Clinical trial results:
An Open-Label, Randomized Phase 2 Study of the Impact of Food on Tolerability when Receiving Abemaciclib for Patients with Previously Treated Hormone Receptor-Positive, HER2-Negative, Metastatic Breast Cancer

Summary

EudraCT number	2018-001853-28
Trial protocol	ES BE
Global end of trial date	09 March 2023

Results information

Result version number	v2 (current)
This version publication date	24 March 2024
First version publication date	02 August 2020
Version creation reason	• New data added to full data set LPV Results Update

Trial information

Trial identification

Sponsor protocol code	I3Y-MC-JPCP

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03703466
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 17041

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	09 March 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 March 2023
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 examine the side effects that participants with metastatic breast cancer experience when taking abemaciclib with or without food.

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	28 November 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Turkey: 18
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Australia: 31
Country: Number of subjects enrolled	Spain: 19
Country: Number of subjects enrolled	Russian Federation: 3
Worldwide total number of subjects	72
EEA total number of subjects	20

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)	53

From 65 to 84 years	19
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

No Text Available

Pre-assignment

Screening details:

Study completers are participants who completed 3 cycles of study treatment (28-day cycle)

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	200 mg Abemaciclib with a Meal

Arm description:

200 mg abemaciclib given twice a day (BID) orally with a meal.

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

Dosage and administration details:

Administered orally.

Arm title	200 mg Abemaciclib without a Meal

Arm description:

200 mg abemaciclib given twice a day (BID) orally without a meal, taken in the modified fasted condition.

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

Dosage and administration details:

Administered orally.

Arm title	200 mg Abemaciclib without Regard to Food

Arm description:

200 mg abemaciclib given twice a day (BID) orally without regard for food.

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

Dosage and administration details:
Administered orally.

Number of subjects in period 1	200 mg Abemaciclib with a Meal	200 mg Abemaciclib without a Meal	200 mg Abemaciclib without Regard to Food
Started	24	24	24
Received at least one dose of study drug	24	23	24
Completed	20	18	22
Not completed	4	6	2
Consent withdrawn by subject	-	3	-
Death	2	1	-
Completed < 3 Cycles	2	2	2

Baseline characteristics

Reporting groups	
Reporting group title	200 mg Abemaciclib with a Meal
Reporting group description:	
200 mg abemaciclib given twice a day (BID) orally with a meal.	
Reporting group title	200 mg Abemaciclib without a Meal
Reporting group description:	
200 mg abemaciclib given twice a day (BID) orally without a meal, taken in the modified fasted condition.	
Reporting group title	200 mg Abemaciclib without Regard to Food
Reporting group description:	
200 mg abemaciclib given twice a day (BID) orally without regard for food.	

Reporting group values	200 mg Abemaciclib with a Meal	200 mg Abemaciclib without a Meal	200 mg Abemaciclib without Regard to Food
Number of subjects	24	24	24
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	58.2	56.9	57.6
standard deviation	± 11.6	± 11.1	± 8.3
Gender categorical Units: Subjects			
Female	23	24	24
Male	1	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	1
Not Hispanic or Latino	24	19	20
Unknown or Not Reported	0	5	3
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	22	24	24
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Region of Enrollment Units: Subjects			
Turkey	6	6	6
Belgium	0	1	0
Australia	11	10	10
Spain	6	6	7

Russia	1	1	1

Reporting group values	Total		
Number of subjects	72		
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	71		
Male	1		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1		
Not Hispanic or Latino	63		
Unknown or Not Reported	8		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	2		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	70		
More than one race	0		
Unknown or Not Reported	0		
Region of Enrollment Units: Subjects			
Turkey	18		
Belgium	1		
Australia	31		
Spain	19		
Russia	3		

End points

End points reporting groups

Reporting group title	200 mg Abemaciclib with a Meal
Reporting group description:	
200 mg abemaciclib given twice a day (BID) orally with a meal.	
Reporting group title	200 mg Abemaciclib without a Meal
Reporting group description:	
200 mg abemaciclib given twice a day (BID) orally without a meal, taken in the modified fasted condition.	
Reporting group title	200 mg Abemaciclib without Regard to Food
Reporting group description:	
200 mg abemaciclib given twice a day (BID) orally without regard for food.	

Primary: Percentage of Participants with Severe Diarrhea (≥ Grade 3)

End point title	Percentage of Participants with Severe Diarrhea (≥ Grade 3)[1]
End point description:	
Percentage of participants with severe diarrhea (≥ grade 3) during the first 3 cycles. Events were as assessed by the investigator and graded according to Common Terminology Criteria for Adverse Events (CTCAE). Grade 3 was defined as an increase of ≥7 stools per day over baseline; incontinence; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self-care activities of daily living (ADL). Analysis Population Description: All participants who received at least one dose of study drug.	
End point type	Primary
End point timeframe:	
Cycle 3 (28 Days Cycle)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistics were planned for this end point.

End point values	200 mg Abemaciclib with a Meal	200 mg Abemaciclib without a Meal	200 mg Abemaciclib without Regard to Food	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	23	24	
Units: percentage of participants				
number (not applicable)	4.2	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Prolonged Grade 2 Diarrhea

End point title	Percentage of Participants with Prolonged Grade 2 Diarrhea[2]
End point description:	
Percentage of participants with prolonged grade 2 diarrhea during first 3 cycles. Events were as	

assessed by the investigator and graded according to Common Terminology Criteria for Adverse Events (CTCAE). Prolonged Grade 2 diarrhea was any event lasting more than 7 days. Grade 2 was defined as Increase of 4-6 stools per day over baseline; moderate increase in ostomy output compared to baseline.

Analysis Population Description: All participants who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Cycle 3 (28 Days Cycle)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistics were planned for this end point.

End point values	200 mg Abemaciclib with a Meal	200 mg Abemaciclib without a Meal	200 mg Abemaciclib without Regard to Food	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	23	24	
Units: percentage of participants				
number (not applicable)	8.3	17.4	20.8	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Dose Reductions Due to Diarrhea

End point title	Percentage of Participants with Dose Reductions Due to Diarrhea[3]

End point description:

Percentage of participants with dose reductions due to diarrhea during first 3 cycles.

Analysis Population Description: All participants who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Cycle 3 (28 Days Cycle)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistics were planned for this end point.

End point values	200 mg Abemaciclib with a Meal	200 mg Abemaciclib without a Meal	200 mg Abemaciclib without Regard to Food	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	23	24	
Units: percentage of participants				
number (not applicable)	16.7	8.7	12.5	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Dose Interruptions Due to Diarrhea

End point title	Percentage of Participants with Dose Interruptions Due to Diarrhea[4]

End point description:

Percentage of participants with dose interruptions due to diarrhea during first 3 cycles.

Analysis Population Description: All participants who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Cycle 3 (28 Days Cycle)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistics were planned for this end point.

End point values	200 mg Abemaciclib with a Meal	200 mg Abemaciclib without a Meal	200 mg Abemaciclib without Regard to Food	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	23	24	
Units: percentage of participants				
number (not applicable)	16.7	4.3	8.3	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants who Discontinue Treatment due to Diarrhea

End point title	Percentage of Participants who Discontinue Treatment due to Diarrhea[5]

End point description:

Percentage of participants who discontinue treatment due to diarrhea

Analysis Population Description: All participants who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Cycle 3 (28 Days Cycle)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistics were planned for this end point.

End point values	200 mg Abemaciclib with a Meal	200 mg Abemaciclib without a Meal	200 mg Abemaciclib without Regard to Food	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	23	24	
Units: percentage of participants				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Utilizing Antidiarrheals

End point title	Percentage of Participants Utilizing Antidiarrheals[6]

End point description:

Percentage of participants who utilized anti diarrheals at least once during the first 3 cycles.

Analysis Population Description: All participants who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Cycle 3 (28 Days Cycle)

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistics were planned for this end point.

End point values	200 mg Abemaciclib with a Meal	200 mg Abemaciclib without a Meal	200 mg Abemaciclib without Regard to Food	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	23	24	
Units: percentage of participants				
number (not applicable)	95.8	91.3	95.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Mean Steady State Exposure of Abemaciclib

End point title	Pharmacokinetics (PK): Mean Steady State Exposure of Abemaciclib

End point description:

PK: Mean steady state exposure of abemaciclib.

Analysis Population Description: All participants who received at least one dose of study drug who had evaluable PK data.

End point type	Secondary

End point timeframe:

Cycle 1: Day 1, Day 15; Cycle 2: Day1, Day 15; Cycle 3: Day 1 (28 Days Cycle)

End point values	200 mg Abemaciclib with a Meal	200 mg Abemaciclib without a Meal	200 mg Abemaciclib without Regard to Food	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24[7]	21[8]	21[9]	
Units: nanogram/milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1: Day 15	305 (± 198)	369 (± 64)	356 (± 75)	
Cycle 2: Day 1	320 (± 91)	280 (± 99)	190 (± 284)	
Cycle 2: Day 15	77.4 (± 731)	345 (± 51)	223 (± 250)	
Cycle 3: Day 1	135 (± 896)	330 (± 54)	85.4 (± 498)	

Notes:

[7] - Cycle 1:Day 15 n=23, Cycle 2 Day 1 n=15, Cycle 2: Day15 n=14 and Cycle 3: Day 1 n=10.

[8] - Cycle 1:Day 15 n=16, Cycle 2 Day 1 n=12, Cycle 2: Day15 n=13 and Cycle 3: Day 1 n=13.

[9] - Cycle 1:Day 15 n=21, Cycle 2 Day 1 n=18, Cycle 2: Day15 n=15 and Cycle 3: Day 1 n=14.

Statistical analyses

No statistical analyses for this end point

Secondary: PK: Mean Steady State Exposure of Abemaciclib Metabolite LSN2839567

End point title	PK: Mean Steady State Exposure of Abemaciclib Metabolite LSN2839567

End point description:

PK: Mean steady state exposure of abemaciclib metabolite LSN2839567.

Analysis Population Description: All participants who received at least one dose of study drug who had evaluable PK data.

End point type	Secondary

End point timeframe:

Cycle 1: Day 1, Day 15; Cycle 2: Day1, Day 15; Cycle 3: Day 1 (28 Days Cycle)

End point values	200 mg Abemaciclib with a Meal	200 mg Abemaciclib without a Meal	200 mg Abemaciclib without Regard to Food	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24[10]	21[11]	21[12]	
Units: nanogram/milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 15	139 (± 109)	129 (± 48)	159 (± 61)	
Cycle 2 Day 1	125 (± 62)	109 (± 84)	96.3 (± 127)	
Cycle 2 Day 15	50.4 (± 276)	121 (± 45)	112 (± 79)	

Cycle 3 Day 1	89.4 (± 110)	125 (± 48)	61.7 (± 122)	

Notes:

[10] - Cycle 1:Day 15 n=23, Cycle 2 Day 1 n=15, Cycle 2: Day15 n=14 and Cycle 3: Day 1 n=10.

[11] - Cycle 1:Day 15 n=16, Cycle 2 Day 1 n=12, Cycle 2: Day15 n=13 and Cycle 3: Day 1 n=13.

[12] - Cycle 1:Day 15 n=21, Cycle 2 Day 1 n=18, Cycle 2: Day15 n=15 and Cycle 3: Day 1 n=14.

Statistical analyses

No statistical analyses for this end point

Secondary: PK: Mean Steady State Exposure of Abemaciclib Metabolite LSN3106726

End point title	PK: Mean Steady State Exposure of Abemaciclib Metabolite LSN3106726

End point description:

PK: Mean steady state exposure of abemaciclib metabolite LSN3106726.

Analysis Population Description: All participants who received at least one dose of study drug who had evaluable PK data.

End point type	Secondary

End point timeframe:

Cycle 1: Day 1, Day 15; Cycle 2: Day1, Day 15; Cycle 3: Day 1 (28 Days Cycle)

End point values	200 mg Abemaciclib with a Meal	200 mg Abemaciclib without a Meal	200 mg Abemaciclib without Regard to Food	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24[13]	21[14]	21[15]	
Units: nanogram/milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 15	231 (± 120)	242 (± 38)	287 (± 63)	
Cycle 2 Day 1	230 (± 59)	210 (± 57)	152 (± 222)	
Cycle 2 Day 15	80.5 (± 377)	221 (± 31)	182 (± 112)	
Cycle 3 Day 1	146 (± 174)	223 (± 33)	107 (± 172)	

Notes:

[13] - Cycle 1:Day 15 n=23, Cycle 2 Day 1 n=15, Cycle 2: Day15 n=14 and Cycle 3: Day 1 n=10.

[14] - Cycle 1:Day 15 n=16, Cycle 2 Day 1 n=12, Cycle 2: Day15 n=13 and Cycle 3: Day 1 n=13.

[15] - Cycle 1:Day 15 n=21, Cycle 2 Day 1 n=18, Cycle 2: Day15 n=15 and Cycle 3: Day 1 n=14.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline until end of the follow-up (Up To 44 months)	
Adverse event reporting additional description:	
All participants who received at least one dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups	
Reporting group title	200 mg Abemaciclib With a Meal
Reporting group description:	
200 mg abemaciclib given twice a day (BID) orally with a meal.	
Reporting group title	200 mg Abemaciclib Without Regard to Food
Reporting group description:	
200 mg abemaciclib given twice a day (BID) orally without regard for food.	
Reporting group title	200 mg Abemaciclib Without a Meal
Reporting group description:	
200 mg abemaciclib given twice a day (BID) orally without a meal, taken in the modified fasted condition.	

Serious adverse events	200 mg Abemaciclib With a Meal	200 mg Abemaciclib Without Regard to Food	200 mg Abemaciclib Without a Meal
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 24 (12.50%)	8 / 24 (33.33%)	5 / 23 (21.74%)
number of deaths (all causes)	3	1	4
number of deaths resulting from adverse events			
Vascular disorders			
superficial vein thrombosis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (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 disorders			
atrial fibrillation			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	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

Nervous system disorders			
guillain-barre syndrome			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (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
cauda equina syndrome			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	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
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	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
General disorders and administration site conditions			
non-cardiac chest pain			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (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
Gastrointestinal disorders			
pancreatitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	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
nausea			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	3 / 23 (13.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

diarrhoea			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
vomiting			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	2 / 23 (8.70%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
hepatic function abnormal			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (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 / 1
cholangitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	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
cholelithiasis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	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
Respiratory, thoracic and mediastinal disorders			
dyspnoea			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (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
respiratory failure			

alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (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 / 1	0 / 0	0 / 0
pulmonary embolism			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pleural effusion			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	2 / 24 (8.33%)	0 / 23 (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
Renal and urinary disorders			
renal failure			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	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
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	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

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	200 mg Abemaciclib With a Meal	200 mg Abemaciclib Without Regard to Food	200 mg Abemaciclib Without a Meal
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 24 (100.00%)	24 / 24 (100.00%)	23 / 23 (100.00%)

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
metastases to meninges			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
malignant melanoma			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
deep vein thrombosis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
hot flush			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
hypertension			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	1 / 23 (4.35%)
occurrences (all)	0	2	1
lymphoedema			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
Surgical and medical procedures			
abdominal cavity drainage			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
tooth extraction			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0

General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	6 / 24 (25.00%)	4 / 24 (16.67%)	5 / 23 (21.74%)
occurrences (all)	10	12	12
chest pain			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
fatigue			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	11 / 24 (45.83%)	10 / 24 (41.67%)	4 / 23 (17.39%)
occurrences (all)	15	20	5
ill-defined disorder			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
malaise			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
mucosal dryness			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
mucosal inflammation			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	3 / 24 (12.50%)	5 / 24 (20.83%)	1 / 23 (4.35%)
occurrences (all)	3	6	1
nodule			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
oedema peripheral			
alternative dictionary used:			

MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	2 / 24 (8.33%)	2 / 23 (8.70%)
occurrences (all)	0	2	2
non-cardiac chest pain			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	3	0	0
pyrexia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 24 (8.33%)	1 / 24 (4.17%)	2 / 23 (8.70%)
occurrences (all)	2	1	2
Immune system disorders			
seasonal allergy			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	4 / 24 (16.67%)	1 / 24 (4.17%)	5 / 23 (21.74%)
occurrences (all)	5	1	6
dry throat			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
dyspnoea			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	5 / 24 (20.83%)	1 / 24 (4.17%)	1 / 23 (4.35%)
occurrences (all)	5	1	1
dyspnoea exertional			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 24 (8.33%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	2	0	1
nasal congestion			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
pleural effusion			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
oropharyngeal pain			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
pulmonary embolism			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
pulmonary haemorrhage			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Psychiatric disorders			
affect lability			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
anxiety			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
depressed mood			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
depression			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	1 / 23 (4.35%)
occurrences (all)	0	1	1
insomnia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 24 (8.33%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	4 / 24 (16.67%)	5 / 24 (20.83%)	2 / 23 (8.70%)
occurrences (all)	7	9	3
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	6 / 24 (25.00%)	4 / 24 (16.67%)	4 / 23 (17.39%)
occurrences (all)	11	8	7
blood alkaline phosphatase increased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 24 (8.33%)	4 / 24 (16.67%)	2 / 23 (8.70%)
occurrences (all)	4	8	2
blood bilirubin increased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	3 / 24 (12.50%)	1 / 24 (4.17%)	3 / 23 (13.04%)
occurrences (all)	3	1	7
blood calcium decreased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
blood creatinine decreased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
blood creatinine increased			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	3 / 24 (12.50%)	4 / 24 (16.67%)	5 / 23 (21.74%)
occurrences (all)	4	8	10
blood lactate dehydrogenase decreased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
blood lactate dehydrogenase increased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	2 / 23 (8.70%)
occurrences (all)	0	0	3
blood phosphorus decreased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	2
gamma-glutamyltransferase increased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	3 / 24 (12.50%)	4 / 24 (16.67%)	4 / 23 (17.39%)
occurrences (all)	5	10	7
haemoglobin decreased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
hepatic enzyme increased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
glomerular filtration rate decreased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
lymphocyte count decreased			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	5 / 24 (20.83%)	5 / 24 (20.83%)	3 / 23 (13.04%)
occurrences (all)	19	20	6
neutrophil count decreased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	7 / 24 (29.17%)	10 / 24 (41.67%)	6 / 23 (26.09%)
occurrences (all)	35	41	15
platelet count decreased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	11 / 24 (45.83%)	5 / 24 (20.83%)	7 / 23 (30.43%)
occurrences (all)	34	12	16
protein total decreased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	3
white blood cell count decreased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	9 / 24 (37.50%)	7 / 24 (29.17%)	7 / 23 (30.43%)
occurrences (all)	31	39	27
weight decreased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 24 (8.33%)	3 / 24 (12.50%)	5 / 23 (21.74%)
occurrences (all)	2	4	7
Injury, poisoning and procedural complications			
contusion			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	3 / 24 (12.50%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	4	0	0
fall			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
spinal fracture			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
palpitations			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
balance disorder			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
brain fog			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
dizziness			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	5 / 24 (20.83%)	1 / 24 (4.17%)	2 / 23 (8.70%)
occurrences (all)	6	1	2
dysgeusia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 24 (8.33%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	2	1	0
disturbance in attention			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
headache			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	5 / 24 (20.83%)	0 / 24 (0.00%)	2 / 23 (8.70%)
occurrences (all)	7	0	2
hemiparesis			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
lethargy			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
memory impairment			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
neuropathy peripheral			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
peripheral sensory neuropathy			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
seizure			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
sensory disturbance			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
sensory loss			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
sleep deficit			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0

somnolence			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	2 / 24 (8.33%)	1 / 23 (4.35%)
occurrences (all)	0	2	1
taste disorder			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	14 / 24 (58.33%)	10 / 24 (41.67%)	11 / 23 (47.83%)
occurrences (all)	34	33	19
leukopenia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	1 / 23 (4.35%)
occurrences (all)	0	2	5
lymphopenia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 24 (8.33%)	2 / 24 (8.33%)	1 / 23 (4.35%)
occurrences (all)	3	3	3
neutropenia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	6 / 24 (25.00%)	9 / 24 (37.50%)	8 / 23 (34.78%)
occurrences (all)	18	25	21
pancytopenia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
thrombocytopenia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	2 / 24 (8.33%)	2 / 23 (8.70%)
occurrences (all)	1	2	4
Ear and labyrinth disorders			

ear pain			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
vertigo			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
dry eye			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
lacrimation increased			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 24 (8.33%)	2 / 24 (8.33%)	2 / 23 (8.70%)
occurrences (all)	3	8	2
lid sulcus deepened			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	5	0
vision blurred			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	2 / 24 (8.33%)	0 / 23 (0.00%)
occurrences (all)	0	9	0
Gastrointestinal disorders			
abdominal discomfort			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
abdominal distension			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 24 (8.33%)	1 / 24 (4.17%)	2 / 23 (8.70%)
occurrences (all)	2	4	2
abdominal pain			

alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	10 / 24 (41.67%)	5 / 24 (20.83%)	4 / 23 (17.39%)
occurrences (all)	12	8	5
abdominal pain upper			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 24 (8.33%)	2 / 24 (8.33%)	2 / 23 (8.70%)
occurrences (all)	3	4	3
angular cheilitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
ascites			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	1 / 23 (4.35%)
occurrences (all)	0	1	2
constipation			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	3 / 24 (12.50%)	1 / 23 (4.35%)
occurrences (all)	1	3	1
diarrhoea			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	21 / 24 (87.50%)	22 / 24 (91.67%)	22 / 23 (95.65%)
occurrences (all)	204	229	187
dry mouth			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
dyspepsia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	4 / 24 (16.67%)	1 / 23 (4.35%)
occurrences (all)	0	12	1
flatulence			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	3 / 24 (12.50%)	1 / 24 (4.17%)	1 / 23 (4.35%)
occurrences (all)	3	1	1
haemorrhoidal haemorrhage			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	1 / 23 (4.35%)
occurrences (all)	0	1	1
mallory-weiss syndrome			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
mouth ulceration			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 24 (8.33%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
nausea			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	15 / 24 (62.50%)	14 / 24 (58.33%)	11 / 23 (47.83%)
occurrences (all)	16	20	21
odynophagia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
oral blood blister			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
rectal haemorrhage			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0

retching			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
stomatitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
toothache			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
vomiting			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	10 / 24 (41.67%)	7 / 24 (29.17%)	10 / 23 (43.48%)
occurrences (all)	23	10	20
Hepatobiliary disorders			
cholelithiasis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
hepatic failure			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
hepatic pain			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
hepatomegaly			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
hypertransaminasaemia			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	1 / 24 (4.17%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
Skin and subcutaneous tissue disorders			
alopecia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 24 (8.33%)	3 / 24 (12.50%)	1 / 23 (4.35%)
occurrences (all)	2	3	2
dry skin			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 24 (8.33%)	1 / 24 (4.17%)	1 / 23 (4.35%)
occurrences (all)	3	1	1
nail ridging			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
onychoclasis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 24 (8.33%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	3	0	0
onychomadesis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
pain of skin			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
palmar-plantar erythrodysaesthesia syndrome			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
photosensitivity reaction			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
pruritus			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	3 / 24 (12.50%)	4 / 23 (17.39%)
occurrences (all)	1	3	6
rash			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	4 / 24 (16.67%)	2 / 24 (8.33%)	2 / 23 (8.70%)
occurrences (all)	4	2	3
rash macular			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 24 (8.33%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
rash maculo-papular			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
skin exfoliation			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
dysuria			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
hydronephrosis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
nocturia			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
cushingoid			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
hyperthyroidism			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
bone pain			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
arthralgia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	4 / 24 (16.67%)	3 / 23 (13.04%)
occurrences (all)	1	4	4
back pain			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	3 / 24 (12.50%)	5 / 24 (20.83%)	0 / 23 (0.00%)
occurrences (all)	4	6	0
groin pain			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
joint stiffness			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
joint swelling			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
limb discomfort			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
musculoskeletal chest pain			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
musculoskeletal pain			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	2 / 24 (8.33%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
myalgia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 24 (8.33%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	2	1	0
neck pain			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
osteonecrosis of jaw			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
pain in extremity			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
sacral pain			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	2 / 24 (8.33%)	0 / 23 (0.00%)
occurrences (all)	0	2	0

tendonitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
bacterial rhinitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
dermatophytosis of nail			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	1 / 23 (4.35%)
occurrences (all)	0	1	1
cellulitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
conjunctivitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
covid-19			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
gastroenteritis viral			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
diverticulitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
gastroenteritis			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
nasopharyngitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
oral herpes			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
paronychia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
pneumonia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	2	0	1
sinusitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	1	2	0
pyelonephritis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
respiratory tract infection			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	2 / 24 (8.33%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
rhinitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0

skin bacterial infection			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
tinea pedis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
tooth infection			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	1 / 23 (4.35%)
occurrences (all)	0	1	2
upper respiratory tract infection			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	4 / 24 (16.67%)	3 / 24 (12.50%)	0 / 23 (0.00%)
occurrences (all)	6	3	0
urinary tract infection			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	4 / 24 (16.67%)	2 / 24 (8.33%)	2 / 23 (8.70%)
occurrences (all)	4	2	2
viral infection			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
viral upper respiratory tract infection			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 24 (8.33%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
vulvovaginal candidiasis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
Metabolism and nutrition disorders			

decreased appetite			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	8 / 24 (33.33%)	9 / 24 (37.50%)	8 / 23 (34.78%)
occurrences (all)	11	11	12
dehydration			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
hypoalbuminaemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 24 (8.33%)	1 / 24 (4.17%)	3 / 23 (13.04%)
occurrences (all)	4	2	10
hypercalcaemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
hypercholesterolaemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
hyperuricaemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
hypocalcaemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	1 / 24 (4.17%)	1 / 23 (4.35%)
occurrences (all)	1	2	2
hypoglycaemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	2
hypokalaemia			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	1 / 24 (4.17%)	2 / 24 (8.33%)	5 / 23 (21.74%)
occurrences (all)	1	4	8
hypomagnesaemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	1 / 23 (4.35%)
occurrences (all)	0	1	1
hyponatraemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	2 / 23 (8.70%)
occurrences (all)	0	0	3
hypophosphataemia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	2 / 24 (8.33%)	2 / 24 (8.33%)	0 / 23 (0.00%)
occurrences (all)	2	2	0
vitamin b12 deficiency			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 January 2019	Amendment B: Revised inclusion criteria for alanine aminotransferase (ALT) and aspartate aminotransferase (AST) values. Dose adjustment rules modified. Incorporated safety monitoring language for hepatic conditions, renal function and venous thromboembolic events (VTEs). Incorporated cystatin C clinical chemistry laboratory test.
18 February 2020	Amendment D: Revised dose modification and delay guidance for interstitial lung disease (ILD)/pneumonitis events to align with the updated Investigator's Brochure. Revised guidance and listing of moderate inducers and additional strong inhibitors of CYP3A.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported