



## Clinical trial results:

### A Phase 1b/2 Dose Escalation and Cohort Expansion Study of the Safety, Tolerability and Efficacy of a Novel Transforming Growth Factor-beta Receptor I Kinase Inhibitor (Galunisertib) Administered in Combination With Anti-PD-1 (Nivolumab) in Advanced Refractory Solid Tumors (Phase 1b) and in Recurrent or Refractory Non-small Cell Lung Cancer, Hepatocellular Carcinoma, or Glioblastoma (Phase 2)

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2015-002093-20 |
| Trial protocol           | DE             |
| Global end of trial date | 08 July 2020   |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1           |
| This version publication date  | 18 July 2021 |
| First version publication date | 18 July 2021 |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | H9H-MC-JBEF |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |                     |
|------------------------------------|---------------------|
| ISRCTN number                      | -                   |
| ClinicalTrials.gov id (NCT number) | NCT02423343         |
| WHO universal trial number (UTN)   | -                   |
| Other trial identifiers            | Trial Number: 15702 |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Eli Lilly and Company   |
| Sponsor organisation address | Lilly Corporate Center, Indianapolis, IN, United States, 46285            |
| Public contact               | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877CTLilly, |
| Scientific contact           | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 8772854559, |

Notes:

#### Paediatric regulatory details

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|  |              |
|--|--------------|
| Analysis stage                                       | Final        |
| Date of interim/final analysis                       | 08 July 2020 |
| Is this the analysis of the primary completion data? | No           |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 08 July 2020 |
| Was the trial ended prematurely?                     | No           |

Notes:

## General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate the safety, tolerability, and efficacy of the study drug known as galunisertib in combination with nivolumab in participants with advanced refractory solid tumors and in recurrent or refractory non-small cell lung cancer (NSCLC) or hepatocellular carcinoma (HCC).

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                          | 01 January 2015 |
| 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: 13 |
| Country: Number of subjects enrolled | Spain: 28         |
| Worldwide total number of subjects   | 41                |
| EEA total number of subjects         | 28                |

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)                      | 28 |
| From 65 to 84 years                       | 13 |

|                   |   |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details:

Due low enrollment, the Hepatocellular Carcinoma (HCC) cohort was terminated early.

### Pre-assignment

Screening details:

Participants who had at least one post baseline tumor assessment were considered to have completed the study.

### Period 1

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

### Arms

|                              |  |
|------------------------------|--|
| Are arms mutually exclusive? | Yes  |
| <b>Arm title</b>             | Galunisertib + Nivolumab (Cohort 1) Phase 1b |

Arm description:

50 milligram (mg) Galunisertib administered orally daily (QD) on Day 1 through Day 14 of each 4-week cycle in combination with 3 milligrams per kilogram (3 mg/kg) nivolumab given intravenously (IV), every 2 weeks (Q2W), on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Galunisertib |
| Investigational medicinal product code |              |
| Other name                             | LY2157299    |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Administered orally

|  |                 |
|--|-----------------|
| Investigational medicinal product name | Nivolumab       |
| Investigational medicinal product code |                 |
| Other name                             | OPDIVO®         |
| Pharmaceutical forms                   | Injection       |
| Routes of administration               | Intravenous use |

Dosage and administration details:

Administered IV

|                  |  |
|------------------|--|
| <b>Arm title</b> | Galunisertib + Nivolumab (Cohort 2) Phase 1b |
|------------------|--|

Arm description:

50 mg Galunisertib administered orally twice daily (BID) on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Galunisertib |
| Investigational medicinal product code |              |
| Other name                             | LY2157299    |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Administered orally

|  |  |
|--|--|
| Investigational medicinal product name | Nivolumab                                    |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Injection                                    |
| Routes of administration               | Intravenous use                              |
| Dosage and administration details:     |  |
| Administered IV                        |  |
| <b>Arm title</b>                       | Galunisertib + Nivolumab (Cohort 3) Phase 1b |

Arm description:

80 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Galunisertib |
| Investigational medicinal product code |              |
| Other name                             | LY2157299    |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Administered orally

|  |                 |
|--|-----------------|
| Investigational medicinal product name | Nivolumab       |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Injection       |
| Routes of administration               | Intravenous use |

Dosage and administration details:

Administered IV

|                  |  |
|------------------|--|
| <b>Arm title</b> | Galunisertib + Nivolumab (Cohort 4) Phase 1b |
|------------------|--|

Arm description:

150 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Galunisertib |
| Investigational medicinal product code |              |
| Other name                             | LY2157299    |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Administered orally

|  |                 |
|--|-----------------|
| Investigational medicinal product name | Nivolumab       |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Injection       |
| Routes of administration               | Intravenous use |

Dosage and administration details:

Administered IV

|                  |  |
|------------------|--|
| <b>Arm title</b> | Galunisertib + Nivolumab (NSCLC) Phase 2 |
|------------------|--|

Arm description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4 week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, (Day 1 and Day 15) of each 4 week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Galunisertib |
| Investigational medicinal product code |              |
| Other name                             | LY2157299    |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Administered orally

|  |                 |
|--|-----------------|
| Investigational medicinal product name | Nivolumab       |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Injection       |
| Routes of administration               | Intravenous use |

Dosage and administration details:

Administered IV

|                  |  |
|------------------|--|
| <b>Arm title</b> | Galunisertib + Nivolumab (HCC) Phase 2 |
|------------------|--|

Arm description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4 week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, (Day 1 and Day 15) of each 4 week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

Hepatocellular Carcinoma (HCC)

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Galunisertib |
| Investigational medicinal product code |              |
| Other name                             | LY2157299    |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Administered orally

|  |                 |
|--|-----------------|
| Investigational medicinal product name | Nivolumab       |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Injection       |
| Routes of administration               | Intravenous use |

Dosage and administration details:

Administered IV

| <b>Number of subjects in period 1</b>  | Galunisertib + Nivolumab (Cohort 1) Phase 1b | Galunisertib + Nivolumab (Cohort 2) Phase 1b | Galunisertib + Nivolumab (Cohort 3) Phase 1b |
|--|--|--|--|
| Started                                | 3  | 5  | 3  |
| Received at Least 1 Dose of Study Drug | 3  | 5  | 3  |
| Completed                              | 3  | 4  | 3  |
| Not completed                          | 0  | 1  | 0  |
| Adverse event, serious fatal           | -  | -  | -  |
| Consent withdrawn by subject           | -  | 1  | -  |
| Adverse event, non-fatal               | -  | -  | -  |
| Progressive Disease                    | -  | -  | -  |

| <b>Number of subjects in period 1</b>  | Galunisertib +<br>Nivolumab (Cohort<br>4) Phase 1b | Galunisertib +<br>Nivolumab (NSCLC)<br>Phase 2 | Galunisertib +<br>Nivolumab (HCC)<br>Phase 2 |
|--|--|--|--|
| Started                                | 4  | 25   | 1  |
| Received at Least 1 Dose of Study Drug | 4  | 25   | 1  |
| Completed                              | 4  | 20   | 1  |
| Not completed                          | 0  | 5  | 0  |
| Adverse event, serious fatal           | -  | 1  | -  |
| Consent withdrawn by subject           | -  | -  | -  |
| Adverse event, non-fatal               | -  | 2  | -  |
| Progressive Disease                    | -  | 2  | -  |

## Baseline characteristics

### Reporting groups

|   |  |
|---|--|
| Reporting group title   | Galunisertib + Nivolumab (Cohort 1) Phase 1b |
| Reporting group description:<br>50 milligram (mg) Galunisertib administered orally daily (QD) on Day 1 through Day 14 of each 4-week cycle in combination with 3 milligrams per kilogram (3 mg/kg) nivolumab given intravenously (IV), every 2 weeks (Q2W), on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met. |  |
| Reporting group title   | Galunisertib + Nivolumab (Cohort 2) Phase 1b |
| Reporting group description:<br>50 mg Galunisertib administered orally twice daily (BID) on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.  |  |
| Reporting group title   | Galunisertib + Nivolumab (Cohort 3) Phase 1b |
| Reporting group description:<br>80 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.  |  |
| Reporting group title   | Galunisertib + Nivolumab (Cohort 4) Phase 1b |
| Reporting group description:<br>150 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.   |  |
| Reporting group title   | Galunisertib + Nivolumab (NSCLC) Phase 2     |
| Reporting group description:<br>150 mg Galunisertib administered orally BID for the first 14 days of each 4 week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, (Day 1 and Day 15) of each 4 week cycle. Participants may continue to receive study drug until discontinuation criteria are met.  |  |
| Hepatocellular Carcinoma (HCC)  |  |
| Reporting group title   | Galunisertib + Nivolumab (HCC) Phase 2       |
| Reporting group description:<br>150 mg Galunisertib administered orally BID for the first 14 days of each 4 week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, (Day 1 and Day 15) of each 4 week cycle. Participants may continue to receive study drug until discontinuation criteria are met.  |  |
| Hepatocellular Carcinoma (HCC)  |  |

| Reporting group values                | Galunisertib + Nivolumab (Cohort 1) Phase 1b | Galunisertib + Nivolumab (Cohort 2) Phase 1b | Galunisertib + Nivolumab (Cohort 3) Phase 1b |
|---------------------------------------|--|--|--|
| Number of subjects                    | 3  | 5  | 3  |
| Age categorical<br>Units: Subjects    |  |  |  |
| Age continuous<br>Units: years        |  |  |  |
| arithmetic mean                       | 60.7   | 47.2   | 36.0   |
| standard deviation                    | ± 15.6                                       | ± 15.8                                       | ± 5.3  |
| Gender categorical<br>Units: Subjects |  |  |  |
| Female                                | 1  | 1  | 1  |
| Male                                  | 2  | 4  | 2  |



|   |   |   |   |
|---|---|---|---|
| Race (NIH/OMB)                            |   |   |   |
| Units: Subjects                           |   |   |   |
| American Indian or Alaska Native          | 0 | 0 | 0 |
| Asian                                     | 0 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American                 | 1 | 0 | 0 |
| White                                     | 2 | 5 | 3 |
| More than one race                        | 0 | 0 | 0 |
| Unknown or Not Reported                   | 0 | 0 | 0 |
| Region of Enrollment                      |   |   |   |
| Units: Subjects                           |   |   |   |
| United States                             | 3 | 3 | 2 |
| Spain                                     | 0 | 2 | 1 |

| <b>Reporting group values</b> | Galunisertib +<br>Nivolumab (Cohort<br>4) Phase 1b | Galunisertib +<br>Nivolumab (NSCLC)<br>Phase 2 | Galunisertib +<br>Nivolumab (HCC)<br>Phase 2 |
|-------------------------------|--|--|--|
| Number of subjects            | 4  | 25   | 1  |
| Age categorical               |  |  |  |
| Units: Subjects               |  |  |  |

|   |       |       |       |
|---|-------|-------|-------|
| Age continuous                            |       |       |       |
| Units: years                              |       |       |       |
| arithmetic mean                           | 61.5  | 61.0  | 64.0  |
| standard deviation                        | ± 9.0 | ± 8.4 | ± 0.0 |
| Gender categorical                        |       |       |       |
| Units: Subjects                           |       |       |       |
| Female                                    | 3     | 9     | 1     |
| Male                                      | 1     | 16    | 0     |
| Race (NIH/OMB)                            |       |       |       |
| Units: Subjects                           |       |       |       |
| American Indian or Alaska Native          | 0     | 0     | 0     |
| Asian                                     | 0     | 0     | 0     |
| Native Hawaiian or Other Pacific Islander | 0     | 0     | 0     |
| Black or African American                 | 1     | 0     | 0     |
| White                                     | 3     | 25    | 1     |
| More than one race                        | 0     | 0     | 0     |
| Unknown or Not Reported                   | 0     | 0     | 0     |
| Region of Enrollment                      |       |       |       |
| Units: Subjects                           |       |       |       |
| United States                             | 4     | 1     | 0     |
| Spain                                     | 0     | 24    | 1     |

| <b>Reporting group values</b> | Total |  |  |
|-------------------------------|-------|--|--|
| Number of subjects            | 41    |  |  |
| Age categorical               |       |  |  |
| Units: Subjects               |       |  |  |

|   |    |  |  |
|---|----|--|--|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | -  |  |  |
| Gender categorical<br>Units: Subjects                                   |    |  |  |
| Female  | 16 |  |  |
| Male  | 25 |  |  |
| Race (NIH/OMB)<br>Units: Subjects                                       |    |  |  |
| American Indian or Alaska Native  | 0  |  |  |
| Asian   | 0  |  |  |
| Native Hawaiian or Other Pacific Islander                               | 0  |  |  |
| Black or African American   | 2  |  |  |
| White   | 39 |  |  |
| More than one race  | 0  |  |  |
| Unknown or Not Reported   | 0  |  |  |
| Region of Enrollment<br>Units: Subjects                                 |    |  |  |
| United States   | 13 |  |  |
| Spain   | 28 |  |  |

## End points

### End points reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | Galunisertib + Nivolumab (Cohort 1) Phase 1b |
|-----------------------|--|

Reporting group description:

50 milligram (mg) Galunisertib administered orally daily (QD) on Day 1 through Day 14 of each 4-week cycle in combination with 3 milligrams per kilogram (3 mg/kg) nivolumab given intravenously (IV), every 2 weeks (Q2W), on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

|                       |  |
|-----------------------|--|
| Reporting group title | Galunisertib + Nivolumab (Cohort 2) Phase 1b |
|-----------------------|--|

Reporting group description:

50 mg Galunisertib administered orally twice daily (BID) on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

|                       |  |
|-----------------------|--|
| Reporting group title | Galunisertib + Nivolumab (Cohort 3) Phase 1b |
|-----------------------|--|

Reporting group description:

80 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

|                       |  |
|-----------------------|--|
| Reporting group title | Galunisertib + Nivolumab (Cohort 4) Phase 1b |
|-----------------------|--|

Reporting group description:

150 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

|                       |  |
|-----------------------|--|
| Reporting group title | Galunisertib + Nivolumab (NSCLC) Phase 2 |
|-----------------------|--|

Reporting group description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4 week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, (Day 1 and Day 15) of each 4 week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

|                       |  |
|-----------------------|--|
| Reporting group title | Galunisertib + Nivolumab (HCC) Phase 2 |
|-----------------------|--|

Reporting group description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4 week cycle in combination with 3 mg/kg nivolumab given IV, Q2W, (Day 1 and Day 15) of each 4 week cycle. Participants may continue to receive study drug until discontinuation criteria are met.  
Hepatocellular Carcinoma (HCC)

|                            |  |
|----------------------------|--|
| Subject analysis set title | Galunisertib + Nivolumab (NSCLC) Phase 2 |
|----------------------------|--|

|                           |              |
|---------------------------|--------------|
| Subject analysis set type | Per protocol |
|---------------------------|--------------|

Subject analysis set description:

150 mg Galunisertib given orally twice daily for the first 14 days of each 4 week cycle in combination with 3 mg/kg nivolumab given IV every 2 weeks (Day 1 and Day 15) of each 4 week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

|                            |                       |
|----------------------------|-----------------------|
| Subject analysis set title | Phase 1b Participants |
|----------------------------|-----------------------|

|                           |              |
|---------------------------|--------------|
| Subject analysis set type | Per protocol |
|---------------------------|--------------|

Subject analysis set description:

Cohort 1: 50 mg Galunisertib administered QD on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV, every Q2W, on Day 1 and Day 15 for 2 cycles.

Cohort 2: 50 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV Q2W on Day 1 and Day 15 for 2 cycles.

Cohort 3: 80 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV Q2W on Day 1 and Day 15 for 2 cycles.

Cohort 4: 150 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in

combination with 3 mg/kg nivolumab given IV Q2W on Day 1 and Day 15 for 2 cycles.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Galunisertib + Nivolumab (NSCLC + HCC) Phase 2 |
| Subject analysis set type  | Per protocol                                   |

Subject analysis set description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4 week cycle in combination with 3 mg/kg nivolumab given IV Q2W (Day 1 and Day 15) of each 4 week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Galunisertib + Nivolumab (NSCLC) Phase 2 |
| Subject analysis set type  | Per protocol                             |

Subject analysis set description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4-week cycle in combination with 3 mg/kg nivolumab given IV Q2W (Day 1 and Day 15) of each 4-week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Galunisertib + Nivolumab (HCC) Phase 2 |
| Subject analysis set type  | Per protocol                           |

Subject analysis set description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4-week cycle in combination with 3 mg/kg nivolumab given IV Q2W (Day 1 and Day 15) of each 4-week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Galunisertib + Nivolumab (NSCLC) Phase 2 |
| Subject analysis set type  | Per protocol                             |

Subject analysis set description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4 week cycle in combination with 3 mg/kg nivolumab given IV Q2W (Day 1 and Day 15) of each 4-week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Galunisertib + Nivolumab (HCC) Phase 2 |
| Subject analysis set type  | Per protocol                           |

Subject analysis set description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4 week cycle in combination with 3 mg/kg nivolumab given IV Q2W (Day 1 and Day 15) of each 4-week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

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### **Primary: Phase 1b: Maximum Tolerated Dose (MTD) of Galunisertib in Combination with Nivolumab**

|                 |   |
|-----------------|---|
| End point title | Phase 1b: Maximum Tolerated Dose (MTD) of Galunisertib in Combination with Nivolumab <sup>[1]</sup> |
|-----------------|---|

End point description:

The MTD is defined as the highest tested dose that has less than 33% probability of causing a dose limiting toxicity (DLT).

Analysis Population Description (APD): All participants who received at least one dose of study drug in Phase 1b per protocol.

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

End point timeframe:

Cycle 1 through Cycle 2 (Up to 2 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: Per protocol, Maximum Tolerated Dose was assessed during Phase 1b only with all Phase 1b cohorts combined.

|                             |                          |  |  |  |
|-----------------------------|--------------------------|--|--|--|
| <b>End point values</b>     | Phase 1b<br>Participants |  |  |  |
| Subject group type          | Subject analysis set     |  |  |  |
| Number of subjects analysed | 15                       |  |  |  |
| Units: milligrams (mg)      |                          |  |  |  |
| number (not applicable)     | 300                      |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics (PK): Minimum Concentration (Cmin) of Nivolumab

|                 |   |
|-----------------|---|
| End point title | Pharmacokinetics (PK): Minimum Concentration (Cmin) of Nivolumab <sup>[2]</sup> |
|-----------------|---|

End point description:

Minimum Concentration (Cmin) of Nivolumab.

APD: All participants who received at least one dose of Nivolumab and had evaluable PK data.  
Enrollment for the HCC cohort was halted early in Phase 2 however enrollment continued for the NSCLC cohort only and data was combined for Phase 2 PK.

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

End point timeframe:

PK: Cycle 1 Day 15 Predose; Cycle 2: Day 1: Pre-dose; Day 15: Predose; Cycle 4: Day 1: Predose

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: Enrollment for the HCC cohort was halted early in Phase 2 (N=1) however enrollment continued for the NSCLC cohort only and data was combined for Phase 2 PK.

| <b>End point values</b>                  | Galunisertib +<br>Nivolumab<br>(Cohort 1)<br>Phase 1b | Galunisertib +<br>Nivolumab<br>(Cohort 2)<br>Phase 1b | Galunisertib +<br>Nivolumab<br>(Cohort 3)<br>Phase 1b | Galunisertib +<br>Nivolumab<br>(Cohort 4)<br>Phase 1b |
|--|---|---|---|---|
| Subject group type                       | Reporting group                                       | Reporting group                                       | Reporting group                                       | Reporting group                                       |
| Number of subjects analysed              | 2   | 5   | 3   | 4   |
| Units: micrograms per milliliter (µg/mL) |   |   |   |   |
| arithmetic mean (full range (min-max))   | 33.5 (19.9 to 53.6)                                   | 36.2 (11.8 to 58.1)                                   | 43.2 (5.45 to 76)                                     | 29.2 (9.39 to 63.7)                                   |

| <b>End point values</b>                  | Galunisertib +<br>Nivolumab<br>(NSCLC +<br>HCC) Phase 2 |  |  |  |
|--|---|--|--|--|
| Subject group type                       | Subject analysis set                                    |  |  |  |
| Number of subjects analysed              | 11  |  |  |  |
| Units: micrograms per milliliter (µg/mL) |   |  |  |  |
| arithmetic mean (full range (min-max))   | 37.6 (1.08 to 105)                                      |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: PK: Area Under the Plasma Concentration -Time Curve of Galunisertib From Time Zero to 24 Hours (AUC [0-24h]) at Steady State

|                 |   |
|-----------------|---|
| End point title | PK: Area Under the Plasma Concentration -Time Curve of Galunisertib From Time Zero to 24 Hours (AUC [0-24h]) at Steady State <sup>[3]</sup> |
|-----------------|---|

End point description:

Area under the plasma concentration curve from time zero to 24 hours of galunisertib for Cycle 1 and Cycle 2.

APD: All participants who received at least one dose of Nivolumab and had evaluable PK data. Enrollment for the HCC cohort was halted early in Phase 2 ) however enrollment continued for the NSCLC cohort only and data was combined for Phase 2 PK.

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

End point timeframe:

PK: Cycle 1 and Cycle 2 Day 1: Predose, 0.5 - 3 hours postdose, Cycle 1 and Cycle 2 Day 14: Predose, 0.5 - 2, 3.5 - 5, and 24 hours postdose through Cycle 4 Day 1 predose

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: Enrollment for the HCC cohort was halted early in Phase 2 (N=1) however enrollment continued for the NSCLC cohort only and data was combined for Phase 2 PK..

| End point values                                    | Galunisertib + Nivolumab (Cohort 1) Phase 1b | Galunisertib + Nivolumab (Cohort 2) Phase 1b | Galunisertib + Nivolumab (Cohort 3) Phase 1b | Galunisertib + Nivolumab (Cohort 4) Phase 1b |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                              | Reporting group                              | Reporting group                              | Reporting group                              |
| Number of subjects analysed                         | 3  | 4  | 3  | 4  |
| Units: micrograms*hour per liter (µg*h/L)           |  |  |  |  |
| geometric mean (geometric coefficient of variation) | 3060 (± 41)                                  | 2350 (± 46)                                  | 2220 (± 164)                                 | 5580 (± 61)                                  |

| End point values                                    | Galunisertib + Nivolumab (NSCLC + HCC) Phase 2 |  |  |  |
|---|--|--|--|--|
| Subject group type                                  | Subject analysis set                           |  |  |  |
| Number of subjects analysed                         | 13   |  |  |  |
| Units: micrograms*hour per liter (µg*h/L)           |  |  |  |  |
| geometric mean (geometric coefficient of variation) | 7160 (± 65)                                    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Anti-Nivolumab Antibodies When Administered in Combination with Galunisertib

|                 |  |
|-----------------|--|
| End point title | Number of Participants with Anti-Nivolumab Antibodies When Administered in Combination with Galunisertib |
|-----------------|--|

End point description:

Participants with treatment-emergent anti-nivolumab antibodies when administered with galunisertib were participants with a 4-fold or greater increase in titer from baseline measurement (treatment-boostered). If baseline result is ADA not present, then the subject is TE ADA+, if there is at least 1 postbaseline result of ADA present with titer  $\geq 40$  (treatment-induced).

APD: All participants who received at least one dose of study drug and were evaluable for TE ADA.

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

End point timeframe:

Cycle 1: Days 1, 14, 15 Predose and Day 100 Follow-up; Cycles 2 and 4: Day 1 Predose and Day 100 Follow-up

| End point values             | Galunisertib + Nivolumab (Cohort 1) Phase 1b | Galunisertib + Nivolumab (Cohort 2) Phase 1b | Galunisertib + Nivolumab (Cohort 3) Phase 1b | Galunisertib + Nivolumab (Cohort 4) Phase 1b |
|------------------------------|--|--|--|--|
| Subject group type           | Reporting group                              | Reporting group                              | Reporting group                              | Reporting group                              |
| Number of subjects analysed  | 3  | 5  | 2  | 3  |
| Units: Count of Participants | 0  | 0  | 0  | 0  |

| End point values             | Galunisertib + Nivolumab (NSCLC) Phase 2 | Galunisertib + Nivolumab (HCC) Phase 2 |  |  |
|------------------------------|--|--|--|--|
| Subject group type           | Reporting group                          | Reporting group                        |  |  |
| Number of subjects analysed  | 13                                       | 1                                      |  |  |
| Units: Count of Participants | 0  | 0                                      |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 2: Progression Free Survival (PFS)

|                 |   |
|-----------------|---|
| End point title | Phase 2: Progression Free Survival (PFS) <sup>[4]</sup> |
|-----------------|---|

End point description:

PFS was defined as the time from the date of first study treatment to the first evidence of disease progression as defined by response evaluation criteria in solid tumors (RECIST) v1.1 or death from any cause. Progressive Disease (PD) was 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 participant does not have a complete baseline disease assessment, then the PFS time was censored at the date of randomization, regardless of whether or not objectively determined disease progression or death has been observed for the participant. If a participant was not known to have died or have objective progression as of the data inclusion cutoff date for the analysis, the PFS time was censored at the last adequate tumor assessment date.

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

End point timeframe:

Date of First Study Treatment to Measured Progressive Disease or Death (Up to 35 Months)

APD: All participants who received at least one dose of study drug in the Phase 2 cohorts. Censored participants Galunisertib + Nivolumab (NSCLC) Phase 2 = 6.

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, anti-tumor activity was assessed only on Phase 2 participants.

| End point values                 | Galunisertib + Nivolumab (NSCLC) Phase 2 | Galunisertib + Nivolumab (HCC) Phase 2 |  |  |
|----------------------------------|--|--|--|--|
| Subject group type               | Reporting group                          | Reporting group                        |  |  |
| Number of subjects analysed      | 25                                       | 1 <sup>[5]</sup>                       |  |  |
| Units: months                    |  |  |  |  |
| median (confidence interval 95%) | 5.26 (1.77 to 9.20)                      | 0 (0 to 0)                             |  |  |

Notes:

[5] - N=1: Median: 5.39, CI: not evaluable (NE)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 2: Percentage of Participants who Achieve Best Overall Tumor Response of Complete Response or Partial Response: Objective Response Rate (ORR)

|                 |  |
|-----------------|--|
| End point title | Phase 2: Percentage of Participants who Achieve Best Overall Tumor Response of Complete Response or Partial Response: Objective Response Rate (ORR) <sup>[6]</sup> |
|-----------------|--|

End point description:

Objective Response Rate was the percentage of participants achieving a best overall response (BOR) of complete response (CR) or partial response (PR) as per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. CR defined as the disappearance of all target and non-target lesions and no appearance of new lesions. PR defined as at least a 30% decrease in the sum of the longest diameters (LD) of target lesions (taking as reference the baseline sum LD), no progression of non-target lesions, and no appearance of new lesions. PD was 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. 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.

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



End point timeframe:

Baseline to Measured Progressive Disease (Up to 35 Months)

Notes:

[6] - 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, anti-tumor activity was assessed only on Phase 2 participants.

| End point values                  | Galunisertib + Nivolumab (NSCLC) Phase 2 | Galunisertib + Nivolumab (HCC) Phase 2 |  |  |
|-----------------------------------|--|--|--|--|
| Subject group type                | Reporting group                          | Reporting group                        |  |  |
| Number of subjects analysed       | 25 <sup>[7]</sup>                        | 1 <sup>[8]</sup>                       |  |  |
| Units: Percentage of Participants |  |  |  |  |
| number (not applicable)           | 24.0                                     | 0.0                                    |  |  |

Notes:

[7] - APD: All participants who received at least one dose of study drug in Phase 2 cohorts.

[8] - APD: All participants who received at least one dose of study drug in Phase 2 cohorts.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 2: Duration of Response (DoR)

|                 |  |
|-----------------|--|
| End point title | Phase 2: Duration of Response (DoR) <sup>[9]</sup> |
|-----------------|--|

End point description:

Duration of response is measured from the date of documented response to the date of first progression of disease or the date of death due to any cause, whichever is earlier.

APD: All participants who received at least one dose of study drug in Phase 2 cohorts and had a response of complete response or partial response. Censored participants Galunisertib + Nivolumab (NSCLC) Phase 2 = 1.

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

End point timeframe:

Date of Complete Response (CR) or Partial Response (PR) to Date of Objective Disease Progression or Death Due to Any Cause (Up to 35 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, anti-tumor activity was assessed only on Phase 2 participants.

| End point values              | Galunisertib + Nivolumab (NSCLC) Phase 2 | Galunisertib + Nivolumab (HCC) Phase 2 |  |  |
|-------------------------------|--|--|--|--|
| Subject group type            | Reporting group                          | Reporting group                        |  |  |
| Number of subjects analysed   | 6  | 1 <sup>[10]</sup>                      |  |  |
| Units: months                 |  |  |  |  |
| median (full range (min-max)) | 9.03 (1.97 to 35)                        | 0 (0 to 0)                             |  |  |

Notes:

[10] - There was no response to treatment for the HCC cohort.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 2: Time to Response

|                 |   |
|-----------------|---|
| End point title | Phase 2: Time to Response <sup>[11]</sup> |
|-----------------|---|

End point description:

Time to response was measured from the date of first study treatment to the first documented response of Complete Response (CR) or Partial Response (PR).

APD: All participants who received at least one dose of study drug in Phase 2 cohorts and had a documented response of CR or PR.

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

End point timeframe:

Date of First Study Treatment to Date of Complete Response or Partial Response (Up to 35 Months)

Notes:

[11] - 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, anti-tumor activity was assessed only on Phase 2 participants.

| End point values              | Galunisertib + Nivolumab (NSCLC) Phase 2 | Galunisertib + Nivolumab (HCC) Phase 2 |  |  |
|-------------------------------|--|--|--|--|
| Subject group type            | Reporting group                          | Reporting group                        |  |  |
| Number of subjects analysed   | 6  | 0 <sup>[12]</sup>                      |  |  |
| Units: months                 |  |  |  |  |
| median (full range (min-max)) | 4.2 (0.5 to 35)                          | ( to )                                 |  |  |

Notes:

[12] - There was no response to treatment for the HCC reporting group.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 2: Overall Survival (OS)

|                 |  |
|-----------------|--|
| End point title | Phase 2: Overall Survival (OS) <sup>[13]</sup> |
|-----------------|--|

End point description:

Overall Survival is determined from the date of first study treatment until death due to any cause.

APD: All participants who received at least one dose of study drug in Phase 2 cohorts. Censored participants Galunisertib + Nivolumab (NSCLC) Phase 2 = 8.

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

End point timeframe:

Date of First Study Treatment to Death from Any Cause (Up to 35 Months)

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, anti-tumor activity was assessed only on Phase 2 participants.

| <b>End point values</b>          | Galunisertib +<br>Nivolumab<br>(NSCLC) Phase<br>2 | Galunisertib +<br>Nivolumab<br>(HCC) Phase 2 |  |  |
|----------------------------------|---|--|--|--|
| Subject group type               | Reporting group                                   | Reporting group                              |  |  |
| Number of subjects analysed      | 25  | 1 <sup>[14]</sup>                            |  |  |
| Units: months                    |   |  |  |  |
| median (confidence interval 95%) | 11.99 (8.15 to<br>16.23)                          | 0 (0 to 0)                                   |  |  |

Notes:

[14] - N=1 median 14.52 months, CI is non-evaluable.

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 34 Months

Adverse event reporting additional description:

All participants who received at least one dose of study drug.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 23.0 |
|--------------------|------|

### Reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | Galunisertib + Nivolumab (Cohort 1) Phase 1b |
|-----------------------|--|

Reporting group description:

50 mg Galunisertib administered orally QD on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV every Q2W on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

|                       |  |
|-----------------------|--|
| Reporting group title | Galunisertib + Nivolumab (Cohort 2) Phase 1b |
|-----------------------|--|

Reporting group description:

50 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV Q2W on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

|                       |  |
|-----------------------|--|
| Reporting group title | Galunisertib + Nivolumab (Cohort 3) Phase 1b |
|-----------------------|--|

Reporting group description:

80 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV Q2W on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

|                       |  |
|-----------------------|--|
| Reporting group title | Galunisertib + Nivolumab (Cohort 4) Phase 1b |
|-----------------------|--|

Reporting group description:

150 mg Galunisertib administered orally BID on Day 1 through Day 14 of each 4-week cycle in combination with 3 mg/kg nivolumab given IV Q2W on Day 1 and Day 15 for 2 cycles. Participants may continue to receive study drug until discontinuation criteria are met.

|                       |  |
|-----------------------|--|
| Reporting group title | Galunisertib + Nivolumab (NSCLC) Phase 2 |
|-----------------------|--|

Reporting group description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4-week cycle in combination with 3 mg/kg nivolumab given IV Q2W (Day 1 and Day 15) of each 4-week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

|                       |  |
|-----------------------|--|
| Reporting group title | Galunisertib + Nivolumab (HCC) Phase 2 |
|-----------------------|--|

Reporting group description:

150 mg Galunisertib administered orally BID for the first 14 days of each 4-week cycle in combination with 3 mg/kg nivolumab given IV Q2W (Day 1 and Day 15) of each 4-week cycle. Participants may continue to receive study drug until discontinuation criteria are met.

| Serious adverse events                            | Galunisertib + Nivolumab (Cohort 1) Phase 1b | Galunisertib + Nivolumab (Cohort 2) Phase 1b | Galunisertib + Nivolumab (Cohort 3) Phase 1b |
|---|--|--|--|
| Total subjects affected by serious adverse events |  |  |  |
| subjects affected / exposed                       | 1 / 3 (33.33%)                               | 2 / 5 (40.00%)                               | 1 / 3 (33.33%)                               |
| 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)<br>adenocarcinoma of colon<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 5 (0.00%)<br>0 / 0<br>0 / 0  | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 |
| Vascular disorders<br>angiopathy<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all   | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 5 (0.00%)<br>0 / 0<br>0 / 0  | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 |
| Cardiac disorders<br>acute myocardial infarction<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all   | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 5 (0.00%)<br>0 / 0<br>0 / 0  | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 |
| pericarditis<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all   | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 5 (0.00%)<br>0 / 0<br>0 / 0  | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 |
| Nervous system disorders<br>cerebrovascular accident<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all   | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 5 (0.00%)<br>0 / 0<br>0 / 0  | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 |
| headache<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all   | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 5 (20.00%)<br>0 / 1<br>0 / 0 | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 |

|  |                                  |                                 |                                  |
|--|----------------------------------|---------------------------------|----------------------------------|
| noninfective encephalitis<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0  | 0 / 5 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0  |
| General disorders and administration<br>site conditions<br>chest pain<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0  | 0 / 5 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0  |
| Gastrointestinal disorders<br>dyspepsia<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                               | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0  | 0 / 5 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 3 (33.33%)<br>0 / 1<br>0 / 0 |
| large intestinal obstruction<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0  | 0 / 5 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 3 (33.33%)<br>0 / 2<br>0 / 0 |
| small intestinal obstruction<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0  | 0 / 5 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0  |
| vomiting<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 1 / 3 (33.33%)<br>0 / 1<br>0 / 0 | 0 / 5 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0  |
| Hepatobiliary disorders  |                                  |                                 |                                  |

|  |                |               |                |
|--|----------------|---------------|----------------|
| cholestasis  |                |               |                |
| alternative dictionary used:<br>MedDRA 23.0        |                |               |                |
| subjects affected / exposed                        | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Respiratory, thoracic and mediastinal<br>disorders |                |               |                |
| chronic obstructive pulmonary<br>disease           |                |               |                |
| alternative dictionary used:<br>MedDRA 23.0        |                |               |                |
| subjects affected / exposed                        | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| cough  |                |               |                |
| alternative dictionary used:<br>MedDRA 23.0        |                |               |                |
| subjects affected / exposed                        | 1 / 3 (33.33%) | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to<br>treatment / all | 1 / 1          | 0 / 0         | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| dyspnoea   |                |               |                |
| alternative dictionary used:<br>MedDRA 23.0        |                |               |                |
| subjects affected / exposed                        | 1 / 3 (33.33%) | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to<br>treatment / all | 1 / 3          | 0 / 0         | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| respiratory failure                                |                |               |                |
| alternative dictionary used:<br>MedDRA 23.0        |                |               |                |
| subjects affected / exposed                        | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Renal and urinary disorders                        |                |               |                |
| hydronephrosis                                     |                |               |                |
| alternative dictionary used:<br>MedDRA 23.0        |                |               |                |
| subjects affected / exposed                        | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Musculoskeletal and connective tissue              |                |               |                |

|  |                |                |                |
|--|----------------|----------------|----------------|
| disorders  |                |                |                |
| arthralgia   |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0        |                |                |                |
| subjects affected / exposed                        | 0 / 3 (0.00%)  | 1 / 5 (20.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| pain in extremity                                  |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0        |                |                |                |
| subjects affected / exposed                        | 1 / 3 (33.33%) | 0 / 5 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences causally related to<br>treatment / all | 0 / 2          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                        |                |                |                |
| bronchitis   |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0        |                |                |                |
| subjects affected / exposed                        | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| lower respiratory tract infection                  |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0        |                |                |                |
| subjects affected / exposed                        | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| pneumonia  |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0        |                |                |                |
| subjects affected / exposed                        | 0 / 3 (0.00%)  | 1 / 5 (20.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| pyelonephritis                                     |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0        |                |                |                |
| subjects affected / exposed                        | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 1 / 3 (33.33%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| respiratory tract infection                        |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0        |                |                |                |



|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (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          |
| septic shock                                    |               |               |                |
| alternative dictionary used: MedDRA 23.0        |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| urinary tract infection                         |               |               |                |
| alternative dictionary used: MedDRA 23.0        |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (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          |
| Metabolism and nutrition disorders              |               |               |                |
| dehydration                                     |               |               |                |
| alternative dictionary used: MedDRA 23.0        |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| failure to thrive                               |               |               |                |
| alternative dictionary used: MedDRA 23.0        |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (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          |

| <b>Serious adverse events</b>                                       | Galunisertib +<br>Nivolumab (Cohort<br>4) Phase 1b | Galunisertib +<br>Nivolumab (NSCLC)<br>Phase 2 | Galunisertib +<br>Nivolumab (HCC)<br>Phase 2 |
|---|--|--|--|
| Total subjects affected by serious adverse events                   |  |  |  |
| subjects affected / exposed   | 2 / 4 (50.00%)                                     | 13 / 25 (52.00%)                               | 0 / 1 (0.00%)                                |
| number of deaths (all causes)                                       | 0  | 1  | 0  |
| number of deaths resulting from adverse events                      | 0  | 0  | 0  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |  |  |
| adenocarcinoma of colon   |  |  |  |
| alternative dictionary used: MedDRA 23.0                            |  |  |  |

|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 1 / 4 (25.00%) | 0 / 25 (0.00%) | 0 / 1 (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         |
| Vascular disorders                              |                |                |               |
| angiopathy                                      |                |                |               |
| alternative dictionary used: MedDRA 23.0        |                |                |               |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 1 / 25 (4.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Cardiac disorders                               |                |                |               |
| acute myocardial infarction                     |                |                |               |
| alternative dictionary used: MedDRA 23.0        |                |                |               |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 1 / 25 (4.00%) | 0 / 1 (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         |
| pericarditis                                    |                |                |               |
| alternative dictionary used: MedDRA 23.0        |                |                |               |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 1 / 25 (4.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Nervous system disorders                        |                |                |               |
| cerebrovascular accident                        |                |                |               |
| alternative dictionary used: MedDRA 23.0        |                |                |               |
| subjects affected / exposed                     | 1 / 4 (25.00%) | 0 / 25 (0.00%) | 0 / 1 (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         |
| headache  |                |                |               |
| alternative dictionary used: MedDRA 23.0        |                |                |               |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 25 (0.00%) | 0 / 1 (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         |
| noninfective encephalitis                       |                |                |               |
| alternative dictionary used: MedDRA 23.0        |                |                |               |

|  |                |                |               |
|--|----------------|----------------|---------------|
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 1 / 25 (4.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 1 / 2          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |
| General disorders and administration site conditions |                |                |               |
| chest pain   |                |                |               |
| alternative dictionary used: MedDRA 23.0             |                |                |               |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 1 / 25 (4.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |
| Gastrointestinal disorders                           |                |                |               |
| dyspepsia  |                |                |               |
| alternative dictionary used: MedDRA 23.0             |                |                |               |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 25 (0.00%) | 0 / 1 (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 23.0             |                |                |               |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 25 (0.00%) | 0 / 1 (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         |
| small intestinal obstruction                         |                |                |               |
| alternative dictionary used: MedDRA 23.0             |                |                |               |
| subjects affected / exposed                          | 1 / 4 (25.00%) | 0 / 25 (0.00%) | 0 / 1 (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         |
| vomiting   |                |                |               |
| alternative dictionary used: MedDRA 23.0             |                |                |               |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 25 (0.00%) | 0 / 1 (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         |
| Hepatobiliary disorders                              |                |                |               |
| cholestasis  |                |                |               |
| alternative dictionary used: MedDRA 23.0             |                |                |               |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 4 (0.00%) | 1 / 25 (4.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 1 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Respiratory, thoracic and mediastinal disorders |               |                |               |
| chronic obstructive pulmonary disease           |               |                |               |
| alternative dictionary used: MedDRA 23.0        |               |                |               |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 1 / 25 (4.00%) | 0 / 1 (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         |
| cough   |               |                |               |
| alternative dictionary used: MedDRA 23.0        |               |                |               |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 25 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| dyspnoea  |               |                |               |
| alternative dictionary used: MedDRA 23.0        |               |                |               |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 2 / 25 (8.00%) | 0 / 1 (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         |
| respiratory failure                             |               |                |               |
| alternative dictionary used: MedDRA 23.0        |               |                |               |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 1 / 25 (4.00%) | 0 / 1 (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         |
| Renal and urinary disorders                     |               |                |               |
| hydronephrosis                                  |               |                |               |
| alternative dictionary used: MedDRA 23.0        |               |                |               |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 25 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Musculoskeletal and connective tissue disorders |               |                |               |
| arthralgia                                      |               |                |               |
| alternative dictionary used:                    |               |                |               |

|   |               |                 |               |
|---|---------------|-----------------|---------------|
| MedDRA 23.0                                     |               |                 |               |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 25 (0.00%)  | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0         |
| pain in extremity                               |               |                 |               |
| alternative dictionary used: MedDRA 23.0        |               |                 |               |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 25 (0.00%)  | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0         |
| Infections and infestations                     |               |                 |               |
| bronchitis                                      |               |                 |               |
| alternative dictionary used: MedDRA 23.0        |               |                 |               |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 1 / 25 (4.00%)  | 0 / 1 (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         |
| lower respiratory tract infection               |               |                 |               |
| alternative dictionary used: MedDRA 23.0        |               |                 |               |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 1 / 25 (4.00%)  | 0 / 1 (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         |
| pneumonia                                       |               |                 |               |
| alternative dictionary used: MedDRA 23.0        |               |                 |               |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 3 / 25 (12.00%) | 0 / 1 (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         |
| pyelonephritis                                  |               |                 |               |
| alternative dictionary used: MedDRA 23.0        |               |                 |               |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 25 (0.00%)  | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0         |
| respiratory tract infection                     |               |                 |               |
| alternative dictionary used: MedDRA 23.0        |               |                 |               |

|   |                |                 |               |
|---|----------------|-----------------|---------------|
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 3 / 25 (12.00%) | 0 / 1 (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         |
| septic shock                                    |                |                 |               |
| alternative dictionary used: MedDRA 23.0        |                |                 |               |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (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         |
| urinary tract infection                         |                |                 |               |
| alternative dictionary used: MedDRA 23.0        |                |                 |               |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (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         |
| Metabolism and nutrition disorders              |                |                 |               |
| dehydration                                     |                |                 |               |
| alternative dictionary used: MedDRA 23.0        |                |                 |               |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 25 (0.00%)  | 0 / 1 (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 23.0        |                |                 |               |
| subjects affected / exposed                     | 1 / 4 (25.00%) | 0 / 25 (0.00%)  | 0 / 1 (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         |

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

| <b>Non-serious adverse events</b>                                   | Galunisertib +<br>Nivolumab (Cohort<br>1) Phase 1b | Galunisertib +<br>Nivolumab (Cohort<br>2) Phase 1b | Galunisertib +<br>Nivolumab (Cohort<br>3) Phase 1b |
|---|--|--|--|
| Total subjects affected by non-serious adverse events               |  |  |  |
| subjects affected / exposed   | 3 / 3 (100.00%)                                    | 4 / 5 (80.00%)                                     | 3 / 3 (100.00%)                                    |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |  |  |

|  |                    |                     |                    |
|--|--------------------|---------------------|--------------------|
| tumour pain<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)             | 0 / 3 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 |
| Vascular disorders   |                    |                     |                    |
| hot flush<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)               | 0 / 3 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 |
| hypertension<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)            | 0 / 3 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 |
| hypotension<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)             | 0 / 3 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 |
| jugular vein thrombosis<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 |
| phlebitis<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)               | 0 / 3 (0.00%)<br>0 | 1 / 5 (20.00%)<br>1 | 0 / 3 (0.00%)<br>0 |
| General disorders and administration<br>site conditions  |                    |                     |                    |
| asthenia<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)                | 0 / 3 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 |
| chest pain<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)              | 0 / 3 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 |
| chills   |                    |                     |                    |

|   |                |               |               |
|---|----------------|---------------|---------------|
| alternative dictionary used:<br>MedDRA 23.0     |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0              | 0             | 0             |
| fatigue   |                |               |               |
| alternative dictionary used:<br>MedDRA 23.0     |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0              | 0             | 0             |
| influenza like illness                          |                |               |               |
| alternative dictionary used:<br>MedDRA 23.0     |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0              | 0             | 0             |
| malaise   |                |               |               |
| alternative dictionary used:<br>MedDRA 23.0     |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0              | 0             | 0             |
| multiple organ dysfunction syndrome             |                |               |               |
| alternative dictionary used:<br>MedDRA 23.0     |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0              | 0             | 0             |
| non-cardiac chest pain                          |                |               |               |
| alternative dictionary used:<br>MedDRA 23.0     |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0              | 0             | 0             |
| oedema peripheral                               |                |               |               |
| alternative dictionary used:<br>MedDRA 23.0     |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0              | 0             | 0             |
| pyrexia   |                |               |               |
| alternative dictionary used:<br>MedDRA 23.0     |                |               |               |
| subjects affected / exposed                     | 1 / 3 (33.33%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 1              | 0             | 0             |
| Respiratory, thoracic and mediastinal disorders |                |               |               |
| aphonia   |                |               |               |
| alternative dictionary used:<br>MedDRA 23.0     |                |               |               |



|   |                |               |                |
|---|----------------|---------------|----------------|
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0              | 0             | 0              |
| bronchial fistula                           |                |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0              | 0             | 0              |
| bronchospasm                                |                |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0              | 0             | 0              |
| chronic obstructive pulmonary<br>disease    |                |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0              | 0             | 0              |
| cough                                       |                |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0              | 0             | 0              |
| dysphonia                                   |                |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0              | 0             | 0              |
| dyspnoea                                    |                |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all)                           | 0              | 0             | 1              |
| haemoptysis                                 |                |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |               |                |
| subjects affected / exposed                 | 1 / 3 (33.33%) | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 1              | 0             | 0              |
| oropharyngeal pain                          |                |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0              | 0             | 0              |

|  |                     |                     |                    |
|--|---------------------|---------------------|--------------------|
| pleural effusion<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 |
| pneumonitis<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 |
| productive cough<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 |
| pulmonary embolism<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 3 (0.00%)<br>0  | 2 / 5 (40.00%)<br>2 | 0 / 3 (0.00%)<br>0 |
| respiratory acidosis<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)                | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 |
| rhinitis allergic<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 |
| rhinorrhoea<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 |
| Psychiatric disorders<br>depression<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all) | 1 / 3 (33.33%)<br>1 | 0 / 5 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 |
| disorientation<br>alternative dictionary used:<br>MedDRA 23.0  |                     |                     |                    |

|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all)                           | 0              | 1              | 0             |
| insomnia                                    |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 1 / 3 (33.33%) | 0 / 5 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                           | 1              | 0              | 0             |
| Investigations                              |                |                |               |
| alanine aminotransferase increased          |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0             |
| amylase increased                           |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0             |
| aspartate aminotransferase increased        |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0             |
| blood alkaline phosphatase increased        |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0             |
| blood creatinine increased                  |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0             |
| cd4 lymphocytes decreased                   |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0             |
| cystatin c increased                        |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |

|  |               |               |               |
|--|---------------|---------------|---------------|
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                        | 0             | 0             | 0             |
| gamma-glutamyltransferase increased      |               |               |               |
| alternative dictionary used: MedDRA 23.0 |               |               |               |
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                        | 0             | 0             | 0             |
| lipase increased                         |               |               |               |
| alternative dictionary used: MedDRA 23.0 |               |               |               |
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                        | 0             | 0             | 0             |
| lymphocyte count decreased               |               |               |               |
| alternative dictionary used: MedDRA 23.0 |               |               |               |
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                        | 0             | 0             | 0             |
| neutrophil count decreased               |               |               |               |
| alternative dictionary used: MedDRA 23.0 |               |               |               |
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                        | 0             | 0             | 0             |
| platelet count decreased                 |               |               |               |
| alternative dictionary used: MedDRA 23.0 |               |               |               |
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                        | 0             | 0             | 0             |
| transaminases increased                  |               |               |               |
| alternative dictionary used: MedDRA 23.0 |               |               |               |
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                        | 0             | 0             | 0             |
| troponin t increased                     |               |               |               |
| alternative dictionary used: MedDRA 23.0 |               |               |               |
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                        | 0             | 0             | 0             |
| weight decreased                         |               |               |               |
| alternative dictionary used: MedDRA 23.0 |               |               |               |
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                        | 0             | 0             | 0             |

|  |  |  |  |
|--|--|--|--|
| white blood cell count decreased<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0   | 0 / 5 (0.00%)<br>0   | 0 / 3 (0.00%)<br>0   |
| Injury, poisoning and procedural complications<br>infusion related reaction<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0   | 0 / 5 (0.00%)<br>0   | 0 / 3 (0.00%)<br>0   |
| Cardiac disorders<br>cardiac failure<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)<br><br>mitral valve incompetence<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)<br><br>pericarditis<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)<br><br>sinus tachycardia<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0<br><br><br>0 / 3 (0.00%)<br>0<br><br><br>0 / 3 (0.00%)<br>0<br><br><br>0 / 3 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0<br><br><br>0 / 5 (0.00%)<br>0<br><br><br>0 / 5 (0.00%)<br>0<br><br><br>0 / 5 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0<br><br><br>0 / 3 (0.00%)<br>0<br><br><br>0 / 3 (0.00%)<br>0<br><br><br>0 / 3 (0.00%)<br>0 |
| Nervous system disorders<br>aura<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)<br><br>dizziness<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0<br><br><br>0 / 3 (0.00%)<br>0   | 1 / 5 (20.00%)<br>1<br><br><br>0 / 5 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0<br><br><br>0 / 3 (0.00%)<br>0   |

|   |               |                |                |
|---|---------------|----------------|----------------|
| epilepsy                                    |               |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0             | 1              | 0              |
| headache                                    |               |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 1 / 5 (20.00%) | 1 / 3 (33.33%) |
| occurrences (all)                           | 0             | 1              | 1              |
| hypersomnia                                 |               |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0             | 0              | 0              |
| neurological decompensation                 |               |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0             | 0              | 0              |
| neurological symptom                        |               |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0             | 0              | 0              |
| neuropathy peripheral                       |               |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0             | 0              | 0              |
| paraesthesia                                |               |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0             | 0              | 0              |
| peripheral motor neuropathy                 |               |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0             | 0              | 0              |
| somnolence                                  |               |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |                |                |

|   |                    |                     |                     |
|---|--------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  | 1 / 3 (33.33%)<br>1 |
| Blood and lymphatic system disorders<br>anaemia<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)    | 0 / 3 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| disseminated intravascular<br>coagulation<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)          | 0 / 3 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| eosinophilia<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 3 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Ear and labyrinth disorders<br>tinnitus<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)            | 0 / 3 (0.00%)<br>0 | 1 / 5 (20.00%)<br>1 | 0 / 3 (0.00%)<br>0  |
| Eye disorders<br>cataract<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 3 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| dry eye<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Gastrointestinal disorders<br>abdominal distension<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| abdominal pain  |                    |                     |                     |

|   |                |                |               |
|---|----------------|----------------|---------------|
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all)                           | 0              | 1              | 0             |
| cheilitis                                   |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0             |
| constipation                                |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0             |
| diarrhoea                                   |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 1 / 3 (33.33%) | 2 / 5 (40.00%) | 0 / 3 (0.00%) |
| occurrences (all)                           | 1              | 5              | 0             |
| dry mouth                                   |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0             |
| dyspepsia                                   |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0             |
| dysphagia                                   |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0             |
| flatulence                                  |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0             |
| gastrooesophageal reflux disease            |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |



|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| haematemesis                                |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |                |
| subjects affected / exposed                 | 1 / 3 (33.33%) | 0 / 5 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 1              | 0              | 0              |
| lower gastrointestinal haemorrhage          |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| nausea                                      |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |                |
| subjects affected / exposed                 | 1 / 3 (33.33%) | 1 / 5 (20.00%) | 1 / 3 (33.33%) |
| occurrences (all)                           | 1              | 1              | 1              |
| oesophageal spasm                           |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| oral pain                                   |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| rectal haemorrhage                          |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| stomatitis                                  |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| vomiting                                    |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |                |
| subjects affected / exposed                 | 2 / 3 (66.67%) | 0 / 5 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                           | 2              | 0              | 2              |

|   |                     |                    |                     |
|---|---------------------|--------------------|---------------------|
| Hepatobiliary disorders<br>cholestasis<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  |
| Skin and subcutaneous tissue disorders<br>dermatitis acneiform<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all) | 1 / 3 (33.33%)<br>1 | 0 / 5 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  |
| dry skin<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  |
| hyperhidrosis<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  |
| livedo reticularis<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  |
| pruritus<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)   | 1 / 3 (33.33%)<br>1 | 0 / 5 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  |
| rash<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 1 / 3 (33.33%)<br>1 |
| rash maculo-papular<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  |
| skin lesion   |                     |                    |                     |

|   |   |   |   |
|---|---|---|---|
| alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1   | 0 / 3 (0.00%)<br>0  |
| Renal and urinary disorders<br>acute kidney injury<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)<br><br>dysuria<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0<br><br><br>0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0<br><br><br>0 / 5 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0<br><br><br>0 / 3 (0.00%)<br>0  |
| Endocrine disorders<br>hyperthyroidism<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)<br><br>hypothyroidism<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0<br><br><br>0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0<br><br><br>1 / 5 (20.00%)<br>1   | 0 / 3 (0.00%)<br>0<br><br><br>0 / 3 (0.00%)<br>0  |
| Musculoskeletal and connective tissue disorders<br>arthralgia<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)<br><br>arthritis<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)<br><br>back pain<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)<br><br>bone pain | 0 / 3 (0.00%)<br>0<br><br><br>0 / 3 (0.00%)<br>0<br><br><br>0 / 3 (0.00%)<br>0<br><br><br>0 | 0 / 5 (0.00%)<br>0<br><br><br>0 / 5 (0.00%)<br>0<br><br><br>0 / 5 (0.00%)<br>0<br><br><br>0 | 0 / 3 (0.00%)<br>0<br><br><br>0 / 3 (0.00%)<br>0<br><br><br>0 / 3 (0.00%)<br>0<br><br><br>0 |

|   |               |               |                |
|---|---------------|---------------|----------------|
| alternative dictionary used:<br>MedDRA 23.0 |               |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0             | 0             | 0              |
| flank pain                                  |               |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0             | 0             | 0              |
| gouty arthritis                             |               |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0             | 0             | 0              |
| muscular weakness                           |               |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0             | 0             | 0              |
| musculoskeletal chest pain                  |               |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0             | 0             | 0              |
| musculoskeletal pain                        |               |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0             | 0             | 0              |
| myalgia                                     |               |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0             | 0             | 0              |
| neck pain                                   |               |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all)                           | 0             | 0             | 1              |
| pain in extremity                           |               |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |               |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| Infections and infestations                 |                |                |                |
| cellulitis                                  |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 1 / 5 (20.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0              | 1              | 0              |
| escherichia infection                       |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| gingivitis                                  |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| influenza                                   |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| otitis externa                              |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| otitis media                                |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| pneumonia                                   |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |                |
| subjects affected / exposed                 | 1 / 3 (33.33%) | 0 / 5 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                           | 1              | 0              | 1              |
| respiratory tract infection                 |                |                |                |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |                |

|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0             |
| rhinitis                                    |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0             |
| skin infection                              |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0             |
| upper respiratory tract infection           |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0             |
| urinary tract infection                     |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0             |
| Metabolism and nutrition disorders          |                |                |               |
| cachexia                                    |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0             |
| decreased appetite                          |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all)                           | 0              | 1              | 0             |
| dehydration                                 |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 1 / 3 (33.33%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all)                           | 1              | 1              | 0             |
| hypercalcaemia                              |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |

|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0             | 0             | 0              |
| hyperglycaemia                              |               |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all)                           | 0             | 0             | 1              |
| hyperkalaemia                               |               |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0             | 0             | 0              |
| hypertriglyceridaemia                       |               |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all)                           | 0             | 0             | 1              |
| hypoalbuminaemia                            |               |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0             | 0             | 0              |
| hypocalcaemia                               |               |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0             | 0             | 0              |
| hypokalaemia                                |               |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0             | 0             | 0              |
| hypomagnesaemia                             |               |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0             | 0             | 0              |
| hypophosphataemia                           |               |               |                |
| alternative dictionary used:<br>MedDRA 23.0 |               |               |                |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0             | 0             | 0              |

| <b>Non-serious adverse events</b>                                   | <b>Galunisertib +<br/>Nivolumab (Cohort<br/>4) Phase 1b</b> | <b>Galunisertib +<br/>Nivolumab (NSCLC)<br/>Phase 2</b> | <b>Galunisertib +<br/>Nivolumab (HCC)<br/>Phase 2</b> |
|---|---|---|---|
| Total subjects affected by non-serious adverse events               |   |   |   |
| subjects affected / exposed   | 4 / 4 (100.00%)   | 23 / 25 (92.00%)  | 1 / 1 (100.00%)                                       |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |   |   |
| tumour pain   |   |   |   |
| alternative dictionary used:<br>MedDRA 23.0                         |   |   |   |
| subjects affected / exposed   | 0 / 4 (0.00%)   | 1 / 25 (4.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)   | 0   | 1   | 0   |
| Vascular disorders  |   |   |   |
| hot flush   |   |   |   |
| alternative dictionary used:<br>MedDRA 23.0                         |   |   |   |
| subjects affected / exposed   | 0 / 4 (0.00%)   | 2 / 25 (8.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)   | 0   | 5   | 0   |
| hypertension  |   |   |   |
| alternative dictionary used:<br>MedDRA 23.0                         |   |   |   |
| subjects affected / exposed   | 1 / 4 (25.00%)  | 0 / 25 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)   | 1   | 0   | 0   |
| hypotension   |   |   |   |
| alternative dictionary used:<br>MedDRA 23.0                         |   |   |   |
| subjects affected / exposed   | 0 / 4 (0.00%)   | 3 / 25 (12.00%)   | 0 / 1 (0.00%)   |
| occurrences (all)   | 0   | 4   | 0   |
| jugular vein thrombosis   |   |   |   |
| alternative dictionary used:<br>MedDRA 23.0                         |   |   |   |
| subjects affected / exposed   | 0 / 4 (0.00%)   | 1 / 25 (4.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)   | 0   | 1   | 0   |
| phlebitis   |   |   |   |
| alternative dictionary used:<br>MedDRA 23.0                         |   |   |   |
| subjects affected / exposed   | 0 / 4 (0.00%)   | 0 / 25 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)   | 0   | 0   | 0   |
| General disorders and administration site conditions                |   |   |   |
| asthenia  |   |   |   |
| alternative dictionary used:<br>MedDRA 23.0                         |   |   |   |



|   |                |                 |               |
|---|----------------|-----------------|---------------|
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 4 / 25 (16.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 5               | 0             |
| chest pain                                  |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 1               | 0             |
| chills                                      |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 1               | 0             |
| fatigue                                     |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 1 / 4 (25.00%) | 6 / 25 (24.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 2              | 10              | 0             |
| influenza like illness                      |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 2               | 0             |
| malaise                                     |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 1               | 0             |
| multiple organ dysfunction syndrome         |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 1               | 0             |
| non-cardiac chest pain                      |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 2 / 4 (50.00%) | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 2              | 1               | 0             |
| oedema peripheral                           |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 1               | 0             |

|  |                     |                      |                    |
|--|---------------------|----------------------|--------------------|
| pyrexia<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 4 (0.00%)<br>0  | 5 / 25 (20.00%)<br>8 | 0 / 1 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal disorders  |                     |                      |                    |
| aphonia<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 4 (0.00%)<br>0  | 1 / 25 (4.00%)<br>1  | 0 / 1 (0.00%)<br>0 |
| bronchial fistula<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 4 (0.00%)<br>0  | 1 / 25 (4.00%)<br>1  | 0 / 1 (0.00%)<br>0 |
| bronchospasm<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 4 (0.00%)<br>0  | 1 / 25 (4.00%)<br>1  | 0 / 1 (0.00%)<br>0 |
| chronic obstructive pulmonary disease<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0  | 1 / 25 (4.00%)<br>1  | 0 / 1 (0.00%)<br>0 |
| cough<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)                                 | 1 / 4 (25.00%)<br>1 | 3 / 25 (12.00%)<br>4 | 0 / 1 (0.00%)<br>0 |
| dysphonia<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 4 (0.00%)<br>0  | 1 / 25 (4.00%)<br>1  | 0 / 1 (0.00%)<br>0 |
| dyspnoea<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 4 (0.00%)<br>0  | 2 / 25 (8.00%)<br>2  | 0 / 1 (0.00%)<br>0 |
| haemoptysis  |                     |                      |                    |

|   |               |                |               |
|---|---------------|----------------|---------------|
| alternative dictionary used:<br>MedDRA 23.0 |               |                |               |
| subjects affected / exposed                 | 0 / 4 (0.00%) | 1 / 25 (4.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 0             | 1              | 0             |
| oropharyngeal pain                          |               |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |               |                |               |
| subjects affected / exposed                 | 0 / 4 (0.00%) | 1 / 25 (4.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 0             | 1              | 0             |
| pleural effusion                            |               |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |               |                |               |
| subjects affected / exposed                 | 0 / 4 (0.00%) | 1 / 25 (4.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 0             | 1              | 0             |
| pneumonitis                                 |               |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |               |                |               |
| subjects affected / exposed                 | 0 / 4 (0.00%) | 2 / 25 (8.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 0             | 2              | 0             |
| productive cough                            |               |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |               |                |               |
| subjects affected / exposed                 | 0 / 4 (0.00%) | 1 / 25 (4.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 0             | 1              | 0             |
| pulmonary embolism                          |               |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |               |                |               |
| subjects affected / exposed                 | 0 / 4 (0.00%) | 0 / 25 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 0             | 0              | 0             |
| respiratory acidosis                        |               |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |               |                |               |
| subjects affected / exposed                 | 0 / 4 (0.00%) | 1 / 25 (4.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 0             | 1              | 0             |
| rhinitis allergic                           |               |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |               |                |               |
| subjects affected / exposed                 | 0 / 4 (0.00%) | 1 / 25 (4.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 0             | 1              | 0             |
| rhinorrhoea                                 |               |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |               |                |               |

|  |                     |                     |                      |
|--|---------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0  | 0 / 25 (0.00%)<br>0 | 1 / 1 (100.00%)<br>1 |
| Psychiatric disorders                            |                     |                     |                      |
| depression                                       |                     |                     |                      |
| alternative dictionary used:<br>MedDRA 23.0      |                     |                     |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0  | 0 / 25 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0   |
| disorientation                                   |                     |                     |                      |
| alternative dictionary used:<br>MedDRA 23.0      |                     |                     |                      |
| subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0  | 0 / 25 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0   |
| insomnia   |                     |                     |                      |
| alternative dictionary used:<br>MedDRA 23.0      |                     |                     |                      |
| subjects affected / exposed<br>occurrences (all) | 1 / 4 (25.00%)<br>1 | 1 / 25 (4.00%)<br>1 | 0 / 1 (0.00%)<br>0   |
| Investigations                                   |                     |                     |                      |
| alanine aminotransferase increased               |                     |                     |                      |
| alternative dictionary used:<br>MedDRA 23.0      |                     |                     |                      |
| subjects affected / exposed<br>occurrences (all) | 1 / 4 (25.00%)<br>3 | 2 / 25 (8.00%)<br>4 | 0 / 1 (0.00%)<br>0   |
| amylase increased                                |                     |                     |                      |
| alternative dictionary used:<br>MedDRA 23.0      |                     |                     |                      |
| subjects affected / exposed<br>occurrences (all) | 3 / 4 (75.00%)<br>6 | 2 / 25 (8.00%)<br>2 | 0 / 1 (0.00%)<br>0   |
| aspartate aminotransferase increased             |                     |                     |                      |
| alternative dictionary used:<br>MedDRA 23.0      |                     |                     |                      |
| subjects affected / exposed<br>occurrences (all) | 2 / 4 (50.00%)<br>4 | 2 / 25 (8.00%)<br>4 | 0 / 1 (0.00%)<br>0   |
| blood alkaline phosphatase increased             |                     |                     |                      |
| alternative dictionary used:<br>MedDRA 23.0      |                     |                     |                      |
| subjects affected / exposed<br>occurrences (all) | 2 / 4 (50.00%)<br>4 | 1 / 25 (4.00%)<br>1 | 0 / 1 (0.00%)<br>0   |
| blood creatinine increased                       |                     |                     |                      |
| alternative dictionary used:<br>MedDRA 23.0      |                     |                     |                      |

|   |                |                 |               |
|---|----------------|-----------------|---------------|
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 1               | 0             |
| cd4 lymphocytes decreased                   |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 1               | 0             |
| cystatin c increased                        |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 1               | 0             |
| gamma-glutamyltransferase increased         |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 2 / 4 (50.00%) | 2 / 25 (8.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 4              | 2               | 0             |
| lipase increased                            |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 2 / 4 (50.00%) | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 7              | 1               | 0             |
| lymphocyte count decreased                  |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 2 / 4 (50.00%) | 0 / 25 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 3              | 0               | 0             |
| neutrophil count decreased                  |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 1 / 4 (25.00%) | 0 / 25 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 2              | 0               | 0             |
| platelet count decreased                    |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 2 / 4 (50.00%) | 3 / 25 (12.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 2              | 3               | 0             |
| transaminases increased                     |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 2 / 25 (8.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 2               | 0             |

|  |                     |                     |                    |
|--|---------------------|---------------------|--------------------|
| troponin t increased<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0  | 1 / 25 (4.00%)<br>1 | 0 / 1 (0.00%)<br>0 |
| weight decreased<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0  | 1 / 25 (4.00%)<br>2 | 0 / 1 (0.00%)<br>0 |
| white blood cell count decreased<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)  | 1 / 4 (25.00%)<br>3 | 0 / 25 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Injury, poisoning and procedural complications<br>infusion related reaction<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0  | 1 / 25 (4.00%)<br>1 | 0 / 1 (0.00%)<br>0 |
| Cardiac disorders<br>cardiac failure<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0  | 1 / 25 (4.00%)<br>1 | 0 / 1 (0.00%)<br>0 |
| mitral valve incompetence<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)   | 0 / 4 (0.00%)<br>0  | 1 / 25 (4.00%)<br>1 | 0 / 1 (0.00%)<br>0 |
| pericarditis<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0  | 1 / 25 (4.00%)<br>1 | 0 / 1 (0.00%)<br>0 |
| sinus tachycardia<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)   | 1 / 4 (25.00%)<br>2 | 0 / 25 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Nervous system disorders   |                     |                     |                    |

|   |                |                 |               |
|---|----------------|-----------------|---------------|
| aura  |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 0 / 25 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 0               | 0             |
| dizziness                                   |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 3 / 25 (12.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 4               | 0             |
| epilepsy                                    |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 0 / 25 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 0               | 0             |
| headache                                    |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 1 / 4 (25.00%) | 5 / 25 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 1              | 6               | 0             |
| hypersomnia                                 |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 1 / 4 (25.00%) | 0 / 25 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 1              | 0               | 0             |
| neurological decompensation                 |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 2               | 0             |
| neurological symptom                        |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 1               | 0             |
| neuropathy peripheral                       |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 1               | 0             |
| paraesthesia                                |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |

|  |  |   |   |
|--|--|---|---|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>peripheral motor neuropathy</p> <p>alternative dictionary used:<br/>MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>somnolence</p> <p>alternative dictionary used:<br/>MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>0 / 4 (0.00%)</p> <p>0</p> <p>0 / 4 (0.00%)</p> <p>0</p> <p>0 / 4 (0.00%)</p> <p>0</p>  | <p>1 / 25 (4.00%)</p> <p>1</p> <p>2 / 25 (8.00%)</p> <p>2</p> <p>0 / 25 (0.00%)</p> <p>0</p>  | <p>0 / 1 (0.00%)</p> <p>0</p> <p>0 / 1 (0.00%)</p> <p>0</p> <p>0 / 1 (0.00%)</p> <p>0</p> |
| <p>Blood and lymphatic system disorders</p> <p>anaemia</p> <p>alternative dictionary used:<br/>MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>disseminated intravascular<br/>coagulation</p> <p>alternative dictionary used:<br/>MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>eosinophilia</p> <p>alternative dictionary used:<br/>MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 4 (25.00%)</p> <p>3</p> <p>0 / 4 (0.00%)</p> <p>0</p> <p>0 / 4 (0.00%)</p> <p>0</p> | <p>3 / 25 (12.00%)</p> <p>3</p> <p>1 / 25 (4.00%)</p> <p>1</p> <p>1 / 25 (4.00%)</p> <p>2</p> | <p>0 / 1 (0.00%)</p> <p>0</p> <p>0 / 1 (0.00%)</p> <p>0</p> <p>0 / 1 (0.00%)</p> <p>0</p> |
| <p>Ear and labyrinth disorders</p> <p>tinnitus</p> <p>alternative dictionary used:<br/>MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>0 / 4 (0.00%)</p> <p>0</p>  | <p>0 / 25 (0.00%)</p> <p>0</p>  | <p>0 / 1 (0.00%)</p> <p>0</p>   |
| <p>Eye disorders</p> <p>cataract</p> <p>alternative dictionary used:<br/>MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>dry eye</p> <p>alternative dictionary used:<br/>MedDRA 23.0</p>  | <p>0 / 4 (0.00%)</p> <p>0</p>  | <p>1 / 25 (4.00%)</p> <p>1</p>  | <p>0 / 1 (0.00%)</p> <p>0</p>   |



|   |                |                 |               |
|---|----------------|-----------------|---------------|
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 2 / 25 (8.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 2               | 0             |
| Gastrointestinal disorders                  |                |                 |               |
| abdominal distension                        |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 3 / 25 (12.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 6               | 0             |
| abdominal pain                              |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 1               | 0             |
| cheilitis                                   |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 1               | 0             |
| constipation                                |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 1 / 4 (25.00%) | 4 / 25 (16.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 1              | 5               | 0             |
| diarrhoea                                   |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 1 / 4 (25.00%) | 7 / 25 (28.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 1              | 10              | 0             |
| dry mouth                                   |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 4 / 25 (16.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 5               | 0             |
| dyspepsia                                   |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 1               | 0             |
| dysphagia                                   |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |

|   |                |                 |               |
|---|----------------|-----------------|---------------|
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 1               | 0             |
| flatulence                                  |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 2 / 25 (8.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 3               | 0             |
| gastrooesophageal reflux disease            |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 1 / 4 (25.00%) | 0 / 25 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 1              | 0               | 0             |
| haematemesis                                |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 0 / 25 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 0               | 0             |
| lower gastrointestinal haemorrhage          |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 1 / 4 (25.00%) | 0 / 25 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 1              | 0               | 0             |
| nausea                                      |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 2 / 4 (50.00%) | 6 / 25 (24.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 2              | 6               | 0             |
| oesophageal spasm                           |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 1               | 0             |
| oral pain                                   |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 2               | 0             |
| rectal haemorrhage                          |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 1 / 4 (25.00%) | 0 / 25 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 1              | 0               | 0             |

|   |                     |                       |                    |
|---|---------------------|-----------------------|--------------------|
| stomatitis<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)   | 0 / 4 (0.00%)<br>0  | 3 / 25 (12.00%)<br>4  | 0 / 1 (0.00%)<br>0 |
| vomiting<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)   | 0 / 4 (0.00%)<br>0  | 3 / 25 (12.00%)<br>3  | 0 / 1 (0.00%)<br>0 |
| Hepatobiliary disorders<br>cholestasis<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 4 (0.00%)<br>0  | 2 / 25 (8.00%)<br>2   | 0 / 1 (0.00%)<br>0 |
| Skin and subcutaneous tissue disorders<br>dermatitis acneiform<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0  | 1 / 25 (4.00%)<br>3   | 0 / 1 (0.00%)<br>0 |
| dry skin<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)   | 0 / 4 (0.00%)<br>0  | 3 / 25 (12.00%)<br>3  | 0 / 1 (0.00%)<br>0 |
| hyperhidrosis<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0  | 1 / 25 (4.00%)<br>1   | 0 / 1 (0.00%)<br>0 |
| livedo reticularis<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)   | 0 / 4 (0.00%)<br>0  | 1 / 25 (4.00%)<br>1   | 0 / 1 (0.00%)<br>0 |
| pruritus<br>alternative dictionary used:<br>MedDRA 23.0<br>subjects affected / exposed<br>occurrences (all)   | 1 / 4 (25.00%)<br>2 | 9 / 25 (36.00%)<br>14 | 0 / 1 (0.00%)<br>0 |
| rash  |                     |                       |                    |

|  |   |  |   |
|--|---|--|---|
| <p>alternative dictionary used:<br/>MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>1 / 4 (25.00%)</p> <p>1</p>                              | <p>2 / 25 (8.00%)</p> <p>4</p>                                 | <p>0 / 1 (0.00%)</p> <p>0</p>                               |
| <p>rash maculo-papular</p> <p>alternative dictionary used:<br/>MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>2 / 4 (50.00%)</p> <p>2</p>                              | <p>5 / 25 (20.00%)</p> <p>10</p>                               | <p>0 / 1 (0.00%)</p> <p>0</p>                               |
| <p>skin lesion</p> <p>alternative dictionary used:<br/>MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>0 / 4 (0.00%)</p> <p>0</p>                               | <p>0 / 25 (0.00%)</p> <p>0</p>                                 | <p>0 / 1 (0.00%)</p> <p>0</p>                               |
| <p>Renal and urinary disorders</p> <p>acute kidney injury</p> <p>alternative dictionary used:<br/>MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>dysuria</p> <p>alternative dictionary used:<br/>MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 4 (0.00%)</p> <p>0</p> <p>0 / 4 (0.00%)</p> <p>0</p> | <p>1 / 25 (4.00%)</p> <p>1</p> <p>1 / 25 (4.00%)</p> <p>1</p>  | <p>0 / 1 (0.00%)</p> <p>0</p> <p>0 / 1 (0.00%)</p> <p>0</p> |
| <p>Endocrine disorders</p> <p>hyperthyroidism</p> <p>alternative dictionary used:<br/>MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>hypothyroidism</p> <p>alternative dictionary used:<br/>MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>      | <p>0 / 4 (0.00%)</p> <p>0</p> <p>0 / 4 (0.00%)</p> <p>0</p> | <p>1 / 25 (4.00%)</p> <p>1</p> <p>4 / 25 (16.00%)</p> <p>4</p> | <p>0 / 1 (0.00%)</p> <p>0</p> <p>0 / 1 (0.00%)</p> <p>0</p> |
| <p>Musculoskeletal and connective tissue disorders</p> <p>arthralgia</p> <p>alternative dictionary used:<br/>MedDRA 23.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>arthritis</p>  | <p>0 / 4 (0.00%)</p> <p>0</p>                               | <p>2 / 25 (8.00%)</p> <p>3</p>                                 | <p>0 / 1 (0.00%)</p> <p>0</p>                               |

|   |                |                 |               |
|---|----------------|-----------------|---------------|
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 8               | 0             |
| back pain                                   |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 6 / 25 (24.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 6               | 0             |
| bone pain                                   |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 2 / 25 (8.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 2               | 0             |
| flank pain                                  |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 1               | 0             |
| gouty arthritis                             |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 1               | 0             |
| muscular weakness                           |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 1               | 0             |
| musculoskeletal chest pain                  |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 1               | 0             |
| musculoskeletal pain                        |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 1 / 4 (25.00%) | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 1              | 1               | 0             |
| myalgia                                     |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed                 | 1 / 4 (25.00%) | 0 / 25 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                           | 1              | 0               | 0               |
| neck pain                                   |                |                 |                 |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |                 |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                           | 0              | 2               | 0               |
| pain in extremity                           |                |                 |                 |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |                 |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 4 / 25 (16.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                           | 0              | 4               | 0               |
| Infections and infestations                 |                |                 |                 |
| cellulitis                                  |                |                 |                 |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |                 |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 0 / 25 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                           | 0              | 0               | 0               |
| escherichia infection                       |                |                 |                 |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |                 |
| subjects affected / exposed                 | 1 / 4 (25.00%) | 0 / 25 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                           | 1              | 0               | 0               |
| gingivitis                                  |                |                 |                 |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |                 |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 0 / 25 (0.00%)  | 1 / 1 (100.00%) |
| occurrences (all)                           | 0              | 0               | 1               |
| influenza                                   |                |                 |                 |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |                 |
| subjects affected / exposed                 | 1 / 4 (25.00%) | 0 / 25 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                           | 1              | 0               | 0               |
| otitis externa                              |                |                 |                 |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |                 |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                           | 0              | 1               | 0               |
| otitis media                                |                |                 |                 |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |                 |

|   |                |                 |               |
|---|----------------|-----------------|---------------|
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 1               | 0             |
| pneumonia                                   |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 0 / 25 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 0               | 0             |
| respiratory tract infection                 |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 4 / 25 (16.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 4               | 0             |
| rhinitis                                    |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 1               | 0             |
| skin infection                              |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 2 / 25 (8.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 2               | 0             |
| upper respiratory tract infection           |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 4 / 25 (16.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 4               | 0             |
| urinary tract infection                     |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 1 / 4 (25.00%) | 2 / 25 (8.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 1              | 4               | 0             |
| Metabolism and nutrition disorders          |                |                 |               |
| cachexia                                    |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 1               | 0             |
| decreased appetite                          |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |

|   |                |                 |               |
|---|----------------|-----------------|---------------|
| subjects affected / exposed                 | 1 / 4 (25.00%) | 7 / 25 (28.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 1              | 11              | 0             |
| dehydration                                 |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 0 / 25 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 0               | 0             |
| hypercalcaemia                              |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 1 / 25 (4.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 2               | 0             |
| hyperglycaemia                              |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 1 / 4 (25.00%) | 3 / 25 (12.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 1              | 3               | 0             |
| hyperkalaemia                               |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 1 / 4 (25.00%) | 0 / 25 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 1              | 0               | 0             |
| hypertriglyceridaemia                       |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 0 / 25 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 0              | 0               | 0             |
| hypoalbuminaemia                            |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 2 / 4 (50.00%) | 0 / 25 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 3              | 0               | 0             |
| hypocalcaemia                               |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 2 / 4 (50.00%) | 0 / 25 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 5              | 0               | 0             |
| hypokalaemia                                |                |                 |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                 |               |
| subjects affected / exposed                 | 2 / 4 (50.00%) | 2 / 25 (8.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                           | 2              | 2               | 0             |



|   |                |                |               |
|---|----------------|----------------|---------------|
| hypomagnesaemia                             |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 1 / 4 (25.00%) | 2 / 25 (8.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 2              | 2              | 0             |
| hypophosphataemia                           |                |                |               |
| alternative dictionary used:<br>MedDRA 23.0 |                |                |               |
| subjects affected / exposed                 | 1 / 4 (25.00%) | 2 / 25 (8.00%) | 0 / 1 (0.00%) |
| occurrences (all)                           | 1              | 2              | 0             |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment   |
|-----------------|---|
| 24 July 2015    | Amendment A: <ul style="list-style-type: none"><li>• Addition of 2 cohorts</li><li>• Addition of study ECG's</li><li>• Addition of <math>\geq</math> CTCAE Grade 3 thrombocytopenia</li><li>• Addition of serum pregnancy test on Day 1 of every cycle</li><li>• Added ECHO at the 30-day follow-up visit</li><li>• Additional patient enrolled predose level to allow for unforeseen discontinuation</li></ul> |
| 30 August 2016  | Amendment B: Removed high-sensitivity C-reactive protein  |
| 31 January 2017 | Amendment C:<br>Removal of glioblastoma cohort <ul style="list-style-type: none"><li>• Requirement for ECHO at the 30-day follow-up visit added back in protocol (c)</li><li>• Add hepatitis B surface antigen testing back in protocol (c)</li></ul>   |

Notes:

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### 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.

Due low enrollment, the HCC cohort was terminated early.

Notes: