Clinical trial results:
A Phase 2 Randomized Study to Investigate the Efficacy and Safety of LY2495655 Versus Placebo in Older Patients Undergoing Elective Total Hip Arthroplasty (eTHA)

Summary

EudraCT number	2011-000426-29
Trial protocol	FI DK EE ES SE AT BE FR
Global end of trial date	19 February 2014

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	I1Q-MC-JDDE

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01369511
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 11671

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 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559,

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	19 February 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 February 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to test the hypothesis that appendicular lean body mass (aLBM) will increase after 12 weeks of LY2495655 treatment versus placebo in older patients undergoing elective total hip arthroplasty (eTHA).

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:

The first injection of study drug was performed 10+/- 6 days before elective total hip replacement.

Evidence for comparator: -

Actual start date of recruitment	14 July 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 26
Country: Number of subjects enrolled	Sweden: 4
Country: Number of subjects enrolled	Austria: 17
Country: Number of subjects enrolled	Belgium: 20
Country: Number of subjects enrolled	Denmark: 34
Country: Number of subjects enrolled	Estonia: 41
Country: Number of subjects enrolled	Finland: 22
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	United States: 113
Country: Number of subjects enrolled	Canada: 74
Country: Number of subjects enrolled	Japan: 45
Worldwide total number of subjects	400
EEA total number of subjects	168

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)	131
From 65 to 84 years	262
85 years and over	7

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

No text entered

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo: Administered subcutaneously every 4 weeks for 12 weeks (administered 4 times)

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo Comparator administered subcutaneously (SC) every 4 weeks (Q4W) for 12 weeks.

Arm title	35 mg LY2495655

Arm description:

LY2495655: 35 milligrams (mg) administered subcutaneously every 4 weeks for 12 weeks (administered 4 times)

Arm type	Experimental
Investigational medicinal product name	LY2495655
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

LY2495655: 35 milligrams (mg) administered subcutaneously every 4 weeks for 12 weeks (administered 4 times)

Arm title	105 mg LY2495655

Arm description:

LY2495655: 105 mg administered subcutaneously every 4 weeks for 12 weeks (administered 4 times)

Arm type	Experimental
Investigational medicinal product name	LY2495655
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:
LY2495655: 105 mg administered subcutaneously every 4 weeks for 12 weeks (administered 4 times)

Arm title	315 mg LY2495655

Arm description:
LY2495655: 315 mg administered subcutaneously every 4 weeks for 12 weeks (administered 4 times)

Arm type	Experimental
Investigational medicinal product name	LY2495655
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:
LY2495655: 315 mg administered subcutaneously every 4 weeks for 12 weeks (administered 4 times)

Number of subjects in period 1	Placebo	35 mg LY2495655	105 mg LY2495655
Started	98	104	98
Received at Least 1 Dose of Study Drug	98	103	98
Completed	85	91	87
Not completed	13	13	11
Physician decision	3	4	-
Consent withdrawn by subject	5	6	4
Adverse event, non-fatal	1	1	5
Protocol violation	-	1	-
Sponsor decision	2	-	1
Lost to follow-up	-	1	1
Entry criteria not met	2	-	-

Number of subjects in period 1	315 mg LY2495655
Started	100
Received at Least 1 Dose of Study Drug	100
Completed	89
Not completed	11
Physician decision	-
Consent withdrawn by subject	6
Adverse event, non-fatal	-
Protocol violation	2
Sponsor decision	-
Lost to follow-up	2

Entry criteria not met	1

Baseline characteristics

Reporting groups

Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	400	400	
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)	131	131	
From 65-84 years	262	262	
85 years and over	7	7	
Gender categorical Units: Subjects			
Female	234	234	
Male	166	166	
Ethnicity Units: Subjects			
Hispanic or Latino	2	2	
Not Hispanic or Latino	214	214	
Unknown or Not Reported	184	184	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	46	46	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	5	5	
White	349	349	
More than one race	0	0	
Unknown or Not Reported	0	0	
Region of Enrollment Units: Subjects			
France	4	4	
United States	113	113	
Estonia	41	41	
Canada	74	74	
Finland	22	22	
Belgium	20	20	
Spain	26	26	
Austria	17	17	

Denmark	34	34	
Japan	45	45	
Sweden	4	4	

Body Mass Index (BMI)			
Measure Description: BMI was calculated by weight in kilograms divided by height in meters squared.			
Units: kilograms per meter squared (kg/m^2)			
arithmetic mean	28.61		
standard deviation	± 4.63	-	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo: Administered subcutaneously every 4 weeks for 12 weeks (administered 4 times)	
Reporting group title	35 mg LY2495655
Reporting group description:	
LY2495655: 35 milligrams (mg) administered subcutaneously every 4 weeks for 12 weeks (administered 4 times)	
Reporting group title	105 mg LY2495655
Reporting group description:	
LY2495655: 105 mg administered subcutaneously every 4 weeks for 12 weeks (administered 4 times)	
Reporting group title	315 mg LY2495655
Reporting group description:	
LY2495655: 315 mg administered subcutaneously every 4 weeks for 12 weeks (administered 4 times)	

Primary: Change From Baseline in Appendicular Lean Body Mass (aLBM) at Week 12

End point title	Change From Baseline in Appendicular Lean Body Mass (aLBM) at Week 12
End point description:	
The percentage change in aLBM of 3 limbs (excluding the operated limb) was measured by dual energy x-ray absorptiometry (DEXA). Least squares (LS) means of the aLBM change from baseline to the 12 week endpoint was adjusted by baseline aLBM values as a covariate and treatment, visit, and the treatment-by-visit interaction were included as fixed effect via a mixed-effects model for repeated measured (MMRM) analysis. Analysis Population Description: Randomized participants with non-missing baseline and at least 1 post-baseline aLBM measure.	
End point type	Primary
End point timeframe:	
Baseline, 12 Weeks	

End point values	Placebo	35 mg LY2495655	105 mg LY2495655	315 mg LY2495655
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	68	76	69
Units: Percentage of change in aLBM				
least squares mean (standard error)	0.297 (± 0.492)	0.741 (± 0.5)	1.018 (± 0.471)	1.357 (± 0.494)

Statistical analyses

Statistical analysis title	Placebo, 35 mg LY2495655
Comparison groups	Placebo v 35 mg LY2495655

Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.527 [2]
Method	Mixed models analysis

Notes:

[1] - At Week 12

[2] - P-values are from type 3 tests.

Statistical analysis title	Placebo, 105 mg LY2495655

Statistical analysis description:

At Week 12

Comparison groups	Placebo v 105 mg LY2495655
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.291 [3]
Method	Mixed models analysis

Notes:

[3] - P-values are from type 3 tests.

Statistical analysis title	Placebo, 315 mg LY2495655
Comparison groups	Placebo v 315 mg LY2495655
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.129 [4]
Method	Mixed models analysis

Notes:

[4] - P-values are from type 3 tests.

Secondary: Change From Baseline in Appendicular Lean Body Mass (aLBM) at Weeks 4, 8, and 16

End point title	Change From Baseline in Appendicular Lean Body Mass (aLBM) at Weeks 4, 8, and 16

End point description:

The percentage change in aLBM of 3 limbs (excluding the operated limb) was measured by DEXA. LS means of the aLBM change from baseline to the 12 week endpoint was adjusted by baseline aLBM values as a covariate and treatment, visit, and the treatment-by-visit interaction were included as fixed effect via an MMRM analysis.

Analysis Population Description: Randomized participants with non-missing baseline and at least 1 post-baseline aLBM measure.

End point type	Secondary

End point timeframe:

Baseline, 4 Weeks, 8 Weeks, and 16 Weeks

End point values	Placebo	35 mg LY2495655	105 mg LY2495655	315 mg LY2495655
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	74[5]	69[6]	80[7]	72[8]
Units: Percentage of change in aLBM (3 Limbs)				
least squares mean (standard error)				
Week 4	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
Week 8 (n=74, 69, 80, 72)	-0.9 (± 0.485)	-0.68 (± 0.498)	0.34 (± 0.466)	0.585 (± 0.488)
Week 16 (n=69, 67, 79, 69)	-0.102 (± 0.494)	0.606 (± 0.502)	2.058 (± 0.467)	1.784 (± 0.494)

Notes:

[5] - Wk 4 data not collected per protocol, swelling associated with surgery would confound results.

[6] - Wk 4 data not collected per protocol, swelling associated with surgery would confound results.

[7] - Wk 4 data not collected per protocol, swelling associated with surgery would confound results.

[8] - Wk 4 data not collected per protocol, swelling associated with surgery would confound results.

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:	
I1Q-MC-JDDE	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	35 mg LY2495655
Reporting group description: -	
Reporting group title	105 mg LY2495655
Reporting group description: -	
Reporting group title	315 mg LY2495655
Reporting group description: -	

Serious adverse events	Placebo	35 mg LY2495655	105 mg LY2495655
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 98 (14.29%)	8 / 104 (7.69%)	16 / 98 (16.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
invasive ductal breast carcinoma			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	1 / 104 (0.96%)	0 / 98 (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
lymphoma			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	0 / 104 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
non-small cell lung cancer			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	0 / 98 (0.00%)	0 / 104 (0.00%)	0 / 98 (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
prostate cancer			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed[1]	0 / 39 (0.00%)	0 / 34 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
venous thrombosis limb			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	0 / 104 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
device dislocation			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	0 / 104 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
oedema peripheral			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	1 / 104 (0.96%)	0 / 98 (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
pyrexia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	1 / 104 (0.96%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
drug hypersensitivity			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	0 / 98 (0.00%)	0 / 104 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
pneumonia aspiration			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 104 (0.00%)	0 / 98 (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
pulmonary embolism			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 104 (0.00%)	0 / 98 (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 failure			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 104 (0.00%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
alcohol abuse			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 104 (0.00%)	0 / 98 (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
delirium			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 104 (0.00%)	0 / 98 (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
mental status changes			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	0 / 98 (0.00%)	1 / 104 (0.96%)	0 / 98 (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
Investigations			
blood creatinine increased			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	1 / 104 (0.96%)	0 / 98 (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			
confusion postoperative			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	0 / 104 (0.00%)	1 / 98 (1.02%)
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			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 98 (2.04%)	0 / 104 (0.00%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
femur fracture			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	0 / 104 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
joint dislocation			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 98 (2.04%)	0 / 104 (0.00%)	0 / 98 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
periprosthetic fracture			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 98 (1.02%)	0 / 104 (0.00%)	0 / 98 (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
post procedural haematoma			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	1 / 104 (0.96%)	0 / 98 (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
wrist fracture			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 104 (0.00%)	0 / 98 (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
Cardiac disorders			
myocardial infarction			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	1 / 104 (0.96%)	0 / 98 (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
sick sinus syndrome			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 104 (0.00%)	0 / 98 (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
tachycardia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	0 / 104 (0.00%)	1 / 98 (1.02%)
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			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 98 (1.02%)	0 / 104 (0.00%)	0 / 98 (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
encephalopathy			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 104 (0.00%)	0 / 98 (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
metabolic encephalopathy			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 104 (0.00%)	0 / 98 (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
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	0 / 104 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
haemorrhagic anaemia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	0 / 104 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	0 / 104 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
petechiae			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 98 (1.02%)	0 / 104 (0.00%)	0 / 98 (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
Renal and urinary disorders			
renal failure			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	0 / 104 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	0 / 104 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
joint ankylosis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	0 / 104 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
osteoarthritis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	3 / 98 (3.06%)	1 / 104 (0.96%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
rotator cuff syndrome			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	1 / 104 (0.96%)	0 / 98 (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			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 98 (1.02%)	0 / 104 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
post procedural infection			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	0 / 104 (0.00%)	1 / 98 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
postoperative wound infection			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	0 / 104 (0.00%)	2 / 98 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
hyperkalaemia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	1 / 104 (0.96%)	0 / 98 (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
hyponatraemia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 104 (0.00%)	0 / 98 (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

Serious adverse events	315 mg LY2495655		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 100 (3.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
invasive ductal breast carcinoma			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
lymphoma			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
non-small cell lung cancer			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
prostate cancer			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed[1]	0 / 46 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
venous thrombosis limb			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
device dislocation			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
oedema peripheral			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pyrexia				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
drug hypersensitivity				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
pneumonia aspiration				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pulmonary embolism				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
respiratory failure				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
alcohol abuse				
alternative dictionary used: MedDRA 16.1				

subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
delirium				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
mental status changes				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
blood creatinine increased				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
confusion postoperative				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
fall				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
femur fracture				
alternative dictionary used: MedDRA 16.1				

subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
joint dislocation				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
periprosthetic fracture				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
post procedural haematoma				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
wrist fracture				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
myocardial infarction				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
sick sinus syndrome				
alternative dictionary used: MedDRA 16.1				

subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
tachycardia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
cerebrovascular accident			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
encephalopathy			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
metabolic encephalopathy			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
haemorrhagic anaemia			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
petechiae			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
renal failure			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
joint ankylosis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
osteoarthritis			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
rotator cuff syndrome				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
pneumonia				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
post procedural infection				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
postoperative wound infection				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	2 / 100 (2.00%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
hyperkalaemia				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	0 / 100 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hyponatraemia				
alternative dictionary used: MedDRA 16.1				

subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

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

Non-serious adverse events	Placebo	35 mg LY2495655	105 mg LY2495655
Total subjects affected by non-serious adverse events			
subjects affected / exposed	72 / 98 (73.47%)	76 / 104 (73.08%)	66 / 98 (67.35%)
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	6 / 98 (6.12%)	3 / 104 (2.88%)	3 / 98 (3.06%)
occurrences (all)	6	3	3
hypotension			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	9 / 98 (9.18%)	9 / 104 (8.65%)	10 / 98 (10.20%)
occurrences (all)	11	10	10
General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	7 / 98 (7.14%)	4 / 104 (3.85%)	4 / 98 (4.08%)
occurrences (all)	9	4	4
injection site erythema			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	1 / 104 (0.96%)	2 / 98 (2.04%)
occurrences (all)	0	1	3
injection site pain			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	3 / 98 (3.06%)	6 / 104 (5.77%)	13 / 98 (13.27%)
occurrences (all)	3	9	30
local swelling			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	5 / 98 (5.10%)	6 / 104 (5.77%)	7 / 98 (7.14%)
occurrences (all)	5	6	7
pyrexia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	11 / 98 (11.22%)	18 / 104 (17.31%)	13 / 98 (13.27%)
occurrences (all)	15	22	24
Psychiatric disorders			
insomnia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	3 / 98 (3.06%)	7 / 104 (6.73%)	7 / 98 (7.14%)
occurrences (all)	3	7	8
Investigations			
oxygen saturation decreased			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	7 / 98 (7.14%)	3 / 104 (2.88%)	3 / 98 (3.06%)
occurrences (all)	7	3	3
Injury, poisoning and procedural complications			
anaemia postoperative			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 98 (2.04%)	3 / 104 (2.88%)	2 / 98 (2.04%)
occurrences (all)	2	4	2
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	13 / 98 (13.27%)	9 / 104 (8.65%)	6 / 98 (6.12%)
occurrences (all)	16	13	7
headache			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	0 / 98 (0.00%)	6 / 104 (5.77%)	3 / 98 (3.06%)
occurrences (all)	0	6	4
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	4 / 98 (4.08%)	8 / 104 (7.69%)	7 / 98 (7.14%)
occurrences (all)	4	8	7
Gastrointestinal disorders			

constipation			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	8 / 98 (8.16%)	14 / 104 (13.46%)	7 / 98 (7.14%)
occurrences (all)	9	15	7
diarrhoea			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 98 (2.04%)	8 / 104 (7.69%)	4 / 98 (4.08%)
occurrences (all)	2	8	4
nausea			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	12 / 98 (12.24%)	20 / 104 (19.23%)	16 / 98 (16.33%)
occurrences (all)	12	23	18
vomiting			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	9 / 98 (9.18%)	16 / 104 (15.38%)	9 / 98 (9.18%)
occurrences (all)	10	20	11
Skin and subcutaneous tissue disorders			
pruritus			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	7 / 98 (7.14%)	3 / 104 (2.88%)	2 / 98 (2.04%)
occurrences (all)	8	3	2
Renal and urinary disorders			
urinary retention			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	8 / 98 (8.16%)	5 / 104 (4.81%)	9 / 98 (9.18%)
occurrences (all)	8	5	9
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	11 / 98 (11.22%)	22 / 104 (21.15%)	11 / 98 (11.22%)
occurrences (all)	15	30	12
back pain			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	3 / 98 (3.06%)	9 / 104 (8.65%)	12 / 98 (12.24%)
occurrences (all)	4	9	14

myalgia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	3 / 98 (3.06%) 3	9 / 104 (8.65%) 10	3 / 98 (3.06%) 4
pain in extremity alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	3 / 98 (3.06%) 3	11 / 104 (10.58%) 13	5 / 98 (5.10%) 6
Infections and infestations influenza alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	6 / 98 (6.12%) 6	1 / 104 (0.96%) 1	2 / 98 (2.04%) 2
nasopharyngitis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 98 (1.02%) 1	3 / 104 (2.88%) 4	2 / 98 (2.04%) 2
Metabolism and nutrition disorders decreased appetite alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	3 / 98 (3.06%) 3	2 / 104 (1.92%) 2	1 / 98 (1.02%) 1

Non-serious adverse events	315 mg LY2495655		
Total subjects affected by non-serious adverse events subjects affected / exposed	68 / 100 (68.00%)		
Vascular disorders hypertension alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	1 / 100 (1.00%) 1		
hypotension alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	12 / 100 (12.00%) 12		
General disorders and administration site conditions			

fatigue alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	9 / 100 (9.00%) 9		
injection site erythema alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	6 / 100 (6.00%) 11		
injection site pain alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	12 / 100 (12.00%) 30		
local swelling alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	3 / 100 (3.00%) 3		
pyrexia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	14 / 100 (14.00%) 14		
Psychiatric disorders insomnia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	5 / 100 (5.00%) 5		
Investigations oxygen saturation decreased alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	6 / 100 (6.00%) 6		
Injury, poisoning and procedural complications anaemia postoperative alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	6 / 100 (6.00%) 6		

Nervous system disorders dizziness alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) headache alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	 9 / 100 (9.00%) 11 2 / 100 (2.00%) 2		
Blood and lymphatic system disorders anaemia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	 11 / 100 (11.00%) 11		
Gastrointestinal disorders constipation alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) diarrhoea alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) nausea alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) vomiting alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	 9 / 100 (9.00%) 9 5 / 100 (5.00%) 5 21 / 100 (21.00%) 21 12 / 100 (12.00%) 12		
Skin and subcutaneous tissue disorders pruritus alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	 3 / 100 (3.00%) 3		

Renal and urinary disorders urinary retention alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	 8 / 100 (8.00%) 8		
Musculoskeletal and connective tissue disorders arthralgia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) back pain alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) myalgia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) pain in extremity alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	 14 / 100 (14.00%) 23 2 / 100 (2.00%) 2 4 / 100 (4.00%) 5 4 / 100 (4.00%) 7		
Infections and infestations influenza alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) nasopharyngitis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all)	 2 / 100 (2.00%) 2 6 / 100 (6.00%) 7		
Metabolism and nutrition disorders decreased appetite alternative dictionary used: MedDRA 16.1			

subjects affected / exposed occurrences (all)	9 / 100 (9.00%) 9		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 March 2011	Addition of fecal occult blood test at screening
05 July 2011	Patient monitoring time was increased from 15 to 30 minutes after study drug injection
23 September 2011	Added 44 patients in Japan, and ensure the third interim analysis did not need to wait for the Japanese patients to have completed. Moved leg strength test from secondary to exploratory objective
09 April 2012	In order to speed up enrollment, changed inclusion criterion [1], from patients 60 years or older to males or females of non child-bearing potential, aged 50 years or older. Also, the window between Visit 2 and surgery was shortened from 14 ± 6 days before the eTHA surgery to 10 ± 6 days. Also, allowed study sites to obtain 25-hydroxyvitamin D levels for eligibility purposes from the local laboratory
17 October 2012	Modification of Inclusion Criterion to further define effective methods of contraception, and addition of Exclusion Criterion for patients who have experienced a severe allergic reaction from a monoclonal antibody.
03 May 2013	Added the following inclusion criteria due to insufficient quality of some scans during first part of the study: Have a baseline DEXA scan (at or before Visit 2) that captures all 4 limbs entirely in the DEXA scan field in the opinion of the investigator site's DEXA technician

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported