Clinical trial results:
Assessment of Safety, Tolerability, and Pharmacodynamic Effects of LY2886721 in Patients with Mild Cognitive Impairment Due to Alzheimer's Disease or Mild Alzheimer's Disease

Summary

EudraCT number	2011-005217-37
Trial protocol	NL ES IT
Global end of trial date	06 August 2013

Results information

Result version number	v1 (current)
This version publication date	09 April 2018
First version publication date	09 April 2018

Trial information

Trial identification

Sponsor protocol code	I4O-MC-BACC

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01561430
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-285-4559,
Scientific contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-CTLILLY,

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	06 August 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this Phase 1/Phase 2 study is to evaluate how the body handles the drug and the drug's effect on the body of participants with mild cognitive impairment (MCI) due to Alzheimer's Disease (AD) or mild AD and who test positive for amyloid plaque.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 March 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 60
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Japan: 5
Worldwide total number of subjects	70
EEA total number of subjects	5

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)	28
From 65 to 84 years	39

85 years and over	3

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

As a result of findings from the I4O-MC-BACJ study (NCT01534273), enrollment was discontinued to the 15 milligrams (mg) arm. The 9 participants already enrolled were allowed to continue study treatment at the 15 mg dose.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	15 mg LY2886721

Arm description:

LY2886721: 15 milligrams (mg), capsules, administered orally, once daily for 26 weeks.

Arm type	Experimental
Investigational medicinal product name	15 mg LY2886721
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

LY2886721: 15 milligrams (mg), capsules, administered orally, once daily for 26 weeks.

Arm title	35 mg LY2886721

Arm description:

LY2886721: 35 mg, capsules, administered orally, once daily for 26 weeks.

Arm type	Experimental
Investigational medicinal product name	35 mg LY2886721
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

LY2886721: 35 mg, capsules, administered orally, once daily for 26 weeks.

Arm title	70 mg LY2886721

Arm description:

LY2886721: 70 mg, capsules, administered orally, once daily for 26 weeks.

Arm type	Experimental
Investigational medicinal product name	70 mg LY2886721
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
LY2886721: 70 mg, capsules, administered orally, once daily for 26 weeks.

Arm title	Placebo
Arm description:	
Placebo: 1 placebo capsule, administered orally, once daily for 26 weeks.	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
Placebo: 1 placebo capsule, administered orally, once daily for 26 weeks.

Number of subjects in period 1	15 mg LY2886721	35 mg LY2886721	70 mg LY2886721
Started	9	23	18
Received at Least One Dose of Study Drug	9	23	18
Completed	8	8	1
Not completed	1	15	17
Physician decision	-	1	-
Consent withdrawn by subject	-	-	1
Adverse event, non-fatal	-	-	3
Sponsor Decision	1	14	13

Number of subjects in period 1	Placebo
Started	20
Received at Least One Dose of Study Drug	20
Completed	7
Not completed	13
Physician decision	-
Consent withdrawn by subject	-
Adverse event, non-fatal	1
Sponsor Decision	12

Baseline characteristics

Reporting groups

Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	70	70	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	28	28	
From 65-84 years	39	39	
85 years and over	3	3	
Gender, Male/Female Units:			
Female	33	33	
Male	37	37	
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	6	6	
Black or African American	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
White	64	64	
Region of Enrollment Units: Subjects			
United States	60	60	
Netherlands	5	5	
Japan	5	5	

End points

End points reporting groups

Reporting group title	15 mg LY2886721
Reporting group description:	
LY2886721: 15 milligrams (mg), capsules, administered orally, once daily for 26 weeks.	
Reporting group title	35 mg LY2886721
Reporting group description:	
LY2886721: 35 mg, capsules, administered orally, once daily for 26 weeks.	
Reporting group title	70 mg LY2886721
Reporting group description:	
LY2886721: 70 mg, capsules, administered orally, once daily for 26 weeks.	
Reporting group title	Placebo
Reporting group description:	
Placebo: 1 placebo capsule, administered orally, once daily for 26 weeks.	

Primary: Change from Baseline to 12 Weeks in Cerebrospinal Fluid (CSF) Amyloid Beta (Aβ)1-40 and Aβ1-42 Concentrations

End point title	Change from Baseline to 12 Weeks in Cerebrospinal Fluid (CSF) Amyloid Beta (Aβ)1-40 and Aβ1-42 Concentrations

End point description:

Percent change in lumbar CSF concentrations of Aβ1-40 and Aβ1-42 from baseline at 12 weeks post-dose was calculated. The units for CSF were picograms per milliliter (pg/mL). Least Squares (LS) means of percent change in concentration from baseline was calculated using analysis of covariance (ANCOVA) with baseline as a covariate and treatment as a fixed effect.

Analysis Population Description: All randomized participants with evaluable post-baseline CSF Aβ1-40 or Aβ1-42 data.

End point type	Primary
End point timeframe:	
Baseline, 12 weeks	

End point values	15 mg LY2886721	35 mg LY2886721	70 mg LY2886721	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	9	5	12
Units: percent change in Aβ1-40 and Aβ1-42				
least squares mean (standard error)				
Aβ1-40 (n=7, 9, 5, 11)	-31.8 (± 7.35)	-57.7 (± 6.67)	-58.9 (± 8.73)	3.7 (± 5.96)
Aβ1-42 (n=7, 9, 5, 12)	-34.4 (± 7.27)	-52 (± 6.8)	-60.7 (± 8.42)	6.5 (± 6.06)

Statistical analyses

Statistical analysis title	15 mg Change from Baseline to Week 12 CSF Aβ1-40
Comparison groups	15 mg LY2886721 v Placebo

Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least Squares Mean
Point estimate	-31.8
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-41.4
upper limit	-22.1
Variability estimate	Standard error of the mean

Statistical analysis title	35 mg Change from Baseline to Week 12 CSF Aβ1-40
Comparison groups	35 mg LY2886721 v Placebo
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least Squre Means
Point estimate	-57.7
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-66.4
upper limit	-48.9
Variability estimate	Standard error of the mean

Statistical analysis title	70 mg Change from Baseline to Week 12 CSF Aβ1-40
Comparison groups	70 mg LY2886721 v Placebo
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least Squares Mean
Point estimate	-58.9
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-70.4
upper limit	-47.4
Variability estimate	Standard error of the mean

Statistical analysis title	15mg Change from Baseline to 12 Weeks CSF Aβ1-42
Comparison groups	Placebo v 15 mg LY2886721
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least Squares Mean
Point estimate	-34.4
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-44
upper limit	-24.9
Variability estimate	Standard error of the mean

Statistical analysis title	35 mg Change from Baseline to 12 Weeks CSF Aβ1-42
Comparison groups	35 mg LY2886721 v Placebo
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least Squares Mean
Point estimate	-52
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-60.9
upper limit	-43.1
Variability estimate	Standard error of the mean

Statistical analysis title	70 mg Change from Baseline to 12 Weeks CSF Aβ1-42
Comparison groups	70 mg LY2886721 v Placebo
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least Squares Mean
Point estimate	-60.7

Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-71.7
upper limit	-49.6
Variability estimate	Standard error of the mean

Primary: Change from Baseline to 26 Weeks in CSF Aβ1-40 and Aβ1-42 Concentrations

End point title	Change from Baseline to 26 Weeks in CSF Aβ1-40 and Aβ1-42 Concentrations[1]

End point description:

Percent change in lumbar CSF concentrations of Aβ1-40 and Aβ1-42 from baseline at 26 weeks post-dose was to be calculated. The units for CSF were picograms per milliliter (pg/mL). LS means of percent change in concentration from baseline was calculated using ANCOVA with baseline as a covariate and treatment as a fixed effect.

9999=Data Not Available (N/A)

End point type	Primary

End point timeframe:

Baseline, 26 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Zero total participants were analyzed for this End point; statistical analysis was not completed.

End point values	15 mg LY2886721	35 mg LY2886721	70 mg LY2886721	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[2]	0[3]	0[4]	0[5]
Units: percent change in Aβ1-40 and Aβ1-42				
least squares mean (standard error)	()	()	()	()

Notes:

[2] - No participants analyzed at 26 weeks due to the termination of the trial.

[3] - No participants analyzed at 26 weeks due to the termination of the trial.

[4] - No participants analyzed at 26 weeks due to the termination of the trial.

[5] - No participants analyzed at 26 weeks due to the termination of the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Plasma Amyloid Beta (Aβ)1-40 and Aβ1-42 Concentrations

End point title	Change from Baseline in Plasma Amyloid Beta (Aβ)1-40 and Aβ1-42 Concentrations

End point description:

Percent change in plasma concentrations of Aβ1-40 and Aβ1-42 from baseline at 12 weeks and 26 weeks post-dose was calculated. The units for CSF were picograms per milliliter (pg/mL).

Analysis Population Description: All randomized participants with evaluable post-baseline CSF Aβ1-40 or Aβ1-42 data.

9999=Data Not Available (N/A)

End point type	Secondary

End point timeframe:

Baseline, 12 weeks, 26 weeks

End point values	15 mg LY2886721	35 mg LY2886721	70 mg LY2886721	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	8	4[6]	12
Units: percent change in Aβ1-40 and Aβ1-42				
arithmetic mean (standard deviation)				
Aβ1-40, Week 12 (n=6, 8, 4, 12)	-73.4 (± 6.22)	-80.8 (± 8.07)	-88.1 (± 2.66)	1.9 (± 15)
Aβ1-40, Week 26 (n=5, 6, 1, 6)	-72.3 (± 11.5)	-85 (± 3.89)	-89.1 (± 9999)	0.944 (± 22.6)
Aβ1-42, Week 12 (n=6, 8, 4, 12	-63.4 (± 6.11)	-71.1 (± 8.38)	-78.2 (± 5.08)	0.541 (± 10.1)
Aβ1-42, Week 26 (n=5, 6, 1, 6)	-65.1 (± 8.85)	-75 (± 4.33)	-80.8 (± 9999)	1.82 (± 9.98)

Notes:

[6] - Standard deviation not reported due to not enough participants for analyses.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to 26 Weeks in Neuropsychological Test Battery (NTB)

End point title	Change from Baseline to 26 Weeks in Neuropsychological Test Battery (NTB)

End point description:

The NTB is a composite cognitive measure in clinical Alzheimer's disease studies and is a collection of several written and oral tests that examines verbal and nonverbal brain functions. Lower scores indicate greater cognitive impairment. LS means were calculated using ANCOVA with baseline as a covariate and treatment as a fixed effect.

Analysis Population Description: All randomized participants with evaluable NTB data.

End point type	Secondary

End point timeframe:

Baseline, 26 weeks

End point values	15 mg LY2886721	35 mg LY2886721	70 mg LY2886721	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	1	9
Units: units on a scale				
least squares mean (standard error)				
NTB z-score	-0.039 (± 0.1096)	-0.161 (± 0.1165)	0.424 (± 0.3156)	-0.262 (± 0.1028)
NTB total score	2 (± 4.77)	-5.9 (± 5.09)	21.2 (± 13.69)	-14.9 (± 4.49)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to 26 Weeks in Alzheimer's Disease Assessment Scale - Cognitive Subscale (ADAS-Cog)

End point title	Change from Baseline to 26 Weeks in Alzheimer's Disease Assessment Scale - Cognitive Subscale (ADAS-Cog)

End point description:

ADAS-Cog11 is an 11-item instrument measuring impairment in memory (Items 1-4, 7, 11), praxis (Items 4 and 5), orientation (Item 6), and language (Items 8-10). Item 1 ranged 0 (all items recalled correctly)-10 (none recalled correctly); Items 2-5 and 8-11 ranged 0 (all items named, performed, drawn, spoken, remember correctly/clearly)-5 (none correct/not clearly spoken); Item 6 ranged 0 (no incorrect responses)-8 (all incorrect); and Item 7 ranged 0 (all words remembered correctly)-12 (no words remembered correctly) for a total ADAS-Cog11 score of 0-70 with higher scores indicating greater disease severity. A score of 0-10 for delayed free recall and a conversion code of 0-5 for digit cancellation and maze completion was added to the total ADAS-Cog11 score for a total ADASCog14 score ranging 0-90 with higher scores indicating greater impairment. LS means were calculated using Mixed Model Repeated Measures (MMRM) with Treatment + Visit + Treatment*Visit + Baseline + Baseline*Visit.

End point type	Secondary

End point timeframe:

Baseline, 26 weeks

End point values	15 mg LY2886721	35 mg LY2886721	70 mg LY2886721	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[7]	9[8]	1[9]	9[10]
Units: units on a scale				
least squares mean (standard error)	1.1 (± 2.77)	0.6 (± 2.48)	0.6 (± 7.41)	1.3 (± 2.44)

Notes:

[7] - All randomized participants with evaluable ADAS-Cog data.

[8] - All randomized participants with evaluable ADAS-Cog data.

[9] - All randomized participants with evaluable ADAS-Cog data.

[10] - All randomized participants with evaluable ADAS-Cog data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to 26 Weeks in the Clinical Dementia Rating Scale - Sum of Boxes (CDR-SB)

End point title	Change from Baseline to 26 Weeks in the Clinical Dementia Rating Scale - Sum of Boxes (CDR-SB)

End point description:

The CDR-SB is a composite measure of 6 domains of cognitive and functional performance: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care.

Scores ranged from 0 to 18, with higher scores indicating greater impairment. LS means were calculated using MMRM with Treatment + Visit + Treatment*Visit + Baseline + Baseline*Visit.

Analysis Population Description: All randomized participants with evaluable CDR-SB data.

End point type	Secondary

End point timeframe:

Baseline, 26 weeks

End point values	15 mg LY2886721	35 mg LY2886721	70 mg LY2886721	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	9	1	8
Units: units on a scale				
least squares mean (standard error)	0.8 (± 0.432)	0.52 (± 0.395)	1.5 (± 1.013)	1.19 (± 0.402)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to 26 Weeks in Mini Mental State Examination (MMSE)

End point title	Change from Baseline to 26 Weeks in Mini Mental State Examination (MMSE)

End point description:

The MMSE (Folstein et al. 1975) is one of the most widely used screening instruments for cognitive impairment. The test consists of five sections (orientation, registration, attention-calculation, recall, and language) and provides a total score ranging from 0 to 30, with lower scores indicative of greater cognitive impairment. LS means were calculated using MMRM with Treatment + Visit + Treatment*Visit + Baseline + Baseline*Visit.

Analysis Population Description: All randomized participants with evaluable MMSE data.

End point type	Secondary

End point timeframe:

Baseline, 26 weeks

End point values	15 mg LY2886721	35 mg LY2886721	70 mg LY2886721	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	9	1	10
Units: units on a scale				
least squares mean (standard error)	-0.7 (± 0.87)	-1.8 (± 0.81)	0.2 (± 2.41)	-3 (± 0.77)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Cerebrospinal Fluid (CSF) Tau and Phosphorylated Tau (Ptau)-181 Concentrations

End point title	Change from Baseline in Cerebrospinal Fluid (CSF) Tau and Phosphorylated Tau (Ptau)-181 Concentrations

End point description:

Percent change in lumbar CSF tau and ptau-181 concentrations from baseline at 12 weeks post-dose and 26 weeks post-dose was calculated. The units for CSF were picograms per milliliter (pg/mL). Least Squares (LS) means of percent change in concentration from baseline was calculated using analysis of covariance (ANCOVA) with baseline as a covariate and treatment as a fixed effect.

Analysis Population Description: All randomized participants with evaluable post-baseline CSF tau or ptau data.

9999=Data Not Available (N/A)

End point type	Secondary

End point timeframe:

Baseline, 12 weeks, 26 weeks

End point values	15 mg LY2886721	35 mg LY2886721	70 mg LY2886721	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[11]	9[12]	5[13]	12[14]
Units: percent change in tau and ptau-181				
least squares mean (standard error)				
CSF Tau, Week 12	14.3 (± 6.06)	2.6 (± 5.42)	6.8 (± 7.49)	-4.4 (± 4.63)
CSF Tau, Week 26	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
CSF Ptau, Week 12	0.7 (± 4.81)	1.7 (± 4.01)	4.3 (± 5.41)	-3.6 (± 3.4)
CSF Ptau, Week 26	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)

Notes:

[11] - No participants analyzed at 26 weeks due to the termination of the trial.

[12] - No participants analyzed at 26 weeks due to the termination of the trial.

[13] - No participants analyzed at 26 weeks due to the termination of the trial.

[14] - No participants analyzed at 26 weeks due to the termination of the trial.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Entire Study	
Adverse event reporting additional description:	
I4O-MC-BACC	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	15 mg LY2886721
Reporting group description: -	
Reporting group title	35 mg LY2886721
Reporting group description: -	
Reporting group title	70 mg LY2886721
Reporting group description: -	

Serious adverse events	Placebo	15 mg LY2886721	35 mg LY2886721
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	2 / 23 (8.70%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
syncope			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
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			
crohn's disease			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
small intestinal obstruction			
alternative dictionary used:			

MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 23 (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

Serious adverse events	70 mg LY2886721		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
syncope			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
crohn's disease			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
small intestinal obstruction			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Placebo	15 mg LY2886721	35 mg LY2886721
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 20 (75.00%)	8 / 9 (88.89%)	13 / 23 (56.52%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

basal cell carcinoma			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
squamous cell carcinoma of skin			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
fatigue			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
oedema peripheral			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
pyrexia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
thirst			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			

abnormal dreams			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
agitation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
anxiety			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
confusional state			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
delusion			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
depression			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
disorientation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
hallucination			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
hallucination, visual			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
hypnopompic hallucination			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
initial insomnia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
insomnia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	1 / 9 (11.11%)	1 / 23 (4.35%)
occurrences (all)	1	1	2
nightmare			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
obsessive thoughts			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
parasomnia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
restlessness			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
sleep talking			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0

stereotypy			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
terminal insomnia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
amylase increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
blood alkaline phosphatase increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
blood creatine phosphokinase increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 20 (10.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
blood pressure increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
colour vision tests abnormal red-green			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
electrocardiogram change			

alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
gamma-glutamyltransferase increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
lipase increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
liver function test abnormal			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	2 / 23 (8.70%)
occurrences (all)	0	1	2
weight increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
accidental overdose			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
alcohol poisoning			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
contusion			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
fall			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
feeding tube complication			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
foot fracture			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
joint injury			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
laceration			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
tooth fracture			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
atrial fibrillation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
bradycardia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
apraxia			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
balance disorder			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
cerebral microhaemorrhage			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
decreased vibratory sense			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
dizziness			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
dysgeusia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
headache			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	2 / 9 (22.22%)	1 / 23 (4.35%)
occurrences (all)	0	2	1
sinus headache			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
leukocytosis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
vertigo			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Eye disorders			
cataract nuclear			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
diplopia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
eye irritation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
lacrimation increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
visual acuity reduced			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
abdominal discomfort			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	2
abdominal distension			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
abdominal pain upper			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
abdominal tenderness			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
dental caries			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
diarrhoea			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
diverticulum intestinal			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
dry mouth			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
flatulence			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1

gastritis erosive			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
gastrointestinal disorder			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
haematochezia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
haemorrhoidal haemorrhage			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
haemorrhoids			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
hiatus hernia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
lip swelling			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
nausea			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
oesophageal disorder			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
oesophagitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
small intestinal obstruction			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
vomiting			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 20 (10.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	2	1	0
Hepatobiliary disorders			
hepatic function abnormal			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
actinic keratosis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
eczema			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
rash			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
rash macular			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
rash vesicular			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
urticaria			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
cystitis interstitial			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
pollakiuria			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
renal failure chronic			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
hypothyroidism			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			

arthralgia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
back pain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
joint range of motion decreased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
joint swelling			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
muscle spasms			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 20 (10.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	2	0	1
muscle tightness			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
musculoskeletal chest pain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
musculoskeletal stiffness			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

herpes zoster			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
nasopharyngitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
sinusitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
upper respiratory tract infection			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	1 / 9 (11.11%)	1 / 23 (4.35%)
occurrences (all)	1	1	1
urinary tract infection			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	1 / 23 (4.35%)
occurrences (all)	0	1	1
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
dehydration			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
hypokalaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
increased appetite			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	70 mg LY2886721		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 18 (88.89%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
basal cell carcinoma			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
squamous cell carcinoma of skin			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
fatigue			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
oedema peripheral			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
pyrexia			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
thirst			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
abnormal dreams			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
agitation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
anxiety			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
confusional state			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
delusion			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
depression			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	3		
disorientation			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
hallucination				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
hallucination, visual				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
hypnopompic hallucination				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
initial insomnia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
insomnia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
nightmare				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
obsessive thoughts				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
parasomnia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			

restlessness alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0			
sleep talking alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1			
stereotypy alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0			
terminal insomnia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0			
Investigations alanine aminotransferase increased alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1			
amylase increased alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0			
blood alkaline phosphatase increased alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1			
blood creatine phosphokinase increased alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0			
blood pressure increased alternative dictionary used:				

MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
colour vision tests abnormal red-green			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
electrocardiogram change			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
gamma-glutamyltransferase increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	3		
lipase increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
liver function test abnormal			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
weight increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
accidental overdose			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
alcohol poisoning			
alternative dictionary used:			

MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
contusion			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
fall			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	3		
feeding tube complication			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
foot fracture			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
joint injury			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
laceration			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	3		
tooth fracture			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Cardiac disorders			
atrial fibrillation			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
bradycardia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
apraxia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
balance disorder			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
cerebral microhaemorrhage			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
decreased vibratory sense			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
dizziness			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
dysgeusia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
headache			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
sinus headache			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	4		
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
leukocytosis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
vertigo			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Eye disorders			
cataract nuclear			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
diplopia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
eye irritation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
lacrimation increased			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
visual acuity reduced			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
abdominal discomfort			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
abdominal distension			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
abdominal pain upper			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
abdominal tenderness			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
dental caries			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
diarrhoea			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
diverticulum intestinal			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
dry mouth				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
flatulence				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
gastritis erosive				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
gastrointestinal disorder				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
gastrooesophageal reflux disease				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
haematochezia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
haemorrhoidal haemorrhage				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
haemorrhoids				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			

hiatus hernia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
lip swelling			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
nausea			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
oesophageal disorder			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
oesophagitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
small intestinal obstruction			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
vomiting			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
hepatic function abnormal			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			

actinic keratosis				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
eczema				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
rash				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
rash macular				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
rash vesicular				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
urticaria				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	0 / 18 (0.00%)			
occurrences (all)	0			
Renal and urinary disorders				
cystitis interstitial				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
pollakiuria				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
renal failure chronic				
alternative dictionary used: MedDRA 16.0				

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Endocrine disorders			
hypothyroidism			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
back pain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
joint range of motion decreased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
joint swelling			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
muscle spasms			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
muscle tightness			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
musculoskeletal chest pain			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
musculoskeletal stiffness			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Infections and infestations			
herpes zoster			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
nasopharyngitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
sinusitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
upper respiratory tract infection			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
urinary tract infection			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
dehydration			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
hypokalaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
increased appetite			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 October 2012	Amendment B: Added the 70 mg dose and dropped the 15 mg dose. Added change in CSF tau and p-tau181 as secondary outcomes.
08 April 2013	Amendment C: Clarified the purpose of the study as a Ph2a PK/PD/safety study. Revised diagnostic criteria to align with contemporary clinical practice. Removed florbetapir scan at Visit 11. Alterations to inclusion/exclusion criteria. Added discontinuation criteria for patients with abnormal liver tests. Altered the randomization ratio to increase the number of subjects assigned to 70 mg dose.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
12 June 2013	The study was terminated early due to hepatic safety finding.	-

Notes:

Limitations and caveats

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

Study was terminated early because of abnormal liver biochemical tests levels for 4 participants.

Notes: