Clinical trial results:
A Phase 2 Study of LY2835219 for Patients with Previously Treated Hormone Receptor Positive, HER2 Negative Metastatic Breast Cancer

Summary

EudraCT number	2013-005548-27
Trial protocol	BE ES
Global end of trial date	22 October 2018

Results information

Result version number	v1 (current)
This version publication date	01 September 2019
First version publication date	01 September 2019

Trial information

Trial identification

Sponsor protocol code	I3Y-MC-JPBN

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02102490
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 15419

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	22 October 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate whether the study drug known as abemaciclib is effective in treating participants with breast cancer who have already tried other drug treatments.

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	10 June 2014
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	Belgium: 28
Country: Number of subjects enrolled	United States: 70
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Spain: 23
Worldwide total number of subjects	132
EEA total number of subjects	62

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)	90
From 65 to 84 years	41

85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

In the Participant Flow, participants who completed were those who died due to any cause or were alive and on study at conclusion but off treatment.

Period 1

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

Arms

Arm title	Abemaciclib

Arm description:

200 mg abemaciclib given orally once every 12 hours for 28 days (1 cycle). Participants may continue to receive treatment until discontinuation criteria are met.

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

Dosage and administration details:

200 mg abemaciclib given orally once every 12 hours for 28 days (1 cycle).

Number of subjects in period 1	Abemaciclib
Started	132
Received at Least 1 Dose of Study Drug	132
Completed	125
Not completed	7
Adverse event, serious fatal	6
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study
Reporting group description:	
200 mg abemaciclib given orally once every 12 hours for 28 days (1 cycle). Participants may continue to receive treatment until discontinuation criteria are met.	

Reporting group values	Overall Study	Total	
Number of subjects	132	132	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	59.13		
standard deviation	± 10.33	-	
Gender categorical Units: Subjects			
Female	132	132	
Male	0	0	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	8	8	
Not Hispanic or Latino	112	112	
Unknown or Not Reported	12	12	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	2	2	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	6	6	
White	112	112	
More than one race	0	0	
Unknown or Not Reported	12	12	
Region of Enrollment Units: Subjects			
Belgium	28	28	
United States	70	70	
France	11	11	
Spain	23	23	

End points

End points reporting groups

Reporting group title	Abemaciclib

Reporting group description:

200 mg abemaciclib given orally once every 12 hours for 28 days (1 cycle). Participants may continue to receive treatment until discontinuation criteria are met.

Primary: Percentage of Participants with Complete Response (CR) or Partial Response (PR) (Objective Response Rate [ORR])

End point title	Percentage of Participants with Complete Response (CR) or Partial Response (PR) (Objective Response Rate [ORR])[1]

End point description:

ORR was the percentage of participants achieving a best overall response (BOR) of complete response (CR) or partial response (PR) as per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. CR defined as the disappearance of all target and non-target lesions and no appearance of new lesions. PR defined as at least a 30% decrease in the sum of the longest diameters (LD) of target lesions (taking as reference the baseline sum LD), no progression of non-target lesions, and no appearance of new lesions. Analysis
population included all enrolled participants who received at least one dose of study drug.

End point type	Primary

End point timeframe:

From Date of First Dose until Disease Progression or Death Due to Any Cause (Up To 14 Months)

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: No inferential statistics were planned or conducted for this endpoint.

End point values	Abemaciclib			
Subject group type	Reporting group			
Number of subjects analysed	132			
Units: Percentage of participants				
number (confidence interval 95%)	19.7 (13.3 to 27.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS defined as the time from first dose date to the date of death due to any cause. For each participant who is not known to have died as of the data-inclusion cutoff date for overall survival analysis, OS time was censored on the last date the participant is known to be alive. 9999=Data Not Available (N/A) as upper limit of the 95% confidence interval (CI) was not calculated due to the high censoring rate. Analysis
population included all enrolled participants who received at least one dose of study drug. Censored participants: Abemaciclib=70.

End point type	Secondary

End point timeframe:

From Date of First Dose until Death Due to Any Cause (Up To 27 Months)

End point values	Abemaciclib			
Subject group type	Reporting group			
Number of subjects analysed	132			
Units: Months				
median (confidence interval 95%)	22.32 (17.72 to 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

DOR was the time from the date of first evidence of complete response or partial response to the date of objective progression or the date of death due to any cause, whichever is earlier. CR and PR were defined using the RECIST v1.1. CR defined as the disappearance of all target and non-target lesions and no appearance of new lesions. PR defined as at least a 30% decrease in the sum of the LD of target lesions (taking as reference the baseline sum LD), no progression of non-target lesions, and no appearance of new lesions. If a responder was not known to have died or have objective progression as of the data inclusion cutoff date, duration of response was censored at the last adequate tumor assessment date. Analysis population included all enrolled participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

From Date of CR, PR until Disease Progression or Death Due to Any Cause (Up To 14 Months)

End point values	Abemaciclib			
Subject group type	Reporting group			
Number of subjects analysed	132			
Units: Months				
median (confidence interval 95%)	8.6 (5.8 to 10.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

PFS defined as the time from the first day of therapy to the first evidence of disease progression as defined by RECIST v1.1 or death from any cause. Progressive Disease (PD) was at least a 20% increase in the sum of the diameters of target lesions, with reference being the smallest sum on study and an absolute increase of at least 5 mm, or unequivocal progression of non-target lesions, or 1 or more new lesions. If a participant does not have a complete baseline disease assessment, then the PFS time was censored at the date of first dose, regardless of whether or not objectively determined disease progression or death has been observed for the participant. If a participant was not known to have died or have objective progression as of the data inclusion cutoff date for the analysis, the PFS time was censored at last adequate tumor assessment date. Analysis population included all enrolled participants who received at least one dose of study drug. Censored participants: Abemaciclib=35.

End point type	Secondary

End point timeframe:

From Date of First Dose until Disease Progression or Death Due to Any Cause (Up To 27 Months)

End point values	Abemaciclib			
Subject group type	Reporting group			
Number of subjects analysed	132			
Units: Months				
median (confidence interval 95%)	6.0 (4.2 to 7.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with CR, PR or SD (Disease Control Rate [DCR])

End point title	Percentage of Participants with CR, PR or SD (Disease Control Rate [DCR])

End point description:

Disease Control Rate (DCR) was the percentage of participants with a best overall response of CR, PR, or Stable Disease (SD) as per Response using RECIST v1.1 criteria. CR defined as the disappearance of all target and non-target lesions and no appearance of new lesions. PR defined as at least a 30% decrease in the sum of the LD of target lesions (taking as reference the baseline sum LD), no progression of non-target lesions, and no appearance of new lesions. SD was neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD for target lesions, no progression of non-target lesions, and no appearance of new lesions. Analysis population included all enrolled participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

From Date of First Dose until Disease Progression or Death Due to Any Cause (Up To 14 Months)

End point values	Abemaciclib			
Subject group type	Reporting group			
Number of subjects analysed	132			
Units: Percentage of participants				
number (confidence interval 95%)	67.4 (58.7 to 75.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Tumor Response of Stable Disease (SD) for at least 6 months, Partial Response (PR) or Complete Response (CR) (Clinical Benefit Rate)

End point title	Percentage of Participants with Tumor Response of Stable Disease (SD) for at least 6 months, Partial Response (PR) or Complete Response (CR) (Clinical Benefit Rate)

End point description:

Clinical benefit rate defined as percentage of patients with best overall response of CR, PR, or SD with a duration of at least 6 months. CR, PR, or SD were defined using RECIST, v1.1 criteria. CR defined as the disappearance of all target and non-target lesions and no appearance of new lesions. PR defined as at least a 30% decrease in the sum of the LD of target lesions (taking as reference the baseline sum LD), no progression of non-target lesions, and no appearance of new lesions. SD was neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD for target lesions, no progression of non-target lesions, and no appearance of new lesions. Percentage of participants = (participants with CR+PR+SD with a duration of at least 6 months /number of participants enrolled) *100. Analysis population included all enrolled participants who received at least one dose of the study drug.

End point type	Secondary

End point timeframe:

From Date of First Dose until Disease Progression or Death Due to Any Cause (Up To 14 Months)

End point values	Abemaciclib			
Subject group type	Reporting group			
Number of subjects analysed	132			
Units: Percentage of participants				
number (confidence interval 95%)	42.4 (33.9 to 51.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Categorical Change From Baseline in Brief Pain Inventory Short Form (mBPI-sf) - Worst Pain Score

End point title	Number of Participants with Categorical Change From Baseline in Brief Pain Inventory Short Form (mBPI-sf) - Worst Pain Score

End point description:

A self-reported scale that measures the severity of pain based on the average pain experienced over the past 24 hours. The severity scores range from 0 (no pain) to 10 (pain as severe as you can imagine). Analysis population included all randomized participants with a baseline and at least 1 post-baseline mBPI-sf data.

End point type	Secondary

End point timeframe:

Cycle 6 Day 1

End point values	Abemaciclib			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: participants	18			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics: Area Under the Concentration versus Time Curve from Time Zero to Infinity (AUC[0-∞]) for Abemaciclib and Metabolites M2 and M20

End point title	Pharmacokinetics: Area Under the Concentration versus Time Curve from Time Zero to Infinity (AUC[0-∞]) for Abemaciclib and Metabolites M2 and M20

End point description:

Area Under the Concentration versus Time Curve from Time Zero to Infinity (AUC[0-∞]) was evaluated for Abemaciclib and Metabolites M2 and M20. Analysis population included all enrolled participants who received at least one dose of study drug (Abemaciclib) with evaluable Abemaciclib, M2 and M20 pharmacokinetic (PK) data.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 pre dose, Cycle 1 Day 15 4 hours (h) and 7 h post dose, Cycle 2 Day 1 pre dose and 3 h post dose, Cycle 3 Day1 pre dose

End point values	Abemaciclib			
Subject group type	Reporting group			
Number of subjects analysed	132			
Units: Nanograms*hour/milliliters (ng*h/mL)]				
geometric mean (geometric coefficient of variation)				
Abemaciclib M2 M20	3510 (± 38.0) 1620 (± 55.0) 2750 (± 55.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Categorical Change from Baseline in European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) - Global Health Status Score

End point title	Number of Participants with Categorical Change from Baseline in European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) - Global Health Status Score

End point description:

EORTC QLQ-C30 v3.0 was a self-administered questionnaire with multidimensional scales that measures 5 functional domains (physical, role, cognitive, emotional, and social), global health status, and symptom scales of fatigue, pain, nausea and vomiting, dyspnea, loss of appetite, insomnia, constipation and diarrhea, and financial difficulties. A linear transformation is applied to standardize the raw scores to range between 0 and 100 per developer guidelines. For functional domains and global health status, higher scores represent a better level of functioning. For symptoms scales, higher scores represented a greater degree of symptoms. Analysis population included all randomized participants who received at least one dose of study drug with baseline and post-baseline EORTC QLQ-C30 data.

End point type	Secondary

End point timeframe:

Cycle 6 Day 1

End point values	Abemaciclib			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: participants				
Better	17			
No Change	16			
Worse	26			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up To 45.57 Months

Adverse event reporting additional description:

All enrolled participants who received at least one dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Abemaciclib

Reporting group description:

200 mg abemaciclib given orally once every 12 hours for 28 days (1 cycle). Participants may continue to receive treatment until discontinuation criteria are met.

Serious adverse events	Abemaciclib		
Total subjects affected by serious adverse events			
subjects affected / exposed	33 / 132 (25.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
arterial thrombosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
pyrexia			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
dyspnoea			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	2 / 132 (1.52%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
pleural effusion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	2 / 132 (1.52%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
pneumonitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
pneumothorax			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
pulmonary embolism			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
blood creatinine increased			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	3 / 132 (2.27%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		
electrocardiogram abnormal			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
liver function test abnormal			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
neutrophil count decreased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
renal function test abnormal			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
white blood cell count decreased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
fall			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
hip fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
tachycardia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
sinus bradycardia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
epilepsy			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
febrile neutropenia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
haematotoxicity			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 132 (0.76%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
neutropenia				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	1 / 132 (0.76%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
abdominal pain				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	2 / 132 (1.52%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
abdominal pain upper				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	1 / 132 (0.76%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
constipation				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	1 / 132 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
large intestinal obstruction				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	1 / 132 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
nausea				
alternative dictionary used: MedDRA 21.1				

subjects affected / exposed	3 / 132 (2.27%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
pancreatic enzyme abnormality				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	1 / 132 (0.76%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
pancreatitis				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	1 / 132 (0.76%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
varices oesophageal				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	1 / 132 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
vomiting				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	1 / 132 (0.76%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
rash				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	1 / 132 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
acute kidney injury				
alternative dictionary used: MedDRA 21.1				

subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
bone pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
muscular weakness			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
atypical pneumonia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
cellulitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	2 / 132 (1.52%)		
occurrences causally related to treatment / all	2 / 5		
deaths causally related to treatment / all	0 / 0		
gastroenteritis viral			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
lung infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
respiratory tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
sepsis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Metabolism and nutrition disorders			
dehydration			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	3 / 132 (2.27%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
decreased appetite			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
hypokalaemia			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Abemaciclib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	132 / 132 (100.00%)		
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	11 / 132 (8.33%)		
occurrences (all)	15		
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	12 / 132 (9.09%)		
occurrences (all)	16		
blood creatinine increased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	15 / 132 (11.36%)		
occurrences (all)	41		
neutrophil count decreased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	31 / 132 (23.48%)		
occurrences (all)	105		
platelet count decreased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	18 / 132 (13.64%)		
occurrences (all)	42		
weight decreased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	18 / 132 (13.64%)		
occurrences (all)	22		

white blood cell count decreased alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	24 / 132 (18.18%) 69		
Nervous system disorders dizziness alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	16 / 132 (12.12%) 18		
dysgeusia alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	18 / 132 (13.64%) 19		
headache alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	26 / 132 (19.70%) 40		
Blood and lymphatic system disorders anaemia alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	35 / 132 (26.52%) 96		
neutropenia alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	24 / 132 (18.18%) 88		
thrombocytopenia alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	11 / 132 (8.33%) 21		
General disorders and administration site conditions asthenia alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	31 / 132 (23.48%) 85		

chills			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	8 / 132 (6.06%)		
occurrences (all)	8		
fatigue			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	63 / 132 (47.73%)		
occurrences (all)	129		
oedema peripheral			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	14 / 132 (10.61%)		
occurrences (all)	16		
pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	13 / 132 (9.85%)		
occurrences (all)	19		
pyrexia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	14 / 132 (10.61%)		
occurrences (all)	17		
Eye disorders			
lacrimation increased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	11 / 132 (8.33%)		
occurrences (all)	12		
Gastrointestinal disorders			
abdominal pain upper			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	16 / 132 (12.12%)		
occurrences (all)	19		
abdominal pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	34 / 132 (25.76%)		
occurrences (all)	54		
constipation			

alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	27 / 132 (20.45%)			
occurrences (all)	33			
diarrhoea				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	120 / 132 (90.91%)			
occurrences (all)	370			
dyspepsia				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	14 / 132 (10.61%)			
occurrences (all)	16			
dry mouth				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	18 / 132 (13.64%)			
occurrences (all)	18			
flatulence				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	9 / 132 (6.82%)			
occurrences (all)	11			
gastrooesophageal reflux disease				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	7 / 132 (5.30%)			
occurrences (all)	13			
nausea				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	89 / 132 (67.42%)			
occurrences (all)	141			
stomatitis				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	12 / 132 (9.09%)			
occurrences (all)	17			
vomiting				
alternative dictionary used: MedDRA 21.1				

subjects affected / exposed	46 / 132 (34.85%)		
occurrences (all)	91		
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	28 / 132 (21.21%)		
occurrences (all)	42		
dyspnoea			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	17 / 132 (12.88%)		
occurrences (all)	23		
Skin and subcutaneous tissue disorders			
alopecia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	20 / 132 (15.15%)		
occurrences (all)	21		
dry skin			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	11 / 132 (8.33%)		
occurrences (all)	13		
pruritus			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	11 / 132 (8.33%)		
occurrences (all)	13		
rash			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	7 / 132 (5.30%)		
occurrences (all)	9		
Psychiatric disorders			
anxiety			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	8 / 132 (6.06%)		
occurrences (all)	8		
Musculoskeletal and connective tissue disorders			

arthralgia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	25 / 132 (18.94%)		
occurrences (all)	32		
back pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	16 / 132 (12.12%)		
occurrences (all)	18		
musculoskeletal chest pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	8 / 132 (6.06%)		
occurrences (all)	9		
musculoskeletal pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	8 / 132 (6.06%)		
occurrences (all)	9		
myalgia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	7 / 132 (5.30%)		
occurrences (all)	8		
Infections and infestations			
upper respiratory tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	9 / 132 (6.82%)		
occurrences (all)	13		
urinary tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	9 / 132 (6.82%)		
occurrences (all)	9		
Metabolism and nutrition disorders			
dehydration			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	11 / 132 (8.33%)		
occurrences (all)	15		
decreased appetite			

alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	60 / 132 (45.45%)		
occurrences (all)	76		
hypokalaemia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	9 / 132 (6.82%)		
occurrences (all)	17		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 March 2015	- Amended to change the time of primary efficacy analysis of ORR from 8 months to 12 months after last patient has entered treatment and to consider the efficacy analysis of ORR at 8 months as an interim efficacy analysis. The time of primary efficacy analysis was changed to ensure adequate response and that durability of response data is available for analysis. The interim efficacy analysis at 8 months allows an earlier assessment of efficacy. In addition, the primary efficacy measure was modified to use investigator-assessed tumor response, which would allow for evaluation earlier than independently reviewed tumor response. - Further modifications were made for 1) supportive management of diarrhea, 2) health outcomes, and 3) Study Schedule for clarity. - Minor typographical and formatting edits were made throughout the document for clarity and consistency.
16 October 2015	- Updated the dosing guidance for cases of hematologic toxicity and diarrhea, and guidance on the use of blood cell growth factors. Lilly conducted a review across several clinical trials of abemaciclib in breast cancer and concluded that there were some inconsistencies. This amendment harmonized the dosing guidance and clarified that blood cell growth factors are only to be used in a manner consistent with American Society of Clinical Oncology (ASCO) guidelines. -Minor typographical and formatting edits were made throughout the document for clarity and consistency.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported