# 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 | |

### Results information

| | |
|---|---|
| Result version number | v1 |
| This version publication date | 02 August 2020 |
| First version publication date | 02 August 2020 |

## 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 | Interim |
| Date of interim/final analysis | 29 July 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 29 July 2019 |
| Global end of trial reached? | No |

Notes:

## General information about the trial

Main objective of the trial:

The main purpose of this study is to 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 (28 days 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 |
| Adverse event, serious fatal | 2 | 1 | - |
| Consent withdrawn by subject | - | 3 | - |
| Completed < 3 Cycles As Of Data Cut-Off | 1 | 2 | 2 |
| Protocol deviation | 1 | - | - |

## 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<br>Units: Subjects | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 58.2 | 56.9 | 57.6 |
| standard deviation | ± 11.6 | ± 11.1 | ± 8.3 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 23 | 24 | 24 |
| Male | 1 | 0 | 0 |
| Ethnicity (NIH/OMB)<br>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)<br>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<br>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<br>Units: Subjects | | | |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | -<br>- | | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 71 | | |
| Male | 1 | | |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 1 | | |
| Not Hispanic or Latino | 63 | | |
| Unknown or Not Reported | 8 | | |
| Race (NIH/OMB)<br>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<br>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).<br><br>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: Per protocol, no statistical analyses (comparison analysis) were specified.

| 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: Per protocol, no statistical analyses (comparison analysis) were specified.

| **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: Per protocol, no statistical analyses (comparison analysis) were specified.

| **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: Per protocol, no statistical analyses (comparison analysis) were specified.

| **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: Per protocol, no statistical analyses (comparison analysis) were specified.

| 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: Per protocol, no statistical analyses (comparison analysis) were specified.

| 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: | |
| Up To 7 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 | 22.0 |

| 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. | |

| Serious adverse events | 200 mg Abemaciclib with a Meal | 200 mg Abemaciclib without a Meal | 200 mg Abemaciclib without Regard to Food |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | 5 / 23 (21.74%) | 6 / 24 (25.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Vascular disorders | | | |
| thrombophlebitis superficial | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 23 (4.35%) | 0 / 24 (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 |
| Cardiac disorders | | | |
| atrial fibrillation | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 1 / 24 (4.17%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Nervous system disorders | | | |
| guillain-barre syndrome | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 23 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| anaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 1 / 24 (4.17%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| 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 22.0 | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 23 (0.00%) | 0 / 24 (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 | | | |
| diarrhoea | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 23 (0.00%) | 0 / 24 (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 |
| nausea | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 3 / 23 (13.04%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| vomiting | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 2 / 23 (8.70%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Hepatobiliary disorders | | | |
| cholangitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 1 / 24 (4.17%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| cholelithiasis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 1 / 24 (4.17%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hepatic function abnormal | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 23 (4.35%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| dyspnoea | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 23 (0.00%) | 0 / 24 (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 |
| pleural effusion | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 2 / 24 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pulmonary embolism | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 23 (4.35%) | 0 / 24 (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 |
| respiratory failure | | | |

| | | | |
|---|---|---|---|
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 23 (0.00%) | 0 / 24 (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 |
| Renal and urinary disorders | | | |
| renal failure | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 1 / 24 (4.17%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| 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 / 24 (0.00%) | 0 / 23 (0.00%) | 1 / 24 (4.17%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| 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** | 200 mg Abemaciclib with a Meal | 200 mg Abemaciclib without a Meal | 200 mg Abemaciclib without Regard to Food |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 24 / 24 (100.00%) | 23 / 23 (100.00%) | 24 / 24 (100.00%) |
| Investigations | | | |
| alanine aminotransferase increased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 24 (16.67%) | 1 / 23 (4.35%) | 4 / 24 (16.67%) |
| occurrences (all) | 7 | 1 | 6 |
| aspartate aminotransferase increased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 5 / 24 (20.83%) | 1 / 23 (4.35%) | 3 / 24 (12.50%) |
| occurrences (all) | 10 | 1 | 4 |
| blood alkaline phosphatase increased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 24 (8.33%) | 1 / 23 (4.35%) | 3 / 24 (12.50%) |
| occurrences (all) | 4 | 1 | 6 |
| blood bilirubin increased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | 1 / 23 (4.35%) | 1 / 24 (4.17%) |
| occurrences (all) | 2 | 1 | 1 |
| blood creatinine increased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | 5 / 23 (21.74%) | 3 / 24 (12.50%) |
| occurrences (all) | 4 | 7 | 5 |
| gamma-glutamyltransferase increased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | 2 / 23 (8.70%) | 2 / 24 (8.33%) |
| occurrences (all) | 4 | 2 | 2 |
| lymphocyte count decreased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 5 / 24 (20.83%) | 2 / 23 (8.70%) | 4 / 24 (16.67%) |
| occurrences (all) | 9 | 2 | 10 |
| neutrophil count decreased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 6 / 24 (25.00%) | 5 / 23 (21.74%) | 7 / 24 (29.17%) |
| occurrences (all) | 21 | 8 | 24 |
| platelet count decreased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 10 / 24 (41.67%) | 4 / 23 (17.39%) | 5 / 24 (20.83%) |
| occurrences (all) | 22 | 9 | 12 |
| weight decreased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | 4 / 23 (17.39%) | 3 / 24 (12.50%) |
| occurrences (all) | 2 | 5 | 3 |
| white blood cell count decreased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 8 / 24 (33.33%) | 7 / 23 (30.43%) | 7 / 24 (29.17%) |
| occurrences (all) | 20 | 18 | 27 |

| | | | |
|---|---|---|---|
| Injury, poisoning and procedural complications | | | |
| contusion | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | 0 / 23 (0.00%) | 0 / 24 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Nervous system disorders | | | |
| dizziness | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 24 (16.67%) | 2 / 23 (8.70%) | 1 / 24 (4.17%) |
| occurrences (all) | 5 | 2 | 1 |
| dysgeusia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | 0 / 23 (0.00%) | 1 / 24 (4.17%) |
| occurrences (all) | 2 | 0 | 1 |
| headache | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 24 (16.67%) | 2 / 23 (8.70%) | 0 / 24 (0.00%) |
| occurrences (all) | 4 | 2 | 0 |
| Blood and lymphatic system disorders | | | |
| anaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 14 / 24 (58.33%) | 9 / 23 (39.13%) | 9 / 24 (37.50%) |
| occurrences (all) | 23 | 12 | 24 |
| lymphopenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | 1 / 23 (4.35%) | 1 / 24 (4.17%) |
| occurrences (all) | 3 | 3 | 2 |
| neutropenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 6 / 24 (25.00%) | 8 / 23 (34.78%) | 9 / 24 (37.50%) |
| occurrences (all) | 15 | 17 | 22 |
| thrombocytopenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 2 / 23 (8.70%) | 1 / 24 (4.17%) |
| occurrences (all) | 1 | 2 | 1 |

| | | | |
|---|---|---|---|
| General disorders and administration site conditions | | | |
| asthenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 5 / 24 (20.83%) | 5 / 23 (21.74%) | 4 / 24 (16.67%) |
| occurrences (all) | 8 | 11 | 11 |
| fatigue | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 10 / 24 (41.67%) | 3 / 23 (13.04%) | 10 / 24 (41.67%) |
| occurrences (all) | 11 | 3 | 17 |
| mucosal inflammation | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | 1 / 23 (4.35%) | 4 / 24 (16.67%) |
| occurrences (all) | 3 | 1 | 5 |
| oedema peripheral | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 2 / 23 (8.70%) | 1 / 24 (4.17%) |
| occurrences (all) | 0 | 2 | 1 |
| pyrexia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 2 / 23 (8.70%) | 0 / 24 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Eye disorders | | | |
| lacrimation increased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 23 (4.35%) | 2 / 24 (8.33%) |
| occurrences (all) | 0 | 1 | 5 |
| vision blurred | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 2 / 24 (8.33%) |
| occurrences (all) | 0 | 0 | 6 |
| Gastrointestinal disorders | | | |
| abdominal distension | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | 2 / 23 (8.70%) | 1 / 24 (4.17%) |
| occurrences (all) | 2 | 2 | 4 |

| | | | |
|---|---|---|---|
| abdominal pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 9 / 24 (37.50%) | 3 / 23 (13.04%) | 5 / 24 (20.83%) |
| occurrences (all) | 10 | 4 | 7 |
| abdominal pain upper | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | 2 / 23 (8.70%) | 2 / 24 (8.33%) |
| occurrences (all) | 3 | 3 | 4 |
| constipation | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 23 (0.00%) | 2 / 24 (8.33%) |
| occurrences (all) | 1 | 0 | 2 |
| diarrhoea | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 21 / 24 (87.50%) | 22 / 23 (95.65%) | 22 / 24 (91.67%) |
| occurrences (all) | 167 | 173 | 175 |
| dyspepsia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 23 (4.35%) | 3 / 24 (12.50%) |
| occurrences (all) | 0 | 1 | 10 |
| gastrooesophageal reflux disease | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | 1 / 23 (4.35%) | 0 / 24 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| nausea | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 14 / 24 (58.33%) | 11 / 23 (47.83%) | 11 / 24 (45.83%) |
| occurrences (all) | 15 | 19 | 16 |
| vomiting | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 10 / 24 (41.67%) | 10 / 23 (43.48%) | 4 / 24 (16.67%) |
| occurrences (all) | 21 | 18 | 6 |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|---|---|---|
| cough | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 4 / 23 (17.39%) | 1 / 24 (4.17%) |
| occurrences (all) | 2 | 5 | 1 |
| Skin and subcutaneous tissue disorders | | | |
| alopecia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | 1 / 23 (4.35%) | 0 / 24 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| dry skin | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | 1 / 23 (4.35%) | 1 / 24 (4.17%) |
| occurrences (all) | 3 | 1 | 1 |
| pruritus | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 3 / 23 (13.04%) | 2 / 24 (8.33%) |
| occurrences (all) | 1 | 3 | 2 |
| rash | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 24 (16.67%) | 2 / 23 (8.70%) | 2 / 24 (8.33%) |
| occurrences (all) | 4 | 3 | 2 |
| Musculoskeletal and connective tissue disorders | | | |
| arthralgia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 2 / 23 (8.70%) | 1 / 24 (4.17%) |
| occurrences (all) | 1 | 2 | 1 |
| back pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | 0 / 23 (0.00%) | 2 / 24 (8.33%) |
| occurrences (all) | 3 | 0 | 3 |
| musculoskeletal pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 23 (4.35%) | 3 / 24 (12.50%) |
| occurrences (all) | 0 | 1 | 3 |
| Infections and infestations | | | |

| | | | |
|---|---|---|---|
| respiratory tract infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 23 (0.00%) | 2 / 24 (8.33%) |
| occurrences (all) | 0 | 0 | 2 |
| urinary tract infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | 1 / 23 (4.35%) | 2 / 24 (8.33%) |
| occurrences (all) | 2 | 1 | 2 |
| viral upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | 0 / 23 (0.00%) | 0 / 24 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| decreased appetite | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 7 / 24 (29.17%) | 8 / 23 (34.78%) | 9 / 24 (37.50%) |
| occurrences (all) | 8 | 11 | 11 |
| hypoalbuminaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | 3 / 23 (13.04%) | 0 / 24 (0.00%) |
| occurrences (all) | 4 | 6 | 0 |
| hypokalaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | 5 / 23 (21.74%) | 0 / 24 (0.00%) |
| occurrences (all) | 1 | 8 | 0 |
| hyponatraemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | 2 / 23 (8.70%) | 0 / 24 (0.00%) |
| occurrences (all) | 0 | 2 | 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