Clinical trial results:
A Randomized, Open-Label, Phase 2 Study of Abemaciclib plus Tamoxifen or Abemaciclib Alone, in Women with Previously Treated Hormone Receptor-Positive, HER2-Negative, Metastatic Breast Cancer

Summary

EudraCT number	2016-000288-18
Trial protocol	ES AT BE DE CZ FR
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	25 June 2022
First version publication date	25 June 2022

Trial information

Trial identification

Sponsor protocol code	I3Y-MC-JPCG

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02747004
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 16339

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	Interim
Date of interim/final analysis	15 June 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 June 2018
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate the safety and efficacy of abemaciclib plus tamoxifen or abemaciclib alone in women with previously treated hormone receptor-positive (HR+), human epidermal growth factor receptor 2 negative (HER2-), metastatic breast cancer.

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	14 September 2016
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	Brazil: 22
Country: Number of subjects enrolled	Argentina: 16
Country: Number of subjects enrolled	Austria: 4
Country: Number of subjects enrolled	Czechia: 16
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Spain: 47
Country: Number of subjects enrolled	Belgium: 12
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	Mexico: 15
Country: Number of subjects enrolled	Russian Federation: 16
Country: Number of subjects enrolled	Turkey: 32
Country: Number of subjects enrolled	Taiwan: 23
Country: Number of subjects enrolled	United States: 9
Worldwide total number of subjects	234
EEA total number of subjects	101

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)	175
From 65 to 84 years	59
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Final results will be posted after the study completion once trial achieves global end date (Last patient visit: LPV).

Pre-assignment

Screening details:

Not Applicable.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	150 milligram (mg) Abemaciclib + 20mg Tamoxifen

Arm description:

Participants received oral dose of 150 mg Abemaciclib every 12 hours (Q12H) along with 20mg Tamoxifen every 24 hours (QD) on days 1 to days 28 of a 28 day cycle.

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

Dosage and administration details:

150 mg Abemaciclib given Q12H on days 1 to days 28 of a 28 day cycle.

Investigational medicinal product name	Tamoxifen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

20mg tamoxifen QD on days 1 to days 28 of a 28 day cycle.

Arm title	150mg Abemaciclib

Arm description:

Participants received oral dose of 150 milligrams (mg) Abemaciclib every 12 hours (Q12H) on days 1 to days 28 of a 28 day cycle.

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

Dosage and administration details:

150 mg Abemaciclib Q12H on days 1 to days 28 of a 28 day cycle.

Arm title	200mg Abemaciclib + 2mg Prophylactic Loperamide

Arm description:

Participants received oral dose of 200 milligrams (mg) Abemaciclib every 12 hours (Q12H) along with 2mg Prophylactic Loperamide on days 1 to days 28 of a 28 day cycle.
Note: During Cycle 1, 2mg prophylactic loperamide was administered orally with the first dose of abemaciclib daily. During Cycle 2 and beyond, loperamide was administered at investigator's discretion and/or if clinically indicated.

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

Dosage and administration details:

200 mg Abemaciclib Q12H on days 1 to days 28 of a 28 day cycle.

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

Dosage and administration details:

2mg Prophylactic Loperamide on days 1 to days 28 of a 28 day cycle.
Note: During Cycle 1, 2mg prophylactic loperamide was administered orally with the first dose of abemaciclib daily. During Cycle 2 and beyond, loperamide was administered at investigator's discretion and/or if clinically indicated.

Number of subjects in period 1	150 milligram (mg) Abemaciclib + 20mg Tamoxifen	150mg Abemaciclib	200mg Abemaciclib + 2mg Prophylactic Loperamide
Started	78	79	77
Received at least one dose of study drug	78	79	77
Completed	21	30	30
Not completed	57	49	47
Consent withdrawn by subject	8	5	4
on study treatment/follow-up	48	42	41
Lost to follow-up	1	2	2

Baseline characteristics

Reporting groups	
Reporting group title	150 milligram (mg) Abemaciclib + 20mg Tamoxifen
Reporting group description:	
Participants received oral dose of 150 mg Abemaciclib every 12 hours (Q12H) along with 20mg Tamoxifen every 24 hours (QD) on days 1 to days 28 of a 28 day cycle.	
Reporting group title	150mg Abemaciclib
Reporting group description:	
Participants received oral dose of 150 milligrams (mg) Abemaciclib every 12 hours (Q12H) on days 1 to days 28 of a 28 day cycle.	
Reporting group title	200mg Abemaciclib + 2mg Prophylactic Loperamide
Reporting group description:	
Participants received oral dose of 200 milligrams (mg) Abemaciclib every 12 hours (Q12H) along with 2mg Prophylactic Loperamide on days 1 to days 28 of a 28 day cycle. Note: During Cycle 1, 2mg prophylactic loperamide was administered orally with the first dose of abemaciclib daily. During Cycle 2 and beyond, loperamide was administered at investigator's discretion and/or if clinically indicated.	

Reporting group values	150 milligram (mg) Abemaciclib + 20mg Tamoxifen	150mg Abemaciclib	200mg Abemaciclib + 2mg Prophylactic Loperamide
Number of subjects	78	79	77
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	54.28	56.18	55.86
standard deviation	± 12.47	± 12.24	± 11.03
Gender categorical Units: Subjects			
Female	78	79	77
Male	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	16	20	21
Not Hispanic or Latino	55	45	46
Unknown or Not Reported	7	14	10
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	4	3	4
Asian	8	6	10
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	1	2
White	63	64	60
More than one race	0	1	0
Unknown or Not Reported	1	4	1

Reporting group values	Total		
Number of subjects	234		

Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	234		
Male	0		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	57		
Not Hispanic or Latino	146		
Unknown or Not Reported	31		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	11		
Asian	24		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	5		
White	187		
More than one race	1		
Unknown or Not Reported	6		

End points

End points reporting groups

Reporting group title	150 milligram (mg) Abemaciclib + 20mg Tamoxifen
Reporting group description:	
Participants received oral dose of 150 mg Abemaciclib every 12 hours (Q12H) along with 20mg Tamoxifen every 24 hours (QD) on days 1 to days 28 of a 28 day cycle.	
Reporting group title	150mg Abemaciclib
Reporting group description:	
Participants received oral dose of 150 milligrams (mg) Abemaciclib every 12 hours (Q12H) on days 1 to days 28 of a 28 day cycle.	
Reporting group title	200mg Abemaciclib + 2mg Prophylactic Loperamide
Reporting group description:	
Participants received oral dose of 200 milligrams (mg) Abemaciclib every 12 hours (Q12H) along with 2mg Prophylactic Loperamide on days 1 to days 28 of a 28 day cycle. Note: During Cycle 1, 2mg prophylactic loperamide was administered orally with the first dose of abemaciclib daily. During Cycle 2 and beyond, loperamide was administered at investigator's discretion and/or if clinically indicated.	

Primary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)
End point description:	
Progression-free survival time was measured from the date of randomization to the date of investigator-determined objective progression as defined by RECIST v1.1, or death from any cause, whichever occurred first. Progressive disease (PD) is defined as 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. Participants who have neither progressed nor died were censored at the day of their last radiographic tumor assessment (if available) or date of randomization if no post baseline radiographic assessment is available. Analysis population description (APD) included all randomized participants who received at least one dose of study drug. Censored participants: 21 in Abemaciclib 150 mg + Tamoxifen 20mg; 25 in Abemaciclib 150 mg; 22 in Abemaciclib 200mg.	
End point type	Primary
End point timeframe:	
Baseline to Objective Disease Progression or Death from Any Cause (Up to 21 Months)	

End point values	150 milligram (mg) Abemaciclib + 20mg Tamoxifen	150mg Abemaciclib	200mg Abemaciclib + 2mg Prophylactic Loperamide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	79	77	
Units: Months				
median (confidence interval 95%)	9.07 (6.90 to 10.95)	6.48 (4.77 to 9.21)	7.43 (5.42 to 9.17)	

Statistical analyses

Statistical analysis title	PFS: Statistical analysis 1
Comparison groups	150 milligram (mg) Abemaciclib + 20mg Tamoxifen v 200mg Abemaciclib + 2mg Prophylactic Loperamide
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.293 [1]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.815
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.556
upper limit	1.193

Notes:

[1] - Two-sided P-value. Stratified by the randomization factors of presence of liver metastases and prior use of Tamoxifen in the advanced/metastatic setting

Statistical analysis title	PFS: Statistical analysis 2
Comparison groups	200mg Abemaciclib + 2mg Prophylactic Loperamide v 150mg Abemaciclib
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.8109 [3]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.045
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.711
upper limit	1.535

Notes:

[2] - Informal phase 2 non-inferiority.

[3] - Stratified by the randomization factors of presence of liver metastases and prior use of Tamoxifen in the advanced/metastatic setting.

Secondary: Objective Response Rate (ORR): Percentage of Participants with a Complete Response (CR) or Partial Response (PR)

End point title	Objective Response Rate (ORR): Percentage of Participants with a Complete Response (CR) or Partial Response (PR)

End point description:

Objective response rate was defined as the percentage of participants with CR or PR according to RECIST v1.1. CR was defined as the disappearance of all target and non-target lesions and no appearance of new lesions. PR was defined as at least a 30% decrease in the sum of the LD (longest diameter) of target lesions (taking as reference the baseline sum LD), no progression of non-target lesions, and no appearance of new lesions. APD included all randomized participants who received at least one dose of study drug and had PR/CR data.

End point type	Secondary

End point timeframe:

Baseline to Objective Disease Progression (Up to 21 Months)

End point values	150 milligram (mg) Abemaciclib + 20mg Tamoxifen	150mg Abemaciclib	200mg Abemaciclib + 2mg Prophylactic Loperamide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	79	77	
Units: Percentage of participants				
number (confidence interval 95%)	34.6 (24.1 to 45.2)	24.1 (14.6 to 33.5)	32.5 (22 to 42.9)	

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 defined as the time from the date of first evidence of a CR or PR to the date of objective progression or death from any cause, whichever is earlier as defined by Recist v1.1. CR was defined as the disappearance of all target and non-target lesions and no appearance of new lesions. PR was 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. APD included all randomized participants who received at least one dose of study drug and achieved CR or PR. Censored participants: 9 in Abemaciclib 150 mg + Tamoxifen 20mg; 9 in Abemaciclib 150 mg; 11 in Abemaciclib 200mg.

End point type	Secondary

End point timeframe:

Date of CR or PR to Date of Objective Disease Progression or Death Due to Any Cause (Up to 21 Months)

End point values	150 milligram (mg) Abemaciclib + 20mg Tamoxifen	150mg Abemaciclib	200mg Abemaciclib + 2mg Prophylactic Loperamide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	27	19[4]	25	
Units: Months				
median (confidence interval 95%)	7.40 (3.88 to 9.27)	9.21 (3.72 to 9999)	7.46 (5.56 to 10.92)	

Notes:

[4] - 9999=Data Not Available (N/A): Upper bound not estimable.

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Mean Single Dose Concentration of Abemaciclib and its Metabolites

End point title	Pharmacokinetics (PK): Mean Single Dose Concentration of Abemaciclib and its Metabolites

End point description:

Mean single dose concentrations of Abemaciclib and its metabolites (M2 & M20) are reported. APD included all randomized participants who received at least one dose of study drug and had evaluable PK samples.

End point type	Secondary

End point timeframe:

Cycle (C) 1 Day (D) 1 post dose

End point values	150 milligram (mg) Abemaciclib + 20mg Tamoxifen	150mg Abemaciclib	200mg Abemaciclib + 2mg Prophylactic Loperamide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	13	20	
Units: Nanogram per Millilitre (ng/mL)				
geometric mean (geometric coefficient of variation)				
Abemaciclib (C1D1)	10.9 (± 231)	3.05 (± 95.4)	8.59 (± 440)	
M2 (C1D1)	6.05 (± 123)	2.14 (± 60.1)	6.85 (± 237)	
M20 (C1D1)	6.50 (± 132)	2.54 (± 54.5)	7.91 (± 220)	

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Steady State Concentration of Abemaciclib and its Metabolites

End point title	Pharmacokinetics (PK): Steady State Concentration of Abemaciclib and its Metabolites

End point description:

Mean steady state concentrations of Abemaciclib and its metabolites (M2 & M20) are reported. APD included all randomized participants who received at least one dose of study drug and had evaluable PK samples.

End point type	Secondary

End point timeframe:

Cycle 1 Day 15, Cycle 2 Day 1, Cycle 2 Day 15, Cycle 3 Day 1 post dose

End point values	150 milligram (mg) Abemaciclib + 20mg Tamoxifen	150mg Abemaciclib	200mg Abemaciclib + 2mg Prophylactic Loperamide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	55	56	46	
Units: Nanogram per Millilitre (ng/mL)				
geometric mean (geometric coefficient of variation)				
Abemaciclib (C1D15)	214 (± 66.4)	256 (± 58.8)	314 (± 74.3)	
M2 (C1D15)	96.5 (± 53.9)	108 (± 45.6)	147 (± 47.1)	
M20 (C1D15)	180 (± 51.1)	199 (± 41.0)	251 (± 48.5)	
Abemaciclib (C2D1)	98.9 (± 196)	182 (± 129)	220 (± 154)	
M2 (C2D1)	56.1 (± 88.0)	85.4 (± 62.1)	105 (± 98.5)	
M20 (C2D1)	100 (± 103)	149 (± 78.9)	164 (± 171)	
Abemaciclib (C2D15)	135 (± 115)	157 (± 173)	175 (± 136)	
M2 (C2D15)	62.3 (± 79.0)	71.7 (± 97.9)	95.4 (± 73.9)	
M20 (C2D15)	120 (± 76.2)	128 (± 121)	154 (± 101)	
Abemaciclib (C3D1)	125 (± 64.3)	177 (± 42.0)	207 (± 49)	
M2 (C3D1)	60.6 (± 39.6)	78.4 (± 38.2)	95.8 (± 44.2)	
M20 (C3D1)	109 (± 39.4)	146 (± 37.7)	171 (± 36.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK: Mean Single Dose Concentration of Tamoxifen and Endoxifen

End point title	PK: Mean Single Dose Concentration of Tamoxifen and Endoxifen[5]

End point description:

Mean single dose concentrations of Tamoxifen and its metabolite (Endoxifen) were reported. APD included all randomized participants who received at least one dose of study drug along with Tamoxifen and had evaluable PK samples. 9999=Data Not Available (N/A): Geometric Mean was not able to be calculated due to small sample size (2 Participants).

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 post dose

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive statistics was added in only specific baseline period reporting arms with evaluable PK data.

End point values	150 milligram (mg) Abemaciclib + 20mg Tamoxifen			
Subject group type	Reporting group			
Number of subjects analysed	21[6]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				

Tamoxifen (C1D1)	7.47 (± 116)			
Endoxifen (C1D1)	9999 (± 9999)			

Notes:

[6] - Endoxifen (C1D1): n = 2; Individual values = 0.653 ng/mL, 3.8 ng/mL.

Statistical analyses

No statistical analyses for this end point

Secondary: PK: Multiple Dose Concentration of Tamoxifen and Endoxifen

End point title	PK: Multiple Dose Concentration of Tamoxifen and Endoxifen[7]

End point description:

Mean multiple dose concentrations of Tamoxifen and its metabolite (Endoxifen) were reported. APD included all randomized participants who received at least one dose of study drug along with Tamoxifen and had evaluable PK samples.

End point type	Secondary

End point timeframe:

Cycle 1 Day 15, Cycle 2 Day 1, Cycle 2 Day 15, Cycle 3 Day 1 post dose

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive statistics was added in only specific baseline period reporting arms with evaluable PK data.

End point values	150 milligram (mg) Abemaciclib + 20mg Tamoxifen			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Tamoxifen (C1D15)	84.5 (± 41.6)			
Endoxifen (C1D15)	4.76 (± 99.7)			
Tamoxifen (C2D1)	98.7 (± 50.2)			
Endoxifen (C2D1)	7.41 (± 89.5)			
Tamoxifen (C2D15)	109 (± 51.9)			
Endoxifen (C2D15)	9.17 (± 73.7)			
Tamoxifen (C3D1)	112 (± 60.2)			
Endoxifen (C3D1)	10.3 (± 84.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Symptom Burden on the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC QLQ-C30)

End point title	Change from Baseline in Symptom Burden on the European

	Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC QLQ-C30)

End point description:

The EORTC QLQ-C30 self-reported general cancer instrument consists of 30 items covered by 1 of 3 dimensions:
1) Global health status/quality of life (2 items) with scores ranging from 1 (Very Poor) to 7 (Excellent).
2) Functional scales (15 total items addressing either physical, role, emotional, cognitive, or social functioning), each item scores ranging from 1 (not at all) to 4 (very much)
3) Symptom scales (13 total items addressing either fatigue, nausea/vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, or financial impact), each item scores ranging from 1 (not at all) to 4 (very much).
Raw scores are linearly converted to a 0–100 scale with higher scores reflecting higher levels of function/QOL or higher levels of symptom burden. APD included all randomized participants who received at least one dose of study drug with baseline and post-baseline EORTC QLQ-C30 score.

End point type	Secondary

End point timeframe:

Baseline, 21 Months

End point values	150 milligram (mg) Abemaciclib + 20mg Tamoxifen	150mg Abemaciclib	200mg Abemaciclib + 2mg Prophylactic Loperamide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	77	75	76	
Units: score on a scale				
least squares mean (standard deviation)				
Global Health Status	1.56 (± 1.83)	4.56 (± 1.90)	-2.77 (± 1.91)	
Functional Scales (Physical Functioning)	-2.01 (± 1.59)	-1.05 (± 1.68)	-2.65 (± 1.68)	
Functional Scales (Role Functioning)	-0.44 (± 2.18)	-3.95 (± 2.30)	-5.87 (± 2.29)	
Functional Scales (Emotional Functioning)	4.40 (± 1.88)	2.58 (± 1.95)	1.86 (± 1.95)	
Functional Scale (Cognitive Functioning)	0.14 (± 1.37)	-1.31 (± 1.44)	-2.39 (± 1.43)	
Functional Scales (Social Functioning)	3.23 (± 2.08)	-0.53 (± 2.16)	-0.94 (± 2.16)	
Symptom Scales (Fatigue)	2.39 (± 2.05)	2.77 (± 2.15)	4.0 (± 2.16)	
Symptom Scales (Nausea and Vomiting)	5.59 (± 1.63)	5.30 (± 1.73)	5.09 (± 1.71)	
Symptom Scales (Pain)	-3.09 (± 2.20)	-1.43 (± 2.30)	-2.01 (± 2.29)	
Symptom Scales (Dyspnoea)	4.21 (± 1.79)	-3.49 (± 1.89)	-2.0 (± 1.87)	
Symptom Scales (Insomnia)	-5.02 (± 2.21)	-3.43 (± 2.36)	-2.98 (± 2.35)	
Symptom Scales (Appetite Loss)	5.82 (± 2.38)	1.87 (± 2.50)	7.76 (± 2.50)	
Symptom Scales (Constipation)	-0.28 (± 1.57)	-6.29 (± 1.71)	0.08 (± 1.67)	
Symptom Scales (Diarrhoea)	13.31 (± 1.97)	20.17 (± 2.10)	17.43 (± 2.09)	
Symptom Scales (Functional Difficulties)	-7.56 (± 2.00)	-3.81 (± 2.08)	-0.09 (± 2.07)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Pain and Symptom Burden Assessment on the Modified Brief Pain Inventory-Short Form (mBPI-sf)

End point title	Change from Baseline in Pain and Symptom Burden

	Assessment on the Modified Brief Pain Inventory-Short Form (mBPI-sf)

End point description:

mBPI-sf is an 11-item instrument used as a multiple-item measure of cancer pain intensity. In addition to pain intensity (4 items), the mBPI-sf is designed for participants to record the presence of pain in general, pain relief, and pain interference with function (general activity, mood, ability to walk, ability to perform normal work, relations with others, sleep, enjoyment of life). Responses for the mBPI-sf items are captured through the use of 11-point numeric rating scales anchored at 0 (no pain or does not interfere) and 10 (pain as bad as you can imagine or completely interferes). The mBPI-sf recall period is 24 hours and typical completion time for this instrument is less than 5 minutes. APD included all randomized participants who received at least one dose of study drug and had baselines and post baseline mBPI-sf measurement.

End point type	Secondary

End point timeframe:

Baseline, 21 Months

End point values	150 milligram (mg) Abemaciclib + 20mg Tamoxifen	150mg Abemaciclib	200mg Abemaciclib + 2mg Prophylactic Loperamide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	76	75	
Units: score on a scale				
least squares mean (standard deviation)				
Pain at its Worst in Last 24 Hours	-0.53 (± 0.20)	-0.43 (± 0.21)	-0.43 (± 0.21)	
Pain at its Least in Last 24 Hours	-0.09 (± 0.15)	-0.01 (± 0.16)	0.14 (± 0.16)	
Pain on the Average	-0.34 (± 0.16)	-0.20 (± 0.17)	-0.11 (± 0.17)	
Pain Right Now	-0.28 (± 0.17)	-0.18 (± 0.17)	-0.04 (± 0.17)	
Mean Interference Score	-0.09 (± 0.18)	0.03 (± 0.18)	0.16 (± 0.18)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 21 Months	
Adverse event reporting additional description:	
All randomized participants who received at least one dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups	
Reporting group title	150mg Abemaciclib + 20mg Tamoxifen
Reporting group description:	
Participants received oral dose of 150 milligrams (mg) Abemaciclib every 12 hours (Q12H) along with 20mg Tamoxifen every 24 hours (QD) on days 1 to days 28 of a 28 day cycle.	
Reporting group title	150mg Abemaciclib
Reporting group description:	
Participants received oral dose of 150 milligrams (mg) Abemaciclib every 12 hours (Q12H) on days 1 to days 28 of a 28 day cycle.	
Reporting group title	200mg Abemaciclib + 2mg Prophylactic Loperamide
Reporting group description:	
Participants received oral dose of 200 milligrams (mg) Abemaciclib every 12 hours (Q12H) along with 2mg Prophylactic Loperamide on days 1 to days 28 of a 28 day cycle. Note: During Cycle 1, 2mg prophylactic loperamide was administered orally with the first dose of abemaciclib daily. During Cycle 2 and beyond, loperamide was administered at investigator's discretion and/or if clinically indicated.	

Serious adverse events	150mg Abemaciclib + 20mg Tamoxifen	150mg Abemaciclib	200mg Abemaciclib + 2mg Prophylactic Loperamide
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 78 (20.51%)	16 / 79 (20.25%)	21 / 77 (27.27%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	0 / 78 (0.00%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
blood creatinine increased			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 78 (1.28%)	0 / 79 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
haemoglobin decreased			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
neutrophil count decreased			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 78 (1.28%)	0 / 79 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
deep vein thrombosis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 78 (1.28%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypertensive crisis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
acute coronary syndrome			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	0 / 78 (0.00%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cardiac arrest			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 78 (1.28%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
cardio-respiratory arrest			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	1 / 79 (1.27%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Nervous system disorders			
cerebral ischaemia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ischaemic stroke			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	1 / 79 (1.27%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
monoparesis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
paraesthesia			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	0 / 78 (0.00%)	1 / 79 (1.27%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
spinal cord compression			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 78 (1.28%)	0 / 79 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 78 (1.28%)	1 / 79 (1.27%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
disseminated intravascular coagulation			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 78 (1.28%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 1
haemolytic anaemia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	1 / 79 (1.27%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
leukopenia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	3 / 79 (3.80%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
neutropenia			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	0 / 78 (0.00%)	2 / 79 (2.53%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pancytopenia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 78 (1.28%)	0 / 79 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
thrombocytopenia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	2 / 79 (2.53%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	2 / 78 (2.56%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
fatigue			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	1 / 79 (1.27%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
multiple organ dysfunction syndrome			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	1 / 79 (1.27%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
pain			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	0 / 78 (0.00%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pyrexia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 78 (1.28%)	2 / 79 (2.53%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 1	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
constipation			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
diarrhoea			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 78 (1.28%)	1 / 79 (1.27%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
dyspepsia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastrointestinal toxicity			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 78 (1.28%)	0 / 79 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intestinal obstruction			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	1 / 78 (1.28%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 4	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
nausea			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	1 / 79 (1.27%)	2 / 77 (2.60%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
vomiting			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 78 (1.28%)	1 / 79 (1.27%)	2 / 77 (2.60%)
occurrences causally related to treatment / all	0 / 1	1 / 1	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
cholangitis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 78 (1.28%)	0 / 79 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hepatic failure			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 78 (1.28%)	1 / 79 (1.27%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
dyspnoea			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 78 (1.28%)	2 / 79 (2.53%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pleural effusion			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	1 / 78 (1.28%)	0 / 79 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia aspiration			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
pneumonitis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	1 / 79 (1.27%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumothorax			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	1 / 79 (1.27%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pulmonary embolism			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	2 / 78 (2.56%)	2 / 79 (2.53%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	2 / 2	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pulmonary oedema			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	1 / 78 (1.28%)	1 / 79 (1.27%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
glomerulonephritis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
influenza			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lung infection			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	1 / 79 (1.27%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pharyngitis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	1 / 79 (1.27%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 78 (1.28%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
respiratory tract infection			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	0 / 78 (0.00%)	1 / 79 (1.27%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sepsis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	1 / 79 (1.27%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
upper respiratory tract infection			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urinary tract infection			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
viral infection			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
dehydration			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	1 / 79 (1.27%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypercalcaemia			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	1 / 78 (1.28%)	0 / 79 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hyponatraemia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	1 / 79 (1.27%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	150mg Abemaciclib + 20mg Tamoxifen	150mg Abemaciclib	200mg Abemaciclib + 2mg Prophylactic Loperamide
Total subjects affected by non-serious adverse events			
subjects affected / exposed	73 / 78 (93.59%)	77 / 79 (97.47%)	75 / 77 (97.40%)
Vascular disorders			
hot flush			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	6 / 78 (7.69%)	2 / 79 (2.53%)	1 / 77 (1.30%)
occurrences (all)	9	2	2
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	14 / 78 (17.95%)	14 / 79 (17.72%)	6 / 77 (7.79%)
occurrences (all)	26	20	7
fatigue			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	22 / 78 (28.21%)	17 / 79 (21.52%)	21 / 77 (27.27%)
occurrences (all)	32	30	41
mucosal inflammation			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	2 / 77 (2.60%)
occurrences (all)	8	4	2
oedema peripheral			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	3 / 78 (3.85%)	6 / 79 (7.59%)	7 / 77 (9.09%)
occurrences (all)	4	8	7
pyrexia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	7 / 78 (8.97%)	5 / 79 (6.33%)	8 / 77 (10.39%)
occurrences (all)	8	7	8
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	7 / 78 (8.97%)	7 / 79 (8.86%)	10 / 77 (12.99%)
occurrences (all)	8	7	14
dyspnoea			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	8 / 78 (10.26%)	12 / 79 (15.19%)	5 / 77 (6.49%)
occurrences (all)	9	15	10
Psychiatric disorders			
anxiety			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	0 / 78 (0.00%)	5 / 79 (6.33%)	2 / 77 (2.60%)
occurrences (all)	0	5	2
insomnia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	3 / 78 (3.85%)	2 / 79 (2.53%)	5 / 77 (6.49%)
occurrences (all)	3	2	5
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	6 / 78 (7.69%)	4 / 79 (5.06%)	5 / 77 (6.49%)
occurrences (all)	10	6	8
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	8 / 78 (10.26%)	4 / 79 (5.06%)	7 / 77 (9.09%)
occurrences (all)	12	5	8
blood alkaline phosphatase increased			
alternative dictionary used:			

MedDRA 20.0			
subjects affected / exposed	4 / 78 (5.13%)	3 / 79 (3.80%)	4 / 77 (5.19%)
occurrences (all)	10	4	4
blood creatinine increased			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	14 / 78 (17.95%)	7 / 79 (8.86%)	8 / 77 (10.39%)
occurrences (all)	35	15	11
gamma-glutamyltransferase increased			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	3 / 78 (3.85%)	5 / 79 (6.33%)	3 / 77 (3.90%)
occurrences (all)	5	13	7
lymphocyte count decreased			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 78 (1.28%)	5 / 79 (6.33%)	3 / 77 (3.90%)
occurrences (all)	1	20	4
neutrophil count decreased			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	11 / 78 (14.10%)	21 / 79 (26.58%)	22 / 77 (28.57%)
occurrences (all)	22	71	81
platelet count decreased			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	8 / 78 (10.26%)	9 / 79 (11.39%)	22 / 77 (28.57%)
occurrences (all)	14	22	49
weight decreased			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	5 / 78 (6.41%)	9 / 79 (11.39%)	5 / 77 (6.49%)
occurrences (all)	9	10	6
white blood cell count decreased			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	12 / 78 (15.38%)	18 / 79 (22.78%)	15 / 77 (19.48%)
occurrences (all)	26	56	52
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	2 / 78 (2.56%)	5 / 79 (6.33%)	2 / 77 (2.60%)
occurrences (all)	2	7	2
dysgeusia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	4 / 78 (5.13%)	4 / 79 (5.06%)	3 / 77 (3.90%)
occurrences (all)	5	4	3
headache			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	7 / 78 (8.97%)	6 / 79 (7.59%)	7 / 77 (9.09%)
occurrences (all)	11	7	7
paraesthesia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	3 / 78 (3.85%)	4 / 79 (5.06%)	3 / 77 (3.90%)
occurrences (all)	5	5	3
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	30 / 78 (38.46%)	24 / 79 (30.38%)	31 / 77 (40.26%)
occurrences (all)	63	36	68
leukopenia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	9 / 78 (11.54%)	10 / 79 (12.66%)	6 / 77 (7.79%)
occurrences (all)	24	23	9
neutropenia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	21 / 78 (26.92%)	20 / 79 (25.32%)	18 / 77 (23.38%)
occurrences (all)	64	46	51
thrombocytopenia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	8 / 78 (10.26%)	1 / 79 (1.27%)	5 / 77 (6.49%)
occurrences (all)	18	1	5
Eye disorders			
dry eye			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	0 / 78 (0.00%)	4 / 79 (5.06%)	0 / 77 (0.00%)
occurrences (all)	0	4	0
lacrimation increased			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	2 / 78 (2.56%)	6 / 79 (7.59%)	4 / 77 (5.19%)
occurrences (all)	2	7	5
Gastrointestinal disorders			
abdominal distension			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	4 / 78 (5.13%)	4 / 79 (5.06%)	3 / 77 (3.90%)
occurrences (all)	5	5	3
abdominal pain upper			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	6 / 78 (7.69%)	8 / 79 (10.13%)	6 / 77 (7.79%)
occurrences (all)	7	10	7
abdominal pain			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	16 / 78 (20.51%)	11 / 79 (13.92%)	19 / 77 (24.68%)
occurrences (all)	21	17	21
constipation			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	10 / 78 (12.82%)	9 / 79 (11.39%)	25 / 77 (32.47%)
occurrences (all)	16	13	28
diarrhoea			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	41 / 78 (52.56%)	53 / 79 (67.09%)	47 / 77 (61.04%)
occurrences (all)	161	244	140
dyspepsia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	7 / 78 (8.97%)	3 / 79 (3.80%)	4 / 77 (5.19%)
occurrences (all)	7	3	6
haemorrhoids			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	4 / 78 (5.13%)	1 / 79 (1.27%)	1 / 77 (1.30%)
occurrences (all)	5	1	2
flatulence			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	4 / 78 (5.13%)	1 / 79 (1.27%)	3 / 77 (3.90%)
occurrences (all)	5	1	4
nausea			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	24 / 78 (30.77%)	26 / 79 (32.91%)	33 / 77 (42.86%)
occurrences (all)	48	47	50
stomatitis			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	5 / 78 (6.41%)	4 / 79 (5.06%)	4 / 77 (5.19%)
occurrences (all)	5	7	6
toothache			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	4 / 78 (5.13%)	0 / 79 (0.00%)	0 / 77 (0.00%)
occurrences (all)	4	0	0
vomiting			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	14 / 78 (17.95%)	20 / 79 (25.32%)	20 / 77 (25.97%)
occurrences (all)	34	62	34
Skin and subcutaneous tissue disorders			
alopecia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	5 / 78 (6.41%)	8 / 79 (10.13%)	3 / 77 (3.90%)
occurrences (all)	5	9	3
pruritus			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	8 / 78 (10.26%)	6 / 79 (7.59%)	4 / 77 (5.19%)
occurrences (all)	8	7	4
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	6 / 78 (7.69%)	5 / 79 (6.33%)	1 / 77 (1.30%)
occurrences (all)	8	7	1
back pain			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	8 / 78 (10.26%)	11 / 79 (13.92%)	2 / 77 (2.60%)
occurrences (all)	9	14	3
bone pain			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	4 / 78 (5.13%)	7 / 79 (8.86%)	0 / 77 (0.00%)
occurrences (all)	8	12	0
myalgia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	5 / 78 (6.41%)	2 / 79 (2.53%)	2 / 77 (2.60%)
occurrences (all)	7	2	2
musculoskeletal pain			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	2 / 78 (2.56%)	4 / 79 (5.06%)	4 / 77 (5.19%)
occurrences (all)	2	4	5
Infections and infestations			
upper respiratory tract infection			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	10 / 78 (12.82%)	4 / 79 (5.06%)	4 / 77 (5.19%)
occurrences (all)	11	6	5
urinary tract infection			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	7 / 78 (8.97%)	5 / 79 (6.33%)	5 / 77 (6.49%)
occurrences (all)	8	6	5
Metabolism and nutrition disorders			
dehydration			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 78 (1.28%)	0 / 79 (0.00%)	5 / 77 (6.49%)
occurrences (all)	1	0	6
decreased appetite			
alternative dictionary used: MedDRA 20.0			

subjects affected / exposed	20 / 78 (25.64%)	12 / 79 (15.19%)	17 / 77 (22.08%)
occurrences (all)	29	21	27
hypocalcaemia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	4 / 78 (5.13%)	2 / 79 (2.53%)	1 / 77 (1.30%)
occurrences (all)	5	2	1
hypoalbuminaemia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	6 / 78 (7.69%)	3 / 79 (3.80%)	6 / 77 (7.79%)
occurrences (all)	9	3	11
hypertriglyceridaemia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	10 / 78 (12.82%)	3 / 79 (3.80%)	2 / 77 (2.60%)
occurrences (all)	22	3	4
hyperglycaemia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	1 / 78 (1.28%)	5 / 79 (6.33%)	3 / 77 (3.90%)
occurrences (all)	1	6	3
hypokalaemia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	3 / 78 (3.85%)	8 / 79 (10.13%)	9 / 77 (11.69%)
occurrences (all)	4	11	10
hyponatraemia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	4 / 78 (5.13%)	1 / 79 (1.27%)	2 / 77 (2.60%)
occurrences (all)	7	1	2
hypophosphataemia			
alternative dictionary used: MedDRA 20.0			
subjects affected / exposed	5 / 78 (6.41%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences (all)	5	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 January 2019	- Inclusion criteria modified; - Safety monitoring information modified for hepatic conditions, renal function and venous thromboembolic events (VTEs); - Cytochromes P450 (CYPs) text updated to align with abemaciclib program information.
07 February 2020	- Dose modification updated and delay guidance for interstitial lung disease (ILD)/pneumonitis events that aligns with the updated Investigator's Brochure; - Investigator's brochure updated.
08 March 2021	- Dose adjustment criteria updated; - Concomitant therapy information was updated for CYP3A modulators and transporter substrates; -Safety monitoring language was updated to align with current guidance and the IB respectively.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported