADL total score ranges from 0 to 78 with a higher score being desirable. An increase in the total score indicates improvement, with a lower score indicating more severe impairment.

End point type	Secondary

End point timeframe:

Baseline through Week 24

End point values	Placebo	ABT-126 25 mg	ABT-126 50 mg	ABT-126 75 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[46]	64[47]	93[48]	62[49]
Units: units on a scale				
least squares mean (standard error)	-2.3 (± 0.76)	-0.44 (± 0.89)	0 (± 0.75)	-0.44 (± 0.9)

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

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

End point values	Donepezil			
Subject group type	Reporting group			
Number of subjects analysed	59[50]			
Units: units on a scale				
least squares mean (standard error)	1.71 (± 0.92)			

Notes:

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

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-126 25 mg

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.053 [51]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	1.86
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.03
upper limit	3.74
Variability estimate	Standard error of the mean
Dispersion value	1.14

Notes:

[51] - 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. Statistically significant at the P = 0.10 level.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-126 50 mg
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.013 [52]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	2.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.6
upper limit	4.01
Variability estimate	Standard error of the mean
Dispersion value	1.04

Notes:

[52] - 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. Statistically significant at the P = 0.05 level.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-126 75 mg
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.054 [53]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	1.86

Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.04
upper limit	3.76
Variability estimate	Standard error of the mean
Dispersion value	1.15

Notes:

[53] - 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. Statistically significant at the P = 0.10 level.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Donepezil
Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [54]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	4.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	2.09
upper limit	5.93
Variability estimate	Standard error of the mean
Dispersion value	1.16

Notes:

[54] - 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. Statistically significant at the P = 0.001 level.

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

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

End point description:

The DEMQOL is a measure of health-related quality of life in dementia and is 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	ABT-126 50 mg	ABT-126 75 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88[55]	64[56]	92[57]	62[58]
Units: units on a scale				
least squares mean (standard error)	0.86 (± 0.88)	2.56 (± 1.04)	2.21 (± 0.89)	1.82 (± 1.03)

Notes:

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

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

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

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

End point values	Donepezil			
Subject group type	Reporting group			
Number of subjects analysed	60[59]			
Units: units on a scale				
least squares mean (standard error)	2.7 (± 1.07)			

Notes:

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

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-126 25 mg
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1 [60]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	1.69
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.48
upper limit	3.87
Variability estimate	Standard error of the mean
Dispersion value	1.32

Notes:

[60] - 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. Statistically significant at the P=0.10 level.

Statistical analysis title	Statistical Analysis 2
Comparison groups	ABT-126 50 mg v Placebo
Number of subjects included in analysis	180
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.13 [61]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	1.34

Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.62
upper limit	3.31
Variability estimate	Standard error of the mean
Dispersion value	1.19

Notes:

[61] - 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.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-126 75 mg
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.235 [62]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	0.96
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.23
upper limit	3.15
Variability estimate	Standard error of the mean
Dispersion value	1.33

Notes:

[62] - 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.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Donepezil
Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.084 [63]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	1.84
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.35
upper limit	4.02
Variability estimate	Standard error of the mean
Dispersion value	1.33

Notes:

[63] - 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. Statistically significant at the 0.10 level.

Secondary: DEMQOL-Proxy Global Score: Change from Baseline to Week 24

End point title	DEMQOL-Proxy Global Score: Change from Baseline to Week 24

End point description:

The DEMQOL-Proxy is a measure of health-related quality of life in dementia and is 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 Proxy contains 31 items and has similar content to the patient-report version, and also includes a self-concept item. The recall period for both versions is 1 week. Items are scored on a 4-point Likert scale, resulting in a global score ranging from 31 to 124. 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	ABT-126 50 mg	ABT-126 75 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88[64]	63[65]	92[66]	62[67]
Units: units on a scale				
least squares mean (standard error)	1.95 (± 0.92)	1.58 (± 1.1)	1.99 (± 0.93)	1.49 (± 1.07)

Notes:

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

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

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

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

End point values	Donepezil			
Subject group type	Reporting group			
Number of subjects analysed	60[68]			
Units: units on a scale				
least squares mean (standard error)	3.64 (± 1.11)			

Notes:

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

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-126 25 mg
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.607 [69]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-0.37
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.64
upper limit	1.89

Variability estimate	Standard error of the mean
Dispersion value	1.37

Notes:

[69] - 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.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-126 50 mg
Number of subjects included in analysis	180
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.489 [70]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	0.03
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.01
upper limit	2.08
Variability estimate	Standard error of the mean
Dispersion value	1.24

Notes:

[70] - 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.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-126 75 mg
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.631 [71]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-0.46
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.74
upper limit	1.81
Variability estimate	Standard error of the mean
Dispersion value	1.38

Notes:

[71] - 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.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Donepezil

Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.111 [72]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	1.69
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.59
upper limit	3.96
Variability estimate	Standard error of the mean
Dispersion value	1.38

Notes:

[72] - 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.

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:

The PPQSA is a caregiver-completed assessment constructed 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. Interference is scored on a 5-point scale ranging from 0 ("not at all") to 4 ("extremely"), with higher scores indicating greater interference in the past week. The PPQSA average score ranges 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	ABT-126 50 mg	ABT-126 75 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[73]	64[74]	92[75]	62[76]
Units: units on a scale				
least squares mean (standard error)	-0.07 (± 0.07)	-0.04 (± 0.08)	-0.08 (± 0.07)	-0.24 (± 0.08)

Notes:

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

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

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

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

End point values	Donepezil			
Subject group type	Reporting group			
Number of subjects analysed	60[77]			
Units: units on a scale				
least squares mean (standard error)	-0.21 (± 0.08)			

Notes:

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

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-126 25 mg
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.382 [78]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	0.03
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.14
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[78] - 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.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-126 50 mg
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.553 [79]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-0.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.16
upper limit	0.14
Variability estimate	Standard error of the mean
Dispersion value	0.09

Notes:

[79] - 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.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-126 75 mg

Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.954 [80]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-0.17
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.34
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[80] - 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.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Donepezil
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.905 [81]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-0.14
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.31
upper limit	0.03
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[81] - 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.

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

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

End point description:

The Wechsler Memory Scale-III (WMS-III) Working Memory Index includes the Letter Number Sequencing (LNS) and Spatial Span (SS) tests. The range of scores from the LNS is 0 to 21 points. The score range for the total of the 2 SS tests ranges from 0 to 32. Raw scores from both LNS and SS were converted to scale scores using the WMS-III Administration and Scoring Manual and an overall Working Memory Index was derived from these scaled scores. The WMS-III Index score ranges from 49 to 155 with a higher score desirable.

End point type	Secondary

End point timeframe:

Baseline through Week 18

End point values	Placebo	ABT-126 25 mg	ABT-126 50 mg	ABT-126 75 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	91[82]	65[83]	93[84]	64[85]
Units: units on a scale				
least squares mean (standard error)	1.17 (± 1.11)	0.24 (± 1.31)	-1.73 (± 1.1)	-2.34 (± 1.27)

Notes:

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

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

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

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

End point values	Donepezil			
Subject group type	Reporting group			
Number of subjects analysed	61[86]			
Units: units on a scale				
least squares mean (standard error)	1.31 (± 1.35)			

Notes:

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

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-126 25 mg
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.715 [87]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-0.93
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.63
upper limit	1.77
Variability estimate	Standard error of the mean
Dispersion value	1.64

Notes:

[87] - 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.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-126 50 mg

Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.975 [88]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-2.91
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.34
upper limit	-0.47
Variability estimate	Standard error of the mean
Dispersion value	1.48

Notes:

[88] - 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.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-126 75 mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.983 [89]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-3.52
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.23
upper limit	-0.8
Variability estimate	Standard error of the mean
Dispersion value	1.65

Notes:

[89] - 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.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Donepezil
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.468 [90]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	0.13
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.6
upper limit	2.86

Variability estimate	Standard error of the mean
Dispersion value	1.65

Notes:

[90] - 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.

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

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

End point description:

RUD-Lite assesses the healthcare resource utilization of participants and their caregivers to determine the level of formal and informal care attributable to Alzheimer's Disease (AD). Components of the RUD-Lite include living accommodations and long-term care, use of respite, home nursing and day care. Outpatient, hospital and social services visits, as well as caregiver informal care time is collected from the baseline and follow-up interviews. The change from baseline to Week 24 in caregiver time is reported.

End point type	Secondary

End point timeframe:

Baseline through Week 24

End point values	Placebo	ABT-126 25 mg	ABT-126 50 mg	ABT-126 75 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86[91]	56[92]	81[93]	55[94]
Units: units on a scale				
least squares mean (standard error)	68.96 (± 22.7)	9.95 (± 28.45)	-14.02 (± 24.36)	-14.9 (± 27.56)

Notes:

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

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

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

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

End point values	Donepezil			
Subject group type	Reporting group			
Number of subjects analysed	58[95]			
Units: units on a scale				
least squares mean (standard error)	-21.5 (± 28.05)			

Notes:

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

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	ABT-126 25 mg v Placebo

Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.044 [96]
Method	ANCOVA
Parameter estimate	least squares mean of difference
Point estimate	-59.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	-115.97
upper limit	-2.05
Variability estimate	Standard error of the mean
Dispersion value	34.52

Notes:

[96] - Statistically significant at the P=0.05 level.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-126 50 mg
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 [97]
Method	ANCOVA
Parameter estimate	least squares mean of difference
Point estimate	-82.98
Confidence interval	
level	90 %
sides	2-sided
lower limit	-134.26
upper limit	-31.71
Variability estimate	Standard error of the mean
Dispersion value	31.08

Notes:

[97] - Statistically significant at the P=0.01 level.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-126 75 mg
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009 [98]
Method	ANCOVA
Parameter estimate	least squares mean of difference
Point estimate	-83.86
Confidence interval	
level	90 %
sides	2-sided
lower limit	-141.6
upper limit	-26.11

Variability estimate	Standard error of the mean
Dispersion value	35

Notes:

[98] - Statistically significant at the P=0.01 level.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Donepezil
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 [99]
Method	ANCOVA
Parameter estimate	least squares mean of difference
Point estimate	-90.46
Confidence interval	
level	90 %
sides	2-sided
lower limit	-145.97
upper limit	-34.95
Variability estimate	Standard error of the mean
Dispersion value	33.64

Notes:

[99] - Statistically significant at the P=0.01 level.

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

End point title	EuroQol-5D (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). The index score ranges from best health (+1) to worst health (-0.59).

End point type	Secondary

End point timeframe:

Baseline through Week 24

End point values	Placebo	ABT-126 25 mg	ABT-126 50 mg	ABT-126 75 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	92[100]	65[101]	93[102]	63[103]
Units: units on a scale				
least squares mean (standard error)	0 (± 0.01)	0 (± 0.01)	0.01 (± 0.01)	0.01 (± 0.01)

Notes:

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

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

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

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

End point values	Donepezil			
Subject group type	Reporting group			
Number of subjects analysed	62[104]			
Units: units on a scale				
least squares mean (standard error)	0.01 (± 0.01)			

Notes:

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

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-126 25 mg
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.516
Method	ANCOVA
Parameter estimate	least squares mean of difference
Point estimate	0
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.03
upper limit	0.03
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-126 50 mg
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.365
Method	ANCOVA
Parameter estimate	least squares mean of difference
Point estimate	0.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.02
upper limit	0.03
Variability estimate	Standard error of the mean
Dispersion value	0.01

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-126 75 mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.338
Method	ANCOVA
Parameter estimate	least squares mean of difference
Point estimate	0.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.02
upper limit	0.03
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Donepezil
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.222
Method	ANCOVA
Parameter estimate	least squares mean of difference
Point estimate	0.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.01
upper limit	0.04
Variability estimate	Standard error of the mean
Dispersion value	0.02

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

End point title	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 vertical graduated visual analog scale (VAS) ranging from 0 (worst imaginable health state) to 100 (best imaginable health state).

End point type	Secondary

End point timeframe:
Baseline through Week 24

End point values	Placebo	ABT-126 25 mg	ABT-126 50 mg	ABT-126 75 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	92[105]	65[106]	93[107]	61[108]
Units: units on a scale				
least squares mean (standard error)	4.18 (± 1.7)	3.11 (± 2.05)	1.34 (± 1.76)	1.94 (± 2.06)

Notes:
[105] - Subjects with a baseline and Week 24 assessment
[106] - Subjects with a baseline and at least one post baseline assessment
[107] - Subjects with a baseline and at least one post baseline assessment
[108] - Subjects with a baseline and at least one post baseline assessment

End point values	Donepezil			
Subject group type	Reporting group			
Number of subjects analysed	62[109]			
Units: units on a scale				
least squares mean (standard error)	3.58 (± 2.09)			

Notes:
[109] - Subjects with a baseline and at least one post baseline assessment

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-126 25 mg
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.662
Method	ANCOVA
Parameter estimate	least squares mean of difference
Point estimate	-1.07
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.3
upper limit	3.16
Variability estimate	Standard error of the mean
Dispersion value	2.56

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-126 50 mg

Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.889
Method	ANCOVA
Parameter estimate	least squares mean of difference
Point estimate	-2.84
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.65
upper limit	0.98
Variability estimate	Standard error of the mean
Dispersion value	2.31

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-126 75 mg
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.807
Method	ANCOVA
Parameter estimate	least squares mean of difference
Point estimate	-2.24
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.52
upper limit	2.03
Variability estimate	Standard error of the mean
Dispersion value	2.59

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Donepezil
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.593
Method	ANCOVA
Parameter estimate	least squares mean of difference
Point estimate	-0.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.81
upper limit	3.61

Variability estimate	Standard error of the mean
Dispersion value	2.55

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

End point title	EQ-5D-3L-Proxy 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. Similar to the EQ-5D-5L, the EQ-5D-3L proxy is also a 5 dimensional tool. However, proxies (e.g., caregivers) rate each dimension using a scale with 3 levels: no problem, some problem, extreme problem. Proxies are asked to rate how he/she (the proxy) believes the patient would rate his/her own Health Related Quality of Life (HRQoL) if he/she (the subject) was able to communicate it. Proxies also rate the overall health of the subject on a VAS scale. The index score ranges from best health (+1) to worst health (-0.59).

End point type	Secondary

End point timeframe:

Baseline through Week 24

End point values	Placebo	ABT-126 25 mg	ABT-126 50 mg	ABT-126 75 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	92[110]	65[111]	94[112]	63[113]
Units: units on a scale				
least squares mean (standard error)	0 (± 0.01)	-0.02 (± 0.02)	0.01 (± 0.01)	0.02 (± 0.02)

Notes:

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

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

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

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

End point values	Donepezil			
Subject group type	Reporting group			
Number of subjects analysed	63[114]			
Units: units on a scale				
least squares mean (standard error)	0.01 (± 0.02)			

Notes:

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

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	ABT-126 25 mg v Placebo

Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.803
Method	ANCOVA
Parameter estimate	least squares mean of difference
Point estimate	-0.02
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.05
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-126 50 mg
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.285
Method	ANCOVA
Parameter estimate	least squares mean of difference
Point estimate	0.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.02
upper limit	0.04
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-126 75 mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.109
Method	ANCOVA
Parameter estimate	least squares mean of difference
Point estimate	0.02
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.01
upper limit	0.06

Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Donepezil
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.306
Method	ANCOVA
Parameter estimate	least squares mean of difference
Point estimate	0.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.02
upper limit	0.04
Variability estimate	Standard error of the mean
Dispersion value	0.02

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

End point title	EQ-5D-3L-Proxy 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. Similar to the EQ-5D-5L, the EQ-5D-3L proxy is also a 5 dimensional tool. However, proxies (e.g., caregivers) rate each dimension using a scale with 3 levels: no problem, some problem, extreme problem. Proxies are asked to rate how he/she (the proxy) believes the patient would rate his/her own Health Related Quality of Life (HRQoL) if he/she (the subject) was able to communicate it. Proxies also rate the overall health of the subject on a vertical graduated VAS ranging from 0 (worst imaginable health state) to 100 (best imaginable health state).

End point type	Secondary

End point timeframe:

Baseline through Week 24

End point values	Placebo	ABT-126 25 mg	ABT-126 50 mg	ABT-126 75 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	92[115]	65[116]	94[117]	63[118]
Units: units on a scale				
least squares mean (standard error)	1.51 (± 1.64)	-1.04 (± 1.97)	1.78 (± 1.67)	3.48 (± 1.93)

Notes:
[115] - Subjects with a baseline and at least one post baseline assessment
[116] - Subjects with a baseline and at least one post baseline assessment
[117] - Subjects with a baseline and at least one post-baseline assessment
[118] - Subjects with a baseline and at least one post baseline assessment

End point values	Donepezil			
Subject group type	Reporting group			
Number of subjects analysed	63[119]			
Units: units on a scale				
least squares mean (standard error)	4.69 (± 1.97)			

Notes:
[119] - Subjects with a baseline and at least one post baseline assessment

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-126 25 mg
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.852
Method	ANCOVA
Parameter estimate	least squares mean of difference
Point estimate	-2.56
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.59
upper limit	1.47
Variability estimate	Standard error of the mean
Dispersion value	2.44

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v ABT-126 50 mg
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.452
Method	ANCOVA
Parameter estimate	least squares mean of difference
Point estimate	0.27
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.38
upper limit	3.91

Variability estimate	Standard error of the mean
Dispersion value	2.21

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-126 75 mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.213
Method	ANCOVA
Parameter estimate	least squares mean of difference
Point estimate	1.97
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.1
upper limit	6.03
Variability estimate	Standard error of the mean
Dispersion value	2.46

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Donepezil
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.097 [120]
Method	ANCOVA
Parameter estimate	least squares mean of difference
Point estimate	3.17
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.84
upper limit	7.19
Variability estimate	Standard error of the mean
Dispersion value	2.44

Notes:

[120] - Statistically significant at the P=0.10 level.

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:

The CIBIC-plus is designed to capture a global impression of change in severity of dementia. The 4 major areas assessed by the CIBIC-plus are general functioning, cognitive functioning, behavioral functioning and activities of daily living. The interview with the caregiver assesses the functional

activities and behavior of the subject. The subject interview primarily assesses cognition. The CIBIC-plus score ranges from 1 to 7 with a lower score being desirable. A decrease in the total score indicates improvement, with a higher score indicating greater impairment.

End point type	Secondary

End point timeframe:

Baseline through Week 24

End point values	Placebo	ABT-126 25 mg	ABT-126 50 mg	ABT-126 75 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89[121]	64[122]	92[123]	61[124]
Units: units on a scale				
least squares mean (standard error)	4.18 (± 0.09)	4.06 (± 0.1)	4.03 (± 0.08)	3.8 (± 0.1)

Notes:

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

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

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

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

End point values	Donepezil			
Subject group type	Reporting group			
Number of subjects analysed	59[125]			
Units: units on a scale				
least squares mean (standard error)	3.75 (± 0.1)			

Notes:

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

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v ABT-126 25 mg
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.184 [126]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-0.12
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.33
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[126] - 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.

	Statistical Analysis 2

Statistical analysis title	
Comparison groups	Placebo v ABT-126 50 mg
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.105 [127]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-0.15
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.34
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[127] - 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.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v ABT-126 75 mg
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 [128]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-0.38
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.59
upper limit	-0.16
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[128] - 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. Statistically significant at the P=0.01 level.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v ABT-126 75 mg v Donepezil
Number of subjects included in analysis	209
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [129]
Method	mixed-effects model for repeated measure
Parameter estimate	least squares mean of difference
Point estimate	-0.43

Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.65
upper limit	-0.21
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[129] - 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. Statistically significant at the P=0.001 level.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Screening up to 2 weeks (± 3 days) after the last dose of study drug (at Week 24 or premature discontinuation).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

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

Reporting group title	ABT-126 50 mg

Reporting group description:

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

Reporting group title	ABT-126 25 mg

Reporting group description:

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

Reporting group title	Donepezil

Reporting group description:

One 5 mg capsule taken orally once daily in the morning for 4 weeks beginning on Day 1, and 1 10 mg capsule taken orally once daily in the morning for 20 weeks thereafter.

Reporting group title	ABT-126 75 mg

Reporting group description:

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

Serious adverse events	Placebo	ABT-126 50 mg	ABT-126 25 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 104 (4.81%)	7 / 107 (6.54%)	6 / 77 (7.79%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma			
subjects affected / exposed	0 / 104 (0.00%)	1 / 107 (0.93%)	0 / 77 (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
Reproductive system and breast disorders			
Uterine prolapse			

subjects affected / exposed	1 / 104 (0.96%)	0 / 107 (0.00%)	0 / 77 (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			
Atelectasis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 107 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 104 (0.00%)	1 / 107 (0.93%)	0 / 77 (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
Psychiatric disorders			
Aggression			
subjects affected / exposed	0 / 104 (0.00%)	0 / 107 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disorientation			
subjects affected / exposed	0 / 104 (0.00%)	0 / 107 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Insomnia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 107 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Weight decreased			
subjects affected / exposed	0 / 104 (0.00%)	1 / 107 (0.93%)	0 / 77 (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			
Brain contusion			

subjects affected / exposed	0 / 104 (0.00%)	0 / 107 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial bones fracture			
subjects affected / exposed	0 / 104 (0.00%)	0 / 107 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 104 (0.00%)	0 / 107 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 104 (0.00%)	0 / 107 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	0 / 104 (0.00%)	0 / 107 (0.00%)	1 / 77 (1.30%)
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			
Atrial fibrillation			
subjects affected / exposed	0 / 104 (0.00%)	0 / 107 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 104 (0.00%)	0 / 107 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 107 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Cerebrovascular accident			
subjects affected / exposed	1 / 104 (0.96%)	0 / 107 (0.00%)	0 / 77 (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
Complex partial seizures			
subjects affected / exposed	1 / 104 (0.96%)	0 / 107 (0.00%)	0 / 77 (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
Convulsion			
subjects affected / exposed	1 / 104 (0.96%)	0 / 107 (0.00%)	0 / 77 (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
Hemiplegia			
subjects affected / exposed	1 / 104 (0.96%)	0 / 107 (0.00%)	0 / 77 (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
Syncope			
subjects affected / exposed	0 / 104 (0.00%)	0 / 107 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 104 (0.96%)	0 / 107 (0.00%)	0 / 77 (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
Constipation			
subjects affected / exposed	0 / 104 (0.00%)	1 / 107 (0.93%)	0 / 77 (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
Duodenitis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 107 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			

subjects affected / exposed	0 / 104 (0.00%)	0 / 107 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 107 (0.00%)	1 / 77 (1.30%)
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			
Cholelithiasis			
subjects affected / exposed	0 / 104 (0.00%)	0 / 107 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urethral stenosis			
subjects affected / exposed	0 / 104 (0.00%)	1 / 107 (0.93%)	0 / 77 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 104 (0.00%)	1 / 107 (0.93%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 107 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 104 (0.00%)	0 / 107 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	1 / 104 (0.96%)	2 / 107 (1.87%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Donepezil	ABT-126 75 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 75 (4.00%)	2 / 73 (2.74%)	
number of deaths (all causes)	2	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Uterine prolapse			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Aggression			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disorientation			

subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Insomnia			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Weight decreased			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Brain contusion			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Complex partial seizures			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiplegia			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urethral stenosis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 75 (1.33%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	ABT-126 50 mg	ABT-126 25 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 104 (18.27%)	31 / 107 (28.97%)	17 / 77 (22.08%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	4 / 104 (3.85%)	5 / 107 (4.67%)	3 / 77 (3.90%)
occurrences (all)	4	6	3
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 104 (6.73%)	4 / 107 (3.74%)	5 / 77 (6.49%)
occurrences (all)	10	7	7
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	3 / 104 (2.88%)	15 / 107 (14.02%)	7 / 77 (9.09%)
occurrences (all)	3	15	10
Diarrhoea			

subjects affected / exposed	2 / 104 (1.92%)	4 / 107 (3.74%)	2 / 77 (2.60%)
occurrences (all)	2	4	2
Nausea			
subjects affected / exposed	3 / 104 (2.88%)	4 / 107 (3.74%)	1 / 77 (1.30%)
occurrences (all)	3	4	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 104 (0.96%)	7 / 107 (6.54%)	1 / 77 (1.30%)
occurrences (all)	1	7	1
Depressed mood			
subjects affected / exposed	1 / 104 (0.96%)	0 / 107 (0.00%)	1 / 77 (1.30%)
occurrences (all)	1	0	1

Non-serious adverse events	Donepezil	ABT-126 75 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 75 (32.00%)	15 / 73 (20.55%)	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	5 / 75 (6.67%)	3 / 73 (4.11%)	
occurrences (all)	5	4	
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 75 (10.67%)	5 / 73 (6.85%)	
occurrences (all)	9	6	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	2 / 75 (2.67%)	2 / 73 (2.74%)	
occurrences (all)	2	2	
Diarrhoea			
subjects affected / exposed	4 / 75 (5.33%)	2 / 73 (2.74%)	
occurrences (all)	4	3	
Nausea			
subjects affected / exposed	6 / 75 (8.00%)	2 / 73 (2.74%)	
occurrences (all)	6	3	
Psychiatric disorders			
Anxiety			

subjects affected / exposed	0 / 75 (0.00%)	2 / 73 (2.74%)	
occurrences (all)	0	2	
Depressed mood			
subjects affected / exposed	4 / 75 (5.33%)	0 / 73 (0.00%)	
occurrences (all)	4	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 September 2011	Significant changes implemented by Amendment 1 included: • Updated Section 3.0 and Section 5.6.4 to incorporate preliminary pharmacokinetic and safety data from the Phase 1 multiple-dose Study M12-843. • Updated exclusion criterion number 3 to clarify that subjects and caregivers may participate in counseling to provide additional information about AD if it is clinically indicated. • Replaced the formula nomenclature used in the synopsis with ABT-126 to maintain proprietary information in a document that will be used in the public domain. • Moved PPQSA assessment from Week 18 to Week 24 to obtain a more appropriate final assessment. • Clarified QTcB interval calculation to determine the QTcB interval that should be used for subject's eligibility. • Added language for subject rescreening to specify terms in which subjects may re-screen for study. • Updated Figure 1, Figure 2, and Figure 3 to better clarify study design. • Updated Section 10.1 Source Documents to clarify specific items being used as source documents.
14 December 2011	Significant changes implemented by Amendment 2 included: • Included preliminary data from 2 recently conducted ABT-126 Phase 1 studies in Section 3.0, Introduction and Section 5.6.4, Selection of Doses in the Study; included an additional electrocardiogram (ECG) assessment; excluded subjects with risk factors for Torsades de Pointes; excluded concomitant medications associated with Torsades de Pointes. An increase in the group mean QTcF interval was observed in healthy volunteers in Phase 1 studies evaluating doses of 100 mg, 125 mg and 150 mg doses of ABT-126, which were higher than those under evaluation in this study. • Updated inclusion criterion 12 to clarify level of education required for subject eligibility to ensure ability to complete assessments accurately. • Added the Wechsler Memory Scale-III Working Memory Index to obtain additional data regarding the effects of ABT-126 on working memory to complement the cognition data obtained from the other outcome measures. • Added the EuroQol-5D-5L and the EuroQol-5D-3L proxy to obtain additional Health Economics and Outcomes Research (HEOR) data. • Clarified circumstances for individual subject withdrawal. Subjects may be discontinued from the study in the event they show pronounced clinical symptom progression. • Updated language in Section 6.0 to comply with the latest sponsor standards. • Updated contact information in Section 7.0, Protocol Deviations since there was a change in personnel.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported