



Clinical trial results:

CYCLONE 1: A Phase 2 Study of Abemaciclib in Metastatic Castration-Resistant Prostate Cancer Patients Previously Treated with a Novel Hormonal Agent and Taxane-based Chemotherapy

Summary

EudraCT number	2020-000290-24
Trial protocol	FR
Global end of trial date	02 June 2023

Results information

Result version number	v2 (current)
This version publication date	15 June 2024
First version publication date	13 May 2023
Version creation reason	<ul style="list-style-type: none">• New data added to full data set New data added to full data set

Trial information

Trial identification

Sponsor protocol code	I3Y-MC-JPCY
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04408924
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 17583

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	02 June 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	02 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The study will evaluate how safe and effective abemaciclib is when given to participants whose metastatic prostate cancer progresses after they had received several previous 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	20 January 2021
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	France: 14
Country: Number of subjects enrolled	Spain: 27
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	44
EEA total number of subjects	41

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)	14
From 65 to 84 years	29

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Not Applicable

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	200 Milligram (mg) Abemaciclib Twice Daily
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Arm description:

Participants received 200 mg abemaciclib administered orally twice daily on a continuous dosing schedule (28-day cycle) until symptomatic and/or radiographic progression, unacceptable toxicity, or until another discontinuation criterion is met.

Arm type	Experimental
Investigational medicinal product name	Abemaciclib
Investigational medicinal product code	LY2835219
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 200 mg abemaciclib administered orally twice daily on a continuous dosing schedule (28-day cycle) until symptomatic and/or radiographic progression, unacceptable toxicity, or until another discontinuation criterion is met.

Number of subjects in period 1	200 Milligram (mg) Abemaciclib Twice Daily
Started	44
Received at Least One Dose of Study Drug	44
Completed	31
Not completed	13
Consent withdrawn by subject	5
Sponsor Decision	2
Off Treatment on Post-Treatment-Discontinuation Fo	3
Lost to follow-up	3

Baseline characteristics

Reporting groups

Reporting group title	200 Milligram (mg) Abemaciclib Twice Daily
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Reporting group description:

Participants received 200 mg abemaciclib administered orally twice daily on a continuous dosing schedule (28-day cycle) until symptomatic and/or radiographic progression, unacceptable toxicity, or until another discontinuation criterion is met.

Reporting group values	200 Milligram (mg) Abemaciclib Twice Daily	Total	
Number of subjects	44	44	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	68.3 ± 9.2	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	44	44	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	3	3	
Unknown or Not Reported	41	41	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	3	3	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	27	27	
More than one race	0	0	
Unknown or Not Reported	14	14	
Region of Enrollment Units: Subjects			
France	14	14	
Spain	27	27	
United States	3	3	

End points

End points reporting groups

Reporting group title	200 Milligram (mg) Abemaciclib Twice Daily
Reporting group description: Participants received 200 mg abemaciclib administered orally twice daily on a continuous dosing schedule (28-day cycle) until symptomatic and/or radiographic progression, unacceptable toxicity, or until another discontinuation criterion is met.	

Primary: Percentage of Participants With Confirmed Objective Response (Objective Response Rate [ORR])

End point title	Percentage of Participants With Confirmed Objective Response (Objective Response Rate [ORR]) ^[1]
End point description: ORR is defined as the percentage of participants with a confirmed complete response (CR) or confirmed partial response (PR) in soft tissue per response evaluation criteria in solid tumors (RECIST) version 1.1 and do not have concurrent bone progression per Prostate Cancer Clinical Trials Working Group 3 (PCWG3), as assessed by the investigator. ORR = (participants with confirmed CR and no bone progression) + (participants with confirmed PR and no bone progression) x 100 / all treated participants. Analysis population description (APD): All participants who received at least one dose of the study drug.	
End point type	Primary
End point timeframe: From Date of First Dose until Objective Progression (Up To 12.8 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 was planned for this endpoint.

End point values	200 Milligram (mg) Abemaciclib Twice Daily			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: percentage of participants				
number (confidence interval 95%)	6.8 (0.0 to 14.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Radiographic Progression-Free Survival (rPFS)

End point title	Radiographic Progression-Free Survival (rPFS)
End point description: The rPFS time is measured from the date of first dose to the earliest date of investigator-assessed radiographic progression per RECIST 1.1 for soft tissue and PCWG3 criteria for bone, or death from any cause, whichever occurred first. Participants who have neither progressed nor died will be censored at the day of their last radiographic tumor assessment (if available) or date of first dose if no post initiation (i.e., postbaseline) radiographic assessment is available. APD: All participants who received at least one	

dose of the study drug. Participants censored = 11.

End point type	Secondary
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End point timeframe:

From Date of First Dose until Objective Progression or Death from Any Cause (Up To 12.8 Months)

End point values	200 Milligram (mg) Abemaciclib Twice Daily			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: months				
median (confidence interval 95%)	2.7 (1.9 to 3.7)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Participants Achieving CR, PR or Stable Disease (SD) (Disease Control Rate [DCR])
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End point description:

The DCR is defined as the percentage of participants with confirmed soft tissue best overall response of CR, PR, or stable disease (SD) per RECIST 1.1, and do not have concurrent bone disease progression per PCWG3. APD: All participants who received at least one dose of the study drug.

End point type	Secondary
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End point timeframe:

From Date of First Dose until Measured Progressive Disease or Death Due to Any Cause (Up To 12.8 Months)

End point values	200 Milligram (mg) Abemaciclib Twice Daily			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: percentage of participants				
number (confidence interval 95%)	45.5 (30.7 to 60.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Prostate-Specific Antigen (PSA) Progression

End point title	Time to Prostate-Specific Antigen (PSA) Progression
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End point description:

Time to PSA progression is defined as the time from the date of treatment initiation to the date of first observation of PSA progression. The PSA progression is defined as a greater than or equal to (\geq) 25 percent (%) increase and an absolute increase of ≥ 2 nanogram/milliliter (ng/mL) above the nadir (or baseline value if baseline is the smallest on study), which is confirmed by a second value obtained 3 or more weeks later. APD: All participants who received at least one dose of the study drug. Participants censored: 31. The upper 95% confidence interval (CI) not achieved as there were insufficient number of events due to high censoring rate.

End point type	Secondary
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End point timeframe:

From Date of First Dose until Confirmed PSA Progression (Up To 12.8 Months)

End point values	200 Milligram (mg) Abemaciclib Twice Daily			
Subject group type	Reporting group			
Number of subjects analysed	44 ^[2]			
Units: months				
median (confidence interval 95%)	6.5 (3.2 to 9999)			

Notes:

[2] - 9999=Data not available.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved Prostate-Specific Antigen (PSA) Response (PSA Response Rate)

End point title	Percentage of Participants Who Achieved Prostate-Specific Antigen (PSA) Response (PSA Response Rate)
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End point description:

The PSA response rate is defined as the percentage of participants with a reduction in PSA level $\geq 50\%$ from baseline, confirmed with a second assessment conducted at least 3 weeks later. APD: All participants who received at least one dose of the study drug.

End point type	Secondary
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End point timeframe:

From Date of First Dose until Confirmed PSA Progression (Up To 12.8 Months)

End point values	200 Milligram (mg) Abemaciclib Twice Daily			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: percentage of participants				
number (not applicable)	4.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Symptomatic Progression

End point title	Time to Symptomatic Progression
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End point description:

Time to symptomatic progression is defined as the time from first dose to any of the following (whichever occurred earlier): 1) symptomatic skeletal event, defined as symptomatic fracture, surgery, or radiation to bone, or spinal cord compression; 2) pain progression or worsening of disease-related symptoms requiring initiation of a new systemic anticancer therapy; and 3) development of clinically significant symptoms due to locoregional tumor progression requiring surgical intervention or radiation therapy. For participants who were not known to have symptomatic progression at the time of data analysis, data were censored on the last date at which no symptomatic progression was indicated. APD: All participants who received at least one dose of the study drug. Participants censored = 28.

End point type	Secondary
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End point timeframe:

From Date of First Dose until Symptomatic Progression (Up to 12.8 Months)

End point values	200 Milligram (mg) Abemaciclib Twice Daily			
Subject group type	Reporting group			
Number of subjects analysed	44 ^[3]			
Units: months				
median (confidence interval 95%)	4.1 (3.7 to 9999)			

Notes:

[3] - 9999=Data not available; Upper 95% confidence interval (CI) not achieved due to high censoring rate.

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Maximum Plasma Concentration at steady state (C_{max,ss}) of Abemaciclib

End point title	Pharmacokinetics (PK): Maximum Plasma Concentration at steady state (C _{max,ss}) of Abemaciclib
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End point description:

PK: C_{max,ss} of abemaciclib is reported. The cycle length was 28 days. APD: All participants who received at least one dose of study drug had evaluable PK data.

End point type	Secondary
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End point timeframe:

Cycle (C) 1 Day (D) 1: Post dose; C1 D15, C2D1, C2D15, C3D1: Pre dose

End point values	200 Milligram (mg) Abemaciclib Twice Daily			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: nanogram per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)	223 (± 47)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK: Minimum/Trough Concentration at Steady State (C_{min,ss}) of Abemaciclib

End point title	PK: Minimum/Trough Concentration at Steady State (C _{min,ss}) of Abemaciclib
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End point description:

PK: C_{min,ss} of abemaciclib is reported. APD: All participants who received at least one dose of study drug had evaluable PK data.

End point type	Secondary
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End point timeframe:

C1 D1: Post dose; C1 D15, C2D1, C2D15, C3D1: Pre dose

End point values	200 Milligram (mg) Abemaciclib Twice Daily			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	176 (± 37)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK: Maximum Plasma Concentration at Steady State (C_{max,ss}) of Abemaciclib Metabolites (Total Active Species)

End point title	PK: Maximum Plasma Concentration at Steady State (C _{max,ss}) of Abemaciclib Metabolites (Total Active Species)
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End point description:

PK: C_{max,ss} of abemaciclib metabolites (Total Active Species) is reported. APD: All participants who received at least one dose of study drug had evaluable PK data.

End point type Secondary

End point timeframe:

C1 D1: Post dose; C1 D15, C2D1, C2D15, C3D1: Pre dose

End point values	200 Milligram (mg) Abemaciclib Twice Daily			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: micromolar per liter (µmol/L)				
geometric mean (geometric coefficient of variation)	1.7 (± 79)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK: Minimum/Trough Concentration at Steady State (C_{min,ss}) of Abemaciclib Metabolites (Total Active Species)

End point title PK: Minimum/Trough Concentration at Steady State (C_{min,ss}) of Abemaciclib Metabolites (Total Active Species)

End point description:

PK: C_{min,ss} of abemaciclib metabolites (Total Active Species) is reported. APD: All participants who received at least one dose of study drug had evaluable PK data.

End point type Secondary

End point timeframe:

C1 D1: Post dose; C1 D15, C2D1, C2D15, C3D1: Pre dose

End point values	200 Milligram (mg) Abemaciclib Twice Daily			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: µmol/L				
geometric mean (geometric coefficient of variation)	1.5 (± 80)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Expression of Ki-67 proliferation marker by Immunohistochemistry (IHC)

End point title	Percentage of Participants with Expression of Ki-67 proliferation marker by Immunohistochemistry (IHC)
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End point description:

Percentage of participants with expression of Ki-67 proliferation marker at baseline by immunohistochemistry.

Baseline expression of the Ki-67 proliferation marker was evaluated by IHC utilizing a 20% or higher score to define high Ki-67 expression. The proportion of Ki-67 positive cells was defined by the number of non-apoptotic tumor cells with unequivocal brown nuclear staining (intensities ≥ 1 using a 0-3 scale) over the total number of non-apoptotic tumor cells. Unit of Measure is percentage of participants with low or high baseline Ki-67 expression. APD: All participants with evaluable tumor tissue specimens

End point type	Secondary
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End point timeframe:

Baseline

End point values	200 Milligram (mg) Abemaciclib Twice Daily			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: percentage of participants				
number (not applicable)				
Low baseline Ki-67 expression	25.8			
High baseline Ki-67 expression	74.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
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End point description:

OS time is measured from the date of first dose to the date of death from any cause. If the participant was alive or lost to follow-up at the time of data analysis, OS data were censored on the last date the participant was known to be alive. APD: All participants who received at least one dose of the study drug. Participants censored = 13.

End point type	Secondary
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End point timeframe:

From Date of First Dose until Date of Death from Any Cause (Up To 28 Months)

End point values	200 Milligram (mg) Abemaciclib Twice Daily			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: months				
median (confidence interval 95%)	8.38 (5.62 to 12.69)			

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 is measured only for confirmed responders (participants with a confirmed soft tissue best overall response of CR or PR per RECIST 1.1 no concurrent bone progression per PCWG3). It is measured from the date of first evidence of soft tissue CR or PR to the earliest date of investigator-assessed radiographic progression or death from any cause, whichever is earlier. APD: All randomized participants who received at least one dose of the study drug and had CR or PR responses. The median was not achieved due to insufficient sample data.	
End point type	Secondary
End point timeframe:	
CR or PR to Disease Progression or Death Due to Any Cause (Up to 12 Months)	

End point values	200 Milligram (mg) Abemaciclib Twice Daily			
Subject group type	Reporting group			
Number of subjects analysed	3 ^[4]			
Units: months				
median (full range (min-max))	9999 (9999 to 9999)			

Notes:

[4] - 9999=Data not available for median due to insufficient sample data. Full range values=3.87 to 11.17.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline Up to 28 Months

Adverse event reporting additional description:

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

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.0
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Reporting groups

Reporting group title	200 mg Abemaciclib Twice Daily
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Reporting group description:

Participants received 200 mg of abemaciclib administered orally twice daily on a continuous dosing schedule (28-day cycle) until symptomatic and/or radiographic progression, unacceptable toxicity, or until another discontinuation criterion is met.

Serious adverse events	200 mg Abemaciclib Twice Daily		
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 44 (40.91%)		
number of deaths (all causes)	31		
number of deaths resulting from adverse events			
General disorders and administration site conditions			
general physical health deterioration			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
pyrexia			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	3 / 44 (6.82%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
pain			
alternative dictionary used: MedDRA 26.0			

subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
pleural effusion			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Product issues			
device occlusion			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
blood creatinine increased			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	2 / 44 (4.55%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
periprosthetic fracture			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
subdural haemorrhage			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
subdural haematoma			

<p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>1 / 44 (2.27%)</p> <p>0 / 1</p> <p>0 / 0</p>		
<p>Cardiac disorders</p> <p>myocardial infarction</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>1 / 44 (2.27%)</p> <p>0 / 1</p> <p>0 / 0</p>		
<p>Nervous system disorders</p> <p>cerebrovascular accident</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>1 / 44 (2.27%)</p> <p>0 / 1</p> <p>0 / 0</p>		
<p>Blood and lymphatic system disorders</p> <p>anaemia</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>2 / 44 (4.55%)</p> <p>1 / 2</p> <p>0 / 0</p>		
<p>Eye disorders</p> <p>diplopia</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>1 / 44 (2.27%)</p> <p>0 / 1</p> <p>0 / 0</p>		
<p>Gastrointestinal disorders</p> <p>diarrhoea</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>1 / 44 (2.27%)</p> <p>0 / 1</p> <p>0 / 0</p>		

<p>haemoperitoneum</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>1 / 44 (2.27%)</p> <p>0 / 2</p> <p>0 / 0</p>		
<p>Skin and subcutaneous tissue disorders</p> <p>dermatitis</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>1 / 44 (2.27%)</p> <p>0 / 1</p> <p>0 / 0</p>		
<p>Renal and urinary disorders</p> <p>urinary retention</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>1 / 44 (2.27%)</p> <p>0 / 1</p> <p>0 / 0</p>		
<p>renal failure</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>3 / 44 (6.82%)</p> <p>1 / 3</p> <p>0 / 0</p>		
<p>Infections and infestations</p> <p>bacteraemia</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>1 / 44 (2.27%)</p> <p>0 / 1</p> <p>0 / 0</p>		
<p>cellulitis</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences causally related to treatment / all</p> <p>deaths causally related to treatment / all</p>	<p>1 / 44 (2.27%)</p> <p>0 / 1</p> <p>0 / 0</p>		
<p>sepsis</p>			

alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
urinary tract infection			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	200 mg Abemaciclib Twice Daily		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 44 (95.45%)		
Investigations			
blood creatinine increased			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	7 / 44 (15.91%)		
occurrences (all)	9		
neutrophil count decreased			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	4 / 44 (9.09%)		
occurrences (all)	4		
platelet count decreased			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	5 / 44 (11.36%)		
occurrences (all)	6		
weight decreased			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	3 / 44 (6.82%)		
occurrences (all)	3		
Nervous system disorders			

dysgeusia alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)	3 / 44 (6.82%) 4		
Blood and lymphatic system disorders anaemia alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) neutropenia alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) thrombocytopenia alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)	16 / 44 (36.36%) 17 13 / 44 (29.55%) 18 4 / 44 (9.09%) 4		
General disorders and administration site conditions asthenia alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) fatigue alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) oedema peripheral alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) pyrexia alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)	24 / 44 (54.55%) 34 5 / 44 (11.36%) 5 6 / 44 (13.64%) 6 6 / 44 (13.64%) 6		
Gastrointestinal disorders			

<p>abdominal pain</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed 5 / 44 (11.36%)</p> <p>occurrences (all) 7</p>			
<p>constipation</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed 9 / 44 (20.45%)</p> <p>occurrences (all) 11</p>			
<p>diarrhoea</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed 36 / 44 (81.82%)</p> <p>occurrences (all) 57</p>			
<p>nausea</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed 21 / 44 (47.73%)</p> <p>occurrences (all) 28</p>			
<p>vomiting</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed 16 / 44 (36.36%)</p> <p>occurrences (all) 19</p>			
<p>Respiratory, thoracic and mediastinal disorders</p> <p>cough</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed 3 / 44 (6.82%)</p> <p>occurrences (all) 3</p> <p>dyspnoea</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed 3 / 44 (6.82%)</p> <p>occurrences (all) 3</p>			
<p>Skin and subcutaneous tissue disorders</p> <p>dry skin</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed 3 / 44 (6.82%)</p> <p>occurrences (all) 3</p>			
<p>Renal and urinary disorders</p>			

<p>haematuria</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 44 (6.82%)</p> <p>4</p>		
<p>Psychiatric disorders</p> <p>insomnia</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 44 (6.82%)</p> <p>3</p>		
<p>Musculoskeletal and connective tissue disorders</p> <p>arthralgia</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>back pain</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>musculoskeletal chest pain</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>5 / 44 (11.36%)</p> <p>6</p> <p>7 / 44 (15.91%)</p> <p>7</p> <p>3 / 44 (6.82%)</p> <p>3</p>		
<p>Infections and infestations</p> <p>urinary tract infection</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 44 (6.82%)</p> <p>4</p>		
<p>Metabolism and nutrition disorders</p> <p>decreased appetite</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>24 / 44 (54.55%)</p> <p>25</p>		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 September 2020	- Clarification of Primary Endpoint; - Added mobile healthcare service option to collect and process lab, PK, Plasma/blood samples; -Added blood microsampling to PK sampling schedule; -Updated new treatment options for metastatic castration-resistant prostate cancer (mCRPC) where approved; - Clarification of Inclusion and Exclusion Criterion; - Text was added to caution participants with known hypersensitivity or suspected intolerance to abemaciclib or any of its excipients; - Clarifications: For Study Intervention(s) Administered; Preparation/Handling/Storage/Accountability regarding study drug; Selection and Timing of Doses; Concomitant Therapy; Discontinuation of Inadvertently Enrolled Participants; Lost to Follow up; Definitions of Efficacy Measures; Clinical Safety Laboratory Assessments; PK; Health Care Resource Utilization; Regulatory and Ethical Considerations; - Updated instructions for Data Quality Assurance
04 March 2021	- Added clarification to Schedule of Activities, Lifestyle Considerations, Selection and Timing of Doses; - Updated language for CYP3A modulators and transporter substrates; - Formatted table for toxicity dose adjustments and delays of abemaciclib; - Updated guidance for monitoring renal function, guidance for venous thromboembolic events, guidance for interstitial lung disease/pneumonitis; - Editorial changes to clarify study statistics; - Added alanine transaminase (ALT) and aspartate transaminase (AST) to the Common Terminology Criteria for Adverse Events (CTCAE) 5.0 table and updated Appendix title and summary text to reflect these additions.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported