



Clinical trial results:

An Adaptive, Open-Label, Randomized Phase 2 Study of Abemaciclib as a Monotherapy and in Combination with Other Agents Versus Choice of Standard of Care (Gemcitabine or Capecitabine) in Patients with Previously Treated Metastatic Pancreatic Ductal Adenocarcinoma Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2016-002218-36 |
| Trial protocol | HU BE GB ES FR |
| Global end of trial date | 09 November 2018 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 27 November 2019 |
| First version publication date | 27 November 2019 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | I3Y-MC-JPCJ |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|---------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02981342 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Trial Number: 16342 |

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 November 2018 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 09 November 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the safety and efficacy of abemaciclib alone and in combination with other drugs versus standard of care in participants with previously treated metastatic pancreatic ductal adenocarcinoma (PDAC).

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 | 12 January 2017 |
| 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 | Belgium: 19 |
| Country: Number of subjects enrolled | United States: 33 |
| Country: Number of subjects enrolled | Taiwan: 14 |
| Country: Number of subjects enrolled | United Kingdom: 1 |
| Country: Number of subjects enrolled | Israel: 11 |
| Country: Number of subjects enrolled | Australia: 5 |
| Country: Number of subjects enrolled | France: 8 |
| Country: Number of subjects enrolled | Spain: 15 |
| Worldwide total number of subjects | 106 |
| EEA total number of subjects | 43 |

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 | 0 |

| | |
|---------------------------|----|
| months) | |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 65 |
| From 65 to 84 years | 40 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details:

Study was planned for stage 1 & stage 2. No participants were enrolled to stage 2; however, results for stage 2 outcomes are reported from the data collected for participants enrolled to stage 1.

Pre-assignment

Screening details:

Per protocol, no efficacy analysis was planned for safety lead in. Purpose of safety lead in was only safety evaluation. All efficacy was done on randomized pts.

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 | 150mg Abemaciclib + 150mg Galunisertib (Safety Lead-in) |

Arm description:

Participants received oral dose of 150mg Abemaciclib twice daily for 28 day cycles along with oral dose of 150 mg Galunisertib twice daily for 14 days of 28 days cycle.

| | |
|--|----------------|
| Arm type | Safety Lead in |
| Investigational medicinal product name | Abemaciclib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received oral dose of 150mg Abemaciclib twice daily for 28 day cycles.

| | |
|--|--------------|
| Investigational medicinal product name | Galunisertib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received oral dose of 150 mg Galunisertib twice daily for 14 days of 28 days cycle.

| | |
|------------------|-------------------|
| Arm title | 200mg Abemaciclib |
|------------------|-------------------|

Arm description:

Participants received oral dose of 200mg Abemaciclib twice daily (BID) for 28 day cycles.

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

Dosage and administration details:

Participants received oral dose of 200mg Abemaciclib twice daily (BID) for 28 day cycles.

| | |
|------------------|-------------------------------------|
| Arm title | 150mg Abemaciclib + 150mg LY3023414 |
|------------------|-------------------------------------|

Arm description:

Participants received oral dose of 150mg Abemaciclib along with 150mg LY3023414 twice daily for 28 day cycles.

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

Dosage and administration details:

Participants received oral dose of 150mg Abemaciclib twice daily for 28 day cycles.

| | |
|--|-----------|
| Investigational medicinal product name | LY3023414 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received oral dose of 150mg LY3023414 twice daily for 28 day cycles.

| | |
|------------------|-----------------------------|
| Arm title | Gemcitabine or Capecitabine |
|------------------|-----------------------------|

Arm description:

Participants received either 1000 milligram per square meter (mg/m²) of Gemcitabine by intravenous infusion on days 1, 8, 15 and 22 of 28 day cycle

or

1250 mg/m² oral dose of Capecitabine twice daily for 14 days of 21 day cycle.

| | |
|--|-----------------|
| Arm type | Standard care |
| Investigational medicinal product name | Gemcitabine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received either 1000 milligram per square meter (mg/m²) of Gemcitabine by intravenous infusion on days 1, 8, 15 and 22 of 28 day cycle.

| | |
|--|--------------|
| Investigational medicinal product name | Capecitabine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received 1250 mg/m² oral dose of Capecitabine twice daily for 14 days of 21 day cycle.

| Number of subjects in period 1 | 150mg Abemaciclib + 150mg Galunisertib (Safety Lead-in) | 200mg Abemaciclib | 150mg Abemaciclib + 150mg LY3023414 |
|--|---|-------------------|-------------------------------------|
| Started | 7 | 33 | 33 |
| Received at least one dose of study drug | 7 | 32 | 33 |
| Completed | 7 | 22 | 20 |
| Not completed | 0 | 11 | 13 |
| Study Closed by Sponsor | - | - | 1 |

| | | | |
|------------------------------|---|---|---|
| Consent withdrawn by subject | - | - | 3 |
| Death | - | 9 | 9 |
| Randomized, Never Treated | - | 1 | - |
| Adverse event | - | - | - |
| Lost to follow-up | - | 1 | - |

| Number of subjects in period 1 | Gemcitabine or Capecitabine |
|--|--------------------------------|
| Started | 33 |
| Received at least one dose of study drug | 26 |
| Completed | 19 |
| Not completed | 14 |
| Study Closed by Sponsor | 1 |
| Consent withdrawn by subject | 1 |
| Death | 4 |
| Randomized, Never Treated | 7 |
| Adverse event | 1 |
| Lost to follow-up | - |

Baseline characteristics

Reporting groups

| | |
|---|---|
| Reporting group title | 150mg Abemaciclib + 150mg Galunisertib (Safety Lead-in) |
| Reporting group description: | |
| Participants received oral dose of 150mg Abemaciclib twice daily for 28 day cycles along with oral dose of 150 mg Galunisertib twice daily for 14 days of 28 days cycle. | |
| Reporting group title | 200mg Abemaciclib |
| Reporting group description: | |
| Participants received oral dose of 200mg Abemaciclib twice daily (BID) for 28 day cycles. | |
| Reporting group title | 150mg Abemaciclib + 150mg LY3023414 |
| Reporting group description: | |
| Participants received oral dose of 150mg Abemaciclib along with 150mg LY3023414 twice daily for 28 day cycles. | |
| Reporting group title | Gemcitabine or Capecitabine |
| Reporting group description: | |
| Participants received either 1000 milligram per square meter (mg/m ²) of Gemcitabine by intravenous infusion on days 1, 8, 15 and 22 of 28 day cycle or 1250 mg/m ² oral dose of Capecitabine twice daily for 14 days of 21 day cycle. | |

| Reporting group values | 150mg Abemaciclib + 150mg Galunisertib (Safety Lead-in) | 200mg Abemaciclib | 150mg Abemaciclib + 150mg LY3023414 |
|---|---|-------------------|-------------------------------------|
| Number of subjects | 7 | 33 | 33 |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: years | | | |
| arithmetic mean | 65.29 | 61.09 | 62.52 |
| standard deviation | ± 6.99 | ± 7.83 | ± 8.97 |
| Gender categorical Units: Subjects | | | |
| Female | 4 | 18 | 16 |
| Male | 3 | 15 | 17 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 0 | 2 | 4 |
| Not Hispanic or Latino | 7 | 30 | 28 |
| Unknown or Not Reported | 0 | 1 | 1 |

| | | | |
|---|---|----|----|
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 7 | 5 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 1 |
| White | 7 | 26 | 26 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 0 | 1 |
| Region of Enrollment | | | |
| Units: Subjects | | | |
| Belgium | 0 | 8 | 6 |
| United States | 7 | 8 | 10 |
| Taiwan | 0 | 7 | 4 |
| United Kingdom | 0 | 1 | 0 |
| Israel | 0 | 2 | 4 |
| Australia | 0 | 1 | 1 |
| France | 0 | 1 | 1 |
| Spain | 0 | 5 | 7 |

| Reporting group values | Gemcitabine or Capecitabine | Total | |
|--|-----------------------------|-------|--|
| Number of subjects | 33 | 106 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | | 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) | | 0 | |
| From 65-84 years | | 0 | |
| 85 years and over | | 0 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 66.85 | | |
| standard deviation | ± 7.61 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 19 | 57 | |
| Male | 14 | 49 | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 3 | 9 | |
| Not Hispanic or Latino | 24 | 89 | |
| Unknown or Not Reported | 6 | 8 | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |

| | | | |
|---|----|----|--|
| Asian | 4 | 16 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 3 | 4 | |
| White | 25 | 84 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 1 | 2 | |
| Region of Enrollment | | | |
| Units: Subjects | | | |
| Belgium | 5 | 19 | |
| United States | 8 | 33 | |
| Taiwan | 3 | 14 | |
| United Kingdom | 0 | 1 | |
| Israel | 5 | 11 | |
| Australia | 3 | 5 | |
| France | 6 | 8 | |
| Spain | 3 | 15 | |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | 150mg Abemaciclib + 150mg Galunisertib (Safety Lead-in) |
| Reporting group description: Participants received oral dose of 150mg Abemaciclib twice daily for 28 day cycles along with oral dose of 150 mg Galunisertib twice daily for 14 days of 28 days cycle. | |
| Reporting group title | 200mg Abemaciclib |
| Reporting group description: Participants received oral dose of 200mg Abemaciclib twice daily (BID) for 28 day cycles. | |
| Reporting group title | 150mg Abemaciclib + 150mg LY3023414 |
| Reporting group description: Participants received oral dose of 150mg Abemaciclib along with 150mg LY3023414 twice daily for 28 day cycles. | |
| Reporting group title | Gemcitabine or Capecitabine |
| Reporting group description: Participants received either 1000 milligram per square meter (mg/m ²) of Gemcitabine by intravenous infusion on days 1, 8, 15 and 22 of 28 day cycle or 1250 mg/m ² oral dose of Capecitabine twice daily for 14 days of 21 day cycle. | |
| Subject analysis set title | 150mg Abemaciclib + 150mg Galunisertib |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Participants received oral dose of 150mg Abemaciclib twice daily for 28 day cycles along with oral dose of 150 mg Galunisertib twice daily for 14 days of 28 days cycle. | |
| Subject analysis set title | 150mg Abemaciclib + 150mg LY3023414 |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Participants received oral dose of 150mg Abemaciclib along with 150mg LY302341 twice daily for 28 day cycles. | |

Primary: Stage 1: Disease Control Rate (DCR): Percentage of Participants with a Best Overall Response of Complete Response (CR), Partial Response (PR) or Stable Disease (SD)

| | |
|-----------------|---|
| End point title | Stage 1: Disease Control Rate (DCR): Percentage of Participants with a Best Overall Response of Complete Response (CR), Partial Response (PR) or Stable Disease (SD) ^[1] |
|-----------------|---|

End point description:

Disease control rate (DCR) is the percentage of participants with a best overall response of CR, PR or SD as defined by RECIST v1.1. CR is defined as the disappearance of all target and non-target lesions and no appearance of new lesions. PR is defined as at least a 30% decrease in the sum of the longest diameter (LD) of target lesions (taking as reference the baseline sum LD), no progression of non-target lesions, and no appearance of new lesions. SD is neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (PD) for target lesions, no progression of non-target lesions, and no appearance of new lesions. PD is defined as at least a 20% increase in the sum of the diameters of target lesions, with reference being the smallest sum on study and an absolute increase of at least 5 mm, or unequivocal progression of non-target lesions, or 1 or more new lesions.

Analysis Population Description (APD): All randomized participants.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline to Measured Progressive Disease or Start of New Anticancer Therapy (Up to 6 Months)

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Per protocol, statistical analysis was not planned for all arms.

| End point values | 200mg Abemaciclib | 150mg Abemaciclib + 150mg LY3023414 | Gemcitabine or Capecitabine | |
|-----------------------------------|--------------------|-------------------------------------|-----------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 33 | 33 | 33 | |
| Units: percentage of Participants | | | | |
| number (confidence interval 95%) | 15.2 (2.9 to 27.4) | 12.1 (1.0 to 23.3) | 36.4 (20 to 52.8) | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 66 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0495 |
| Method | Cochran-Mantel-Haenszel |

| Statistical analysis title | Statistical Analysis 2 |
|---|---|
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 66 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.023 |
| Method | Cochran-Mantel-Haenszel |

Primary: Stage 2: Progression Free Survival (PFS)

| | |
|-----------------|---|
| End point title | Stage 2: Progression Free Survival (PFS) ^[2] |
|-----------------|---|

End point description:

PFS was defined as the time from the date of randomization until first observation of objective progressive disease as defined by RECIST v1.1 or death from any cause, whichever comes first. PD is defined as at least a 20% increase in the sum of the diameters of target lesions, with reference being the smallest sum on study and an absolute increase of at least 5 mm, or unequivocal progression of non-target lesions, or 1 or more new lesions. If a patient does not have a complete baseline disease assessment, then the PFS time will be censored at the randomization date, regardless of whether or not objectively determined disease progression or death has been observed for the patient; otherwise, if a patient is not known to have died or have objective progression as of the data inclusion cutoff date for the analysis, the PFS time will be censored at the last complete objective progression-free disease assessment date.

APD: All randomized participants.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline to Measured Progressive Disease or Death Due to Any Cause (Up to 6 Months)

Censored participants: Abemaciclib 200 mg: 3, Abemaciclib 150mg + LY3023414 150mg: 8, Gemcitabine & Capecitabine: 18;

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No participants were enrolled in stage 2; however, results for stage 2 outcomes are reported from the data collected for participants enrolled in stage 1.

Per protocol, statistical analysis was not planned for all arms.

| End point values | 200mg Abemaciclib | 150mg Abemaciclib + 150mg LY3023414 | Gemcitabine or Capecitabine | |
|----------------------------------|---------------------|-------------------------------------|-----------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 33 | 33 | 33 | |
| Units: Months | | | | |
| median (confidence interval 95%) | 1.68 (1.35 to 1.84) | 1.81 (1.28 to 1.91) | 3.25 (1.05 to 5.65) | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 66 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0085 |
| Method | Logrank |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 2 |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 66 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0123 |
| Method | Logrank |

Secondary: Stage 1: Objective Response Rate (ORR): Percentage of Participants with a Best Overall Response (BOR) of CR or PR

| | |
|-----------------|--|
| End point title | Stage 1: Objective Response Rate (ORR): Percentage of Participants with a Best Overall Response (BOR) of CR or PR ^[3] |
|-----------------|--|

End point description:

Objective response rate (ORR) is the percentage of participants with a BOR of CR or PR as defined by RECIST v1.1. CR is defined as the disappearance of all target and non-target lesions and no appearance of new lesions. PR is defined as at least a 30% decrease in the sum of the LD of target lesions (taking as reference the baseline sum LD), no progression of non-target lesions, and no appearance of new lesions.

APD: All randomized participants.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Measured Progressive Disease or Start of New Anti-Cancer Therapy (Up to 6 Months)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Per protocol, statistical analysis was not planned for all arms.

| End point values | 200mg Abemaciclib | 150mg Abemaciclib + 150mg LY3023414 | Gemcitabine or Capecitabine | |
|-----------------------------------|-------------------|-------------------------------------|-----------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 33 | 33 | 33 | |
| Units: percentage of Participants | | | | |
| number (confidence interval 95%) | 3 (0 to 8.9) | 0 (0 to 0) | 3 (0 to 8.9) | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 66 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 1 |
| Method | Cochran-Mantel-Haenszel |

| Statistical analysis title | Statistical Analysis 2 |
|---|---|
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 66 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3017 |
| Method | Cochran-Mantel-Haenszel |

Secondary: Stage 1: Pharmacokinetics (PK): Mean Steady State Exposure of Abemaciclib and Its Metabolites (LSN2839567 (M2), LSN3106726 (M20))

| | |
|-----------------|--|
| End point title | Stage 1: Pharmacokinetics (PK): Mean Steady State Exposure of Abemaciclib and Its Metabolites (LSN2839567 (M2), LSN3106726 (M20)) ^[4] |
|-----------------|--|

End point description:

Mean steady state exposure was reported as measured by maximum observed plasma concentration (C_{max}).

All randomized participants who received at least one dose of Abemaciclib along with Galunisertib and had evaluable PK samples.

Geometric CV is expressed as %.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Cycle(C)1 Day(D)14: 0 hour(h),0.5h,1h,2h,4h,6h,8h post dose | |

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol, statistical analysis was not planned for all arms.

| | | | | |
|---|---|--|--|--|
| End point values | 150mg Abemaciclib + 150mg Galunisertib (Safety Lead-in) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 4 | | | |
| Units: Nanogram per Millilitre (ng/mL) | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Abemaciclib LSN2839567 (M2) LSN3106726 (M20) | 356 (± 137) 85.1 (± 66) 153 (± 58) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 1: PK: Area Under the Curve (AUC) (AUC[Tau]) of LY3023414

| | |
|-----------------|--|
| End point title | Stage 1: PK: Area Under the Curve (AUC) (AUC[Tau]) of LY3023414 ^[5] |
|-----------------|--|

End point description:

APD: Zero Participants Analyzed: AUC was not analyzed due to insufficient data collected.

Geometric CV is expressed as %.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Cycle 1 Day 1 through Cycle 4 Day 1 (28 Day Cycles) | |

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol, statistical analysis was not planned for all arms.

| | | | | |
|---|--|--|--|--|
| End point values | 150mg Abemaciclib + 150mg LY3023414 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[6] | | | |
| Units: nanogram*hour per Milliliter | | | | |
| geometric mean (geometric coefficient of variation) | () | | | |

Notes:

[6] - Zero Participants Analyzed: AUC was not analyzed due to insufficient data collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 1: PK: Maximum Concentration (Cmax) at Steady State of LY3023414

| | |
|-----------------|---|
| End point title | Stage 1: PK: Maximum Concentration (Cmax) at Steady State of LY3023414 ^[7] |
|-----------------|---|

End point description:

Zero Participants Analyzed: Cmax was not analyzed due to insufficient data collected.

Geometric CV is expressed as %.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Cycle 1 Day 1 through Cycle 4 Day 1 (28 Day Cycles)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Per protocol, statistical analysis was not planned.

| | | | | |
|---|--|--|--|--|
| End point values | 150mg Abemaciclib + 150mg LY3023414 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[8] | | | |
| Units: mm | | | | |
| geometric mean (geometric coefficient of variation) | () | | | |

Notes:

[8] - Zero Participants Analyzed: Cmax was not analyzed due to insufficient data collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 2: Disease Control Rate (DCR): Percentage of Participants With a Best Overall Response of CR, PR, and SD

| | |
|-----------------|---|
| End point title | Stage 2: Disease Control Rate (DCR): Percentage of Participants With a Best Overall Response of CR, PR, and SD ^[9] |
|-----------------|---|

End point description:

APD: Data not reported, no patients were enrolled to stage 2.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Measured Progressive Disease or Start of New Anticancer Therapy (Up to 6 Months)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol, statistical analysis was not planned for all arms.

| End point values | 200mg Abemaciclib | 150mg Abemaciclib + 150mg LY3023414 | Gemcitabine or Capecitabine | |
|-----------------------------------|----------------------|--|--------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[10] | 0 ^[11] | 0 ^[12] | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | (to) | (to) | (to) | |

Notes:

[10] - Data not reported, no patients were enrolled to stage 2.

[11] - Data not reported, no patients were enrolled to stage 2.

[12] - Data not reported, no patients were enrolled to stage 2.

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 2: Clinical Benefit Rate (CBR): Percentage of Participants with Best Overall Response of CR, PR, or SD with Duration of SD for at Least 6 Months

| | |
|-----------------|--|
| End point title | Stage 2: Clinical Benefit Rate (CBR): Percentage of Participants with Best Overall Response of CR, PR, or SD with Duration of SD for at Least 6 Months ^[13] |
|-----------------|--|

End point description:

Clinical benefit rate (CBR) is the percentage of participants with a BOR of CR or PR, or SD ≥ 6 months. CR is defined as the disappearance of all target and non-target lesions & no appearance of new lesions. PR is defined as at least a 30% decrease in the sum of the LD of target lesions (taking as reference the baseline sum LD), no progression of non-target lesions, and no appearance of new lesions. SD is neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD for target lesions, no progression of non-target lesions, and no appearance of new lesions. PD is defined as at least a 20% increase in the sum of the diameters of target lesions, with reference being the smallest sum on study and an absolute increase of at least 5 mm, or unequivocal progression of non-target lesions, or 1 or more new lesions.

No participants were enrolled to stage 2; however, results for stage 2 outcomes are reported from the data collected for participants enrolled to stage 1.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Disease Progression or Start of New Anticancer Therapy (Up to 6 Months)

APD: All randomized participants.

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Per protocol, statistical analysis was not planned for all arms.

| End point values | 200mg Abemaciclib | 150mg Abemaciclib + 150mg LY3023414 | Gemcitabine or Capecitabine | |
|-----------------------------------|----------------------|--|--------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 33 | 33 | 33 | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 3 (0 to 8.9) | 0 (0 to 0) | 3 (0 to 8.9) | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 66 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 1 |
| Method | Cochran-Mantel-Haenszel |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 2 |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 66 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3017 |
| Method | Cochran-Mantel-Haenszel |

Secondary: Stage 2: Duration of Response (DoR)

| | |
|------------------------|--|
| End point title | Stage 2: Duration of Response (DoR) ^[14] |
| End point description: | DoR was not analyzed due to small sample size with PR data. |
| End point type | Secondary |
| End point timeframe: | Date of CR or PR to Date of Disease Progression or Death Due to Any Cause (Up to 6 Months) |

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Per protocol, statistical analysis was not planned for all arms.

| End point values | 200mg Abemaciclib | 150mg Abemaciclib + 150mg LY3023414 | Gemcitabine or Capecitabine | |
|----------------------------------|-------------------|-------------------------------------|-----------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[15] | 0 ^[16] | 0 ^[17] | |
| Units: Months | | | | |
| median (confidence interval 95%) | (to) | (to) | (to) | |

Notes:

[15] - DoR was not analyzed due to small sample size with PR data.

[16] - DoR was not analyzed due to small sample size with PR data.

[17] - DoR was not analyzed due to small sample size with PR data.

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 2: Overall Survival (OS)

| | |
|-----------------|--|
| End point title | Stage 2: Overall Survival (OS) ^[18] |
|-----------------|--|

End point description:

OS duration is measured from the date of randomization to the date of death from any cause. for participants who is not known to have died as of the data-inclusion cutoff date, OS was censored at the last known alive date.

No participants were enrolled to stage 2; however, results for stage 2 outcomes are reported from the data collected for participants enrolled to stage 1.

APD: All randomized participants.

Censored participants: Abemaciclib 200mg: 11, Abemaciclib 150mg + LY3023414 150mg: 12,

Gemcitabine + Capecitabine: 21;

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Death from Any Cause (Up to 10 Months)

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Per protocol, statistical analysis was not planned for all arms.

| End point values | 200mg Abemaciclib | 150mg Abemaciclib + 150mg LY3023414 | Gemcitabine or Capecitabine | |
|----------------------------------|------------------------|--|--------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 33 | 33 | 33 ^[19] | |
| Units: Months | | | | |
| median (confidence interval 95%) | 2.71 (1.97 to 5.36) | 3.29 (1.97 to 5.03) | 9999 (2.53 to 9999) | |

Notes:

[19] - 9999 = N/A

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 66 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1938 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.6 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.782 |
| upper limit | 3.272 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 2 |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 66 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2477 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.533 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.746 |
| upper limit | 3.15 |

Secondary: Stage 2: Change from Baseline in Carbohydrate Antigen 19.9 (CA 19-9) Level

| | |
|-----------------|--|
| End point title | Stage 2: Change from Baseline in Carbohydrate Antigen 19.9 (CA 19-9) Level ^[20] |
|-----------------|--|

End point description:

No participants were enrolled to stage 2; however, results for stage 2 outcomes are reported from the data collected for participants enrolled to stage 1.

APD: All randomized participants with baseline and post baseline CA 19-9 measurement.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, 6 Months

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Per protocol, statistical analysis was not planned for all arms.

| End point values | 200mg Abemaciclib | 150mg Abemaciclib + 150mg LY3023414 | Gemcitabine or Capecitabine | |
|--------------------------------------|---------------------|-------------------------------------|-----------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 24 | 21 | 20 | |
| Units: U/mL | | | | |
| arithmetic mean (standard deviation) | 4281.53 (± 8177.89) | 3225.29 (± 5730.25) | -501.17 (± 7198.70) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 2: Change from Baseline in Pain and Symptom Burden Assessment on the Modified Brief Pain Inventory-Short Form (mBPI-sf)

| | |
|-----------------|---|
| End point title | Stage 2: Change from Baseline in Pain and Symptom Burden Assessment on the Modified Brief Pain Inventory-Short Form (mBPI-sf) ^[21] |
|-----------------|---|

End point description:

mBPI-sf is an 11-item instrument used as a multiple-item measure of cancer pain intensity. In addition to pain intensity (4 items), the mBPI-sf is designed for participants to record the presence of pain in general, pain relief, and pain interference with function (general activity, mood, ability to walk, ability to perform normal work, relations with others, sleep, and enjoyment of life). Responses for the mBPI-sf items are captured through the use of 11-point numeric rating scales anchored at 0 (no pain or does not interfere) and ranged through 10 (pain as bad as you can imagine or completely interferes). The mBPI-sf recall period is 24 hours, and typical completion time for this instrument is less than 5 minutes. No participants were enrolled to stage 2; however, results for stage 2 outcomes are reported from the data collected for participants enrolled to stage 1.

APD: All randomized participants with baseline & post baseline value for the mBPI-sf specified item.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, 6 Months

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Per protocol, statistical analysis was not planned for all arms.

| End point values | 200mg Abemaciclib | 150mg Abemaciclib + 150mg LY3023414 | Gemcitabine or Capecitabine | |
|-------------------------------------|-------------------|-------------------------------------|-----------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 19 | 14 | 13 | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | | | | |
| Pain at its Worst in Last 24 hours | 0.63 (± 0.47) | -0.33 (± 0.55) | -0.02 (± 0.57) | |
| Pain at its Least in Last 24 hours | 0.86 (± 0.42) | 0.18 (± 0.49) | 0.39 (± 0.51) | |
| Pain on the Average | 0.62 (± 0.45) | -0.03 (± 0.51) | -0.07 (± 0.53) | |
| Pain Right Now | 0.38 (± 0.34) | 0.34 (± 0.59) | -0.38 (± 0.61) | |
| Pain Interfered General Activity | 0.64 (± 0.47) | 0.07 (± 0.55) | 0.22 (± 0.57) | |
| Pain Interfered with Mood | 0.54 (± 0.41) | 0.28 (± 0.48) | 0.60 (± 0.50) | |
| Pain Interfered Walking Ability | 0.05 (± 0.55) | 0.83 (± 0.64) | 0.19 (± 0.67) | |
| Pain Interfered with Normal Work | 1.07 (± 0.51) | 0.66 (± 0.59) | 0.19 (± 0.61) | |
| Pain Interfered with Relations | 0.39 (± 0.52) | 0.67 (± 0.61) | 0.26 (± 0.63) | |
| Pain Interfered with Sleep | 0.19 (± 0.53) | 0.34 (± 0.61) | -0.56 (± 0.65) | |
| Pain Interfered Enjoyment of Life | 0.69 (± 0.62) | 0.39 (± 0.72) | -0.13 (± 0.75) | |
| BPI Mean Pain Interference Score | 0.55 (± 0.44) | 0.50 (± 0.51) | 0.05 (± 0.54) | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: Pain at its Worst in Last 24 Hours | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[22] |
| P-value | = 0.383 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 0.65 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.84 |
| upper limit | 2.13 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.74 |

Notes:

[22] - Pain at its Worst in Last 24 Hours

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 2 |
| Statistical analysis description: Pain at its Worst in Last 24 Hours | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[23] |
| P-value | = 0.692 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -0.31 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.91 |
| upper limit | 1.28 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.79 |

Notes:

[23] - Pain at its Worst in Last 24 Hours

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 3 |
| Statistical analysis description: | |
| Pain at its Least in Last 24 Hours | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.469 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 0.48 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.85 |
| upper limit | 1.8 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.66 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 4 |
| Statistical analysis description: | |
| Pain at its Least in Last 24 Hours | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[24] |
| P-value | = 0.776 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.62 |
| upper limit | 1.22 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.7 |

Notes:

[24] - Pain at its Least in Last 24 Hours

| | |
|-----------------------------------|---|
| Statistical analysis title | Statistical Analysis 5 |
| Statistical analysis description: | |
| Pain on the Average | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |

| | |
|---|-----------------------------|
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[25] |
| P-value | = 0.328 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 0.69 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.72 |
| upper limit | 2.11 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.7 |

Notes:

[25] - Pain on the Average

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 6 |
| Statistical analysis description: | |
| Pain on the Average | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[26] |
| P-value | = 0.954 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 0.04 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.45 |
| upper limit | 1.54 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.74 |

Notes:

[26] - Pain on the Average

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 7 |
| Statistical analysis description: | |
| Pain Right Now | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[27] |
| P-value | = 0.35 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 0.75 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.85 |
| upper limit | 2.36 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.8 |

Notes:

[27] - Pain Right Now

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 8 |
|-----------------------------------|------------------------|

Statistical analysis description:

Pain on the Average

| | |
|---|---|
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[28] |
| P-value | = 0.405 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 0.72 |

Confidence interval

| | |
|----------------------|----------------------------|
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.01 |
| upper limit | 2.44 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.85 |

Notes:

[28] - Pain on the Average

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 9 |
|-----------------------------------|------------------------|

Statistical analysis description:

Pain Interfered General Activity

| | |
|---|---|
| Comparison groups | Gemcitabine or Capecitabine v 200mg Abemaciclib |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[29] |
| P-value | = 0.565 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 0.43 |

Confidence interval

| | |
|----------------------|----------------------------|
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.06 |
| upper limit | 1.91 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.73 |

Notes:

[29] - Pain Interfered General Activity

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 10 |
| Statistical analysis description: Pain Interfered General Activity | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[30] |
| P-value | = 0.848 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -0.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.74 |
| upper limit | 1.43 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.79 |

Notes:

[30] - Pain Interfered General Activity

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 11 |
| Statistical analysis description: Pain Interfered with Mood | |
| Comparison groups | Gemcitabine or Capecitabine v 200mg Abemaciclib |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[31] |
| P-value | = 0.928 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -0.06 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.37 |
| upper limit | 1.25 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.65 |

Notes:

[31] - Pain Interfered with Mood

| | |
|--|--|
| Statistical analysis title | Statistical Analysis 12 |
| Statistical analysis description: Pain Interfered with Mood | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or |

| | |
|---|-----------------------------|
| | Capecitabine |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[32] |
| P-value | = 0.65 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -0.32 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.71 |
| upper limit | 1.08 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.69 |

Notes:

[32] - Pain Interfered with Mood

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 13 |
| Statistical analysis description: Pain Interfered Walking Ability | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[33] |
| P-value | = 0.865 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -0.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.89 |
| upper limit | 1.6 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.86 |

Notes:

[33] - Pain Interfered Walking Ability

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 14 |
| Statistical analysis description: Pain Interfered Walking Ability | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[34] |
| P-value | = 0.497 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 0.63 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.23 |
| upper limit | 2.5 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.92 |

Notes:

[34] - Pain Interfered Walking Ability

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 15 |
| Statistical analysis description: Pain Interfered with Normal Work | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[35] |
| P-value | = 0.272 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 0.89 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.72 |
| upper limit | 2.5 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.8 |

Notes:

[35] - Pain Interfered with Normal Work

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 16 |
| Statistical analysis description: Pain Interfered with Normal Work | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[36] |
| P-value | = 0.583 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 0.47 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.25 |
| upper limit | 2.19 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.85 |

Notes:

[36] - Pain Interfered with Normal Work

| Statistical analysis title | Statistical Analysis 17 |
|---|---|
| Statistical analysis description: Pain Interfered with Relations | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[37] |
| P-value | = 0.876 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 0.13 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.53 |
| upper limit | 1.79 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.82 |

Notes:

[37] - Pain Interfered with Relations

| Statistical analysis title | Statistical Analysis 18 |
|--|---|
| Statistical analysis description: Pain Interfered with relations. | |
| Comparison groups | Gemcitabine or Capecitabine v 150mg Abemaciclib + 150mg LY3023414 |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.644 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 0.41 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.37 |
| upper limit | 2.19 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.88 |

| Statistical analysis title | Statistical Analysis 19 |
|---|---|
| Statistical analysis description: Pain Interfered with Sleep | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |

| | |
|---|-----------------------------|
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[38] |
| P-value | = 0.384 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 0.75 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.97 |
| upper limit | 2.48 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.85 |

Notes:

[38] - Pain Interfered with Sleep

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 20 |
| Statistical analysis description: Pain Interfered with sleep. | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.318 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.9 |
| upper limit | 2.71 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.89 |

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 21 |
| Statistical analysis description: Pain Interfered Enjoyment of Life | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[39] |
| P-value | = 0.407 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 0.81 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.15 |
| upper limit | 2.78 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.97 |

Notes:

[39] - Pain Interfered Enjoyment of Life

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 22 |
| Statistical analysis description: Pain Interfered Enjoyment of Life | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[40] |
| P-value | = 0.62 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 0.52 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.58 |
| upper limit | 2.62 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.04 |

Notes:

[40] - Pain Interfered Enjoyment of Life

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 23 |
| Statistical analysis description: BPI-Mean Interference Score | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[41] |
| P-value | = 0.475 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 0.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.9 |
| upper limit | 1.91 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.7 |

Notes:

[41] - BPI-Mean Interference Score

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 24 |
| Statistical analysis description: BPI-Mean Interference Score | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[42] |
| P-value | = 0.54 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 0.46 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.04 |
| upper limit | 1.96 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.74 |

Notes:

[42] - BPI-Mean Interference Score

Secondary: Stage 2: Change from Baseline in Symptom Burden on the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC QLQ-C30)

| | |
|-----------------|---|
| End point title | Stage 2: Change from Baseline in Symptom Burden on the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC QLQ-C30) ^[43] |
|-----------------|---|

End point description:

The EORTC QLQ-C30 self-reported general cancer instrument consists of 30 items covered by 1 of 3 dimensions:

- 1) Global health status/quality of life (2 items) with scores ranging from 1 (Very Poor) to 7 (Excellent).
- 2) Functional scales (15 total items addressing either physical, role, emotional, cognitive, or social functioning), each item scores ranging from 1 (not at all) to 4 (very much)
- 3) Symptom scales (13 total items addressing either fatigue, nausea/vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, or financial impact), each item scores ranging from 1 (not at all) to 4 (very much).

Raw scores are linearly converted to a 0–100 scale with higher scores reflecting higher levels of function/QOL or higher levels of symptom burden.

No participants were enrolled to stage 2; however, results for stage 2 outcomes are reported from the data collected for participants enrolled to stage 1.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, 6 Months

APD: All randomized participants with baseline & post baseline value for the EORTC QLQ-C30 specified item.

Notes:

[43] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Per protocol, statistical analysis was not planned for all arms.

| End point values | 200mg Abemaciclib | 150mg Abemaciclib + 150mg LY3023414 | Gemcitabine or Capecitabine | |
|--|----------------------|--|--------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 19 | 14 | 14 | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | | | | |
| Global Health Status | -6.21 (± 3.87) | -4.82 (± 4.50) | -2.40 (± 4.64) | |
| Functional Scales: Physical Functioning | -14.44 (± 4.40) | -11.65 (± 5.12) | -5.42 (± 5.12) | |
| Functional Scales: Role Functioning | -17.09 (± 6.17) | -18.05 (± 7.32) | -17.10 (± 7.36) | |
| Functional Scales: Emotional Functioning | -4.89 (± 4.49) | -0.63 (± 5.22) | 2.06 (± 5.41) | |
| Functional Scales: Cognitive Functioning | -10.43 (± 4.10) | -8.39 (± 4.77) | -5.18 (± 4.95) | |
| Functional Scale: Social Functioning | -21.12 (± 4.90) | -17.09 (± 5.72) | -2.00 (± 5.95) | |
| Symptom Scales: Fatigue | 14.13 (± 4.92) | 14.90 (± 5.73) | 5.64 (± 5.71) | |
| Symptom Scales: Nausea and Vomiting | 7.98 (± 5.57) | 9.42 (± 6.47) | 11.88 (± 6.50) | |
| Symptom Scales: Pain | 9.79 (± 5.63) | 2.68 (± 6.61) | 5.43 (± 6.62) | |
| Symptom Scale: Dysopnea | 0.35 (± 5.48) | 11.19 (± 6.38) | -4.51 (± 6.36) | |
| Symptom Scale: Insomnia | -5.19 (± 5.17) | 1.83 (± 6.01) | -6.71 (± 6.05) | |
| Symptom Scale: Appetite Loss | 12.54 (± 5.79) | 15.32 (± 6.77) | 9.51 (± 7.30) | |
| Symptom Scale: Constipation | 2.96 (± 5.95) | -6.51 (± 6.96) | 12.93 (± 7.15) | |
| Symptom Scale: Diarrhoea | 15.71 (± 6.76) | 26.28 (± 7.83) | 20.51 (± 7.98) | |
| Symptom Scale: Financial difficulties | 3.96 (± 4.82) | 2.45 (± 5.68) | -3.30 (± 5.87) | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Statistical analysis description: | |
| Global health status | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.818 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -1.39 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -13.46 |
| upper limit | 10.68 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 5.98 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 2 |
| Statistical analysis description: | |
| Global health status | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.533 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -3.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -16.03 |
| upper limit | 8.42 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 6.06 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 3 |
| Statistical analysis description: | |
| Functional Scales: Physical functioning | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.681 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -2.79 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -16.4 |
| upper limit | 10.82 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 6.75 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 4 |
| Statistical analysis description: | |
| Functional Scales: Physical functioning | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.189 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -9.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -22.63 |
| upper limit | 4.59 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 6.75 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 5 |
| Statistical analysis description: | |
| Functional Scales: Role functioning | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.921 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 0.96 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -18.29 |
| upper limit | 20.21 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 9.54 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 6 |
| Statistical analysis description: | |
| Functional Scales: Role functioning | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.999 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 0.01 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -19.4 |
| upper limit | 19.42 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 9.62 |

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 7 |
| Statistical analysis description: | |
| Functional Scales: Emotional functioning | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.541 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -4.26 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -18.2 |
| upper limit | 9.68 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 6.91 |

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 8 |
| Statistical analysis description: | |
| Functional Scales: Emotional functioning | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.33 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -6.95 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -21.17 |
| upper limit | 7.27 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 7.05 |

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 9 |
| Statistical analysis description: | |
| Functional Scales: Cognitive Functioning | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.747 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -2.04 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14.74 |
| upper limit | 10.66 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 6.29 |

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 10 |
| Statistical analysis description: | |
| Functional Scales: Cognitive Functioning | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.419 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -5.25 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -18.22 |
| upper limit | 7.73 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 6.43 |

| | |
|---------------------------------------|---|
| Statistical analysis title | Statistical Analysis 11 |
| Statistical analysis description: | |
| Functional Scales: Social functioning | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.596 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -4.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -19.23 |
| upper limit | 11.19 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 7.53 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 12 |
| Statistical analysis description: | |
| Functional Scales: Social functioning | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.017 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -19.12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -34.68 |
| upper limit | -3.55 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 7.71 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 13 |
| Statistical analysis description: | |
| Symptoms Scales: Fatigue | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.919 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -0.77 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -16.03 |
| upper limit | 14.49 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 7.57 |

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 14 |
| Statistical analysis description: Symptom Scales: Fatigue | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.267 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 8.48 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.72 |
| upper limit | 23.69 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 7.54 |

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 15 |
| Statistical analysis description: Symptom Scales: Nausea and Vomiting | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.866 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -1.45 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -18.66 |
| upper limit | 15.77 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 8.54 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 16 |
| Statistical analysis description: | |
| Symptom Scales: Nausea and Vomiting | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.652 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -3.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -21.23 |
| upper limit | 13.43 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 8.59 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 17 |
| Statistical analysis description: | |
| Symptom Scales: Pain | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.417 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 7.11 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.39 |
| upper limit | 24.6 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 8.67 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Statistical Analysis 18 |
| Statistical analysis description: | |
| Symptom Scales: Pain | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or |

| | |
|---|----------------------------|
| | Capecitabine |
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.618 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 4.36 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -13.16 |
| upper limit | 21.89 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 8.69 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 19 |
| Statistical analysis description: | |
| Symptom Scales: Dyspnoea | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.206 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -10.84 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -27.85 |
| upper limit | 6.18 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 8.44 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 20 |
| Statistical analysis description: | |
| Symptom Scales: Dyspnoea | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.566 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 4.86 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12.08 |
| upper limit | 21.8 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 8.4 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 21 |
| Statistical analysis description: Symptom Scales: Insomnia | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.38 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -7.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -23.01 |
| upper limit | 8.96 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 7.93 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 22 |
| Statistical analysis description: Symptom Scales: Insomnia | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.85 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 1.52 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14.6 |
| upper limit | 17.64 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 7.99 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 23 |
| Statistical analysis description: | |
| Symptom Scales: Appetite loss | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.756 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -2.79 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -20.78 |
| upper limit | 15.21 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 8.91 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 24 |
| Statistical analysis description: | |
| Symptom Scales: Appetite loss | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.747 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 3.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -15.77 |
| upper limit | 21.82 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 9.31 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Statistical Analysis 25 |
| Statistical analysis description: | |
| Symptom Scales: Constipation | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.311 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 9.47 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.16 |
| upper limit | 28.09 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 9.23 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 26 |
| Statistical analysis description: | |
| Symptom Scales: Constipation | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.29 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -9.97 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -28.75 |
| upper limit | 8.8 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 9.3 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 27 |
| Statistical analysis description: | |
| Symptom Scales: Diarrhoea | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.323 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -10.57 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -31.93 |
| upper limit | 10.78 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 10.58 |

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 28 |
| Statistical analysis description: Symptom Scales: Diarrhoea | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.651 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | -4.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -26.08 |
| upper limit | 16.48 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 10.54 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 29 |
| Statistical analysis description: Symptom Scales: Financial Difficulties | |
| Comparison groups | 200mg Abemaciclib v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.841 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 1.51 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -13.57 |
| upper limit | 16.59 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 7.47 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 30 |
| Statistical analysis description: Symptom Scales: Financial Difficulties | |
| Comparison groups | 150mg Abemaciclib + 150mg LY3023414 v Gemcitabine or Capecitabine |
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.344 |
| Method | Mixed models analysis |
| Parameter estimate | LSMean Difference |
| Point estimate | 7.26 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.03 |
| upper limit | 22.54 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 7.57 |

Secondary: Stage 1: PK: Steady state trough pre dose concentration of LY3023414

| | |
|-----------------|--|
| End point title | Stage 1: PK: Steady state trough pre dose concentration of LY3023414 ^[44] |
|-----------------|--|

End point description:

Mean steady state exposure was reported by trough pre-dose plasma concentrations.

Geometric CV is expressed as %.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

C2D1: 0h, C3D1: 0h, C4D1: 0h

Notes:

[44] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Per protocol, statistical analysis was not planned for all arms.

| | | | | |
|---|-------------------------------------|--|--|--|
| End point values | 150mg Abemaciclib + 150mg LY3023414 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 9 | | | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | 27.3 (± 450) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Stage 1: PK: Mean Single Dose Concentration of LY3023414 at 2h Post-dose

| | |
|-----------------|--|
| End point title | Stage 1: PK: Mean Single Dose Concentration of LY3023414 at 2h Post-dose ^[45] |
|-----------------|--|

End point description:

Mean single dose exposure was reported by plasma concentrations collected approximately 2 hours post-dose.

Geometric CV is expressed as %.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

C1D1: 2h Post dose

Notes:

[45] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Per protocol, statistical analysis was not planned.

| | | | | |
|---|--|--|--|--|
| End point values | 150mg Abemaciclib + 150mg LY3023414 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 28 | | | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | 518 (± 67) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 30 weeks

Adverse event reporting additional description:

All randomized participants who received at least one dose of study drug. There are gender specific adverse events, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 20.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Abema200mg |
|-----------------------|------------|

Reporting group description: -

| | |
|-----------------------|----------------------|
| Reporting group title | Abema150mg+LY3023414 |
|-----------------------|----------------------|

Reporting group description: -

| | |
|-----------------------|-------------------|
| Reporting group title | Abema150mg+Gal_LI |
|-----------------------|-------------------|

Reporting group description: -

| | |
|-----------------------|------------|
| Reporting group title | Gem or Cap |
|-----------------------|------------|

Reporting group description: -

| Serious adverse events | Abema200mg | Abema150mg+LY3023414 | Abema150mg+Gal_LI |
|---|------------------|----------------------|-------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 17 / 32 (53.13%) | 18 / 33 (54.55%) | 4 / 7 (57.14%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| tumour pain | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| deep vein thrombosis | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 1 / 7 (14.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| embolism | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hypotension | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 33 (0.00%) | 0 / 7 (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 |
| General disorders and administration site conditions | | | |
| asthenia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 1 / 7 (14.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| chills | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 33 (0.00%) | 0 / 7 (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 |
| fatigue | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 1 / 33 (3.03%) | 1 / 7 (14.29%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| general physical health deterioration | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| malaise | | | |
| alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 0 / 7 (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 |
| multiple organ dysfunction syndrome alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 0 / 7 (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 |
| pyrexia alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 2 / 33 (6.06%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| systemic inflammatory response syndrome alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 1 / 7 (14.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| hypoxia alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 0 / 7 (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 |
| pleural effusion alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 1 / 7 (14.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pulmonary embolism alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 2 / 32 (6.25%) | 1 / 33 (3.03%) | 1 / 7 (14.29%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| respiratory failure | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| confusional state | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| mental status changes | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 0 / 7 (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 |
| Investigations | | | |
| blood creatinine increased | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 1 / 33 (3.03%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| platelet count decreased | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 1 / 7 (14.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| white blood cell count decreased | | | |
| alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 1 / 7 (14.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| cerebrovascular accident | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 1 / 33 (3.03%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| ischaemic cerebral infarction | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 33 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| anaemia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 1 / 7 (14.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| febrile neutropenia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 1 / 33 (3.03%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| neutropenia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 0 / 7 (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 |
| thrombocytopenia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 32 (0.00%) | 2 / 33 (6.06%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 8 / 8 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| abdominal pain | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | 0 / 33 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ascites | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 33 (0.00%) | 0 / 7 (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 |
| diarrhoea | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 1 / 33 (3.03%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| duodenal stenosis | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 0 / 7 (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 |
| gastric ulcer haemorrhage | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 1 / 7 (14.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| gastrointestinal perforation | | | |
| alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|---|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 0 / 7 (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 |
| intestinal obstruction | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| large intestinal obstruction | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 33 (0.00%) | 0 / 7 (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 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 0 / 7 (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 |
| obstruction gastric | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 33 (0.00%) | 0 / 7 (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 |
| oesophagitis | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 0 / 7 (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 |
| stomatitis | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 2 / 33 (6.06%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------------------------|----------------------------------|----------------------------------|
| subileus alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 32 (3.13%) 0 / 1 0 / 0 | 0 / 33 (0.00%) 0 / 0 0 / 0 | 0 / 7 (0.00%) 0 / 0 0 / 0 |
| vomiting alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 32 (3.13%) 0 / 2 0 / 0 | 2 / 33 (6.06%) 2 / 2 0 / 0 | 0 / 7 (0.00%) 0 / 0 0 / 0 |
| Hepatobiliary disorders bile duct obstruction alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 32 (6.25%) 0 / 2 0 / 0 | 0 / 33 (0.00%) 0 / 0 0 / 0 | 0 / 7 (0.00%) 0 / 0 0 / 0 |
| cholangitis alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 32 (3.13%) 0 / 1 0 / 0 | 1 / 33 (3.03%) 2 / 2 0 / 0 | 0 / 7 (0.00%) 0 / 0 0 / 0 |
| cholangitis acute alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 32 (0.00%) 0 / 0 0 / 0 | 0 / 33 (0.00%) 0 / 0 0 / 0 | 0 / 7 (0.00%) 0 / 0 0 / 0 |
| Renal and urinary disorders acute kidney injury alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 32 (0.00%) 0 / 0 0 / 0 | 0 / 33 (0.00%) 0 / 0 0 / 0 | 1 / 7 (14.29%) 0 / 1 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|--|----------------|----------------|---------------|
| back pain | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 33 (0.00%) | 0 / 7 (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 |
| muscular weakness | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 0 / 7 (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 |
| Infections and infestations | | | |
| abdominal infection | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 0 / 7 (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 |
| bacteraemia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 1 / 33 (3.03%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| escherichia bacteraemia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 0 / 7 (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 |
| peritonitis bacterial | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| sepsis | | | |
| alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 32 (3.13%) | 1 / 33 (3.03%) | 1 / 7 (14.29%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| upper respiratory tract infection alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 33 (0.00%) | 0 / 7 (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 |
| urosepsis alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 1 / 7 (14.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| acidosis alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 0 / 7 (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 |
| decreased appetite alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 0 / 7 (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 |
| dehydration alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| failure to thrive alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|--|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 0 / 7 (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 |
| hypokalaemia alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 33 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hyponatraemia alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 1 / 33 (3.03%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hypophosphataemia alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 0 / 7 (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 |
| tumour lysis syndrome alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |

| Serious adverse events | Gem or Cap | | |
|---|------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 15 / 26 (57.69%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) tumour pain alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| deep vein thrombosis | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| embolism | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| hypotension | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| asthenia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| chills | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| fatigue | | | |
| alternative dictionary used: MedDRA 20.0 | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 26 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| general physical health deterioration | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| malaise | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| multiple organ dysfunction syndrome | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| pyrexia | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| systemic inflammatory response syndrome | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Respiratory, thoracic and mediastinal disorders | | | | |
| hypoxia | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| pleural effusion | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| pulmonary embolism | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| respiratory failure | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Psychiatric disorders | | | |
| confusional state | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| mental status changes | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| blood creatinine increased | | | |
| alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| platelet count decreased | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| white blood cell count decreased | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| cerebrovascular accident | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ischaemic cerebral infarction | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| anaemia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| febrile neutropenia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| neutropenia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| thrombocytopenia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| abdominal pain | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ascites | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| diarrhoea | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| duodenal stenosis | | | |
| alternative dictionary used: MedDRA 20.0 | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 26 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| gastric ulcer haemorrhage | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| gastrointestinal perforation | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| intestinal obstruction | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| large intestinal obstruction | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| nausea | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| obstruction gastric | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

| | | | | |
|--|-----------------|--|--|--|
| oesophagitis | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| stomatitis | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| subileus | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| vomiting | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 4 / 26 (15.38%) | | | |
| occurrences causally related to treatment / all | 2 / 4 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatobiliary disorders | | | | |
| bile duct obstruction | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| cholangitis | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| cholangitis acute | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Renal and urinary disorders | | | |
| acute kidney injury | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| back pain | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| muscular weakness | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| abdominal infection | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| bacteraemia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| escherichia bacteraemia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| peritonitis bacterial | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| sepsis | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| urosepsis | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| acidosis | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| decreased appetite | | | |
| alternative dictionary used: MedDRA 20.0 | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 26 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| dehydration | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| failure to thrive | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| hypokalaemia | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| hyponatraemia | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| hypophosphataemia | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| tumour lysis syndrome | | | | |
| alternative dictionary used: MedDRA 20.0 | | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

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

| Non-serious adverse events | Abema200mg | Abema150mg+LY30 23414 | Abema150mg+Gal_ LI |
|---|------------------|--------------------------|-----------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 30 / 32 (93.75%) | 33 / 33 (100.00%) | 7 / 7 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| tumour pain | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | 0 / 33 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Vascular disorders | | | |
| hot flush | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 1 / 7 (14.29%) |
| occurrences (all) | 0 | 1 | 1 |
| hypotension | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | 1 / 33 (3.03%) | 1 / 7 (14.29%) |
| occurrences (all) | 3 | 1 | 1 |
| peripheral coldness | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all) | 0 | 0 | 1 |
| General disorders and administration site conditions | | | |
| asthenia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 4 / 32 (12.50%) | 0 / 33 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all) | 5 | 0 | 1 |
| chills | | | |
| alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|---|------------------|------------------|----------------|
| subjects affected / exposed | 1 / 32 (3.13%) | 2 / 33 (6.06%) | 0 / 7 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| fatigue | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 16 / 32 (50.00%) | 17 / 33 (51.52%) | 4 / 7 (57.14%) |
| occurrences (all) | 22 | 25 | 7 |
| feeling cold | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all) | 0 | 0 | 1 |
| general physical health deterioration | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 2 / 33 (6.06%) | 0 / 7 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| malaise | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 33 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all) | 1 | 0 | 1 |
| non-cardiac chest pain | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| oedema | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all) | 0 | 0 | 1 |
| oedema peripheral | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 4 / 32 (12.50%) | 5 / 33 (15.15%) | 2 / 7 (28.57%) |
| occurrences (all) | 4 | 6 | 2 |
| peripheral swelling | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|--|--|---|
| pyrexia alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 3 / 32 (9.38%) 5 | 5 / 33 (15.15%) 6 | 2 / 7 (28.57%) 2 |
| Reproductive system and breast disorders prostatomegaly alternative dictionary used: MedDRA 20.0 subjects affected / exposed ^[1] occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 17 (5.88%) 1 | 0 / 3 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders atelectasis alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) cough alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) dysphonia alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) dyspnoea alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) hypoxia alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) pleural effusion alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 2 / 32 (6.25%) 2 0 / 32 (0.00%) 0 2 / 32 (6.25%) 2 0 / 32 (0.00%) 0 2 / 32 (6.25%) 0 | 0 / 33 (0.00%) 0 2 / 33 (6.06%) 2 0 / 33 (0.00%) 0 4 / 33 (12.12%) 5 2 / 33 (6.06%) 2 | 1 / 7 (14.29%) 1 1 / 7 (14.29%) 1 1 / 7 (14.29%) 2 2 / 7 (28.57%) 2 0 / 7 (0.00%) 0 1 / 7 (14.29%) 1 |

| | | | |
|---|----------------------|---------------------|---------------------|
| pneumothorax alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 7 (0.00%) 0 |
| upper-airway cough syndrome alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | 0 / 33 (0.00%) 0 | 1 / 7 (14.29%) 1 |
| Psychiatric disorders anxiety alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 1 / 32 (3.13%) 1 | 0 / 33 (0.00%) 0 | 1 / 7 (14.29%) 1 |
| confusional state alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 3 / 32 (9.38%) 3 | 0 / 33 (0.00%) 0 | 0 / 7 (0.00%) 0 |
| depression alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 1 / 32 (3.13%) 1 | 1 / 33 (3.03%) 1 | 1 / 7 (14.29%) 1 |
| insomnia alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | 2 / 33 (6.06%) 3 | 0 / 7 (0.00%) 0 |
| Investigations alanine aminotransferase increased alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 4 / 32 (12.50%) 8 | 0 / 33 (0.00%) 0 | 1 / 7 (14.29%) 1 |
| aspartate aminotransferase increased alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 3 / 32 (9.38%) 6 | 0 / 33 (0.00%) 0 | 2 / 7 (28.57%) 3 |
| blood alkaline phosphatase increased | | | |

| | | | |
|---|-----------------|----------------|----------------|
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 5 / 32 (15.63%) | 3 / 33 (9.09%) | 1 / 7 (14.29%) |
| occurrences (all) | 9 | 5 | 1 |
| blood creatinine increased | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 3 / 33 (9.09%) | 1 / 7 (14.29%) |
| occurrences (all) | 2 | 5 | 1 |
| blood bilirubin increased | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 5 / 32 (15.63%) | 1 / 33 (3.03%) | 0 / 7 (0.00%) |
| occurrences (all) | 16 | 1 | 0 |
| blood potassium decreased | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | 0 / 33 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| blood sodium decreased | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | 0 / 33 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| international normalised ratio increased | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | 0 / 33 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| lymphocyte count decreased | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | 0 / 33 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| neutrophil count decreased | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 4 / 32 (12.50%) | 1 / 33 (3.03%) | 0 / 7 (0.00%) |
| occurrences (all) | 7 | 3 | 0 |
| occult blood positive | | | |
| alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|---|--|--|--|
| <p>subjects affected / exposed</p> <p>0 / 32 (0.00%)</p> <p>0 / 33 (0.00%)</p> <p>1 / 7 (14.29%)</p> <p>occurrences (all)</p> <p>0</p> <p>0</p> <p>1</p> | | | |
| <p>platelet count decreased</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>10 / 32 (31.25%)</p> <p>5 / 33 (15.15%)</p> <p>0 / 7 (0.00%)</p> <p>occurrences (all)</p> <p>20</p> <p>11</p> <p>0</p> | | | |
| <p>weight decreased</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>0 / 32 (0.00%)</p> <p>3 / 33 (9.09%)</p> <p>2 / 7 (28.57%)</p> <p>occurrences (all)</p> <p>0</p> <p>3</p> <p>2</p> | | | |
| <p>white blood cell count decreased</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>4 / 32 (12.50%)</p> <p>1 / 33 (3.03%)</p> <p>2 / 7 (28.57%)</p> <p>occurrences (all)</p> <p>4</p> <p>3</p> <p>3</p> | | | |
| <p>Injury, poisoning and procedural complications</p> <p>fall</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>1 / 32 (3.13%)</p> <p>2 / 33 (6.06%)</p> <p>0 / 7 (0.00%)</p> <p>occurrences (all)</p> <p>1</p> <p>2</p> <p>0</p> | | | |
| <p>Cardiac disorders</p> <p>tachycardia</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>1 / 32 (3.13%)</p> <p>1 / 33 (3.03%)</p> <p>1 / 7 (14.29%)</p> <p>occurrences (all)</p> <p>1</p> <p>1</p> <p>1</p> | | | |
| <p>Nervous system disorders</p> <p>dizziness</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>1 / 32 (3.13%)</p> <p>3 / 33 (9.09%)</p> <p>2 / 7 (28.57%)</p> <p>occurrences (all)</p> <p>1</p> <p>3</p> <p>2</p> <p>dysgeusia</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>3 / 32 (9.38%)</p> <p>4 / 33 (12.12%)</p> <p>0 / 7 (0.00%)</p> <p>occurrences (all)</p> <p>3</p> <p>4</p> <p>0</p> | | | |
| <p>Blood and lymphatic system disorders</p> | | | |

| | | | |
|---|-----------------------------------|---------------------------------|---------------------------------|
| <p>anaemia</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>10 / 32 (31.25%)</p> <p>18</p> | <p>6 / 33 (18.18%)</p> <p>7</p> | <p>3 / 7 (42.86%)</p> <p>14</p> |
| <p>cytopenia</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 32 (0.00%)</p> <p>0</p> | <p>0 / 33 (0.00%)</p> <p>0</p> | <p>1 / 7 (14.29%)</p> <p>1</p> |
| <p>leukopenia</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 32 (0.00%)</p> <p>0</p> | <p>0 / 33 (0.00%)</p> <p>0</p> | <p>1 / 7 (14.29%)</p> <p>1</p> |
| <p>neutropenia</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>4 / 32 (12.50%)</p> <p>9</p> | <p>0 / 33 (0.00%)</p> <p>0</p> | <p>2 / 7 (28.57%)</p> <p>2</p> |
| <p>thrombocytopenia</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 32 (0.00%)</p> <p>0</p> | <p>5 / 33 (15.15%)</p> <p>5</p> | <p>0 / 7 (0.00%)</p> <p>0</p> |
| <p>Eye disorders</p> <p>photopsia</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 32 (0.00%)</p> <p>0</p> | <p>0 / 33 (0.00%)</p> <p>0</p> | <p>1 / 7 (14.29%)</p> <p>1</p> |
| <p>visual impairment</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 32 (0.00%)</p> <p>0</p> | <p>0 / 33 (0.00%)</p> <p>0</p> | <p>1 / 7 (14.29%)</p> <p>1</p> |
| <p>Gastrointestinal disorders</p> <p>abdominal distension</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 32 (3.13%)</p> <p>1</p> | <p>0 / 33 (0.00%)</p> <p>0</p> | <p>1 / 7 (14.29%)</p> <p>2</p> |
| <p>abdominal discomfort</p> | | | |

| | | | |
|---|------------------|------------------|----------------|
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 2 / 7 (28.57%) |
| occurrences (all) | 0 | 0 | 2 |
| abdominal pain | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 7 / 32 (21.88%) | 5 / 33 (15.15%) | 1 / 7 (14.29%) |
| occurrences (all) | 8 | 5 | 1 |
| abdominal pain upper | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 1 / 7 (14.29%) |
| occurrences (all) | 0 | 1 | 1 |
| ascites | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 4 / 32 (12.50%) | 2 / 33 (6.06%) | 0 / 7 (0.00%) |
| occurrences (all) | 5 | 2 | 0 |
| constipation | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 5 / 32 (15.63%) | 2 / 33 (6.06%) | 1 / 7 (14.29%) |
| occurrences (all) | 6 | 2 | 2 |
| diarrhoea | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 12 / 32 (37.50%) | 17 / 33 (51.52%) | 4 / 7 (57.14%) |
| occurrences (all) | 21 | 19 | 4 |
| dry mouth | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 2 / 33 (6.06%) | 0 / 7 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| dyspepsia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | 0 / 33 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| eructation | | | |
| alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|---|-----------------------------------|-----------------------------------|--------------------------------|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 32 (0.00%)</p> <p>0</p> | <p>0 / 33 (0.00%)</p> <p>0</p> | <p>1 / 7 (14.29%)</p> <p>1</p> |
| <p>flatulence</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 32 (6.25%)</p> <p>2</p> | <p>1 / 33 (3.03%)</p> <p>1</p> | <p>0 / 7 (0.00%)</p> <p>0</p> |
| <p>gastrointestinal pain</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 32 (3.13%)</p> <p>1</p> | <p>0 / 33 (0.00%)</p> <p>0</p> | <p>1 / 7 (14.29%)</p> <p>1</p> |
| <p>nausea</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>9 / 32 (28.13%)</p> <p>14</p> | <p>15 / 33 (45.45%)</p> <p>18</p> | <p>5 / 7 (71.43%)</p> <p>5</p> |
| <p>stomatitis</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 32 (0.00%)</p> <p>0</p> | <p>12 / 33 (36.36%)</p> <p>16</p> | <p>0 / 7 (0.00%)</p> <p>0</p> |
| <p>vomiting</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>10 / 32 (31.25%)</p> <p>12</p> | <p>15 / 33 (45.45%)</p> <p>22</p> | <p>2 / 7 (28.57%)</p> <p>3</p> |
| <p>Hepatobiliary disorders</p> <p>bile duct obstruction</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>4 / 32 (12.50%)</p> <p>4</p> | <p>0 / 33 (0.00%)</p> <p>0</p> | <p>0 / 7 (0.00%)</p> <p>0</p> |
| <p>Skin and subcutaneous tissue disorders</p> <p>dry skin</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>ecchymosis</p> <p>alternative dictionary used: MedDRA 20.0</p> | <p>1 / 32 (3.13%)</p> <p>1</p> | <p>1 / 33 (3.03%)</p> <p>1</p> | <p>1 / 7 (14.29%)</p> <p>1</p> |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all) | 0 | 0 | 1 |
| palmar-plantar erythrodysaesthesia syndrome | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 2 / 33 (6.06%) | 0 / 7 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| pruritus | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | 2 / 33 (6.06%) | 2 / 7 (28.57%) |
| occurrences (all) | 2 | 2 | 2 |
| rash | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 1 / 33 (3.03%) | 2 / 7 (28.57%) |
| occurrences (all) | 0 | 1 | 3 |
| rash maculo-papular | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 3 / 33 (9.09%) | 0 / 7 (0.00%) |
| occurrences (all) | 3 | 3 | 0 |
| skin discolouration | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all) | 0 | 0 | 1 |
| skin ulcer | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| acute kidney injury | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 33 (0.00%) | 0 / 7 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| haematuria | | | |
| alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | 0 / 33 (0.00%) 0 | 1 / 7 (14.29%) 1 |
| hydronephrosis alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | 0 / 33 (0.00%) 0 | 1 / 7 (14.29%) 1 |
| Endocrine disorders hypothyroidism alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | 0 / 33 (0.00%) 0 | 1 / 7 (14.29%) 1 |
| Musculoskeletal and connective tissue disorders arthropathy alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | 0 / 33 (0.00%) 0 | 1 / 7 (14.29%) 1 |
| back pain alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 3 / 32 (9.38%) 3 | 0 / 33 (0.00%) 0 | 1 / 7 (14.29%) 1 |
| flank pain alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | 1 / 33 (3.03%) 1 | 1 / 7 (14.29%) 2 |
| musculoskeletal pain alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | 0 / 33 (0.00%) 0 | 1 / 7 (14.29%) 1 |
| muscular weakness alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 0 / 32 (0.00%) 0 | 2 / 33 (6.06%) 3 | 0 / 7 (0.00%) 0 |
| myalgia alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|--|--|---|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>pain in extremity</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 32 (6.25%)</p> <p>3</p> <p>0 / 32 (0.00%)</p> <p>0</p> | <p>1 / 33 (3.03%)</p> <p>2</p> <p>1 / 33 (3.03%)</p> <p>1</p> | <p>0 / 7 (0.00%)</p> <p>0</p> <p>1 / 7 (14.29%)</p> <p>1</p> |
| <p>Infections and infestations</p> <p>bacterial sepsis</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>upper respiratory tract infection</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>urinary tract infection</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 32 (0.00%)</p> <p>0</p> <p>0 / 32 (0.00%)</p> <p>0</p> <p>1 / 32 (3.13%)</p> <p>1</p> | <p>0 / 33 (0.00%)</p> <p>0</p> <p>0 / 33 (0.00%)</p> <p>0</p> <p>0 / 33 (0.00%)</p> <p>0</p> | <p>1 / 7 (14.29%)</p> <p>1</p> <p>0 / 7 (0.00%)</p> <p>0</p> <p>1 / 7 (14.29%)</p> <p>1</p> |
| <p>Metabolism and nutrition disorders</p> <p>decreased appetite</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>dehydration</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>failure to thrive</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>fluid retention</p> <p>alternative dictionary used: MedDRA 20.0</p> | <p>9 / 32 (28.13%)</p> <p>11</p> <p>0 / 32 (0.00%)</p> <p>0</p> <p>0 / 32 (0.00%)</p> <p>0</p> | <p>8 / 33 (24.24%)</p> <p>9</p> <p>2 / 33 (6.06%)</p> <p>2</p> <p>0 / 33 (0.00%)</p> <p>0</p> | <p>3 / 7 (42.86%)</p> <p>4</p> <p>1 / 7 (14.29%)</p> <p>1</p> <p>1 / 7 (14.29%)</p> <p>1</p> |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all) | 0 | 0 | 1 |
| hyperglycaemia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 3 / 33 (9.09%) | 1 / 7 (14.29%) |
| occurrences (all) | 0 | 5 | 1 |
| hyperkalaemia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 2 / 33 (6.06%) | 0 / 7 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| hypoalbuminaemia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 3 / 33 (9.09%) | 2 / 7 (28.57%) |
| occurrences (all) | 1 | 3 | 5 |
| hypokalaemia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | 3 / 33 (9.09%) | 0 / 7 (0.00%) |
| occurrences (all) | 4 | 3 | 0 |
| hypocalcaemia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 0 / 33 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all) | 4 | 0 | 2 |
| hypomagnesaemia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | 1 / 33 (3.03%) | 1 / 7 (14.29%) |
| occurrences (all) | 3 | 1 | 1 |
| hyponatraemia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | 3 / 33 (9.09%) | 4 / 7 (57.14%) |
| occurrences (all) | 1 | 6 | 6 |
| hypophagia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 32 (0.00%) | 0 / 33 (0.00%) | 1 / 7 (14.29%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|--|-------------------------|-------------------------|------------------------|
| hypophosphataemia alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 2 / 32 (6.25%) 3 | 1 / 33 (3.03%) 2 | 0 / 7 (0.00%) 0 |
|--|-------------------------|-------------------------|------------------------|

| Non-serious adverse events | Gem or Cap | | |
|--|---|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 25 / 26 (96.15%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) tumour pain alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Vascular disorders hot flush alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) hypotension alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) peripheral coldness alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 0 / 26 (0.00%) 0 0 / 26 (0.00%) 0 | | |
| General disorders and administration site conditions asthenia alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) chills alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 0 / 26 (0.00%) 0 | | |

| | | | |
|---|------------------|--|--|
| fatigue | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 11 / 26 (42.31%) | | |
| occurrences (all) | 12 | | |
| feeling cold | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| general physical health deterioration | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 3 / 26 (11.54%) | | |
| occurrences (all) | 3 | | |
| malaise | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| non-cardiac chest pain | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | | |
| occurrences (all) | 2 | | |
| oedema | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| oedema peripheral | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| peripheral swelling | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| pyrexia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|--|---|--|--|
| subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Reproductive system and breast disorders prostatomegaly alternative dictionary used: MedDRA 20.0 subjects affected / exposed ^[1] occurrences (all) | 0 / 10 (0.00%) 0 | | |
| Respiratory, thoracic and mediastinal disorders atelectasis alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) cough alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) dysphonia alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) dyspnoea alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) hypoxia alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) pleural effusion alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) pneumothorax alternative dictionary used: MedDRA 20.0 | 0 / 26 (0.00%) 0 2 / 26 (7.69%) 2 1 / 26 (3.85%) 1 3 / 26 (11.54%) 5 0 / 26 (0.00%) 0 1 / 26 (3.85%) 1 | | |

| | | | |
|--|---|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>upper-airway cough syndrome</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 26 (7.69%)</p> <p>4</p> <p>0 / 26 (0.00%)</p> <p>0</p> | | |
| <p>Psychiatric disorders</p> <p>anxiety</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>confusional state</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>depression</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>insomnia</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 26 (3.85%)</p> <p>1</p> <p>1 / 26 (3.85%)</p> <p>1</p> <p>0 / 26 (0.00%)</p> <p>0</p> <p>0 / 26 (0.00%)</p> <p>0</p> | | |
| <p>Investigations</p> <p>alanine aminotransferase increased</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>aspartate aminotransferase increased</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>blood alkaline phosphatase increased</p> <p>alternative dictionary used: MedDRA 20.0</p> | <p>1 / 26 (3.85%)</p> <p>1</p> <p>1 / 26 (3.85%)</p> <p>3</p> | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| blood creatinine increased | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 3 | | |
| blood bilirubin increased | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 2 | | |
| blood potassium decreased | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| blood sodium decreased | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| international normalised ratio increased | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| lymphocyte count decreased | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | | |
| occurrences (all) | 4 | | |
| neutrophil count decreased | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | | |
| occurrences (all) | 8 | | |
| occult blood positive | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|---|----------------------|--|--|
| platelet count decreased alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 4 / 26 (15.38%) 9 | | |
| weight decreased alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| white blood cell count decreased alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 3 / 26 (11.54%) 5 | | |
| Injury, poisoning and procedural complications fall alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Cardiac disorders tachycardia alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Nervous system disorders dizziness alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| dysgeusia alternative dictionary used: MedDRA 20.0 subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Blood and lymphatic system disorders anaemia alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|---|--|--|--|
| <p>subjects affected / exposed</p> <p>11 / 26 (42.31%)</p> <p>occurrences (all)</p> <p>19</p> <p>cytopenia</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>0 / 26 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>leukopenia</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>0 / 26 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>neutropenia</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>2 / 26 (7.69%)</p> <p>occurrences (all)</p> <p>5</p> <p>thrombocytopenia</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>4 / 26 (15.38%)</p> <p>occurrences (all)</p> <p>17</p> | | | |
| <p>Eye disorders</p> <p>photopsia</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>0 / 26 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>visual impairment</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>0 / 26 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> | | | |
| <p>Gastrointestinal disorders</p> <p>abdominal distension</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>1 / 26 (3.85%)</p> <p>occurrences (all)</p> <p>1</p> <p>abdominal discomfort</p> <p>alternative dictionary used: MedDRA 20.0</p> | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| abdominal pain | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 6 / 26 (23.08%) | | |
| occurrences (all) | 8 | | |
| abdominal pain upper | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 4 / 26 (15.38%) | | |
| occurrences (all) | 4 | | |
| ascites | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 3 / 26 (11.54%) | | |
| occurrences (all) | 3 | | |
| constipation | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 7 / 26 (26.92%) | | |
| occurrences (all) | 7 | | |
| diarrhoea | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 8 / 26 (30.77%) | | |
| occurrences (all) | 16 | | |
| dry mouth | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| dyspepsia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| eructation | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|---|--|--|--|
| <p>flatulence</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>0 / 26 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> | | | |
| <p>gastrointestinal pain</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>0 / 26 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> | | | |
| <p>nausea</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>9 / 26 (34.62%)</p> <p>occurrences (all)</p> <p>10</p> | | | |
| <p>stomatitis</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>6 / 26 (23.08%)</p> <p>occurrences (all)</p> <p>9</p> | | | |
| <p>vomiting</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>6 / 26 (23.08%)</p> <p>occurrences (all)</p> <p>8</p> | | | |
| <p>Hepatobiliary disorders</p> <p>bile duct obstruction</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>0 / 26 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> | | | |
| <p>Skin and subcutaneous tissue disorders</p> <p>dry skin</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>1 / 26 (3.85%)</p> <p>occurrences (all)</p> <p>1</p> <p>ecchymosis</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>0 / 26 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>palmar-plantar erythrodysesthesia syndrome</p> | | | |

| | | | |
|---|-----------------------------------|--|--|
| <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>10 / 26 (38.46%)</p> <p>24</p> | | |
| <p>pruritus</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 26 (3.85%)</p> <p>1</p> | | |
| <p>rash</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 26 (0.00%)</p> <p>0</p> | | |
| <p>rash maculo-papular</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 26 (3.85%)</p> <p>1</p> | | |
| <p>skin discolouration</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 26 (0.00%)</p> <p>0</p> | | |
| <p>skin ulcer</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 26 (7.69%)</p> <p>2</p> | | |
| <p>Renal and urinary disorders</p> <p>acute kidney injury</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 26 (11.54%)</p> <p>3</p> | | |
| <p>haematuria</p> <p>alternative dictionary used: MedDRA 20.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 26 (0.00%)</p> <p>0</p> | | |
| <p>hydronephrosis</p> <p>alternative dictionary used: MedDRA 20.0</p> | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| Endocrine disorders | | | |
| hypothyroidism | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| arthropathy | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| back pain | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| flank pain | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| musculoskeletal pain | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| muscular weakness | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| myalgia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| pain in extremity | | | |
| alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| Infections and infestations | | | |
| bacterial sepsis | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | | |
| occurrences (all) | 2 | | |
| urinary tract infection | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| Metabolism and nutrition disorders | | | |
| decreased appetite | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 8 / 26 (30.77%) | | |
| occurrences (all) | 8 | | |
| dehydration | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| failure to thrive | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| fluid retention | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| hyperglycaemia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| hyperkalaemia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | | |
| occurrences (all) | 2 | | |
| hypoalbuminaemia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| hypokalaemia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 4 / 26 (15.38%) | | |
| occurrences (all) | 5 | | |
| hypocalcaemia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| hypomagnesaemia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| hyponatraemia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| hypophagia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| hypophosphataemia | | | |
| alternative dictionary used: MedDRA 20.0 | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: There are gender specific adverse events, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

| |
|---|
| Study was planned for stage 1 & stage 2. Stage 2 did not occur, no participants were enrolled to stage 2; |
|---|

Notes: