



Clinical trial results:

A Phase 2 Study to Evaluate LY2603618 in Combination with Pemetrexed in Patients with Advanced or Metastatic Non-small Cell Lung Cancer

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2009-013787-39 |
| Trial protocol | IT |
| Global end of trial date | 11 November 2014 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 30 July 2017 |
| First version publication date | 30 July 2017 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | I2I-MC-JMMD |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|---------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00988858 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Trial Number: 12092 |

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 | 11 November 2014 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 11 November 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary purpose of this study is to evaluate the efficacy and safety of LY2603618 in combination with pemetrexed and any side effects that might be associated with it along with determining the effects of LY2603618 in combination with pemetrexed in participants with advanced or metastatic Non-small Cell Lung Cancer (NSCLC).

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 November 2009 |
| 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 | United States: 24 |
| Country: Number of subjects enrolled | Taiwan: 5 |
| Country: Number of subjects enrolled | Korea, Republic of: 14 |
| Country: Number of subjects enrolled | Italy: 12 |
| Worldwide total number of subjects | 55 |
| EEA total number of subjects | 12 |

Notes:

Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |

| | |
|----------------------|----|
| Adults (18-64 years) | 32 |
| From 65 to 84 years | 23 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants that had progressive disease were completers.

Period 1

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

Arms

| | |
|------------------|--------------------------|
| Arm title | LY2603618 and Pemetrexed |
|------------------|--------------------------|

Arm description:

LY2603618: 150 milligram per square meter mg/m² intravenously on Day 2 of each 21 day cycle repeating every 21 days for a planned minimum of 2 cycles or until disease progression

Pemetrexed: 500mg/m² intravenously on Day 1 of each 21 Day cycle repeating every 21 days for a planned minimum of 2 cycles or until disease progression

| | |
|--|-------------------|
| Arm type | Experimental |
| Investigational medicinal product name | LY2603618 |
| Investigational medicinal product code | |
| Other name | CHK-1 Inhibitor I |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

150 milligram per square meter (mg/m²) intravenously on Day 2 of each 21 day cycle repeating every 21 days for a planned minimum of 2 cycles continuing until disease progression

| | |
|--|-----------------|
| Investigational medicinal product name | Pemetrexed |
| Investigational medicinal product code | |
| Other name | LY231514 |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

500 mg/m² intravenously on Day 1 of each 21 Day cycle repeating every 21 days for a planned minimum of 2 cycles or until disease progression

| Number of subjects in period 1 | LY2603618 and Pemetrexed |
|--------------------------------|--------------------------|
| Started | 55 |
| Completed | 45 |
| Not completed | 10 |
| Physician decision | 1 |
| Adverse event, non-fatal | 7 |
| Death | 1 |

| | |
|------------------|---|
| Sponsor Decision | 1 |
|------------------|---|

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | Overall Study |
|-----------------------|---------------|

Reporting group description: -

| Reporting group values | Overall Study | Total | |
|---|---------------|-------|--|
| Number of subjects | 55 | 55 | |
| 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 | 61.2 | | |
| standard deviation | ± 8.6 | - | |
| Gender, Male/Female | | | |
| Units: | | | |
| Male | 34 | 34 | |
| Female | 21 | 21 | |
| Region of Enrollment | | | |
| Units: Subjects | | | |
| United States | 24 | 24 | |
| Taiwan | 5 | 5 | |
| Korea, Republic of | 14 | 14 | |
| Italy | 12 | 12 | |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | |
| Not Hispanic or Latino | 55 | 55 | |
| Unknown or Not Reported | 0 | 0 | |
| Race | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 21 | 21 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 1 | 1 | |
| White | 33 | 33 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 0 | 0 | |

End points

End points reporting groups

| | |
|--|--------------------------|
| Reporting group title | LY2603618 and Pemetrexed |
| Reporting group description: | |
| LY2603618: 150 milligram per square meter mg/m ² intravenously on Day 2 of each 21 day cycle repeating every 21 days for a planned minimum of 2 cycles or until disease progression | |
| Pemetrexed: 500mg/m ² intravenously on Day 1 of each 21 Day cycle repeating every 21 days for a planned minimum of 2 cycles or until disease progression | |

Primary: Overall Tumor Response - Percentage of Participants Achieving Complete Response (CR) or Partial Response (PR) [Overall Response Rate (ORR)]

| | |
|-----------------|--|
| End point title | Overall Tumor Response - Percentage of Participants Achieving Complete Response (CR) or Partial Response (PR) [Overall Response Rate (ORR)] ^[1] |
|-----------------|--|

End point description:

Overall response rate is the best response of complete response (CR) or partial response (PR) as classified by the investigators according to the Response Evaluation Criteria In Solid Tumors (RECIST v1.1). CR is a disappearance of all target and non-target lesions and normalization of tumor marker level. PR is an at least 30% decrease in the sum of the diameters of target lesions (taking as reference the baseline sum diameter) without progression of not-target lesions or appearance of new lesions. Overall response rate is calculated as a total number of participants with CR or PR divided by the total number of participants with at least 1 measurable lesion, multiplied by 100.

Analysis Population Description : All randomized participants who received at least 1 dose of drug.

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

End point timeframe:

Baseline until Progressive Disease or Study Discontinuation (Up to 23 Months)

Notes:

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

Justification: This is a single arm study with no comparison groups therefore statistical analyses (comparison analysis) were not conducted.

| | | | | |
|-----------------------------------|--------------------------|--|--|--|
| End point values | LY2603618 and Pemetrexed | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 55 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 9.1 (3.7 to 18.2) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved a Best Response of Complete Response (CR), Partial Response (PR), or Stable Disease (SD) (Clinical Benefit Rate)

| | |
|-----------------|--|
| End point title | Percentage of Participants Who Achieved a Best Response of Complete Response (CR), Partial Response (PR), or Stable Disease (SD) (Clinical Benefit Rate) |
|-----------------|--|

End point description:

Clinical benefit rate is the best response CR, PR, or stable disease (SD) as classified by the investigators according to the RECIST v1.1. CR is a disappearance of all target and non-target lesions and normalization of tumor marker level. PR is an at least 30% decrease in the sum of the diameters of target lesions (taking as reference the baseline sum diameter) without progression of not-target lesions or appearance of new lesions. SD is neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease, taking as reference the smallest sum diameter since treatment started. Clinical benefit rate is calculated as a total number of participants with CR, PR, or SD divided by the total number of participants with at least 1 measurable lesion, multiplied by 100.

Analysis Population Description : All randomized participants who received at least 1 dose of drug.

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

End point timeframe:

Baseline until Progressive Disease or Study Discontinuation (Up to 23 Months)

| | | | | |
|-----------------------------------|--------------------------|--|--|--|
| End point values | LY2603618 and Pemetrexed | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 55 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 90%) | 45.5 (33.9 to 57.4) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS)

| | |
|-----------------|---------------------------------|
| End point title | Progression-free survival (PFS) |
|-----------------|---------------------------------|

End point description:

Progression-free survival (PFS) time was defined as the time from the date of randomization to the first date of progressive disease (symptomatic or objective) or death due to any cause, whichever occurred first. For participants who were not known to have died or progressed as of the data-inclusion cutoff date, PFS time was censored at the date of the last objective progression-free disease assessment prior to the date of any subsequent systematic anticancer therapy. PFS was summarized using Kaplan-Meier estimates.

Analysis Population Description : All randomized participants who received at least 1 dose of drug. 9 participants were censored.

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

End point timeframe:

Baseline to Progressive Disease or Death Due to Any Cause (Up to 27.1 Months)

| | | | | |
|----------------------------------|--------------------------|--|--|--|
| End point values | LY2603618 and Pemetrexed | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 55 | | | |
| Units: months | | | | |
| median (confidence interval 90%) | 2.3 (1.4 to 3.3) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

| | |
|-----------------|----------------------|
| End point title | Duration of Response |
|-----------------|----------------------|

End point description:

Duration of Response is defined as the time from the first observation of CR or PR to the first observation of progressive disease (PD) or death from any cause. A response is defined as a confirmed objective status of CR or PR. For participants who are not known to have died as of the data inclusion cut-off date and who do not have PD, the duration will be censored at the date of the last objective progression free disease assessment prior to the date of any subsequent anticancer therapy.

Analysis Population Description: All randomized participants who received at least 1 dose of drug with Best Overall Response of Complete Response or Partial Response. 5 participants were censored.

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

End point timeframe:

First Observation of CR or PR until Progressive Disease or Death Due to Any Cause (Up to 23 Months)

| | | | | |
|----------------------------------|--------------------------|--|--|--|
| End point values | LY2603618 and Pemetrexed | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 55 ^[2] | | | |
| Units: months | | | | |
| median (confidence interval 90%) | 8.7 (7 to 99999) | | | |

Notes:

[2] - 99999 = Upper limit is not estimable based on sample size.

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Symptom Burden Scores of Lung Cancer Symptom Scale (LCSS)

| | |
|-----------------|---|
| End point title | Change in Symptom Burden Scores of Lung Cancer Symptom Scale (LCSS) |
|-----------------|---|

End point description:

The LCSS participants scale is a 9-item questionnaire. Six questions are symptom-specific measures for lung cancer (appetite, fatigue, cough, dyspnea, hemoptysis and pain), and 3 summation items describe total symptomatic distress, activity status, and overall quality of life. Participant responses were measured using visual analogue scales (VAS) with 100-milliliter (mm) lines. Scores range from 0 (for best outcome) to 100 (for worst outcome). The Average Symptom Burden Index (ASBI) was calculated as the mean of 6 symptom-specific questions from the LCSS.

Analysis Population Description: The LCSS evaluable population consisted of all enrolled participants who had a baseline LCSS measurement and at least 1 post-baseline measurement. The population was evaluated for changes in the ASBI (improved, stable, worsened), with improvement/worsening based on trends seen in sets of consecutive ASBI assessments with respect to baseline ASBI.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline until End of Study (Up to 27.1 Months) | |

| | | | | |
|-----------------------------|--------------------------|--|--|--|
| End point values | LY2603618 and Pemetrexed | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 46 | | | |
| Units: participants | | | | |
| number (not applicable) | | | | |
| Improved | 12 | | | |
| Worsened | 6 | | | |
| Stable | 18 | | | |
| Unknown | 10 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Maximum Plasma Concentration (Cmax) of LY2603618

| | |
|-----------------|---|
| End point title | Pharmacokinetics (PK): Maximum Plasma Concentration (Cmax) of LY2603618 |
|-----------------|---|

End point description:

Analysis Population Description : All randomized participants who received at least 1 dose of drug and had evaluable PK data

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

End point timeframe:

Day 2 and Day 3 of Cycle 1 and Cycle 2: Prior to End of Infusion (EOI); EOI + 1-2 hr; EOI + 4-6 hr; EOI + 20-28 hr; anytime on Day 8 of Cycle 1 and Cycle 2

| | | | | |
|---|--------------------------|--|--|--|
| End point values | LY2603618 and Pemetrexed | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 48 ^[3] | | | |
| Units: nanogram per milliliter (ng/mL) | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Day 2/Cycle 1 (n=41) | 3430 (± 50) | | | |
| Day 2/Cycle 2 (n=48) | 3560 (± 40) | | | |

Notes:

[3] - The geometric coefficient of variation is a percentage.

Statistical analyses

No statistical analyses for this end point

Secondary: PK: Maximum Plasma Concentration (C_{max}) of Pemetrexed

| | |
|-----------------|--|
| End point title | PK: Maximum Plasma Concentration (C _{max}) of Pemetrexed |
|-----------------|--|

End point description:

Analysis Population Description : All randomized participants who received at least 1 dose of drug and evaluable PK data.

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

End point timeframe:

Day 1 and Day 2 of Cycle 1 and Cycle 2: Prior to End of Infusion (EOI); EOI + 1-2 hour (hr); EOI + 4-6-hr; EOI + 20-28 hr

| | | | | |
|---|--------------------------|--|--|--|
| End point values | LY2603618 and Pemetrexed | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 ^[4] | | | |
| Units: microgram per milliliter (µg/mL) | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Day 1/Cycle 1 (n=40) | 102 (± 50) | | | |
| Day 1/Cycle 2 (n=43) | 96.8 (± 42) | | | |

Notes:

[4] - The geometric coefficient of variation is a percentage.

Statistical analyses

No statistical analyses for this end point

Secondary: PK: Area Under the plasma concentration vs. time Curve from time zero to infinity [AUC(0-∞)] of Pemetrexed

| | |
|-----------------|--|
| End point title | PK: Area Under the plasma concentration vs. time Curve from time zero to infinity [AUC(0-∞)] of Pemetrexed |
|-----------------|--|

End point description:

Analysis Population Description : All randomized participants who received at least 1 dose of drug and had evaluable PK data.

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

End point timeframe:

Day 1 and Day 2 of Cycle 1 and Cycle 2: Prior to End of Infusion (EOI); EOI + 1-2 hour (hr); EOI + 4-6-hr; EOI + 20-28 hr

| | | | | |
|---|--------------------------|--|--|--|
| End point values | LY2603618 and Pemetrexed | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 ^[5] | | | |
| Units: microgram*hour per milliliter (µg*hr/mL) | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Day 1/Cycle 1(n=40) | 193 (± 31) | | | |
| Day 1/Cycle 2(n=43) | 202 (± 33) | | | |

Notes:

[5] - The geometric coefficient of variation is a percentage.

Statistical analyses

No statistical analyses for this end point

Secondary: PK: Area Under the plasma concentration vs. time Curve from time zero to infinity [AUC(0-∞)] of LY2603618

| | |
|---|---|
| End point title | PK: Area Under the plasma concentration vs. time Curve from time zero to infinity [AUC(0-∞)] of LY2603618 |
| End point description: | |
| Analysis Population Description: All randomized participants who received at least 1 dose of drug and had evaluable PK data. | |
| End point type | Secondary |
| End point timeframe: | |
| Day 2 and Day 3 of Cycle 1 and Cycle 2: Prior to End of Infusion (EOI); EOI + 1-2 hr; EOI + 4-6 hr; EOI + 20-28 hr; anytime on Day 8 of Cycle 1 and Cycle 2 | |

| | | | | |
|---|--------------------------|--|--|--|
| End point values | LY2603618 and Pemetrexed | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 48 ^[6] | | | |
| Units: nanograms*hour per milliliter (ng*h/mL) | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Day 2/Cycle 1(n=41) | 38000 (± 85) | | | |
| Day 2/Cycle 2(n=48) | 41500 (± 88) | | | |

Notes:

[6] - The geometric coefficient of variation is a percentage.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Entire Study

Adverse event reporting additional description:

I2I-MC-JMMD

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 14.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | LY2603618-150mg/m2+PEMETREXED-500mg/m2 |
|-----------------------|--|

Reporting group description: -

| Serious adverse events | LY2603618-150mg/m2+PEMETREXED-500mg/m2 | | |
|---|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 16 / 55 (29.09%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| pericardial effusion malignant | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| road traffic accident | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| spinal compression fracture | | | |
| alternative dictionary used: MedDRA 14.1 | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 1 / 55 (1.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| tibia fracture | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| convulsion | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| asthenia | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| febrile neutropenia | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| neutropenia | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| thrombocytopenia | | | |
| alternative dictionary used: MedDRA 14.1 | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 2 / 55 (3.64%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| diarrhoea | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| gastritis | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| dyspnoea | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| haemoptysis | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| pleural effusion | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| pneumothorax | | | |
| alternative dictionary used: MedDRA 14.1 | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 2 / 55 (3.64%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| pulmonary embolism | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| dermatitis | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| confusional state | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| pneumonia | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| pseudomembranous colitis | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| sepsis | | | |
| alternative dictionary used: MedDRA 14.1 | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 55 (1.82%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| | | | |
|---|--|--|--|
| Non-serious adverse events | LY2603618- 150mg/m2+PEMETR EXED-500mg/m2 | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 52 / 55 (94.55%) | | |
| Investigations | | | |
| alanine aminotransferase increased alternative dictionary used: MedDRA 14.1 subjects affected / exposed occurrences (all) | 7 / 55 (12.73%) 7 | | |
| aspartate aminotransferase increased alternative dictionary used: MedDRA 14.1 subjects affected / exposed occurrences (all) | 6 / 55 (10.91%) 6 | | |
| Vascular disorders | | | |
| flushing alternative dictionary used: MedDRA 14.1 subjects affected / exposed occurrences (all) | 3 / 55 (5.45%) 3 | | |
| Nervous system disorders | | | |
| dizziness alternative dictionary used: MedDRA 14.1 subjects affected / exposed occurrences (all) | 5 / 55 (9.09%) 5 | | |
| headache alternative dictionary used: MedDRA 14.1 subjects affected / exposed occurrences (all) | 4 / 55 (7.27%) 5 | | |
| peripheral sensory neuropathy alternative dictionary used: MedDRA 14.1 | | | |

| | | | |
|---|------------------------|--|--|
| subjects affected / exposed occurrences (all) | 4 / 55 (7.27%) 6 | | |
| Blood and lymphatic system disorders | | | |
| anaemia alternative dictionary used: MedDRA 14.1 subjects affected / exposed occurrences (all) | 10 / 55 (18.18%) 12 | | |
| leukopenia alternative dictionary used: MedDRA 14.1 subjects affected / exposed occurrences (all) | 8 / 55 (14.55%) 13 | | |
| neutropenia alternative dictionary used: MedDRA 14.1 subjects affected / exposed occurrences (all) | 15 / 55 (27.27%) 35 | | |
| thrombocytopenia alternative dictionary used: MedDRA 14.1 subjects affected / exposed occurrences (all) | 4 / 55 (7.27%) 6 | | |
| General disorders and administration site conditions | | | |
| face oedema alternative dictionary used: MedDRA 14.1 subjects affected / exposed occurrences (all) | 4 / 55 (7.27%) 4 | | |
| fatigue alternative dictionary used: MedDRA 14.1 subjects affected / exposed occurrences (all) | 20 / 55 (36.36%) 27 | | |
| pyrexia alternative dictionary used: MedDRA 14.1 subjects affected / exposed occurrences (all) | 5 / 55 (9.09%) 5 | | |
| Gastrointestinal disorders | | | |

| | | | |
|---|-----------------------------------|--|--|
| <p>abdominal pain</p> <p>alternative dictionary used: MedDRA 14.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>6 / 55 (10.91%)</p> <p>6</p> | | |
| <p>constipation</p> <p>alternative dictionary used: MedDRA 14.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>11 / 55 (20.00%)</p> <p>15</p> | | |
| <p>diarrhoea</p> <p>alternative dictionary used: MedDRA 14.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>7 / 55 (12.73%)</p> <p>7</p> | | |
| <p>dyspepsia</p> <p>alternative dictionary used: MedDRA 14.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 55 (5.45%)</p> <p>3</p> | | |
| <p>nausea</p> <p>alternative dictionary used: MedDRA 14.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>18 / 55 (32.73%)</p> <p>28</p> | | |
| <p>stomatitis</p> <p>alternative dictionary used: MedDRA 14.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>5 / 55 (9.09%)</p> <p>5</p> | | |
| <p>vomiting</p> <p>alternative dictionary used: MedDRA 14.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>12 / 55 (21.82%)</p> <p>12</p> | | |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>cough</p> <p>alternative dictionary used: MedDRA 14.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>dyspnoea</p> <p>alternative dictionary used:</p> | <p>7 / 55 (12.73%)</p> <p>8</p> | | |

| | | | |
|---|-----------------|--|--|
| MedDRA 14.1 | | | |
| subjects affected / exposed | 7 / 55 (12.73%) | | |
| occurrences (all) | 7 | | |
| haemoptysis | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 3 / 55 (5.45%) | | |
| occurrences (all) | 3 | | |
| nasal congestion | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 3 / 55 (5.45%) | | |
| occurrences (all) | 3 | | |
| Skin and subcutaneous tissue disorders | | | |
| rash | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 4 / 55 (7.27%) | | |
| occurrences (all) | 4 | | |
| Musculoskeletal and connective tissue disorders | | | |
| back pain | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 5 / 55 (9.09%) | | |
| occurrences (all) | 6 | | |
| myalgia | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 3 / 55 (5.45%) | | |
| occurrences (all) | 3 | | |
| Infections and infestations | | | |
| herpes zoster | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 3 / 55 (5.45%) | | |
| occurrences (all) | 3 | | |
| Metabolism and nutrition disorders | | | |
| decreased appetite | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 9 / 55 (16.36%) | | |
| occurrences (all) | 9 | | |

| | | | |
|---|----------------|--|--|
| dehydration | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 3 / 55 (5.45%) | | |
| occurrences (all) | 3 | | |
| hypokalaemia | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 4 / 55 (7.27%) | | |
| occurrences (all) | 4 | | |
| hyponatraemia | | | |
| alternative dictionary used: MedDRA 14.1 | | | |
| subjects affected / exposed | 3 / 55 (5.45%) | | |
| occurrences (all) | 4 | | |

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

None reported