Clinical trial results:
A Phase 2 Study of Abemaciclib in Patients with Brain Metastases Secondary to Hormone Receptor Positive Breast Cancer

Summary

EudraCT number	2014-004010-28
Trial protocol	AT BE FR ES IT
Global end of trial date	08 November 2019

Results information

Result version number	v1 (current)
This version publication date	10 December 2020
First version publication date	10 December 2020

Trial information

Trial identification

Sponsor protocol code	I3Y-MC-JPBO

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02308020
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 15450

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	08 November 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 November 2019
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 the safety and effectiveness of the study drug known as abemaciclib in participants with hormone receptor positive breast cancer, non-small cell lung cancer (NSCLC), or melanoma that has spread to the brain.

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 April 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Belgium: 18
Country: Number of subjects enrolled	United States: 71
Country: Number of subjects enrolled	Italy: 15
Country: Number of subjects enrolled	Israel: 6
Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	France: 32
Country: Number of subjects enrolled	Spain: 7
Worldwide total number of subjects	162
EEA total number of subjects	73

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)	123
From 65 to 84 years	39
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

No Text Available

Pre-assignment

Screening details:

Completers include participants who died or discontinued study treatment due to progressive disease and is in follow up.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A Abemaciclib: Hormone Receptor (HR+) HER2+ Breast Cancer

Arm description:

Abemaciclib 200 milligram (mg) was administered orally once every 12 hours on days 1-21 of a 21-day cycle when administered as a single agent or in combination with endocrine therapy (ET). Participants with hormone receptor positive (HR+), hormone epidermal growth factor receptor 2 positive (HER2+) breast cancer receiving concurrent trastuzumab, 150 mg abemaciclib was given orally once every 12 hours on days 1-21 of a 21-day 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:

Abemaciclib 200 milligram (mg) was administered orally once every 12 hours on days 1-21 of a 21-day cycle.

Arm title	Part B Abemaciclib: HR+, HER2- Breast Cancer

Arm description:

Abemaciclib 200 mg was administered orally once every 12 hours on days 1-21 of a 21-day cycle when administered as a single agent or in combination with endocrine therapy (ET).

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	LY2835219
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Abemaciclib 200 mg was administered orally once every 12 hours on days 1-21 of a 21-day cycle

Arm title	Part C Abemaciclib: Surgical Resection

Arm description:

Abemaciclib 200 mg was administered orally once every 12 hours on days 1-21 of a 21-day cycle when administered as a single agent or for participants with breast cancer in combination with endocrine

therapy (ET). Participants with HR+, HER2+ breast cancer, NSCLC, or melanoma with intracranial lesions for which surgical resection is clinically indicated receiving concurrent trastuzumab, gemcitabine, or pemetrexed, 150 mg abemaciclib was given orally once every 12 hours for 5-14 days prior to surgical resection. Dosing may resume following wound healing on a 21-day 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:

Abemaciclib 200 mg was administered orally once every 12 hours on days 1-21 of a 21-day cycle

Arm title	Part D Abemaciclib: Non-Small Cell Lung Cancer (NSCLC)

Arm description:

Abemaciclib 200 mg was administered orally once every 12 hours on days 1-21 of a 21-day cycle. Participants with NSCLC receiving concurrent gemcitabine or pemetrexed, 150 mg abemaciclib was given orally once every 12 hours on days 1-21 of a 21-day 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	LY2835219
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Abemaciclib 200 mg was administered orally once every 12 hours on days 1-21 of a 21-day cycle

Arm title	Part E Abemaciclib: Melanoma

Arm description:

Abemaciclib 200 mg was administered orally once every 12 hours on days 1-21 of a 21-day 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	LY2835219
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Abemaciclib 200 mg was administered orally once every 12 hours on days 1-21 of a 21-day cycle

Arm title	Part F Abemaciclib: HR+ Breast Cancer, NSCLC, or Melanoma

Arm description:

Abemaciclib 200 mg was administered orally once every 12 hours on days 1-21 of a 21-day cycle when administered as a single agent or for participants with breast cancer in combination with endocrine therapy (ET). Participants with HR+ (either HER2+ or HER2-) breast cancer, NSCLC, or melanoma and leptomeningeal metastases received concurrent trastuzumab, gemcitabine, or pemetrexed, 150 mg abemaciclib was given orally once every 12 hours on days 1-21 of a 21-day 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	LY2835219
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Abemaciclib 200 mg was administered orally once every 12 hours on days 1-21 of a 21-day cycle

Number of subjects in period 1	Part A Abemaciclib: Hormone Receptor (HR+) HER2+ Breast Cancer	Part B Abemaciclib: HR+, HER2- Breast Cancer	Part C Abemaciclib: Surgical Resection
Started	27	58	9
Received at least one dose of study drug	27	58	9
Completed	23	38	6
Not completed	4	20	3
Consent withdrawn by subject	3	5	3
Sponsor Decision	-	8	-
Lost to follow-up	1	7	-

Number of subjects in period 1	Part D Abemaciclib: Non-Small Cell Lung Cancer (NSCLC)	Part E Abemaciclib: Melanoma	Part F Abemaciclib: HR+ Breast Cancer, NSCLC, or Melanoma
Started	28	23	17
Received at least one dose of study drug	28	23	17
Completed	24	19	12
Not completed	4	4	5
Consent withdrawn by subject	2	1	2
Sponsor Decision	2	2	1
Lost to follow-up	-	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Part A Abemaciclib: Hormone Receptor (HR+) HER2+ Breast Cancer

Reporting group description:

Abemaciclib 200 milligram (mg) was administered orally once every 12 hours on days 1-21 of a 21-day cycle when administered as a single agent or in combination with endocrine therapy (ET). Participants with hormone receptor positive (HR+), hormone epidermal growth factor receptor 2 positive (HER2+) breast cancer receiving concurrent trastuzumab, 150 mg abemaciclib was given orally once every 12 hours on days 1-21 of a 21-day cycle. Participants may continue to receive treatment until discontinuation criteria are met.

Reporting group title	Part B Abemaciclib: HR+, HER2- Breast Cancer

Reporting group description:

Abemaciclib 200 mg was administered orally once every 12 hours on days 1-21 of a 21-day cycle when administered as a single agent or in combination with endocrine therapy (ET).

Participants may continue to receive treatment until discontinuation criteria are met.

Reporting group title	Part C Abemaciclib: Surgical Resection

Reporting group description:

Abemaciclib 200 mg was administered orally once every 12 hours on days 1-21 of a 21-day cycle when administered as a single agent or for participants with breast cancer in combination with endocrine therapy (ET). Participants with HR+, HER2+ breast cancer, NSCLC, or melanoma with intracranial lesions for which surgical resection is clinically indicated receiving concurrent trastuzumab, gemcitabine, or pemetrexed, 150 mg abemaciclib was given orally once every 12 hours for 5-14 days prior to surgical resection. Dosing may resume following wound healing on a 21-day cycle. Participants may continue to receive treatment until discontinuation criteria are met.

Reporting group title	Part D Abemaciclib: Non-Small Cell Lung Cancer (NSCLC)

Reporting group description:

Abemaciclib 200 mg was administered orally once every 12 hours on days 1-21 of a 21-day cycle. Participants with NSCLC receiving concurrent gemcitabine or pemetrexed, 150 mg abemaciclib was given orally once every 12 hours on days 1-21 of a 21-day cycle. Participants may continue to receive treatment until discontinuation criteria are met.

Reporting group title	Part E Abemaciclib: Melanoma

Reporting group description:

Abemaciclib 200 mg was administered orally once every 12 hours on days 1-21 of a 21-day cycle. Participants may continue to receive treatment until discontinuation criteria are met.

Reporting group title	Part F Abemaciclib: HR+ Breast Cancer, NSCLC, or Melanoma

Reporting group description:

Abemaciclib 200 mg was administered orally once every 12 hours on days 1-21 of a 21-day cycle when administered as a single agent or for participants with breast cancer in combination with endocrine therapy (ET). Participants with HR+ (either HER2+ or HER2-) breast cancer, NSCLC, or melanoma and leptomeningeal metastases received concurrent trastuzumab, gemcitabine, or pemetrexed, 150 mg abemaciclib was given orally once every 12 hours on days 1-21 of a 21-day cycle. Participants may continue to receive treatment until discontinuation criteria are met.

Reporting group values	Part A Abemaciclib: Hormone Receptor (HR+) HER2+ Breast Cancer	Part B Abemaciclib: HR+, HER2- Breast Cancer	Part C Abemaciclib: Surgical Resection
Number of subjects	27	58	9
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	49.9	54.1	57.0
standard deviation	± 10.9	± 10.5	± 17.9
Gender categorical Units: Subjects			
Female	27	57	8
Male	0	1	1
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	3	0
Not Hispanic or Latino	21	42	8
Unknown or Not Reported	6	13	1
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	3	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	4	0
White	17	35	7
More than one race	1	1	0
Unknown or Not Reported	7	15	1
Region of Enrollment Units: Subjects			
Canada	0	1	0
Austria	0	1	0
Belgium	4	8	0
United States	11	24	7
Italy	0	4	0
Israel	1	2	0
Australia	2	2	1
France	7	14	1
Spain	2	2	0

Reporting group values	Part D Abemaciclib: Non-Small Cell Lung Cancer (NSCLC)	Part E Abemaciclib: Melanoma	Part F Abemaciclib: HR+ Breast Cancer, NSCLC, or Melanoma
Number of subjects	28	23	17
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	58.4	55.1	50.1
standard deviation	± 10.9	± 14.4	± 12.3
Gender categorical Units: Subjects			
Female	14	11	14
Male	14	12	3

Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	1
Not Hispanic or Latino	20	20	14
Unknown or Not Reported	8	2	2
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	1
White	20	22	14
More than one race	0	0	0
Unknown or Not Reported	7	1	2
Region of Enrollment Units: Subjects			
Canada	0	0	2
Austria	0	0	0
Belgium	3	3	0
United States	12	7	10
Italy	2	9	0
Israel	1	1	1
Australia	2	1	1
France	7	1	2
Spain	1	1	1

Reporting group values	Total		
Number of subjects	162		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	131		
Male	31		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	5		
Not Hispanic or Latino	125		
Unknown or Not Reported	32		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	5		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	7		

White	115		
More than one race	2		
Unknown or Not Reported	33		
Region of Enrollment Units: Subjects			
Canada	3		
Austria	1		
Belgium	18		
United States	71		
Italy	15		
Israel	6		
Australia	9		
France	32		
Spain	7		

End points reporting groups

Reporting group title	Part A Abemaciclib: Hormone Receptor (HR+) HER2+ Breast Cancer

Reporting group description:

Abemaciclib 200 milligram (mg) was administered orally once every 12 hours on days 1-21 of a 21-day cycle when administered as a single agent or in combination with endocrine therapy (ET). Participants with hormone receptor positive (HR+), hormone epidermal growth factor receptor 2 positive (HER2+) breast cancer receiving concurrent trastuzumab, 150 mg abemaciclib was given orally once every 12 hours on days 1-21 of a 21-day cycle. Participants may continue to receive treatment until discontinuation criteria are met.

Reporting group title	Part B Abemaciclib: HR+, HER2- Breast Cancer

Reporting group description:

Abemaciclib 200 mg was administered orally once every 12 hours on days 1-21 of a 21-day cycle when administered as a single agent or in combination with endocrine therapy (ET).

Participants may continue to receive treatment until discontinuation criteria are met.

Reporting group title	Part C Abemaciclib: Surgical Resection

Reporting group description:

Abemaciclib 200 mg was administered orally once every 12 hours on days 1-21 of a 21-day cycle when administered as a single agent or for participants with breast cancer in combination with endocrine therapy (ET). Participants with HR+, HER2+ breast cancer, NSCLC, or melanoma with intracranial lesions for which surgical resection is clinically indicated receiving concurrent trastuzumab, gemcitabine, or pemetrexed, 150 mg abemaciclib was given orally once every 12 hours for 5-14 days prior to surgical resection. Dosing may resume following wound healing on a 21-day cycle. Participants may continue to receive treatment until discontinuation criteria are met.

Reporting group title	Part D Abemaciclib: Non-Small Cell Lung Cancer (NSCLC)

Reporting group description:

Abemaciclib 200 mg was administered orally once every 12 hours on days 1-21 of a 21-day cycle. Participants with NSCLC receiving concurrent gemcitabine or pemetrexed, 150 mg abemaciclib was given orally once every 12 hours on days 1-21 of a 21-day cycle. Participants may continue to receive treatment until discontinuation criteria are met.

Reporting group title	Part E Abemaciclib: Melanoma

Reporting group description:

Abemaciclib 200 mg was administered orally once every 12 hours on days 1-21 of a 21-day cycle. Participants may continue to receive treatment until discontinuation criteria are met.

Reporting group title	Part F Abemaciclib: HR+ Breast Cancer, NSCLC, or Melanoma

Reporting group description:

Abemaciclib 200 mg was administered orally once every 12 hours on days 1-21 of a 21-day cycle when administered as a single agent or for participants with breast cancer in combination with endocrine therapy (ET). Participants with HR+ (either HER2+ or HER2-) breast cancer, NSCLC, or melanoma and leptomeningeal metastases received concurrent trastuzumab, gemcitabine, or pemetrexed, 150 mg abemaciclib was given orally once every 12 hours on days 1-21 of a 21-day cycle. Participants may continue to receive treatment until discontinuation criteria are met.

Subject analysis set title	Part A Abemaciclib: HR+, HER2+ Breast Cancer
Subject analysis set type	Per protocol

Subject analysis set description:

Abemaciclib 200 mg was administered orally once every 12 hours on days 1-21 of a 21-day cycle when administered as a single agent or in combination with endocrine therapy (ET). Participants with hormone receptor positive HR+, HER2+ breast cancer receiving concurrent trastuzumab, 150 mg abemaciclib was given orally once every 12 hours on days 1-21 of a 21-day cycle. Participants may continue to receive treatment until discontinuation criteria are met.

Subject analysis set title	Part D Abemaciclib: NSCLC
Subject analysis set type	Per protocol

Subject analysis set description:

Abemaciclib 200 mg was administered orally once every 12 hours on days 1-21 of a 21-day cycle. Participants with NSCLC receiving concurrent gemcitabine or pemetrexed, 150 mg abemaciclib was given orally once every 12 hours on days 1-21 of a 21-day cycle. Participants may continue to receive

treatment until discontinuation criteria are met.

Subject analysis set title	Part A 150 mg Abemaciclib: HR+, HER2+ Breast Cancer
Subject analysis set type	Per protocol

Subject analysis set description:

Participants with HR+, HER2+ breast cancer received 150 mg abemaciclib orally once every 12 hours on days 1-21 of a 21-day cycle.

Subject analysis set title	Part B 200 mg Abemaciclib: HR+, HER2- Breast Cancer
Subject analysis set type	Per protocol

Subject analysis set description:

Participants with HR+, HER2- breast cancer received 200 mg abemaciclib given orally once every 12 hours on days 1-21 of a 21-day cycle.

Subject analysis set title	Part C 200 mg Abemaciclib: Surgical Resection
Subject analysis set type	Per protocol

Subject analysis set description:

Participants with HR+ breast cancer, NSCLC, or melanoma with intracranial lesions for which surgical resection is clinically indicated received 200 mg abemaciclib given orally once every 12 hours for 5-14 days prior to surgical resection.

Subject analysis set title	Part D 200 mg Abemaciclib: NSCLC
Subject analysis set type	Per protocol

Subject analysis set description:

Participants with NSCLC received 200 mg abemaciclib given orally once every 12 hours on days 1-21 of a 21-day cycle.

Subject analysis set title	Part E 200 mg Abemaciclib: Melanoma
Subject analysis set type	Per protocol

Subject analysis set description:

Participants with melanoma received 200 mg abemaciclib given orally once every 12 hours on days 1-21 of a 21-day cycle.

Subject analysis set title	Part F 200 mg Abemaciclib: HR+ Breast Cancer, NSCLC, Melanoma
Subject analysis set type	Per protocol

Subject analysis set description:

Participants with HR+ (either HER2+ or HER2-) breast cancer, NSCLC, or melanoma and leptomeningeal metastases received 200 mg abemaciclib given orally once every 12 hours on days 1-21 of a 21-day cycle.

Primary: Percentage of Participants Achieving Complete Response (CR) or Partial Response (PR): Objective Intracranial Response Rate (OIRR)

End point title	Percentage of Participants Achieving Complete Response (CR) or Partial Response (PR): Objective Intracranial Response Rate (OIRR)[1][2]

End point description:

OIRR is the percentage of participants with a (CR) or (PR) based on the Response Assessment in Neuro-Oncology Brain Metastasis (RANO-BM) response criteria. CR is measurable target lesions, the disappearance of all central nervous system (CNS) target lesions for at least 4 weeks; no new lesions; no corticosteroids; stable or improved clinically. PR is at least a 30% decrease in the sum longest duration (LD) of CNS target lesions, taking as reference the baseline sum LD for at least 4 weeks; no new lesions; stable to decreased corticosteroid dose; stable or improved clinically. Nontarget lesions requires disappearance CNS non-target lesions and no new CNS lesions. Stable disease (SD) is less than (<)30% decrease relative to baseline but <20% increase in sum LD relative to nadir. Progressive disease (PD) is greater than or equal to (≥) 20% increase in sum LD relative to nadir and a relative increase of 20%, ≥1 lesion must increase by absolute value of ≥5 millimeter (mm).

End point type	Primary

End point timeframe:

Baseline to Objective Disease Progression (Up to 36 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: This is single arm cohort study, no comparison between arms were analyzed.

[2] - 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: All participants who had evaluable OIRR data with at least one measurable brain lesion at baseline (per RANO-BM) and for whom at least one post-baseline overall response assessment for intracranial disease is available. Parts C and F were exploratory per protocol.

End point values	Part A Abemaciclib: Hormone Receptor (HR+) HER2+ Breast Cancer	Part B Abemaciclib: HR+, HER2- Breast Cancer	Part D Abemaciclib: Non-Small Cell Lung Cancer (NSCLC)	Part E Abemaciclib: Melanoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23[3]	52[4]	23[5]	22[6]
Units: percentage of participants				
number (not applicable)	0	5.8	0	0

Notes:

[3] - All participants who had evaluable OIRR data per RANO-BM.

[4] - All participants who had evaluable OIRR data per RANO-BM.

[5] - All participants who had evaluable OIRR data per RANO-BM.

[6] - All participants who had evaluable OIRR data per RANO-BM.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with CR, PR, Stable Disease (SD), Progressive Disease (PD), or Not Evaluable (NE): Best Overall Intracranial Response (BOIR)

End point title	Percentage of Participants with CR, PR, Stable Disease (SD), Progressive Disease (PD), or Not Evaluable (NE): Best Overall Intracranial Response (BOIR)[7]

End point description:

Percentage of Participants with BOIR was categorized as CR, PR, SD, PD or NE, as defined by RANO-BM, from baseline until the earliest of objective progression according to brain metastases response criteria or start of new anticancer therapy. CR is measurable target lesions, the disappearance of all CNS target lesions for at least 4 weeks; no new lesions; no corticosteroids; stable or improved clinically. PR is at least a 30% decrease in the sum LD of CNS target lesions, taking as reference the baseline sum LD for at least 4 weeks; no new lesions; stable to decreased corticosteroid dose; stable or improved clinically. SD is <30% decrease relative to baseline but <20% increase in sum LD relative to nadir. PD is greater than or equal to (≥) 20% increase in sum LD relative to nadir and a relative increase of 20%, ≥1 lesion must increase by absolute value of ≥5 mm. NE is absent (no abnormality; normal), or non-evaluable (NE).

End point type	Secondary

End point timeframe:

Baseline to Earliest Objective Progression or Start of New Anticancer Therapy (Up to 36 Months)

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: All participants who had evaluable OIRR data with at least one measurable brain lesion at baseline (per RANO-BM) and for whom at least one post-baseline overall response assessment for intracranial disease is available. Parts C and F were exploratory per protocol.

End point values	Part A Abemaciclib: Hormone Receptor (HR+) HER2+ Breast Cancer	Part B Abemaciclib: HR+, HER2- Breast Cancer	Part D Abemaciclib: Non-Small Cell Lung Cancer (NSCLC)	Part E Abemaciclib: Melanoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23[8]	52[9]	23[10]	22[11]

Units: percentage of participants				
number (not applicable)				
Partial Response	0	5.8	0	0
Stable Disease	52.2	65.4	43.5	31.8
Progressive Disease	47.8	28.8	56.5	68.2
Not Evaluable	0	0	0	0

Notes:

[8] - All participants who had evaluable OIRR data per RANO-BM.

[9] - All participants who had evaluable OIRR data per RANO-BM.

[10] - All participants who had evaluable OIRR data per RANO-BM.

[11] - All participants who had evaluable OIRR data per RANO-BM.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of CR or PR: Duration of Intracranial Response (DOIR)

End point title	Duration of CR or PR: Duration of Intracranial Response

End point description:

DOIR is measured from the date of first evidence of a confirmed response (CR or PR), as defined by RANO-BM, to the date objective progression or death from any cause. CR is measurable target lesions, the disappearance of all CNS target lesions for at least 4 weeks; no new lesions; no corticosteroids; stable or improved clinically. PR is at least a 30% decrease in the sum LD of CNS target lesions, taking as reference the baseline sum LD for at least 4 weeks; no new lesions; stable to decreased corticosteroid dose; stable or improved clinically. Participants who have neither progressed nor died were censored on the day of their last radiographic tumor assessment or on the date of response. PD is greater than or equal to (≥) 20% increase in sum LD relative to nadir and a relative increase of 20%, ≥1 lesion must increase by absolute value of ≥5 mm. DOIR was summarized using Kaplan-Meier estimates.

End point type	Secondary

End point timeframe:

Date of CR or PR to Date of Objective Disease Progression or Death from Any Cause (Up to 36 Months)

Notes:

[12] - 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: All participants who had evaluable OIRR data with at least one measurable brain lesion at baseline (per RANO-BM) and for whom at least one post-baseline overall response assessment for intracranial disease is available. Parts C and F were exploratory per protocol.

End point values	Part A Abemaciclib: Hormone Receptor (HR+) HER2+ Breast Cancer	Part B Abemaciclib: HR+, HER2- Breast Cancer	Part D Abemaciclib: Non-Small Cell Lung Cancer (NSCLC)	Part E Abemaciclib: Melanoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[13]	3[14]	0[15]	0[16]
Units: Months				
median (full range (min-max))	(to)	8.8 (3.0 to 14.3)	(to)	(to)

Notes:

[13] - All participants who had evaluable OIRR data per RANO-BM.

[14] - All participants who had evaluable OIRR data per RANO-BM.

[15] - All participants who had evaluable OIRR data per RANO-BM.

[16] - All participants who had evaluable OIRR data per RANO-BM.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Best Overall Intracranial Response (BOIR) of CR, PR, or SD: Intracranial Disease Control Rate (IDCR)

End point title	Percentage of Participants with Best Overall Intracranial Response (BOIR) of CR, PR, or SD: Intracranial Disease Control Rate (IDCR)[17]

End point description:

Percentage of participants with BOIR of CR, PR, or SD: IDCR, as defined by RANO-BM is reported. CR is measurable target lesions, the disappearance of all central nervous system CNS target lesions for at least 4 weeks; no new lesions; no corticosteroids; stable or improved clinically. PR is at least a 30% decrease in the sum LD of CNS target lesions, taking as reference the baseline sum LD for at least 4 weeks; no new lesions; stable to decreased corticosteroid dose; stable or improved clinically. Nontarget lesions requires disappearance CNS non-target lesions and no new CNS lesions. SD is less than (<)30% decrease relative to baseline but <20% increase in sum LD relative to nadir. PD is greater than or equal to (≥) 20% increase in sum LD relative to nadir and a relative increase of 20%, ≥1 lesion must increase by absolute value of ≥5 mm.

End point type	Secondary

End point timeframe:

Baseline to Disease Progression or Start of New Anticancer Therapy (Up to 36 Months)

Notes:

[17] - 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: All participants who had evaluable OIRR data with at least one measurable brain lesion at baseline (per RANO-BM) and for whom at least one post-baseline overall response assessment for intracranial disease is available. Parts C and F were exploratory per protocol.

End point values	Part A Abemaciclib: Hormone Receptor (HR+) HER2+ Breast Cancer	Part B Abemaciclib: HR+, HER2- Breast Cancer	Part D Abemaciclib: Non-Small Cell Lung Cancer (NSCLC)	Part E Abemaciclib: Melanoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23[18]	52[19]	23[20]	22[21]
Units: percentage of participants				
number (not applicable)	52.2	71.2	43.5	31.8

Notes:

[18] - All participants who had evaluable OIRR data per RANO-BM.

[19] - All participants who had evaluable OIRR data per RANO-BM.

[20] - All participants who had evaluable OIRR data per RANO-BM.

[21] - All participants who had evaluable OIRR data per RANO-BM.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with BOIR of CR, PR, or SD with Duration of SD for at Least 6 Months: Intracranial Clinical Benefit Rate (ICBR)

End point title	Percentage of Participants with BOIR of CR, PR, or SD with Duration of SD for at Least 6 Months: Intracranial Clinical Benefit Rate (ICBR)[22]

End point description:

ICBR is the percentage of participants with BOIR of CR, PR, or SD with duration of SD for at least 6 months, as defined by RANO-BM. CR is measurable target lesions, the disappearance of all CNS target lesions for at least 4 weeks; no new lesions; no corticosteroids; stable or improved clinically. PR is at

least a 30% decrease in the sum LD of CNS target lesions, taking as reference the baseline sum LD for at least 4 weeks; no new lesions; stable to decreased corticosteroid dose; stable or improved clinically. SD is <30% decrease relative to baseline but <20% increase in sum LD relative to nadir. PD is greater than or equal to (≥) 20% increase in sum LD relative to nadir and a relative increase of 20%, ≥1 lesion must increase by absolute value of ≥5 mm.

End point type	Secondary

End point timeframe:

Baseline to Disease Progression or Start of New Anticancer Therapy (Up to 36 Months)

Notes:

[22] - 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: All participants who had evaluable OIRR data with at least one measurable brain lesion at baseline (per RANO-BM) and for whom at least one post-baseline overall response assessment for intracranial disease is available. Parts C and F were exploratory per protocol.

End point values	Part A Abemaciclib: Hormone Receptor (HR+) HER2+ Breast Cancer	Part B Abemaciclib: HR+, HER2- Breast Cancer	Part D Abemaciclib: Non-Small Cell Lung Cancer (NSCLC)	Part E Abemaciclib: Melanoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23[23]	52[24]	23[25]	22[26]
Units: percentage of participants				
number (not applicable)	13.0	26.9	26.1	9.1

Notes:

[23] - All participants who had evaluable OIRR data per RANO-BM.

[24] - All participants who had evaluable OIRR data per RANO-BM.

[25] - All participants who had evaluable OIRR data per RANO-BM.

[26] - All participants who had evaluable OIRR data per RANO-BM.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)[27]

End point description:

OS was measured from baseline to the date of death from any cause. For each participant who is not known to have died as of the data-inclusion cutoff date for a particular analysis, OS was censored for that analysis at the date of last contact prior to the data inclusion cutoff date (contacts considered in the determination of last contact date include adverse event (AE) date, tumor assessment date, visit date, and last known alive date). OS was summarized using Kaplan-Meier estimates.

End point type	Secondary

End point timeframe:

Baseline to the Date of Death from Any Cause (Up to 5 Years)

Notes:

[27] - 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: All participants who had evaluable OIRR data with at least one measurable brain lesion at baseline (per RANO-BM) and for whom at least one post-baseline overall response assessment for intracranial disease is available. Parts C and F were exploratory per protocol.

End point values	Part A Abemaciclib: Hormone Receptor (HR+) HER2+ Breast Cancer	Part B Abemaciclib: HR+, HER2- Breast Cancer	Part D Abemaciclib: Non-Small Cell Lung Cancer (NSCLC)	Part E Abemaciclib: Melanoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27[28]	58[29]	28[30]	23[31]
Units: percentage of participants				
median (confidence interval 95%)	10.06 (4.21 to 14.30)	13.38 (9.60 to 20.84)	7.13 (3.65 to 9.37)	2.93 (1.22 to 4.31)

Notes:

[28] - All participants who received at least one dose of study drug.

[29] - All participants who received at least one dose of study drug.

[30] - All participants who received at least one dose of study drug.

[31] - All participants who received at least one dose of study drug.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Best Response of CR or PR: Extracranial Objective Response Rate (EORR)

End point title	Percentage of Participants with a Best Response of CR or PR: Extracranial Objective Response Rate (EORR)[32]

End point description:

The percentage of participants with a best response of CR or PR objective response rate is complete response (CR) + partial response (PR), as classified by the investigators according to the Response Evaluation Criteria In Solid Tumors (RECIST v1.1) guidelines. CR is disappearance of all target and non-target lesions; PR is ≥30% decrease in sum of longest diameter of target lesions. PD is defined as at least a 20% increase in the sum LD of CNS target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study) and the 20% increase must be at least one lesion must increase by an absolute value of ≥5 mm to be considered progression.

End point type	Secondary

End point timeframe:

Baseline to Disease Progression (Up to 36 Months)

Notes:

[32] - 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: All participants who had evaluable OIRR data with at least one measurable brain lesion at baseline (per RANO-BM) and for whom at least one post-baseline overall response assessment for intracranial disease is available. Parts C and F were exploratory per protocol.

End point values	Part A Abemaciclib: Hormone Receptor (HR+) HER2+ Breast Cancer	Part B Abemaciclib: HR+, HER2- Breast Cancer	Part D Abemaciclib: Non-Small Cell Lung Cancer (NSCLC)	Part E Abemaciclib: Melanoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27[33]	58[34]	28[35]	23[36]
Units: percentage of participants				
number (not applicable)	0	1.7	3.6	0

Notes:

[33] - All participants who received at least one dose of study drug.

[34] - All participants who received at least one dose of study drug.

[35] - All participants who received at least one dose of study drug.

[36] - All participants who received at least one dose of study drug.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Best Overall Response of CR, PR, or SD: Extracranial Disease Control Rate (EDCR)

End point title	Percentage of Participants with a Best Overall Response of CR, PR, or SD: Extracranial Disease Control Rate (EDCR)[37]

End point description:

Disease control rate (DCR) (CR+ PR+ SD) per RECIST v1.1. is defined as the percentage of participants with best overall response of CR, PR, or SD. CR is disappearance of all target and non-target lesions; PR is ≥30% decrease in sum of longest diameter of target lesions. PD is defined as at least a 20% increase in the sum LD of CNS target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study) and the 20% increase must be at least one lesion must increase by an absolute value of ≥5 mm to be considered progression.

End point type	Secondary

End point timeframe:

Baseline to Disease Progression or Start of New Anticancer Therapy (Up to 36 Months)

Notes:

[37] - 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: All participants who had evaluable OIRR data with at least one measurable brain lesion at baseline (per RANO-BM) and for whom at least one post-baseline overall response assessment for intracranial disease is available. Parts C and F were exploratory per protocol.

End point values	Part A Abemaciclib: Hormone Receptor (HR+) HER2+ Breast Cancer	Part B Abemaciclib: HR+, HER2- Breast Cancer	Part D Abemaciclib: Non-Small Cell Lung Cancer (NSCLC)	Part E Abemaciclib: Melanoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27[38]	58[39]	28[40]	23[41]
Units: percentage of participants				
number (not applicable)	40.7	51.7	39.3	26.1

Notes:

[38] - All participants who received at least one dose of study drug.

[39] - All participants who received at least one dose of study drug.

[40] - All participants who received at least one dose of study drug.

[41] - All participants who received at least one dose of study drug.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) Bi-compartmental

End point title	Progression Free Survival (PFS) Bi-compartmental[42]

End point description:

PFS was measured from baseline to objective progression (intracranial or extracranial) as defined by

(RANO-BM.) or death from any cause. Participants who have neither progressed nor died were censored at the day of their last radiographic tumor assessment. PD is greater than or equal to (≥) 20% increase in sum LD relative to nadir and a relative increase of 20%, ≥1 lesion must increase by absolute value of ≥5 mm. PFS was summarized using Kaplan-Meier estimates.

End point type	Secondary

End point timeframe:

Baseline to Objective Disease Progression or Death from Any Cause (Up to 36 Months)

Notes:

[42] - 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: All participants who had evaluable OIRR data with at least one measurable brain lesion at baseline (per RANO-BM) and for whom at least one post-baseline overall response assessment for intracranial disease is available. Parts C and F were exploratory per protocol.

End point values	Part A Abemaciclib: Hormone Receptor (HR+) HER2+ Breast Cancer	Part B Abemaciclib: HR+, HER2- Breast Cancer	Part D Abemaciclib: Non-Small Cell Lung Cancer (NSCLC)	Part E Abemaciclib: Melanoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27[43]	58[44]	28[45]	23[46]
Units: Months				
median (confidence interval 95%)	2.07 (1.35 to 3.32)	4.41 (2.60 to 5.46)	1.45 (1.35 to 2.76)	1.22 (1.02 to 1.55)

Notes:

[43] - All participants who received at least one dose of study drug.

[44] - All participants who received at least one dose of study drug.

[45] - All participants who received at least one dose of study drug.

[46] - All participants who received at least one dose of study drug.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Neurologic Symptoms on the MD Anderson Inventory-Brain Tumor (MDASI-BT) Subscale

End point title	Change from Baseline in Neurologic Symptoms on the MD Anderson Inventory-Brain Tumor (MDASI-BT) Subscale[47]

End point description:

The MDASI-BT is an instrument to assess multi-symptoms in participants with brain tumor metastases (including those with brain metastases secondary to breast cancer). The MDASI-BT of participants with a change from baseline is reported as mean core symptoms, mean brain tumor symptoms, and symptom groupings (mean focal neurologic deficit, mean generalized/disease status symptoms, and mean gastrointestinal symptoms). The mean of all symptom subscale items was calculated where 0 equals "not present" and 10 equals "as bad as you can imagine." A change from baseline with negative values indicate improvement, positive values indicate worsening.

End point type	Secondary

End point timeframe:

Baseline, Cycle 3 (Up to 63 Days)

Notes:

[47] - 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: All participants who had evaluable OIRR data with at least one measurable brain lesion at baseline (per RANO-BM) and for whom at least one post-baseline overall response assessment for intracranial disease is available. Parts C and F were exploratory per protocol.

End point values	Part A Abemaciclib: Hormone Receptor (HR+) HER2+ Breast Cancer	Part B Abemaciclib: HR+, HER2- Breast Cancer	Part D Abemaciclib: Non-Small Cell Lung Cancer (NSCLC)	Part E Abemaciclib: Melanoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11[48]	35[49]	10[50]	7[51]
Units: units on a scale				
arithmetic mean (standard deviation)				
mean core symptom severity	-0.98 (± 0.86)	-0.17 (± 0.99)	-0.38 (± 1.19)	-0.53 (± 0.62)
mean brain tumor symptom severity	-0.47 (± 0.57)	-0.29 (± 1.05)	-0.10 (± 1.22)	0.31 (± 1.11)
mean focal neurologic deficit symptom severity	-0.84 (± 0.92)	-0.36 (± 1.23)	-0.44 (± 0.58)	0.54 (± 1.16)
mean generalized disease status	-0.47 (± 1.03)	0 (± 1.39)	0.28 (± 1.51)	0.01 (± 0.89)
mean gastrointestinal symptom	-1.35 (± 2.11)	0.40 (± 1.91)	1.00 (± 1.46)	0 (± 0.29)

Notes:

[48] - All participants had at least 1 baseline and an evaluable post baseline assessment.

[49] - All participants had at least 1 baseline and an evaluable post baseline assessment.

[50] - All participants had at least 1 baseline and an evaluable post baseline assessment.

[51] - All participants had at least 1 baseline and an evaluable post baseline assessment.

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Steady State Minimum Concentration (Cmin) of Abemaciclib and its Metabolites LSN2839567 (M2), LSN3106726 (M20), and LSN3106729 (M18)

End point title	Pharmacokinetics (PK): Steady State Minimum Concentration (Cmin) of Abemaciclib and its Metabolites LSN2839567 (M2), LSN3106726 (M20), and LSN3106729 (M18)

End point description:

A PK plasma sample was taken prior to abemaciclib dose to analyze the minimum concentrations of abemaciclib and its metabolites (Cmin) - Individual Cmin values were averaged if there were 3 or more available data points, otherwise individual data are reported.

End point type	Secondary

End point timeframe:

Parts A, B, D, E, F, Cycle 3, Day 1: Predose; Part C, Cycle 4, Day 1: Predose

End point values	Part A 150 mg Abemaciclib: HR+, HER2+ Breast Cancer	Part B 200 mg Abemaciclib: HR+, HER2- Breast Cancer	Part C 200 mg Abemaciclib: Surgical Resection	Part D 200 mg Abemaciclib: NSCLC
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3[52]	12[53]	1[54]	5[55]
Units: nanogram/milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Abemaciclib	133 (± 13.4)	120 (± 186)	0 (± 0)	306 (± 33.5)
LSN2839567 (M2)	72.6 (± 8.23)	77.3 (± 121)	0 (± 0)	100 (± 77.5)
LSN3106726 (M20)	158 (± 25.0)	133 (± 160)	0 (± 0)	203 (± 43.3)
LSN3106729 (M18)	36.8 (± 39.3)	42.4 (± 85.6)	0 (± 0)	28.9 (± 108)

Notes:

[52] - All participants who had evaluable PK data. geometric coefficient of variation is a percent.

[53] - All participants who had evaluable PK data.

[54] - Abemaciclib value 256 ng/mL
(M2) value 98.8 ng/mL
(M20) value 181 ng/mL
(M18) value 28.2 ng/mL

[55] - All participants who had evaluable PK data.

End point values	Part E 200 mg Abemaciclib: Melanoma	Part F 200 mg Abemaciclib: HR+ Breast Cancer, NSCLC, Melanoma		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2[56]	4[57]		
Units: nanogram/milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Abemaciclib	0 (± 0)	142 (± 80.0)		
LSN2839567 (M2)	0 (± 0)	68.5 (± 150)		
LSN3106726 (M20)	0 (± 0)	122 (± 137)		
LSN3106729 (M18)	0 (± 0)	27.0 (± 242)		

Notes:

[56] - Abemaciclib: 99.7 and 222 ng/mL
(M2) 61.6 and 90.7
(M20) 109 and 172
(M18) 22.2 and 44.2

[57] - All participants who had evaluable PK data.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 36 Months	
Adverse event reporting additional description: I3Y-MC-JPBO	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	Study Part A Abemaciclib: HR+, HER2+ Breast Cancer
Reporting group description: -	
Reporting group title	Study Part B Abemaciclib: HR+, HER2- Breast Cancer
Reporting group description: -	
Reporting group title	Study Part E Abemaciclib: Melanoma
Reporting group description: -	
Reporting group title	Study Part D Abemaciclib: NSCLC
Reporting group description: -	
Reporting group title	Study Part F Abemaciclib HR+ Breast Cancer, NSCLC, or Melanoma
Reporting group description: -	
Reporting group title	Study Part C Abemaciclib: Surgery
Reporting group description: -	

Serious adverse events	Study Part A Abemaciclib: HR+, HER2+ Breast Cancer	Study Part B Abemaciclib: HR+, HER2- Breast Cancer	Study Part E Abemaciclib: Melanoma
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 27 (22.22%)	16 / 58 (27.59%)	4 / 23 (17.39%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
tumour pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
embolism			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 27 (0.00%)	2 / 58 (3.45%)	0 / 23 (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
shock haemorrhagic			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
general physical health deterioration			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (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
pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pyrexia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	2 / 58 (3.45%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
aspiration			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (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
cough			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
dyspnoea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
pulmonary hypertension			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
confusional state			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	1 / 58 (1.72%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
mental status changes			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
ankle fracture			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
fracture			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
acute coronary syndrome			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cardiac failure			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
myocardial infarction			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
aphasia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ataxia			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
brain oedema			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
headache			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (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
seizure			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 27 (7.41%)	0 / 58 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
syncope			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
thrombocytopenia			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	1 / 27 (3.70%)	0 / 58 (0.00%)	0 / 23 (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
Eye disorders			
glaucoma			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 27 (7.41%)	2 / 58 (3.45%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	1 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
enterocolitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	0 / 58 (0.00%)	0 / 23 (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
haemorrhoidal haemorrhage			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lower gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
nausea			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pancreatitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
upper gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
vomiting			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	0 / 58 (0.00%)	0 / 23 (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
Hepatobiliary disorders			
hepatocellular injury			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
jaundice cholestatic			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
chronic kidney disease			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal failure			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (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
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
lung infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (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
sepsis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (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
shunt infection			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
skin infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urinary tract infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
dehydration			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	2 / 23 (8.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypercalcaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypokalaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hyponatraemia			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Study Part D Abemaciclib: NSCLC	Study Part F Abemaciclib HR+ Breast Cancer, NSCLC, or Melanoma	Study Part C Abemaciclib: Surgery
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 28 (28.57%)	7 / 17 (41.18%)	3 / 9 (33.33%)
number of deaths (all causes)	3	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
tumour pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (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
Vascular disorders			
embolism			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
shock haemorrhagic			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (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
General disorders and administration site conditions			
general physical health deterioration			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pain			

alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pyrexia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
aspiration			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cough			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (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
dyspnoea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
pneumonitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pulmonary hypertension			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
confusional state			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
mental status changes			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
ankle fracture			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
fracture			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
acute coronary syndrome			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cardiac failure			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	0 / 9 (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
myocardial infarction			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	0 / 9 (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
Nervous system disorders			
aphasia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	0 / 9 (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
ataxia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
brain oedema			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	0 / 9 (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
headache			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
seizure			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	1 / 28 (3.57%)	2 / 17 (11.76%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
syncope			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (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
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (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
thrombocytopenia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
glaucoma			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
enterocolitis			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
haemorrhoidal haemorrhage			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	0 / 9 (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
lower gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
nausea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (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
pancreatitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
upper gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (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
vomiting			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hepatobiliary disorders			
hepatocellular injury			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	0 / 9 (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
jaundice cholestatic			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	0 / 9 (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
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	0 / 9 (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
chronic kidney disease			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal failure			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

lung infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 28 (10.71%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
sepsis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
shunt infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (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
skin infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	0 / 9 (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
urinary tract infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	0 / 9 (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
Metabolism and nutrition disorders			
dehydration			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (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
hypercalcaemia			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypokalaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hyponatraemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Study Part A Abemaciclib: HR+, HER2+ Breast Cancer	Study Part B Abemaciclib: HR+, HER2- Breast Cancer	Study Part E Abemaciclib: Melanoma
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 27 (85.19%)	55 / 58 (94.83%)	16 / 23 (69.57%)
Vascular disorders			
embolism			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	3 / 58 (5.17%)	0 / 23 (0.00%)
occurrences (all)	0	3	0
hypertension			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	2 / 58 (3.45%)	0 / 23 (0.00%)
occurrences (all)	0	4	0
hypotension			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	2 / 58 (3.45%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
General disorders and administration site conditions			

chills			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
fatigue			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	9 / 27 (33.33%)	28 / 58 (48.28%)	4 / 23 (17.39%)
occurrences (all)	9	31	4
gait disturbance			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 27 (11.11%)	4 / 58 (6.90%)	0 / 23 (0.00%)
occurrences (all)	3	4	0
general physical health deterioration			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	2 / 23 (8.70%)
occurrences (all)	0	1	2
influenza like illness			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	3 / 58 (5.17%)	1 / 23 (4.35%)
occurrences (all)	1	3	1
localised oedema			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 27 (11.11%)	3 / 58 (5.17%)	0 / 23 (0.00%)
occurrences (all)	3	3	0
malaise			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	2 / 58 (3.45%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
oedema peripheral			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	3 / 58 (5.17%)	3 / 23 (13.04%)
occurrences (all)	0	3	3
non-cardiac chest pain			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 27 (0.00%)	3 / 58 (5.17%)	0 / 23 (0.00%)
occurrences (all)	0	5	0
pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
pyrexia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	3 / 58 (5.17%)	0 / 23 (0.00%)
occurrences (all)	1	3	0
Reproductive system and breast disorders			
breast pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	5 / 58 (8.62%)	0 / 23 (0.00%)
occurrences (all)	1	7	0
dyspnoea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	9 / 58 (15.52%)	0 / 23 (0.00%)
occurrences (all)	1	9	0
epistaxis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
nasal congestion			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
oropharyngeal pain			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
sinus pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
agitation			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	1 / 58 (1.72%)	2 / 23 (8.70%)
occurrences (all)	1	1	2
anxiety			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	3 / 58 (5.17%)	1 / 23 (4.35%)
occurrences (all)	1	3	1
confusional state			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 27 (7.41%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences (all)	2	2	0
depression			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	4 / 58 (6.90%)	0 / 23 (0.00%)
occurrences (all)	1	4	0
insomnia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	3 / 58 (5.17%)	1 / 23 (4.35%)
occurrences (all)	1	3	1
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 27 (11.11%)	4 / 58 (6.90%)	2 / 23 (8.70%)
occurrences (all)	3	4	2
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	4 / 27 (14.81%)	2 / 58 (3.45%)	4 / 23 (17.39%)
occurrences (all)	4	2	4
blood alkaline phosphatase increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	1 / 58 (1.72%)	1 / 23 (4.35%)
occurrences (all)	1	1	1
blood bilirubin increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
blood creatinine increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	5 / 58 (8.62%)	2 / 23 (8.70%)
occurrences (all)	1	6	3
haemoglobin increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
international normalised ratio increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
weight decreased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	6 / 58 (10.34%)	1 / 23 (4.35%)
occurrences (all)	0	6	2
weight increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	2 / 58 (3.45%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
Injury, poisoning and procedural complications			
contusion			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
fall			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	4 / 58 (6.90%)	0 / 23 (0.00%)
occurrences (all)	1	6	0
fracture			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
incision site pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
skin laceration			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
vascular access complication			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
palpitations			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
amnesia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
aphasia			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	2 / 27 (7.41%)	3 / 58 (5.17%)	0 / 23 (0.00%)
occurrences (all)	3	3	0
balance disorder			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
cognitive disorder			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
dizziness			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 27 (7.41%)	8 / 58 (13.79%)	0 / 23 (0.00%)
occurrences (all)	2	8	0
disturbance in attention			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
dysarthria			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	1 / 23 (4.35%)
occurrences (all)	0	1	1
dysgeusia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	2 / 58 (3.45%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
headache			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 27 (7.41%)	14 / 58 (24.14%)	2 / 23 (8.70%)
occurrences (all)	2	23	3
hemiparesis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0

neuropathy			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 27 (11.11%)	12 / 58 (20.69%)	1 / 23 (4.35%)
occurrences (all)	3	19	2
peripheral motor neuropathy			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	2 / 58 (3.45%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
presyncope			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
seizure			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 27 (14.81%)	3 / 58 (5.17%)	3 / 23 (13.04%)
occurrences (all)	5	3	3
somnolence			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
tremor			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	3 / 58 (5.17%)	0 / 23 (0.00%)
occurrences (all)	0	3	0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 27 (11.11%)	12 / 58 (20.69%)	2 / 23 (8.70%)
occurrences (all)	3	14	5
haemorrhagic diathesis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
leukocytosis			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
leukopenia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 27 (7.41%)	7 / 58 (12.07%)	3 / 23 (13.04%)
occurrences (all)	2	10	5
lymphopenia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 27 (14.81%)	6 / 58 (10.34%)	1 / 23 (4.35%)
occurrences (all)	4	9	2
neutropenia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	6 / 27 (22.22%)	17 / 58 (29.31%)	5 / 23 (21.74%)
occurrences (all)	8	32	8
thrombocytopenia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 27 (14.81%)	11 / 58 (18.97%)	3 / 23 (13.04%)
occurrences (all)	5	12	4
Ear and labyrinth disorders			
hypoacusis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	2 / 58 (3.45%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
Eye disorders			
diplopia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
eye pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
photopsia			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
vision blurred			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	3 / 58 (5.17%)	1 / 23 (4.35%)
occurrences (all)	1	3	1
Gastrointestinal disorders			
abdominal distension			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
abdominal pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 27 (11.11%)	9 / 58 (15.52%)	5 / 23 (21.74%)
occurrences (all)	3	14	5
anal incontinence			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
ascites			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
constipation			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 27 (7.41%)	9 / 58 (15.52%)	2 / 23 (8.70%)
occurrences (all)	2	11	2
diarrhoea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	15 / 27 (55.56%)	45 / 58 (77.59%)	5 / 23 (21.74%)
occurrences (all)	26	100	6
dry mouth			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	2 / 27 (7.41%)	4 / 58 (6.90%)	1 / 23 (4.35%)
occurrences (all)	2	4	1
dysphagia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
gastritis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 27 (7.41%)	5 / 58 (8.62%)	0 / 23 (0.00%)
occurrences (all)	2	5	0
haemorrhoids			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
nausea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	9 / 27 (33.33%)	26 / 58 (44.83%)	1 / 23 (4.35%)
occurrences (all)	11	32	1
oral pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
stomatitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 27 (7.41%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences (all)	2	1	0
vomiting			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	7 / 27 (25.93%)	20 / 58 (34.48%)	1 / 23 (4.35%)
occurrences (all)	8	31	1

Skin and subcutaneous tissue disorders			
alopecia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 27 (7.41%)	2 / 58 (3.45%)	0 / 23 (0.00%)
occurrences (all)	2	2	0
dry skin			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 27 (7.41%)	4 / 58 (6.90%)	1 / 23 (4.35%)
occurrences (all)	2	5	1
rash			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 27 (11.11%)	3 / 58 (5.17%)	0 / 23 (0.00%)
occurrences (all)	3	6	0
skin ulcer			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 27 (7.41%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	2 / 58 (3.45%)	1 / 23 (4.35%)
occurrences (all)	0	2	1
cystitis noninfective			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	3 / 58 (5.17%)	0 / 23 (0.00%)
occurrences (all)	0	3	0
urinary incontinence			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
urinary retention			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			

arthralgia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	3 / 58 (5.17%)	1 / 23 (4.35%)
occurrences (all)	1	4	1
back pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	3 / 58 (5.17%)	1 / 23 (4.35%)
occurrences (all)	0	4	1
bone pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	3 / 58 (5.17%)	2 / 23 (8.70%)
occurrences (all)	0	7	3
flank pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	2 / 58 (3.45%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
muscle spasms			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	5 / 58 (8.62%)	0 / 23 (0.00%)
occurrences (all)	0	5	0
muscular weakness			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	7 / 27 (25.93%)	4 / 58 (6.90%)	2 / 23 (8.70%)
occurrences (all)	8	5	2
myalgia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	4 / 58 (6.90%)	3 / 23 (13.04%)
occurrences (all)	0	5	3
pain in extremity			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	5 / 58 (8.62%)	3 / 23 (13.04%)
occurrences (all)	1	5	3
Infections and infestations			

ear infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
sinusitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	3 / 58 (5.17%)	0 / 23 (0.00%)
occurrences (all)	0	3	0
upper respiratory tract infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
urinary tract infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	3 / 58 (5.17%)	0 / 23 (0.00%)
occurrences (all)	0	3	0
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 27 (11.11%)	19 / 58 (32.76%)	2 / 23 (8.70%)
occurrences (all)	4	19	2
dehydration			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 27 (11.11%)	6 / 58 (10.34%)	1 / 23 (4.35%)
occurrences (all)	3	6	1
hyperglycaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
hyperkalaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 58 (1.72%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
hypermagnesaemia			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
hypernatraemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 27 (0.00%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
hypoalbuminaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 27 (3.70%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
hypocalcaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 27 (7.41%)	0 / 58 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
hypokalaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 27 (14.81%)	11 / 58 (18.97%)	1 / 23 (4.35%)
occurrences (all)	7	17	1
hyponatraemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 27 (11.11%)	1 / 58 (1.72%)	1 / 23 (4.35%)
occurrences (all)	4	2	1

Non-serious adverse events	Study Part D Abemaciclib: NSCLC	Study Part F Abemaciclib HR+ Breast Cancer, NSCLC, or Melanoma	Study Part C Abemaciclib: Surgery
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 28 (96.43%)	16 / 17 (94.12%)	8 / 9 (88.89%)
Vascular disorders			
embolism			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
hypertension			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	3
hypotension			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
chills			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
fatigue			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	11 / 28 (39.29%)	9 / 17 (52.94%)	2 / 9 (22.22%)
occurrences (all)	16	9	2
gait disturbance			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
general physical health deterioration			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
influenza like illness			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
localised oedema			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
malaise			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
oedema peripheral			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	1 / 17 (5.88%)	1 / 9 (11.11%)
occurrences (all)	1	1	1
non-cardiac chest pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	2 / 17 (11.76%)	1 / 9 (11.11%)
occurrences (all)	1	2	1
pyrexia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 28 (7.14%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
Reproductive system and breast disorders			
breast pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
dyspnoea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	5 / 28 (17.86%)	2 / 17 (11.76%)	1 / 9 (11.11%)
occurrences (all)	5	2	2
epistaxis			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	2 / 28 (7.14%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
nasal congestion			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
oropharyngeal pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
sinus pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
agitation			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
anxiety			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 28 (7.14%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
confusional state			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	5 / 28 (17.86%)	1 / 17 (5.88%)	2 / 9 (22.22%)
occurrences (all)	8	1	2
depression			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
insomnia			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	2
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 28 (7.14%)	2 / 17 (11.76%)	6 / 9 (66.67%)
occurrences (all)	4	2	7
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 28 (7.14%)	2 / 17 (11.76%)	3 / 9 (33.33%)
occurrences (all)	2	3	3
blood alkaline phosphatase increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 28 (7.14%)	1 / 17 (5.88%)	3 / 9 (33.33%)
occurrences (all)	5	1	4
blood bilirubin increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
blood creatinine increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 28 (7.14%)	1 / 17 (5.88%)	1 / 9 (11.11%)
occurrences (all)	4	2	1
haemoglobin increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
international normalised ratio increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
weight decreased			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	4 / 28 (14.29%)	2 / 17 (11.76%)	2 / 9 (22.22%)
occurrences (all)	5	2	2
weight increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	2 / 17 (11.76%)	1 / 9 (11.11%)
occurrences (all)	0	2	1
Injury, poisoning and procedural complications			
contusion			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
fall			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 28 (10.71%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
fracture			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
incision site pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
skin laceration			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
vascular access complication			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 28 (7.14%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Cardiac disorders			
palpitations			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	1 / 9 (11.11%)
occurrences (all)	0	1	2
Nervous system disorders			
amnesia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
aphasia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
balance disorder			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
cognitive disorder			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
dizziness			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	1 / 17 (5.88%)	1 / 9 (11.11%)
occurrences (all)	1	1	1
disturbance in attention			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
dysarthria			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 28 (7.14%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
dysgeusia			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	2 / 9 (22.22%)
occurrences (all)	0	1	2
headache			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 28 (14.29%)	3 / 17 (17.65%)	2 / 9 (22.22%)
occurrences (all)	4	3	3
hemiparesis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
neuropathy			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	2
peripheral motor neuropathy			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
presyncope			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
seizure			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
somnolence			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
tremor			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0

Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	5 / 28 (17.86%)	5 / 17 (29.41%)	4 / 9 (44.44%)
occurrences (all)	6	5	7
haemorrhagic diathesis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
leukocytosis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
leukopenia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 28 (14.29%)	3 / 17 (17.65%)	4 / 9 (44.44%)
occurrences (all)	6	3	6
lymphopenia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 28 (14.29%)	3 / 17 (17.65%)	3 / 9 (33.33%)
occurrences (all)	7	3	8
neutropenia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	7 / 28 (25.00%)	2 / 17 (11.76%)	4 / 9 (44.44%)
occurrences (all)	9	2	6
thrombocytopenia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	8 / 28 (28.57%)	3 / 17 (17.65%)	4 / 9 (44.44%)
occurrences (all)	11	3	5
Ear and labyrinth disorders			
hypoacusis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Eye disorders			

diplopia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
eye pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
photopsia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
vision blurred			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 28 (10.71%)	2 / 17 (11.76%)	1 / 9 (11.11%)
occurrences (all)	3	2	1
Gastrointestinal disorders			
abdominal distension			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	2 / 17 (11.76%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
abdominal pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 28 (7.14%)	4 / 17 (23.53%)	2 / 9 (22.22%)
occurrences (all)	2	4	4
anal incontinence			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
ascites			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
constipation			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	7 / 28 (25.00%)	3 / 17 (17.65%)	0 / 9 (0.00%)
occurrences (all)	7	3	0
diarrhoea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	15 / 28 (53.57%)	6 / 17 (35.29%)	4 / 9 (44.44%)
occurrences (all)	21	6	6
dry mouth			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 28 (7.14%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
dysphagia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
gastritis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
haemorrhoids			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
nausea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	8 / 28 (28.57%)	7 / 17 (41.18%)	2 / 9 (22.22%)
occurrences (all)	10	10	2
oral pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	0	1	0

stomatitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
vomiting			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 28 (14.29%)	5 / 17 (29.41%)	2 / 9 (22.22%)
occurrences (all)	4	6	2
Skin and subcutaneous tissue disorders			
alopecia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
dry skin			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 28 (7.14%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
rash			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
skin ulcer			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 28 (7.14%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
cystitis noninfective			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
urinary incontinence			

alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
urinary retention			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
back pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 28 (10.71%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	3	2	0
bone pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
flank pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
muscle spasms			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
muscular weakness			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 28 (7.14%)	4 / 17 (23.53%)	2 / 9 (22.22%)
occurrences (all)	2	4	2
myalgia			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
pain in extremity			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Infections and infestations			
ear infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
sinusitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
upper respiratory tract infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 28 (7.14%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
urinary tract infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	7 / 28 (25.00%)	2 / 17 (11.76%)	2 / 9 (22.22%)
occurrences (all)	10	2	2
dehydration			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 28 (10.71%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences (all)	4	0	0
hyperglycaemia			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	2 / 28 (7.14%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
hyperkalaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 17 (0.00%)	3 / 9 (33.33%)
occurrences (all)	0	0	9
hypermagnesaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	1 / 17 (5.88%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
hypernatraemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
hypoalbuminaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	2 / 17 (11.76%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
hypocalcaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	3 / 17 (17.65%)	4 / 9 (44.44%)
occurrences (all)	0	3	5
hypokalaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 28 (7.14%)	2 / 17 (11.76%)	2 / 9 (22.22%)
occurrences (all)	2	2	5
hyponatraemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 28 (3.57%)	3 / 17 (17.65%)	2 / 9 (22.22%)
occurrences (all)	1	3	9

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 August 2015	Protocol amendment (a) Incorporated patients with brain metastases secondary to NSCLC or Replaced CDK 4/6 with CDK4 and CDK6 for clarity Updated accordingly to incorporate NSCLC and melanoma information and clarify breast cancer Included Parts D and E and clarified previously Irradiated progressive lesions; Specified parts for HR+ and HER2+ breast cancer patients, and NSCLC patients with respect to concomitant/concurrent therapies; Clarified use of trastuzumab in HER2+ breast cancer patient parts; Clarified Parts for breast cancer patients Incorporated male birth control and sperm donation language Updated exclusion criteria breast cancer patients; parts for evidence of leptomeningeal metastases; parts for previous treatment with CDK4 and CDK6 inhibitor; deleted criterion Clarified discontinuation of abemaciclib Incorporated NSCLC and melanoma language and updated study design illustration Updated treatment regimens, modified supportive management for diarrhea, permitted combination therapies, surgery/surgical resection, efficacy assessments and measures, drug concentration Incorporated NSCLC and melanoma information in sample size Updated the Parts in secondary outcomes and methodology, trail making tests, drug concentrations in samples, health outcomes analyses, and interim analyses Updated Study Schedule Incorporated RANO-BM and RANO LM information Modified sampling and sampling summary Parts
08 February 2019	Protocol amendment (d) Included TBL and VTE in abbreviations Incorporated rationale for Amendment (d) to update safety monitoring Information for hepatic conditions, renal function, and VTEs. Modified alignment with safety updates. Updated requirements for AE/SAE reporting Incorporated safety monitoring language for hepatic conditions, renal function, and VTEs. CYPs text updated to align with abemaciclib program information

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported