



## Clinical trial results:

### A Phase 1b (Open-Label) / Phase 2 (Randomized, Double-Blinded) Study Evaluating Gemcitabine and Docetaxel With or Without Olaratumab in the Treatment of Advanced Soft Tissue Sarcoma

#### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2015-001316-34    |
| Trial protocol           | HU ES DE PL GB IT |
| Global end of trial date | 27 April 2021     |

#### Results information

|                                |                                                  |
|--------------------------------|--------------------------------------------------|
| Result version number          | v2 (current)                                     |
| This version publication date  | 01 May 2022                                      |
| First version publication date | 11 August 2021                                   |
| Version creation reason        | • New data added to full data set<br>LPV results |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | I5B-MC-JGDL |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |                     |
|------------------------------------|---------------------|
| ISRCTN number                      | -                   |
| ClinicalTrials.gov id (NCT number) | NCT02659020         |
| WHO universal trial number (UTN)   | -                   |
| Other trial identifiers            | Trial Number: 15839 |

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                       | 28 July 2020  |
| Is this the analysis of the primary completion data? | No            |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 27 April 2021 |
| 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 and efficacy of two anti-cancer drugs (gemcitabine and docetaxel) with and without the study drug known as olaratumab in participants with advanced soft tissue sarcoma (STS) or STS that has spread to another part(s) of the body.

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 March 2016 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | Yes           |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Australia: 9       |
| Country: Number of subjects enrolled | Germany: 24        |
| Country: Number of subjects enrolled | Spain: 37          |
| Country: Number of subjects enrolled | Hungary: 11        |
| Country: Number of subjects enrolled | United States: 161 |
| Country: Number of subjects enrolled | Poland: 8          |
| Country: Number of subjects enrolled | United Kingdom: 31 |
| Country: Number of subjects enrolled | Italy: 6           |
| Country: Number of subjects enrolled | Israel: 18         |
| Country: Number of subjects enrolled | France: 5          |
| Worldwide total number of subjects   | 310                |
| EEA total number of subjects         | 91                 |

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)                     | 227 |
| From 65 to 84 years                      | 83  |
| 85 years and over                        | 0   |

## Subject disposition

### Recruitment

Recruitment details:

No Text Available

### Pre-assignment

Screening details:

Completers included participants who died from any cause.

### Period 1

|                                                 |                                |
|-------------------------------------------------|--------------------------------|
| Period 1 title                                  | Overall Study (overall period) |
| Is this the baseline period?                    | Yes                            |
| Allocation method                               | Randomised - controlled        |
| Blinding used                                   | Double blind                   |
| Roles blinded                                   | Subject, Investigator          |
| Blinding implementation details:                |                                |
| Phase 1b (Open-Label), Phase 2 (Double-Blinded) |                                |

### Arms

|                              |                                                              |
|------------------------------|--------------------------------------------------------------|
| Are arms mutually exclusive? | Yes                                                          |
| <b>Arm title</b>             | Phase1b:Cohort1: 15mg/kg<br>Olaratumab+Gemcitabine+Docetaxel |

Arm description:

Participants received intravenous infusions of olaratumab 15 milligrams per kilogram (mg/kg) on days 1, 8 plus gemcitabine 900 milligrams per meter square (mg/m<sup>2</sup>) on days 1, 8 plus docetaxel 75 mg/m<sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

|                                        |                   |
|----------------------------------------|-------------------|
| Arm type                               | Experimental      |
| Investigational medicinal product name | Olaratumab        |
| Investigational medicinal product code |                   |
| Other name                             | LY3012207,IMC-3G3 |
| Pharmaceutical forms                   | Infusion          |
| Routes of administration               | Intravenous use   |

Dosage and administration details:

Intravenous infusions of olaratumab 15 mg/kg on days 1, 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

|                                        |                 |
|----------------------------------------|-----------------|
| Investigational medicinal product name | Gemcitabine     |
| Investigational medicinal product code |                 |
| Other name                             | LY188011,Gemzar |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

Dosage and administration details:

Intravenous infusions of gemcitabine 900 mg/m<sup>2</sup> on days 1, 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

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

Dosage and administration details:

Intravenous infusions of docetaxel 75 mg/m<sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

|                  |                                                              |
|------------------|--------------------------------------------------------------|
| <b>Arm title</b> | Phase1b:Cohort2: 20mg/kg<br>Olaratumab+Gemcitabine+Docetaxel |
|------------------|--------------------------------------------------------------|

**Arm description:**

Participants received intravenous infusions of olaratumab 20 mg/kg on days 1, 8 in combination with gemcitabine 900 mg/m<sup>2</sup> on days 1, 8 and docetaxel 75 mg/m<sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

|                                        |                   |
|----------------------------------------|-------------------|
| Arm type                               | Experimental      |
| Investigational medicinal product name | Olaratumab        |
| Investigational medicinal product code |                   |
| Other name                             | LY3012207,IMC-3G3 |
| Pharmaceutical forms                   | Infusion          |
| Routes of administration               | Intravenous use   |

**Dosage and administration details:**

Intravenous infusions of olaratumab 20 mg/kg on days 1, 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

|                                        |                 |
|----------------------------------------|-----------------|
| Investigational medicinal product name | Gemcitabine     |
| Investigational medicinal product code |                 |
| Other name                             | LY188011,Gemzar |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

**Dosage and administration details:**

Intravenous infusions of gemcitabine 900 mg/m<sup>2</sup> on days 1, 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

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

**Dosage and administration details:**

Intravenous infusions of docetaxel 75 mg/m<sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

|                  |                                                               |
|------------------|---------------------------------------------------------------|
| <b>Arm title</b> | Phase1b:Cohort2Expand:20mg/kgOlaratumab+Gemcitabine+Docetaxel |
|------------------|---------------------------------------------------------------|

**Arm description:**

Following a protocol amendment, additional participants were enrolled into this group to confirm the safety of the 20 mg/kg dose level prior to opening the Phase 2. Participants received intravenous infusions of olaratumab 20 milligrams per kilogram (mg/kg) on days 1, 8 plus gemcitabine 900 milligrams per meter square (mg/m<sup>2</sup>) on days 1, 8 plus docetaxel 75 mg/m<sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

|                                        |                   |
|----------------------------------------|-------------------|
| Arm type                               | Experimental      |
| Investigational medicinal product name | Olaratumab        |
| Investigational medicinal product code |                   |
| Other name                             | LY3012207,IMC-3G3 |
| Pharmaceutical forms                   | Infusion          |
| Routes of administration               | Intravenous use   |

**Dosage and administration details:**

Intravenous infusions of olaratumab 20 mg/kg on days 1, 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

|                                        |                 |
|----------------------------------------|-----------------|
| Investigational medicinal product name | Gemcitabine     |
| Investigational medicinal product code |                 |
| Other name                             | LY188011,Gemzar |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

**Dosage and administration details:**

Intravenous infusions of gemcitabine 900 mg/m<sup>2</sup> on days 1, 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------|
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Docetaxel                                                      |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                |
| Other name                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                |
| Pharmaceutical forms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Infusion                                                       |
| Routes of administration                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Intravenous use                                                |
| Dosage and administration details:                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                |
| Intravenous infusions of docetaxel 75 mg/m <sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.                                                                                                                                                                                                                                                                                                                        |                                                                |
| <b>Arm title</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive)      |
| Arm description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                |
| This cohort included participants who never received olaratumab prior to enrollment. Participants received intravenous infusions of olaratumab loading dose 20 mg/kg on days 1, 8 of cycle 1 followed by 15 mg/kg on days 1, 8 of all subsequent cycles in combination with gemcitabine 900 mg/m <sup>2</sup> on days 1, 8 and docetaxel 75 mg/m <sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.                  |                                                                |
| Arm type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Experimental                                                   |
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Olaratumab                                                     |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                |
| Other name                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | LY3012207,IMC-3G3                                              |
| Pharmaceutical forms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Infusion                                                       |
| Routes of administration                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Intravenous use                                                |
| Dosage and administration details:                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                |
| Intravenous infusions of olaratumab loading dose 20 mg/kg on days 1, 8 of cycle 1 followed by 15 mg/kg on days 1, 8 of all subsequent cycles of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.                                                                                                                                                                                                                                            |                                                                |
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Gemcitabine                                                    |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                |
| Other name                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | LY188011,Gemzar                                                |
| Pharmaceutical forms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Infusion                                                       |
| Routes of administration                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Intravenous use                                                |
| Dosage and administration details:                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                |
| Intravenous infusions of gemcitabine 900 mg/m <sup>2</sup> on days 1, 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.                                                                                                                                                                                                                                                                                                                 |                                                                |
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Docetaxel                                                      |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                |
| Other name                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                |
| Pharmaceutical forms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Infusion                                                       |
| Routes of administration                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Intravenous use                                                |
| Dosage and administration details:                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                |
| Intravenous infusions of docetaxel 75 mg/m <sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.                                                                                                                                                                                                                                                                                                                        |                                                                |
| <b>Arm title</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) |
| Arm description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                |
| This cohort included participants who received commercially available olaratumab prior to enrollment. Participants received intravenous infusions of olaratumab loading dose 20 mg/kg on days 1, 8 of cycle 1 followed by 15 mg/kg on days 1, 8 of all subsequent cycles in combination with gemcitabine 900 mg/m <sup>2</sup> on days 1, 8 and docetaxel 75 mg/m <sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met. |                                                                |
| Arm type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Experimental                                                   |
| Investigational medicinal product name                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Olaratumab                                                     |
| Investigational medicinal product code                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                |
| Other name                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | LY3012207,IMC-3G3                                              |
| Pharmaceutical forms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Infusion                                                       |
| Routes of administration                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Intravenous use                                                |

Dosage and administration details:

Intravenous infusions of olaratumab loading dose 20 mg/kg on days 1, 8 of cycle 1 followed by 15 mg/kg on days 1, 8 of all subsequent cycles of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

|                                        |                 |
|----------------------------------------|-----------------|
| Investigational medicinal product name | Gemcitabine     |
| Investigational medicinal product code |                 |
| Other name                             | LY188011,Gemzar |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

Dosage and administration details:

Intravenous infusions of gemcitabine 900 mg/m<sup>2</sup> on days 1, 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

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

Dosage and administration details:

Intravenous infusions of docetaxel 75 mg/m<sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

|                  |                                                        |
|------------------|--------------------------------------------------------|
| <b>Arm title</b> | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) |
|------------------|--------------------------------------------------------|

Arm description:

This cohort included participants who never received olaratumab prior to enrollment. Participants received intravenous infusions of placebo on days 1, 8 in combination with gemcitabine 900 mg/m<sup>2</sup> on days 1, 8 and docetaxel 75 mg/m<sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

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

Dosage and administration details:

Intravenous infusions of placebo on days 1, 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

|                                        |                 |
|----------------------------------------|-----------------|
| Investigational medicinal product name | Gemcitabine     |
| Investigational medicinal product code |                 |
| Other name                             | LY188011,Gemzar |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

Dosage and administration details:

Intravenous infusions of gemcitabine 900 mg/m<sup>2</sup> on days 1, 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

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

Dosage and administration details:

Intravenous infusions of docetaxel 75 mg/m<sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

|                  |                                                             |
|------------------|-------------------------------------------------------------|
| <b>Arm title</b> | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab pretreated) |
|------------------|-------------------------------------------------------------|

Arm description:

This cohort included participants who received commercially available olaratumab prior to enrollment.

Participants received intravenous infusions of placebo on days 1, 8 in combination with gemcitabine 900 mg/m<sup>2</sup> on days 1, 8 and docetaxel 75 mg/m<sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

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

Dosage and administration details:

Intravenous infusions of placebo on days 1, 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

|                                        |                  |
|----------------------------------------|------------------|
| Investigational medicinal product name | Gemcitabine      |
| Investigational medicinal product code |                  |
| Other name                             | LY188011, Gemzar |
| Pharmaceutical forms                   | Infusion         |
| Routes of administration               | Intravenous use  |

Dosage and administration details:

Intravenous infusions of gemcitabine 900 mg/m<sup>2</sup> on days 1, 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

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

Dosage and administration details:

Intravenous infusions of docetaxel 75 mg/m<sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

| Number of subjects in period 1       | Phase1b:Cohort1:<br>15mg/kg<br>Olaratumab+Gemcitabine+Docetaxel | Phase1b:Cohort2:<br>20mg/kg<br>Olaratumab+Gemcitabine+Docetaxel | Phase1b:Cohort2Exp<br>and:20mg/kgOlaratumab+Gemcitabine+Docetaxel |
|--------------------------------------|-----------------------------------------------------------------|-----------------------------------------------------------------|-------------------------------------------------------------------|
|                                      |                                                                 |                                                                 |                                                                   |
| Started                              | 21                                                              | 18                                                              | 15                                                                |
| Received atLeast 1 Doseof Study Drug | 21                                                              | 18                                                              | 15                                                                |
| Completed                            | 18                                                              | 15                                                              | 14                                                                |
| Not completed                        | 3                                                               | 3                                                               | 1                                                                 |
| Consent withdrawn by subject         | 2                                                               | 1                                                               | -                                                                 |
| Physician decision                   | -                                                               | -                                                               | -                                                                 |
| Adverse event, non-fatal             | -                                                               | -                                                               | -                                                                 |
| Progressive Disease                  | -                                                               | -                                                               | -                                                                 |
| Lost to follow-up                    | 1                                                               | 2                                                               | 1                                                                 |

| Number of subjects in period 1 | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) |
|--------------------------------|-----------------------------------------------------------|----------------------------------------------------------------|--------------------------------------------------------|
|                                |                                                           |                                                                |                                                        |
| Started                        | 81                                                        | 46                                                             | 86                                                     |

|                                      |    |    |    |
|--------------------------------------|----|----|----|
| Received atLeast 1 Doseof Study Drug | 81 | 45 | 86 |
| Completed                            | 65 | 40 | 75 |
| Not completed                        | 16 | 6  | 11 |
| Consent withdrawn by subject         | 3  | 3  | -  |
| Physician decision                   | 1  | 1  | -  |
| Adverse event, non-fatal             | 2  | -  | 6  |
| Progressive Disease                  | 4  | 1  | -  |
| Lost to follow-up                    | 6  | 1  | 5  |

|                                       |                                                             |
|---------------------------------------|-------------------------------------------------------------|
| <b>Number of subjects in period 1</b> | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab pretreated) |
| Started                               | 43                                                          |
| Received atLeast 1 Doseof Study Drug  | 43                                                          |
| Completed                             | 35                                                          |
| Not completed                         | 8                                                           |
| Consent withdrawn by subject          | 3                                                           |
| Physician decision                    | 1                                                           |
| Adverse event, non-fatal              | 2                                                           |
| Progressive Disease                   | 2                                                           |
| Lost to follow-up                     | -                                                           |

## Baseline characteristics

| Reporting groups                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Phase1b:Cohort1: 15mg/kg<br>Olaratumab+Gemcitabine+Docetaxel   |
| Reporting group description:<br>Participants received intravenous infusions of olaratumab 15 milligrams per kilogram (mg/kg) on days 1, 8 plus gemcitabine 900 milligrams per meter square (mg/m <sup>2</sup> ) on days 1, 8 plus docetaxel 75 mg/m <sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.                                                                                                                                                                      |                                                                |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Phase1b:Cohort2: 20mg/kg<br>Olaratumab+Gemcitabine+Docetaxel   |
| Reporting group description:<br>Participants received intravenous infusions of olaratumab 20 mg/kg on days 1, 8 in combination with gemcitabine 900 mg/m <sup>2</sup> on days 1, 8 and docetaxel 75 mg/m <sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.                                                                                                                                                                                                                 |                                                                |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Phase1b:Cohort2Expand:20mg/kgOlaratumab+Gemcitabine+Docetaxel  |
| Reporting group description:<br>Following a protocol amendment, additional participants were enrolled into this group to confirm the safety of the 20 mg/kg dose level prior to opening the Phase 2. Participants received intravenous infusions of olaratumab 20 milligrams per kilogram (mg/kg) on days 1, 8 plus gemcitabine 900 milligrams per meter square (mg/m <sup>2</sup> ) on days 1, 8 plus docetaxel 75 mg/m <sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met. |                                                                |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive)      |
| Reporting group description:<br>This cohort included participants who never received olaratumab prior to enrollment. Participants received intravenous infusions of olaratumab loading dose 20 mg/kg on days 1, 8 of cycle 1 followed by 15 mg/kg on days 1, 8 of all subsequent cycles in combination with gemcitabine 900 mg/m <sup>2</sup> on days 1, 8 and docetaxel 75 mg/m <sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.                                         |                                                                |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) |
| Reporting group description:<br>This cohort included participants who received commercially available olaratumab prior to enrollment. Participants received intravenous infusions of olaratumab loading dose 20 mg/kg on days 1, 8 of cycle 1 followed by 15 mg/kg on days 1, 8 of all subsequent cycles in combination with gemcitabine 900 mg/m <sup>2</sup> on days 1, 8 and docetaxel 75 mg/m <sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.                        |                                                                |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive)         |
| Reporting group description:<br>This cohort included participants who never received olaratumab prior to enrollment. Participants received intravenous infusions of placebo on days 1, 8 in combination with gemcitabine 900 mg/m <sup>2</sup> on days 1, 8 and docetaxel 75 mg/m <sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.                                                                                                                                        |                                                                |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab pretreated)    |
| Reporting group description:<br>This cohort included participants who received commercially available olaratumab prior to enrollment. Participants received intravenous infusions of placebo on days 1, 8 in combination with gemcitabine 900 mg/m <sup>2</sup> on days 1, 8 and docetaxel 75 mg/m <sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.                                                                                                                       |                                                                |

| Reporting group values | Phase1b:Cohort1:<br>15mg/kg<br>Olaratumab+Gemcitabine+Docetaxel | Phase1b:Cohort2:<br>20mg/kg<br>Olaratumab+Gemcitabine+Docetaxel | Phase1b:Cohort2Expand:<br>20mg/kgOlaratumab+Gemcitabine+Docetaxel |
|------------------------|-----------------------------------------------------------------|-----------------------------------------------------------------|-------------------------------------------------------------------|
|------------------------|-----------------------------------------------------------------|-----------------------------------------------------------------|-------------------------------------------------------------------|

|                                           |    |    |    |
|-------------------------------------------|----|----|----|
| Number of subjects                        | 21 | 18 | 15 |
| Age categorical                           |    |    |    |
| Units: Subjects                           |    |    |    |
| <65 years                                 | 20 | 12 | 6  |
| >=65 years                                | 1  | 6  | 9  |
| <=18 years                                | 0  | 0  | 0  |
| Gender categorical                        |    |    |    |
| Units: Subjects                           |    |    |    |
| Female                                    | 11 | 8  | 7  |
| Male                                      | 10 | 10 | 8  |
| Ethnicity (NIH/OMB)                       |    |    |    |
| Units: Subjects                           |    |    |    |
| Hispanic or Latino                        | 5  | 0  | 1  |
| Not Hispanic or Latino                    | 16 | 18 | 11 |
| Unknown or Not Reported                   | 0  | 0  | 3  |
| Race (NIH/OMB)                            |    |    |    |
| Units: Subjects                           |    |    |    |
| American Indian or Alaska Native          | 0  | 0  | 1  |
| Asian                                     | 0  | 1  | 1  |
| Native Hawaiian or Other Pacific Islander | 0  | 0  | 0  |
| Black or African American                 | 0  | 2  | 0  |
| White                                     | 15 | 10 | 13 |
| More than one race                        | 6  | 5  | 0  |
| Unknown or Not Reported                   | 0  | 0  | 0  |
| Region of Enrollment                      |    |    |    |
| Units: Subjects                           |    |    |    |
| Hungary                                   | 0  | 0  | 0  |
| United States                             | 10 | 14 | 14 |
| Poland                                    | 0  | 0  | 0  |
| United Kingdom                            | 0  | 0  | 0  |
| Italy                                     | 0  | 0  | 0  |
| Israel                                    | 0  | 0  | 0  |
| France                                    | 0  | 0  | 0  |
| Australia                                 | 0  | 0  | 1  |
| Germany                                   | 0  | 0  | 0  |
| Spain                                     | 11 | 4  | 0  |

| <b>Reporting group values</b> | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) |
|-------------------------------|-----------------------------------------------------------|----------------------------------------------------------------|--------------------------------------------------------|
| Number of subjects            | 81                                                        | 46                                                             | 86                                                     |
| Age categorical               |                                                           |                                                                |                                                        |
| Units: Subjects               |                                                           |                                                                |                                                        |
| <65 years                     | 66                                                        | 27                                                             | 66                                                     |
| >=65 years                    | 15                                                        | 19                                                             | 20                                                     |
| <=18 years                    | 0                                                         | 0                                                              | 0                                                      |
| Gender categorical            |                                                           |                                                                |                                                        |
| Units: Subjects               |                                                           |                                                                |                                                        |
| Female                        | 48                                                        | 28                                                             | 58                                                     |
| Male                          | 33                                                        | 18                                                             | 28                                                     |

|                                           |    |    |    |
|-------------------------------------------|----|----|----|
| Ethnicity (NIH/OMB)                       |    |    |    |
| Units: Subjects                           |    |    |    |
| Hispanic or Latino                        | 8  | 4  | 6  |
| Not Hispanic or Latino                    | 71 | 39 | 73 |
| Unknown or Not Reported                   | 2  | 3  | 7  |
| Race (NIH/OMB)                            |    |    |    |
| Units: Subjects                           |    |    |    |
| American Indian or Alaska Native          | 0  | 0  | 0  |
| Asian                                     | 3  | 2  | 2  |
| Native Hawaiian or Other Pacific Islander | 0  | 1  | 0  |
| Black or African American                 | 1  | 8  | 1  |
| White                                     | 61 | 30 | 70 |
| More than one race                        | 15 | 3  | 10 |
| Unknown or Not Reported                   | 1  | 2  | 3  |
| Region of Enrollment                      |    |    |    |
| Units: Subjects                           |    |    |    |
| Hungary                                   | 5  | 0  | 6  |
| United States                             | 29 | 36 | 28 |
| Poland                                    | 6  | 0  | 2  |
| United Kingdom                            | 11 | 3  | 12 |
| Italy                                     | 2  | 0  | 4  |
| Israel                                    | 4  | 3  | 7  |
| France                                    | 2  | 0  | 3  |
| Australia                                 | 6  | 0  | 2  |
| Germany                                   | 7  | 4  | 11 |
| Spain                                     | 9  | 0  | 11 |

| Reporting group values           | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab pretreated) | Total |  |
|----------------------------------|-------------------------------------------------------------|-------|--|
| Number of subjects               | 43                                                          | 310   |  |
| Age categorical                  |                                                             |       |  |
| Units: Subjects                  |                                                             |       |  |
| <65 years                        | 30                                                          | 227   |  |
| >=65 years                       | 13                                                          | 83    |  |
| <=18 years                       | 0                                                           | 0     |  |
| Gender categorical               |                                                             |       |  |
| Units: Subjects                  |                                                             |       |  |
| Female                           | 28                                                          | 188   |  |
| Male                             | 15                                                          | 122   |  |
| Ethnicity (NIH/OMB)              |                                                             |       |  |
| Units: Subjects                  |                                                             |       |  |
| Hispanic or Latino               | 4                                                           | 28    |  |
| Not Hispanic or Latino           | 36                                                          | 264   |  |
| Unknown or Not Reported          | 3                                                           | 18    |  |
| Race (NIH/OMB)                   |                                                             |       |  |
| Units: Subjects                  |                                                             |       |  |
| American Indian or Alaska Native | 0                                                           | 1     |  |
| Asian                            | 2                                                           | 11    |  |

|                                           |    |     |  |
|-------------------------------------------|----|-----|--|
| Native Hawaiian or Other Pacific Islander | 0  | 1   |  |
| Black or African American                 | 2  | 14  |  |
| White                                     | 34 | 233 |  |
| More than one race                        | 3  | 42  |  |
| Unknown or Not Reported                   | 2  | 8   |  |
| Region of Enrollment                      |    |     |  |
| Units: Subjects                           |    |     |  |
| Hungary                                   | 0  | 11  |  |
| United States                             | 30 | 161 |  |
| Poland                                    | 0  | 8   |  |
| United Kingdom                            | 5  | 31  |  |
| Italy                                     | 0  | 6   |  |
| Israel                                    | 4  | 18  |  |
| France                                    | 0  | 5   |  |
| Australia                                 | 0  | 9   |  |
| Germany                                   | 2  | 24  |  |
| Spain                                     | 2  | 37  |  |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                    |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Phase1b:Cohort1: 15mg/kg<br>Olaratumab+Gemcitabine+Docetaxel       |
| Reporting group description:<br>Participants received intravenous infusions of olaratumab 15 milligrams per kilogram (mg/kg) on days 1, 8 plus gemcitabine 900 milligrams per meter square (mg/m <sup>2</sup> ) on days 1, 8 plus docetaxel 75 mg/m <sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.                                                                                                                                                                      |                                                                    |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Phase1b:Cohort2: 20mg/kg<br>Olaratumab+Gemcitabine+Docetaxel       |
| Reporting group description:<br>Participants received intravenous infusions of olaratumab 20 mg/kg on days 1, 8 in combination with gemcitabine 900 mg/m <sup>2</sup> on days 1, 8 and docetaxel 75 mg/m <sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.                                                                                                                                                                                                                 |                                                                    |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Phase1b:Cohort2Expand:20mg/kgOlaratumab+Gemcitabine+D<br>ocetaxel  |
| Reporting group description:<br>Following a protocol amendment, additional participants were enrolled into this group to confirm the safety of the 20 mg/kg dose level prior to opening the Phase 2. Participants received intravenous infusions of olaratumab 20 milligrams per kilogram (mg/kg) on days 1, 8 plus gemcitabine 900 milligrams per meter square (mg/m <sup>2</sup> ) on days 1, 8 plus docetaxel 75 mg/m <sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met. |                                                                    |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-<br>naive)      |
| Reporting group description:<br>This cohort included participants who never received olaratumab prior to enrollment. Participants received intravenous infusions of olaratumab loading dose 20 mg/kg on days 1, 8 of cycle 1 followed by 15 mg/kg on days 1, 8 of all subsequent cycles in combination with gemcitabine 900 mg/m <sup>2</sup> on days 1, 8 and docetaxel 75 mg/m <sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.                                         |                                                                    |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab<br>Pretreated)  |
| Reporting group description:<br>This cohort included participants who received commercially available olaratumab prior to enrollment. Participants received intravenous infusions of olaratumab loading dose 20 mg/kg on days 1, 8 of cycle 1 followed by 15 mg/kg on days 1, 8 of all subsequent cycles in combination with gemcitabine 900 mg/m <sup>2</sup> on days 1, 8 and docetaxel 75 mg/m <sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.                        |                                                                    |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive)             |
| Reporting group description:<br>This cohort included participants who never received olaratumab prior to enrollment. Participants received intravenous infusions of placebo on days 1, 8 in combination with gemcitabine 900 mg/m <sup>2</sup> on days 1, 8 and docetaxel 75 mg/m <sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.                                                                                                                                        |                                                                    |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab<br>pretreated)     |
| Reporting group description:<br>This cohort included participants who received commercially available olaratumab prior to enrollment. Participants received intravenous infusions of placebo on days 1, 8 in combination with gemcitabine 900 mg/m <sup>2</sup> on days 1, 8 and docetaxel 75 mg/m <sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.                                                                                                                       |                                                                    |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Phase1b:Cohort2overall-<br>20mg/kgOlaratumab+Gemcitabine+Docetaxel |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Per protocol                                                       |
| Subject analysis set description:<br>Participants received intravenous infusions of olaratumab 20 mg/kg on days 1, 8 in combination with gemcitabine 900 mg/m <sup>2</sup> on days 1, 8 and docetaxel 75 mg/m <sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met (cohort 2).                                                                                                                                                                                                 |                                                                    |

Following a protocol amendment, additional participants were enrolled into this group to confirm the safety of the 20 mg/kg dose level prior to opening the Phase 2 (cohort 2 expansion).

|                            |                                         |
|----------------------------|-----------------------------------------|
| Subject analysis set title | Phase2:Olaratumab+Gemcitabine+Docetaxel |
|----------------------------|-----------------------------------------|

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

Subject analysis set description:

Participants received intravenous infusions of olaratumab loading dose 20 mg/kg on days 1, 8 of cycle 1 followed by 15 mg/kg on days 1, 8 of all subsequent cycles in combination with gemcitabine 900 mg/m<sup>2</sup> on days 1, 8 and docetaxel 75 mg/m<sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met. This cohort is a combination of participants who never received olaratumab (olaratumab-naïve) and who received commercially available olaratumab (olaratumab pre-treated) prior to enrollment.

|                            |                                      |
|----------------------------|--------------------------------------|
| Subject analysis set title | Phase2:Placebo+Gemcitabine+Docetaxel |
|----------------------------|--------------------------------------|

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

Subject analysis set description:

Participants received intravenous infusions of placebo on days 1, 8 in combination with gemcitabine 900 mg/m<sup>2</sup> on days 1, 8 and docetaxel 75 mg/m<sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met. This cohort is a combination of participants who never received olaratumab (olaratumab-naïve) and who received commercially available olaratumab (olaratumab pre-treated) prior to enrollment.

|                            |                                      |
|----------------------------|--------------------------------------|
| Subject analysis set title | Olaratumab + Gemcitabine + Docetaxel |
|----------------------------|--------------------------------------|

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

Subject analysis set description:

Participants received intravenous infusions of olaratumab on days 1, 8 (phase 1: 15 or 20 mg/kg; phase 2: 20 mg/kg only in cycle 1 and 15 mg/kg in subsequent cycles) plus gemcitabine 900 mg/m<sup>2</sup> on days 1, 8 plus docetaxel 75 mg/m<sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

### Primary: Phase 1b: Number of Participants with Dose Limiting Toxicity (DLT)

|                 |                                                                                      |
|-----------------|--------------------------------------------------------------------------------------|
| End point title | Phase 1b: Number of Participants with Dose Limiting Toxicity (DLT) <sup>[1][2]</sup> |
|-----------------|--------------------------------------------------------------------------------------|

End point description:

A Dose Limiting Toxicity is defined as an Adverse Event (AE) that is likely related to the study medication or combination, and fulfils any one of the following criteria, graded according to the NCI-CTCAE Version 4.0:

1. Febrile neutropenia with documented Grade  $\geq 3$  infection or sepsis
2. Grade 4 neutropenia lasting 7 days or longer.
3. Grade 4 thrombocytopenia, or Grade 3 thrombocytopenia complicated by hemorrhage.
4. Nonhematologic Grade  $\geq 3$  toxicity, except for toxicities such as nausea, vomiting, transient electrolyte abnormalities, or diarrhoea that can be controlled with optimal medical management within 48 hours.

Analysis Population Description: Phase 1b: All participants who received at least one dose of Olaratumab.

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

End point timeframe:

Cycle 1 (Up To 21 Days)

Notes:

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

Justification: No inferential statistics were planned for this endpoint.

[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: Outcome reporting is only for Phase 1b participants.

|                             |                                                           |                                                           |                                                               |  |
|-----------------------------|-----------------------------------------------------------|-----------------------------------------------------------|---------------------------------------------------------------|--|
| <b>End point values</b>     | Phase1b:Cohort1: 15mg/kg Olaratumab+Gemcitabine+Docetaxel | Phase1b:Cohort2: 20mg/kg Olaratumab+Gemcitabine+Docetaxel | Phase1b:Cohort2Expand:20mg/kgOlaratumab+Gemcitabine+Docetaxel |  |
| Subject group type          | Reporting group                                           | Reporting group                                           | Reporting group                                               |  |
| Number of subjects analysed | 21                                                        | 18                                                        | 15                                                            |  |
| Units: participants         | 1                                                         | 4                                                         | 3                                                             |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Phase 2: Overall Survival (OS) (Olaratumab-Naive)

|                 |                                                                  |
|-----------------|------------------------------------------------------------------|
| End point title | Phase 2: Overall Survival (OS) (Olaratumab-Naive) <sup>[3]</sup> |
|-----------------|------------------------------------------------------------------|

End point description:

OS was defined as the time from the date of randomization to the date of death from any cause. For each participant who is not known to have died as of the data-inclusion cut-off date for a particular analysis, overall survival duration was censored for that analysis at the date of last prior contact.

Analysis Population Description: Phase 2: All randomized participants (including the censored participants). Number of participants censored in "Olaratumab+ Gemcitabine+Docetaxel(Olaratumab-naive)=30," "Placebo+Gemcitabine+Docetaxel(Olaratumab-naive)=28."

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

End point timeframe:

Baseline to Date of Death Due to Any Cause (Up To 38 Months)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Outcome reporting is only for Phase 2 Olaratumab-Naive participants.

|                                  |                                                           |                                                        |  |  |
|----------------------------------|-----------------------------------------------------------|--------------------------------------------------------|--|--|
| <b>End point values</b>          | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) |  |  |
| Subject group type               | Reporting group                                           | Reporting group                                        |  |  |
| Number of subjects analysed      | 81                                                        | 86                                                     |  |  |
| Units: Months                    |                                                           |                                                        |  |  |
| median (confidence interval 95%) | 16.76 (15.28 to 25.40)                                    | 18.04 (13.17 to 22.90)                                 |  |  |

## Statistical analyses

|                                   |                                                                                                                    |
|-----------------------------------|--------------------------------------------------------------------------------------------------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 1                                                                                             |
| Comparison groups                 | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) v Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) |

|                                         |                        |
|-----------------------------------------|------------------------|
| Number of subjects included in analysis | 167                    |
| Analysis specification                  | Pre-specified          |
| Analysis type                           | superiority            |
| P-value                                 | = 0.775 <sup>[4]</sup> |
| Method                                  | Logrank                |
| Parameter estimate                      | Hazard ratio (HR)      |
| Point estimate                          | 0.945                  |
| Confidence interval                     |                        |
| level                                   | 95 %                   |
| sides                                   | 2-sided                |
| lower limit                             | 0.639                  |
| upper limit                             | 1.397                  |

Notes:

[4] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and Eastern Cooperative Oncology Group Performance Status (ECOG PS) (0 vs1).

### Secondary: Phase 1b: Pharmacokinetics (PK): Maximum Serum Concentration (Cmax) of Olaratumab

|                 |                                                                                                  |
|-----------------|--------------------------------------------------------------------------------------------------|
| End point title | Phase 1b: Pharmacokinetics (PK): Maximum Serum Concentration (Cmax) of Olaratumab <sup>[5]</sup> |
|-----------------|--------------------------------------------------------------------------------------------------|

End point description:

Cmax of Olaratumab.

Analysis Population Description: Phase 1b: All participants who received at least one dose of Olaratumab and had evaluable PK data.

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

End point timeframe:

Pre-dose, 5 minutes (min), 1, 4, 4.5, 24, 96, 168, 336 hours (h) post-dose on Cycle 1 Day 1, Cycle 1 Day 8, Cycle 3 Day 1, Cycle 3 Day 8

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Outcome reporting is only for Phase 1b participants.

| End point values                                    | Phase1b:Cohort1: 15mg/kg Olaratumab+Gemcitabine+Docetaxel | Phase1b:Cohort2overall-20mg/kgOlaratumab+Gemcitabine+Docetaxel |  |  |
|-----------------------------------------------------|-----------------------------------------------------------|----------------------------------------------------------------|--|--|
| Subject group type                                  | Reporting group                                           | Subject analysis set                                           |  |  |
| Number of subjects analysed                         | 20 <sup>[6]</sup>                                         | 33 <sup>[7]</sup>                                              |  |  |
| Units: micrograms per milliliter (µg/mL)            |                                                           |                                                                |  |  |
| geometric mean (geometric coefficient of variation) |                                                           |                                                                |  |  |
| Cycle 1 (Day 1)                                     | 432 (± 24)                                                | 572 (± 25)                                                     |  |  |
| Cycle 1 (Day 8)                                     | 460 (± 25)                                                | 697 (± 20)                                                     |  |  |
| Cycle 3 (Day 1)                                     | 523 (± 38)                                                | 644 (± 20)                                                     |  |  |
| Cycle 3 (Day 8)                                     | 513 (± 21)                                                | 689 (± 20)                                                     |  |  |

Notes:

[6] - Cycle 1 (Day 1) = 19;  
Cycle 3 (Day 1), Cycle 3 (Day 8) = 14

[7] - Cycle 3 (Day 1) = 23;  
Cycle 3 (Day 8) = 22

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1b: PK: Minimum Serum Concentration (Cmin) of Olaratumab

|                 |                                                                               |
|-----------------|-------------------------------------------------------------------------------|
| End point title | Phase 1b: PK: Minimum Serum Concentration (Cmin) of Olaratumab <sup>[8]</sup> |
|-----------------|-------------------------------------------------------------------------------|

End point description:  
Cmin of Olaratumab.

Analysis Population Description: Phase 1b: All participants who received at least one dose of Olaratumab and had evaluable PK data.

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

End point timeframe:

Pre-dose, 5 min, 1, 4, 4.5, 24, 96, 168, 336 h post-dose on Cycle 1 Day 1, Cycle 1 Day 8, Cycle 3 Day 1

Notes:

[8] - 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: Outcome reporting is only for Phase 1b participants.

| End point values                                    | Phase1b:Cohort1: 15mg/kg Olaratumab+Gemcitabine+Docetaxel | Phase1b:Cohort2overall- 20mg/kgOlaratumab+Gemcitabine+Docetaxel |  |  |
|-----------------------------------------------------|-----------------------------------------------------------|-----------------------------------------------------------------|--|--|
| Subject group type                                  | Reporting group                                           | Subject analysis set                                            |  |  |
| Number of subjects analysed                         | 20 <sup>[9]</sup>                                         | 31 <sup>[10]</sup>                                              |  |  |
| Units: µg/mL                                        |                                                           |                                                                 |  |  |
| geometric mean (geometric coefficient of variation) |                                                           |                                                                 |  |  |
| Cycle 1 (Day 1)                                     | 95.9 (± 37)                                               | 142 (± 38)                                                      |  |  |
| Cycle 1 (Day 8)                                     | 64.3 (± 64)                                               | 93.3 (± 47)                                                     |  |  |
| Cycle 3 (Day 1)                                     | 137 (± 40)                                                | 252 (± 36)                                                      |  |  |

Notes:

[9] - Cycle 1 (Day 8) = 19;  
Cycle 3 (Day 1) = 14

[10] - Cycle 1 (Day 8) = 30;  
Cycle 3 (Day 1) = 22

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1b: PK: Elimination Half-Life (T1/2) of Olaratumab

|                 |                                                                          |
|-----------------|--------------------------------------------------------------------------|
| End point title | Phase 1b: PK: Elimination Half-Life (T1/2) of Olaratumab <sup>[11]</sup> |
|-----------------|--------------------------------------------------------------------------|

End point description:  
T1/2 of Olaratumab.

Analysis Population Description: Phase 1b: All participants who received at least one dose of Olaratumab and had evaluable PK data.

|                                                                                                                        |           |
|------------------------------------------------------------------------------------------------------------------------|-----------|
| End point type                                                                                                         | Secondary |
| End point timeframe:                                                                                                   |           |
| Pre-dose, 5 min, 1, 4, 4.5, 24, 96, 168, 336 h post-dose on Cycle 1 Day 1, Cycle 1 Day 8, Cycle 3 Day 1, Cycle 3 Day 8 |           |

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: Outcome reporting is only for Phase 1b participants.

|                                                     |                                                           |                                                                 |  |  |
|-----------------------------------------------------|-----------------------------------------------------------|-----------------------------------------------------------------|--|--|
| <b>End point values</b>                             | Phase1b:Cohort1: 15mg/kg Olaratumab+Gemcitabine+Docetaxel | Phase1b:Cohort2overall: 20mg/kgOlaratumab+Gemcitabine+Docetaxel |  |  |
| Subject group type                                  | Reporting group                                           | Subject analysis set                                            |  |  |
| Number of subjects analysed                         | 19 <sup>[12]</sup>                                        | 33 <sup>[13]</sup>                                              |  |  |
| Units: days                                         |                                                           |                                                                 |  |  |
| geometric mean (geometric coefficient of variation) |                                                           |                                                                 |  |  |
| Cycle 1 (Day 1)                                     | 4.60 (± 34)                                               | 4.29 (± 28)                                                     |  |  |
| Cycle 1 (Day 8)                                     | 6.25 (± 25)                                               | 6.62 (± 27)                                                     |  |  |
| Cycle 3 (Day 1)                                     | 5.17 (± 36)                                               | 6.36 (± 41)                                                     |  |  |
| Cycle 3 (Day 8)                                     | 5.82 (± 30)                                               | 6.39 (± 32)                                                     |  |  |

Notes:

[12] - Cycle 3 (Day 1), Cycle 3 (Day 8) = 14

[13] - Cycle 3 (Day 1) = 23;  
Cycle 3 (Day 8) = 21

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 1b/2: PK: Cmax of Gemcitabine

|                        |                                                     |
|------------------------|-----------------------------------------------------|
| End point title        | Phase 1b/2: PK: Cmax of Gemcitabine <sup>[14]</sup> |
| End point description: |                                                     |
| Cmax of Gemcitabine.   |                                                     |

Analysis Population Description: Phase 1b/2: All participants who received at least one dose of Gemcitabine and had evaluable PK data.

|                                                                     |           |
|---------------------------------------------------------------------|-----------|
| End point type                                                      | Secondary |
| End point timeframe:                                                |           |
| Day 8 of Cycle 1 (end of infusion, 1, 2, 4, 24 hours post-infusion) |           |

Notes:

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

Justification: Outcomes were reported by combining phase 1b cohort 2+cohort2expand arms [i.e. Cohort2overall: 20mg/kgOlaratumab+Gemcitabine+Docetaxel]; Phase2Olaratumab+Gemcitabine+Docetaxel (Olaratumab-naïve) +Phase2Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) arms [i.e.Phase2: Olaratumab+Gemcitabine+Docetaxel]; Phase2Placebo+Gemcitabine+Docetaxel (Olaratumab-naïve) +Phase2Placebo+Gemcitabine+Docetaxel(Olaratumab Pretreated) arms [i.e.Phase2: Placebo+Gemcitabine+Docetaxel]

| End point values                                    | Phase1b:Cohort1: 15mg/kg Olaratumab+Gemcitabine+Docetaxel | Phase1b:Cohort2overall-20mg/kgOlaratumab+Gemcitabine+Docetaxel | Phase2:Olaratumab+Gemcitabine+Docetaxel | Phase2:Placebo+Gemcitabine+Docetaxel |
|-----------------------------------------------------|-----------------------------------------------------------|----------------------------------------------------------------|-----------------------------------------|--------------------------------------|
| Subject group type                                  | Reporting group                                           | Subject analysis set                                           | Subject analysis set                    | Subject analysis set                 |
| Number of subjects analysed                         | 18                                                        | 24                                                             | 87                                      | 88                                   |
| Units: µg/mL                                        |                                                           |                                                                |                                         |                                      |
| geometric mean (geometric coefficient of variation) | 2.79 (± 70)                                               | 3.49 (± 50)                                                    | 3.01 (± 122)                            | 2.35 (± 105)                         |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 1b/2: PK: Area Under the Concentration-Time Curve From Time Zero to Infinity (AUC[0-∞]) of Gemcitabine

|                        |                                                                                                                                                                         |
|------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title        | Phase 1b/2: PK: Area Under the Concentration-Time Curve From Time Zero to Infinity (AUC[0-∞]) of Gemcitabine <sup>[15]</sup>                                            |
| End point description: | Phase 1b/2: Due to short half-life of Gemcitabine, there was insufficient quantifiable data in the elimination phase to calculate AUC[0-∞] for any of the participants. |
| End point type         | Secondary                                                                                                                                                               |
| End point timeframe:   | Day 8 of Cycle 1 (end of infusion, 1, 2, 4, 24 hours post-infusion)                                                                                                     |

Notes:

[15] - 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: Outcomes were reported by combining phase 1b cohort 2+cohort2expand arms [i.e. Cohort2overall:20mg/kgOlaratumab+Gemcitabine+Docetaxel]; Phase2Olaratumab+Gemcitabine+Docetaxel (Olaratumab-naïve) +Phase2Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) arms [i.e.Phase2:Olaratumab+Gemcitabine+Docetaxel]; Phase2Placebo+Gemcitabine+Docetaxel (Olaratumab-naïve) +Phase2Placebo+Gemcitabine+Docetaxel(Olaratumab Pretreated) arms [i.e.Phase2:Placebo+Gemcitabine+Docetaxel]

| End point values                                    | Phase1b:Cohort1: 15mg/kg Olaratumab+Gemcitabine+Docetaxel | Phase1b:Cohort2overall-20mg/kgOlaratumab+Gemcitabine+Docetaxel | Phase2:Olaratumab+Gemcitabine+Docetaxel | Phase2:Placebo+Gemcitabine+Docetaxel |
|-----------------------------------------------------|-----------------------------------------------------------|----------------------------------------------------------------|-----------------------------------------|--------------------------------------|
| Subject group type                                  | Reporting group                                           | Subject analysis set                                           | Subject analysis set                    | Subject analysis set                 |
| Number of subjects analysed                         | 0 <sup>[16]</sup>                                         | 0 <sup>[17]</sup>                                              | 0 <sup>[18]</sup>                       | 0 <sup>[19]</sup>                    |
| Units: nanograms*hours per milliliter               |                                                           |                                                                |                                         |                                      |
| geometric mean (geometric coefficient of variation) | ()                                                        | ()                                                             | ()                                      | ()                                   |

Notes:

[16] - Zero participants analysed due to insufficient quantifiable data in the elimination phase.

[17] - Zero participants analysed due to insufficient quantifiable data in the elimination phase.

[18] - Zero participants analysed due to insufficient quantifiable data in the elimination phase.

[19] - Zero participants analysed due to insufficient quantifiable data in the elimination phase.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1b/2: PK: Cmax of Docetaxel

|                                                                                                                                      |                                                   |
|--------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|
| End point title                                                                                                                      | Phase 1b/2: PK: Cmax of Docetaxel <sup>[20]</sup> |
| End point description:<br>Cmax of Docetaxel.                                                                                         |                                                   |
| Analysis Population Description: Phase 1b/2: All participants who received at least one dose of Docetaxel and had evaluable PK data. |                                                   |
| End point type                                                                                                                       | Secondary                                         |
| End point timeframe:<br>5 min, 1, 3, 24, 48 h post-dose on Cycle 1 Day 8                                                             |                                                   |

Notes:

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

Justification: Outcomes were reported by combining phase 1b cohort 2+cohort2expand arms [i.e. Cohort2overall: 20mg/kgOlaratumab+Gemcitabine+Docetaxel]; Phase2Olaratumab+Gemcitabine+Docetaxel (Olaratumab-naïve) +Phase2Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) arms [i.e.Phase2: Olaratumab+Gemcitabine+Docetaxel]; Phase2Placebo+Gemcitabine+Docetaxel (Olaratumab-naïve) +Phase2Placebo+Gemcitabine+Docetaxel(Olaratumab Pretreated) arms [i.e.Phase2: Placebo+Gemcitabine+Docetaxel]

| End point values                                    | Phase1b:Cohort1: 15mg/kg Olaratumab+Gemcitabine+Docetaxel | Phase1b:Cohort2overall: 20mg/kgOlaratumab+Gemcitabine+Docetaxel | Phase2:Olaratumab+Gemcitabine+Docetaxel | Phase2:Placebo+Gemcitabine+Docetaxel |
|-----------------------------------------------------|-----------------------------------------------------------|-----------------------------------------------------------------|-----------------------------------------|--------------------------------------|
| Subject group type                                  | Reporting group                                           | Subject analysis set                                            | Subject analysis set                    | Subject analysis set                 |
| Number of subjects analysed                         | 18                                                        | 30                                                              | 71                                      | 73                                   |
| Units: Nanograms per milliliter                     |                                                           |                                                                 |                                         |                                      |
| geometric mean (geometric coefficient of variation) | 903 (± 143)                                               | 1110 (± 84)                                                     | 1030 (± 134)                            | 827 (± 102)                          |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1b/2: PK: Area Under the Concentration Versus Time Curve From Time Zero to Infinity (AUC [0-∞]) of Docetaxel

|                                                                                                                                                                                                                                                              |                                                                                                                                    |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                              | Phase 1b/2: PK: Area Under the Concentration Versus Time Curve From Time Zero to Infinity (AUC [0-∞]) of Docetaxel <sup>[21]</sup> |
| End point description:<br>Analysis Population Description: Phase 1b/2: All participants who received at least one dose of Docetaxel and had evaluable PK data. For phase 2, zero participants analysed due to data not collected for AUC [0-∞] of Docetaxel. |                                                                                                                                    |
| End point type                                                                                                                                                                                                                                               | Secondary                                                                                                                          |
| End point timeframe:<br>5 min, 1, 3, 24, 48 h post-dose on Cycle 1 Day 8                                                                                                                                                                                     |                                                                                                                                    |

Notes:

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

Justification: Outcomes were reported by combining phase 1b cohort 2+cohort2expand arms [i.e. Cohort2overall:20mg/kgOlaratumab+Gemcitabine+Docetaxel]; Phase2Olaratumab+Gemcitabine+Docetaxel (Olaratumab-naive) +Phase2Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) arms [i.e.Phase2: Olaratumab+Gemcitabine+Docetaxel]; Phase2Placebo+Gemcitabine+Docetaxel (Olaratumab-naive) +Phase2Placebo+Gemcitabine+Docetaxel(Olaratumab Pretreated) arms [i.e.Phase2: Placebo+Gemcitabine+Docetaxel]

| End point values                                    | Phase1b:Cohort1: 15mg/kg Olaratumab+Gemcitabine+Docetaxel | Phase1b:Cohort2overall- 20mg/kgOlaratumab+Gemcitabine+Docetaxel | Phase2:Olaratumab+Gemcitabine+Docetaxel | Phase2:Placebo+Gemcitabine+Docetaxel |
|-----------------------------------------------------|-----------------------------------------------------------|-----------------------------------------------------------------|-----------------------------------------|--------------------------------------|
| Subject group type                                  | Reporting group                                           | Subject analysis set                                            | Subject analysis set                    | Subject analysis set                 |
| Number of subjects analysed                         | 7                                                         | 18                                                              | 0 <sup>[22]</sup>                       | 0 <sup>[23]</sup>                    |
| Units: nanograms*hours per milliliter               |                                                           |                                                                 |                                         |                                      |
| geometric mean (geometric coefficient of variation) | 4440 (± 103)                                              | 2990 (± 83)                                                     | ()                                      | ()                                   |

Notes:

[22] - Data not collected.

[23] - Data not collected.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 1b/2: Population PK: Clearance of Olaratumab

|                                                                                                                                                                                                                                                                                                                                                                                  |                                                    |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                  | Phase 1b/2: Population PK: Clearance of Olaratumab |
| End point description:                                                                                                                                                                                                                                                                                                                                                           |                                                    |
| Analysis Population Description: Phase 1b/2: All participants who received at least one dose of Olaratumab and had evaluable PK data. Phase 1b and phase 2 participants olaratumab PK data was planned to be pooled for the population PK analysis and compared to a validated PK model to confirm that PK parameters were similar to analyses from previous olaratumab studies. |                                                    |
| End point type                                                                                                                                                                                                                                                                                                                                                                   | Secondary                                          |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                             |                                                    |
| Cycle 1-19: Pre-dose, 5 min, 1, 4, 4.5, 24, 96, 168, 336 h post-dose on days 1, 8                                                                                                                                                                                                                                                                                                |                                                    |

| End point values                          | Olaratumab + Gemcitabine + Docetaxel |  |  |  |
|-------------------------------------------|--------------------------------------|--|--|--|
| Subject group type                        | Subject analysis set                 |  |  |  |
| Number of subjects analysed               | 178                                  |  |  |  |
| Units: Liter Per Hour                     |                                      |  |  |  |
| arithmetic mean (confidence interval 95%) | 0.0186 (0.0175 to 0.0192)            |  |  |  |

## Statistical analyses

No statistical analyses for this end point

**Secondary: Phase 1b/2: Population PK: Volume of Distribution at Steady State (Vss) of Olaratumab**

|                 |                                                                                       |
|-----------------|---------------------------------------------------------------------------------------|
| End point title | Phase 1b/2: Population PK: Volume of Distribution at Steady State (Vss) of Olaratumab |
|-----------------|---------------------------------------------------------------------------------------|

End point description:

The Vss is the sum of central volume of distribution (V1) + peripheral volume of distribution (V2).

Analysis Population Description: Phase 1b/2: All participants who received at least one dose of Olaratumab and had evaluable PK data. Phase 1b and phase 2 participants olaratumab PK data was planned to be pooled for the population PK analysis and compared to a validated PK model to confirm that PK parameters were similar to analyses from previous olaratumab studies.

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

End point timeframe:

Cycle 1-19: Pre-dose, 5 min, 1, 4, 4.5, 24, 96, 168, 336 h post-dose on days 1, 8

|                                           |                                      |  |  |  |
|-------------------------------------------|--------------------------------------|--|--|--|
| <b>End point values</b>                   | Olaratumab + Gemcitabine + Docetaxel |  |  |  |
| Subject group type                        | Subject analysis set                 |  |  |  |
| Number of subjects analysed               | 178                                  |  |  |  |
| Units: Liter                              |                                      |  |  |  |
| arithmetic mean (confidence interval 95%) | 5.14 (4.68 to 5.54)                  |  |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Phase 2: Overall Survival (Olaratumab Pre-Treated)**

|                 |                                                                    |
|-----------------|--------------------------------------------------------------------|
| End point title | Phase 2: Overall Survival (Olaratumab Pre-Treated) <sup>[24]</sup> |
|-----------------|--------------------------------------------------------------------|

End point description:

OS was defined as the time from the date of randomization to the date of death from any cause. For each participant who is not known to have died as of the data-inclusion cut-off date for a particular analysis, overall survival duration was censored for that analysis at the date of last prior contact.

Analysis Population Description: Phase 2: All randomized participants (including the censored participants). Number of participants censored in "Olaratumab+ Gemcitabine+Docetaxel(Olaratumab Pre-Treated)=20," "Placebo+Gemcitabine+Docetaxel(Olaratumab Pre-Treated)=15."

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

End point timeframe:

Baseline to Date of Death Due to Any Cause (Up To 38 Months)

Notes:

[24] - 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: Outcome reporting is only for Phase 2 Olaratumab Pre-Treated participants.

|                                  |                                                                |                                                             |  |  |
|----------------------------------|----------------------------------------------------------------|-------------------------------------------------------------|--|--|
| <b>End point values</b>          | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab pretreated) |  |  |
| Subject group type               | Reporting group                                                | Reporting group                                             |  |  |
| Number of subjects analysed      | 46 <sup>[25]</sup>                                             | 43                                                          |  |  |
| Units: Months                    |                                                                |                                                             |  |  |
| median (confidence interval 95%) | 19.84 (14.19 to 9999)                                          | 17.31 (10.81 to 20.30)                                      |  |  |

Notes:

[25] - 9999 = N/A, There were not enough events to estimate the upper confidence limit.

## Statistical analyses

|                                         |                                                                                                                              |
|-----------------------------------------|------------------------------------------------------------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 1                                                                                                       |
| Comparison groups                       | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) v Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab Pretreated) |
| Number of subjects included in analysis | 89                                                                                                                           |
| Analysis specification                  | Pre-specified                                                                                                                |
| Analysis type                           | superiority                                                                                                                  |
| P-value                                 | = 0.148 <sup>[26]</sup>                                                                                                      |
| Method                                  | Logrank                                                                                                                      |
| Parameter estimate                      | Hazard ratio (HR)                                                                                                            |
| Point estimate                          | 0.667                                                                                                                        |
| Confidence interval                     |                                                                                                                              |
| level                                   | 95 %                                                                                                                         |
| sides                                   | 2-sided                                                                                                                      |
| lower limit                             | 0.385                                                                                                                        |
| upper limit                             | 1.158                                                                                                                        |

Notes:

[26] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs ≥1), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

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

|                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|----------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title                  | Phase 2: Progression Free Survival (PFS) <sup>[27]</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| End point description:           | PFS was defined as the time from randomization to the first date of radiologic disease progression (as defined by Response Evaluation Criteria In Solid Tumors, Version 1.1 [RECIST v.1.1]) or death due to any cause. Progressive disease (PD) was defined as at least a 20% increase in the sum of the diameters of target lesions, with reference being the smallest sum on study and an absolute increase of at least 5 mm, or unequivocal progression of non-target lesions, or 1 or more new lesions. Participants who have neither progressed nor died were censored at the day of their last radiographic tumor assessment, if available, or date of randomization if no post-baseline radiographic assessment is available. |
| Analysis Population Description: | Phase 2: All randomized participants (including censored). Number of participants censored in Olaratumab+Gemcitabine+Docetaxel (Olaratumab-naive=20, Olaratumab pretreated=12), Placebo+Gemcitabine+Docetaxel(Olaratumab-naive=21, Olaratumab pretreated=16).                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| End point type                   | Secondary                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |

End point timeframe:

Baseline to Objective Disease Progression or Death from Any Cause (Up To 38 Months)

Notes:

[27] - 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.

| <b>End point values</b>          | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab pretreated) |
|----------------------------------|-----------------------------------------------------------|----------------------------------------------------------------|--------------------------------------------------------|-------------------------------------------------------------|
| Subject group type               | Reporting group                                           | Reporting group                                                | Reporting group                                        | Reporting group                                             |
| Number of subjects analysed      | 81                                                        | 46                                                             | 86                                                     | 43                                                          |
| Units: Months                    |                                                           |                                                                |                                                        |                                                             |
| median (confidence interval 95%) | 7.62 (5.13 to 8.54)                                       | 5.45 (2.76 to 8.71)                                            | 4.37 (2.86 to 6.87)                                    | 4.17 (2.20 to 6.90)                                         |

### Statistical analyses

| <b>Statistical analysis title</b>       | Statistical analysis 1                                                                                             |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------|
| Comparison groups                       | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) v Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) |
| Number of subjects included in analysis | 167                                                                                                                |
| Analysis specification                  | Pre-specified                                                                                                      |
| Analysis type                           | superiority                                                                                                        |
| P-value                                 | = 0.055 <sup>[28]</sup>                                                                                            |
| Method                                  | Logrank                                                                                                            |
| Parameter estimate                      | Hazard ratio (HR)                                                                                                  |
| Point estimate                          | 0.692                                                                                                              |
| Confidence interval                     |                                                                                                                    |
| level                                   | 95 %                                                                                                               |
| sides                                   | 2-sided                                                                                                            |
| lower limit                             | 0.476                                                                                                              |
| upper limit                             | 1.007                                                                                                              |

Notes:

[28] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs ≥1), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

| <b>Statistical analysis title</b>       | Statistical analysis 2                                                                                           |
|-----------------------------------------|------------------------------------------------------------------------------------------------------------------|
| Comparison groups                       | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) v Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab |
| Number of subjects included in analysis | 89                                                                                                               |
| Analysis specification                  | Pre-specified                                                                                                    |
| Analysis type                           | superiority                                                                                                      |
| P-value                                 | = 0.482 <sup>[29]</sup>                                                                                          |
| Method                                  | Logrank                                                                                                          |
| Parameter estimate                      | Hazard ratio (HR)                                                                                                |
| Point estimate                          | 0.828                                                                                                            |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.49    |
| upper limit         | 1.398   |

Notes:

[29] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs ≥1), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

## Secondary: Phase 2: Percentage of Participants With a Complete or Partial Response (Objective Response Rate [ORR])

|                 |                                                                                                                         |
|-----------------|-------------------------------------------------------------------------------------------------------------------------|
| End point title | Phase 2: Percentage of Participants With a Complete or Partial Response (Objective Response Rate [ORR]) <sup>[30]</sup> |
|-----------------|-------------------------------------------------------------------------------------------------------------------------|

End point description:

ORR is the best overall tumor response of complete response (CR) or partial response (PR) as classified by the investigator according to the Response Evaluation Criteria In Solid Tumors (RECIST v1.1). CR is a disappearance of all target and non-target lesions and normalization of tumor marker level. PR is an at least 30% decrease in the sum of the diameters of target lesions (taking as reference the baseline sum diameter) without progression of non-target lesions or appearance of new lesions.

Analysis Population Description: Phase 2: All randomized participants.

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

End point timeframe:

Baseline to Objective Disease Progression or Start of New Anti-Cancer Therapy (Up To 38 Months)

Notes:

[30] - 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: Outcome reporting is only for Phase 2 participants.

| End point values                  | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab pretreated) |
|-----------------------------------|-----------------------------------------------------------|----------------------------------------------------------------|--------------------------------------------------------|-------------------------------------------------------------|
| Subject group type                | Reporting group                                           | Reporting group                                                | Reporting group                                        | Reporting group                                             |
| Number of subjects analysed       | 81                                                        | 46                                                             | 86                                                     | 43                                                          |
| Units: Percentage of participants |                                                           |                                                                |                                                        |                                                             |
| number (confidence interval 95%)  | 32.1 (22.2 to 43.4)                                       | 30.4 (17.7 to 45.8)                                            | 23.3 (14.8 to 33.6)                                    | 14 (5.3 to 27.9)                                            |

## Statistical analyses

|                            |                                                                                                                    |
|----------------------------|--------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical analysis 1                                                                                             |
| Comparison groups          | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) v Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 167                        |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | superiority                |
| P-value                                 | = 0.1891 <sup>[31]</sup>   |
| Method                                  | Exact Mantel-Haenszel test |
| Parameter estimate                      | Odds ratio (OR)            |
| Point estimate                          | 1.589                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 0.794                      |
| upper limit                             | 3.179                      |

Notes:

[31] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs 1).

|                                         |                                                                                                                     |
|-----------------------------------------|---------------------------------------------------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 2                                                                                              |
| Comparison groups                       | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) v<br>Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab |
| Number of subjects included in analysis | 89                                                                                                                  |
| Analysis specification                  | Pre-specified                                                                                                       |
| Analysis type                           | superiority                                                                                                         |
| P-value                                 | = 0.0642 <sup>[32]</sup>                                                                                            |
| Method                                  | Exact Mantel-Haenszel test                                                                                          |
| Parameter estimate                      | Odds ratio (OR)                                                                                                     |
| Point estimate                          | 2.668                                                                                                               |
| Confidence interval                     |                                                                                                                     |
| level                                   | 95 %                                                                                                                |
| sides                                   | 2-sided                                                                                                             |
| lower limit                             | 0.923                                                                                                               |
| upper limit                             | 7.71                                                                                                                |

Notes:

[32] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs 1).

### **Secondary: Phase 2: Disease Control Rate (DCR): Percentage of Participants With a Best Overall Response of Complete Response (CR), Partial Response (PR), and Stable Disease (SD)**

|                 |                                                                                                                                                                                        |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Phase 2: Disease Control Rate (DCR): Percentage of Participants With a Best Overall Response of Complete Response (CR), Partial Response (PR), and Stable Disease (SD) <sup>[33]</sup> |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

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

Analysis Population Description: Phase 2: All randomized participants

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

End point timeframe:

Baseline to Measured Progressive Disease or Start of New Anti-Cancer Therapy (Up To 38 Months)

Notes:

[33] - 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: Outcome reporting is only for Phase 2 participants.

| End point values                  | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab pretreated) |
|-----------------------------------|-----------------------------------------------------------|----------------------------------------------------------------|--------------------------------------------------------|-------------------------------------------------------------|
| Subject group type                | Reporting group                                           | Reporting group                                                | Reporting group                                        | Reporting group                                             |
| Number of subjects analysed       | 81                                                        | 46                                                             | 86                                                     | 43                                                          |
| Units: Percentage of participants |                                                           |                                                                |                                                        |                                                             |
| number (confidence interval 95%)  | 74.1 (63.1 to 83.2)                                       | 67.4 (52.0 to 80.5)                                            | 72.1 (61.4 to 81.2)                                    | 62.8 (46.7 to 77.0)                                         |

## Statistical analyses

| Statistical analysis title              | Statistical analysis 1                                                                                             |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------|
| Comparison groups                       | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) v Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) |
| Number of subjects included in analysis | 167                                                                                                                |
| Analysis specification                  | Pre-specified                                                                                                      |
| Analysis type                           | superiority                                                                                                        |
| P-value                                 | = 0.7724 [34]                                                                                                      |
| Method                                  | Exact Mantel-Haenszel test                                                                                         |
| Parameter estimate                      | Odds ratio (OR)                                                                                                    |
| Point estimate                          | 1.106                                                                                                              |
| Confidence interval                     |                                                                                                                    |
| level                                   | 95 %                                                                                                               |
| sides                                   | 2-sided                                                                                                            |
| lower limit                             | 0.558                                                                                                              |
| upper limit                             | 2.194                                                                                                              |

Notes:

[34] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs ≥1), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

| Statistical analysis title              | Statistical analysis 2                                                                                           |
|-----------------------------------------|------------------------------------------------------------------------------------------------------------------|
| Comparison groups                       | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) v Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab |
| Number of subjects included in analysis | 89                                                                                                               |
| Analysis specification                  | Pre-specified                                                                                                    |
| Analysis type                           | superiority                                                                                                      |
| P-value                                 | = 0.6508 [35]                                                                                                    |
| Method                                  | Exact Mantel-Haenszel test                                                                                       |
| Parameter estimate                      | Odds ratio (OR)                                                                                                  |
| Point estimate                          | 1.222                                                                                                            |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.513   |
| upper limit         | 2.911   |

Notes:

[35] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs 1).

## Secondary: Phase 2: Time to First Worsening of the Brief Pain Inventory Short Form Modified (mBPI-sf) "Worst Pain Score"

|                 |                                                                                                                               |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------|
| End point title | Phase 2: Time to First Worsening of the Brief Pain Inventory Short Form Modified (mBPI-sf) "Worst Pain Score" <sup>[36]</sup> |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------|

End point description:

The mBPI-sf is a 11-item instrument used as a multiple-item measure of cancer pain intensity ranging from 0 (no pain or does not interfere) to 10 (pain as bad as you can imagine or completely interferes). Time to first worsening of the mBPI-sf "worst pain score" (TWP) was defined as the time from the date of randomization to the first date of either a "worst pain" score increase of greater than or equal to ( $\geq$ ) 2 points from baseline or an analgesic drug class increase of  $\geq 1$  level. If the patient has not worsened by either of these criteria, TWP was censored for analysis on the last date the mBPI-sf was administered.

Analysis Population Description: Phase 2: All randomized participants who had baseline and at least one post-baseline assessment (including the censored participants). Number of participants censored in Olaratumab+Gemcitabine+Docetaxel (Olaratumab-naive=30, Olaratumab pretreated=17), Placebo+Gemcitabine+Docetaxel(Olaratumab-naive=23, Olaratumab pretreated=8).

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

End point timeframe:

Baseline to Follow-up (Up To 24 Months)

Notes:

[36] - 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: Outcome reporting is only for Phase 2 participants.

| End point values                 | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab pretreated) |
|----------------------------------|-----------------------------------------------------------|----------------------------------------------------------------|--------------------------------------------------------|-------------------------------------------------------------|
| Subject group type               | Reporting group                                           | Reporting group                                                | Reporting group                                        | Reporting group                                             |
| Number of subjects analysed      | 68                                                        | 41                                                             | 71                                                     | 34                                                          |
| Units: Months                    |                                                           |                                                                |                                                        |                                                             |
| median (confidence interval 95%) | 3.61 (2.66 to 8.57)                                       | 3.15 (1.41 to 7.62)                                            | 2.27 (1.41 to 6.54)                                    | 2.20 (0.76 to 3.02)                                         |

## Statistical analyses

|                            |                                                                                                                    |
|----------------------------|--------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title | Statistical analysis 1                                                                                             |
| Comparison groups          | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) v Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) |

|                                         |                         |
|-----------------------------------------|-------------------------|
| Number of subjects included in analysis | 139                     |
| Analysis specification                  | Pre-specified           |
| Analysis type                           | superiority             |
| P-value                                 | = 0.073 <sup>[37]</sup> |
| Method                                  | Logrank                 |
| Parameter estimate                      | Hazard ratio (HR)       |
| Point estimate                          | 0.661                   |
| Confidence interval                     |                         |
| level                                   | 95 %                    |
| sides                                   | 2-sided                 |
| lower limit                             | 0.419                   |
| upper limit                             | 1.041                   |

Notes:

[37] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

|                                         |                                                                                                                     |
|-----------------------------------------|---------------------------------------------------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 2                                                                                              |
| Comparison groups                       | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) v<br>Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab |
| Number of subjects included in analysis | 75                                                                                                                  |
| Analysis specification                  | Pre-specified                                                                                                       |
| Analysis type                           | superiority                                                                                                         |
| P-value                                 | = 0.225 <sup>[38]</sup>                                                                                             |
| Method                                  | Logrank                                                                                                             |
| Parameter estimate                      | Hazard ratio (HR)                                                                                                   |
| Point estimate                          | 0.703                                                                                                               |
| Confidence interval                     |                                                                                                                     |
| level                                   | 95 %                                                                                                                |
| sides                                   | 2-sided                                                                                                             |
| lower limit                             | 0.395                                                                                                               |
| upper limit                             | 1.253                                                                                                               |

Notes:

[38] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

### **Secondary: Phase 2: Time to First Worsening of Symptom Burden on the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) - Symptom Scales.**

|                 |                                                                                                                                                                                                              |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Phase 2: Time to First Worsening of Symptom Burden on the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) - Symptom Scales. <sup>[39]</sup> |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

The EORTC QLQ-C30 is a self-reported general cancer instrument consisting of 30 items covered by 1 of 3 dimensions: global health status/quality of life(2 items), functional scales(15 items addressing either physical,role,emotional,cognitive,or social functioning), symptom scales (13 items addressing either fatigue,nausea/vomiting,pain,dyspnoea,insomnia,appetite loss,constipation,diarrhoea,or financial impact). Time to first worsening of Symptom Burden was the time from randomization to the first observation of worsening on symptom scales (i.e.,) increase of at least 10 points from baseline. For symptom scales, a linear transformation was used to obtain total score ranging from 0 to 100, a high score represents a high level of symptomatology or problems.

Analysis Population Description: Phase 2: All randomized participants who had baseline and at least one post-baseline assessment.

9999=N/A, There were not enough events to estimate the median/upper confidence limit, as applicable.

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

End point timeframe:

Baseline to Follow-up (Up to 33 months)

Notes:

[39] - 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: Outcome reporting is only for Phase 2 participants.

| End point values                 | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab pretreated) |
|----------------------------------|-----------------------------------------------------------|----------------------------------------------------------------|--------------------------------------------------------|-------------------------------------------------------------|
| Subject group type               | Reporting group                                           | Reporting group                                                | Reporting group                                        | Reporting group                                             |
| Number of subjects analysed      | 75 <sup>[40]</sup>                                        | 45 <sup>[41]</sup>                                             | 78 <sup>[42]</sup>                                     | 41 <sup>[43]</sup>                                          |
| Units: Months                    |                                                           |                                                                |                                                        |                                                             |
| median (confidence interval 95%) |                                                           |                                                                |                                                        |                                                             |
| Fatigue                          | 0.95 (0.76 to 1.12)                                       | 0.85 (0.72 to 1.41)                                            | 0.95 (0.76 to 1.45)                                    | 0.76 (0.72 to 1.84)                                         |
| Nausea and vomiting              | 3.78 (2.14 to 9999)                                       | 3.98 (1.41 to 9999)                                            | 2.46 (0.99 to 13.34)                                   | 13.17 (1.64 to 9999)                                        |
| Pain                             | 4.67 (2.33 to 9.53)                                       | 2.43 (1.41 to 8.77)                                            | 0.99 (0.79 to 2.76)                                    | 3.06 (0.76 to 5.55)                                         |
| Dyspnoea                         | 2.14 (1.51 to 3.06)                                       | 2.33 (1.45 to 14.09)                                           | 2.14 (1.48 to 2.86)                                    | 2.79 (1.45 to 8.05)                                         |
| Insomnia                         | 5.32 (2.33 to 7.72)                                       | 1.91 (1.41 to 6.47)                                            | 4.24 (1.48 to 16.82)                                   | 5.09 (1.45 to 9999)                                         |
| Appetite loss                    | 1.12 (0.82 to 2.14)                                       | 1.41 (0.85 to 3.52)                                            | 2.56 (1.64 to 3.98)                                    | 1.97 (1.38 to 4.04)                                         |
| Constipation                     | 3.25 (2.14 to 5.98)                                       | 4.63 (1.91 to 12.91)                                           | 2.86 (1.48 to 9999)                                    | 3.81 (1.97 to 9999)                                         |
| Diarrhoea                        | 1.41 (0.99 to 3.68)                                       | 3.55 (1.41 to 6.05)                                            | 1.81 (1.41 to 4.24)                                    | 3.52 (1.97 to 9999)                                         |
| Financial difficulties           | 9999 (5.32 to 9999)                                       | 7.29 (2.33 to 7.85)                                            | 7.66 (3.29 to 9999)                                    | 9999 (3.94 to 9999)                                         |

Notes:

[40] - Nausea/vomiting,Dyspnoea=74, Pain,Constipation,Appetite loss=73, Insomnia=68,Financial difficulty=67

[41] - Fatigue,Nausea&vomiting,Pain,Constipation,Diarrhoea=44, Financial,Dyspnoea=43,Insomnia=41

[42] - Constipation,Fatigue,Pain=77,Insomnia=74,Appetite loss=76,Diarrhoea=80,Financial difficulty=71

[43] - Fatigue,Dyspnoea,=39,Pain,Financial difficulty=35,Insomnia=38,Appetite loss=37, Constipation=40

## Statistical analyses

| Statistical analysis title        | Statistical analysis 1                                                                                             |
|-----------------------------------|--------------------------------------------------------------------------------------------------------------------|
| Statistical analysis description: |                                                                                                                    |
| Fatigue                           |                                                                                                                    |
| Comparison groups                 | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) v Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) |

|                                         |                             |
|-----------------------------------------|-----------------------------|
| Number of subjects included in analysis | 153                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | superiority <sup>[44]</sup> |
| P-value                                 | = 0.332 <sup>[45]</sup>     |
| Method                                  | Logrank                     |
| Parameter estimate                      | Hazard ratio (HR)           |
| Point estimate                          | 1.213                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.834                       |
| upper limit                             | 1.764                       |

Notes:

[44] - Fatigue

[45] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

|                                         |                                                                                                                    |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 2                                                                                             |
| Statistical analysis description:       |                                                                                                                    |
| Nausea and vomiting                     |                                                                                                                    |
| Comparison groups                       | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) v Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) |
| Number of subjects included in analysis | 153                                                                                                                |
| Analysis specification                  | Pre-specified                                                                                                      |
| Analysis type                           | superiority <sup>[46]</sup>                                                                                        |
| P-value                                 | = 0.389 <sup>[47]</sup>                                                                                            |
| Method                                  | Logrank                                                                                                            |
| Parameter estimate                      | Hazard ratio (HR)                                                                                                  |
| Point estimate                          | 0.813                                                                                                              |
| Confidence interval                     |                                                                                                                    |
| level                                   | 95 %                                                                                                               |
| sides                                   | 2-sided                                                                                                            |
| lower limit                             | 0.514                                                                                                              |
| upper limit                             | 1.287                                                                                                              |

Notes:

[46] - Nausea and vomiting

[47] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

|                                         |                                                                                                                    |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 3                                                                                             |
| Statistical analysis description:       |                                                                                                                    |
| Pain                                    |                                                                                                                    |
| Comparison groups                       | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) v Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) |
| Number of subjects included in analysis | 153                                                                                                                |
| Analysis specification                  | Pre-specified                                                                                                      |
| Analysis type                           | superiority <sup>[48]</sup>                                                                                        |
| P-value                                 | = 0.02 <sup>[49]</sup>                                                                                             |
| Method                                  | Logrank                                                                                                            |
| Parameter estimate                      | Hazard ratio (HR)                                                                                                  |
| Point estimate                          | 0.598                                                                                                              |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.386   |
| upper limit         | 0.926   |

Notes:

[48] - Pain

[49] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

|                                         |                                                                                                                    |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 4                                                                                             |
| Statistical analysis description:       |                                                                                                                    |
| Dyspnoea                                |                                                                                                                    |
| Comparison groups                       | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) v Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) |
| Number of subjects included in analysis | 153                                                                                                                |
| Analysis specification                  | Pre-specified                                                                                                      |
| Analysis type                           | superiority <sup>[50]</sup>                                                                                        |
| P-value                                 | = 0.821 <sup>[51]</sup>                                                                                            |
| Method                                  | Logrank                                                                                                            |
| Parameter estimate                      | Hazard ratio (HR)                                                                                                  |
| Point estimate                          | 0.947                                                                                                              |
| Confidence interval                     |                                                                                                                    |
| level                                   | 95 %                                                                                                               |
| sides                                   | 2-sided                                                                                                            |
| lower limit                             | 0.622                                                                                                              |
| upper limit                             | 1.442                                                                                                              |

Notes:

[50] - Dyspnoea

[51] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

|                                         |                                                                                                                    |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 5                                                                                             |
| Statistical analysis description:       |                                                                                                                    |
| Insomnia                                |                                                                                                                    |
| Comparison groups                       | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) v Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) |
| Number of subjects included in analysis | 153                                                                                                                |
| Analysis specification                  | Pre-specified                                                                                                      |
| Analysis type                           | superiority <sup>[52]</sup>                                                                                        |
| P-value                                 | = 0.812 <sup>[53]</sup>                                                                                            |
| Method                                  | Logrank                                                                                                            |
| Parameter estimate                      | Hazard ratio (HR)                                                                                                  |
| Point estimate                          | 0.931                                                                                                              |
| Confidence interval                     |                                                                                                                    |
| level                                   | 95 %                                                                                                               |
| sides                                   | 2-sided                                                                                                            |
| lower limit                             | 0.574                                                                                                              |
| upper limit                             | 1.509                                                                                                              |

Notes:

[52] - Insomnia

[53] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

| Statistical analysis title              | Statistical analysis 6                                                                                             |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------|
| Statistical analysis description:       |                                                                                                                    |
| Appetite loss                           |                                                                                                                    |
| Comparison groups                       | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) v Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) |
| Number of subjects included in analysis | 153                                                                                                                |
| Analysis specification                  | Pre-specified                                                                                                      |
| Analysis type                           | superiority <sup>[54]</sup>                                                                                        |
| P-value                                 | = 0.162 <sup>[55]</sup>                                                                                            |
| Method                                  | Logrank                                                                                                            |
| Parameter estimate                      | Hazard ratio (HR)                                                                                                  |
| Point estimate                          | 1.355                                                                                                              |
| Confidence interval                     |                                                                                                                    |
| level                                   | 95 %                                                                                                               |
| sides                                   | 2-sided                                                                                                            |
| lower limit                             | 0.893                                                                                                              |
| upper limit                             | 2.055                                                                                                              |

Notes:

[54] - Appetite loss

[55] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

| Statistical analysis title              | Statistical analysis 7                                                                                             |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------|
| Statistical analysis description:       |                                                                                                                    |
| Constipation                            |                                                                                                                    |
| Comparison groups                       | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) v Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) |
| Number of subjects included in analysis | 153                                                                                                                |
| Analysis specification                  | Pre-specified                                                                                                      |
| Analysis type                           | superiority <sup>[56]</sup>                                                                                        |
| P-value                                 | = 0.619 <sup>[57]</sup>                                                                                            |
| Method                                  | Logrank                                                                                                            |
| Parameter estimate                      | Hazard ratio (HR)                                                                                                  |
| Point estimate                          | 0.881                                                                                                              |
| Confidence interval                     |                                                                                                                    |
| level                                   | 95 %                                                                                                               |
| sides                                   | 2-sided                                                                                                            |
| lower limit                             | 0.55                                                                                                               |
| upper limit                             | 1.413                                                                                                              |

Notes:

[56] - Constipation

[57] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

| Statistical analysis title        | Statistical analysis 8                                                                                             |
|-----------------------------------|--------------------------------------------------------------------------------------------------------------------|
| Statistical analysis description: |                                                                                                                    |
| Diarrhoea                         |                                                                                                                    |
| Comparison groups                 | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) v Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) |

|                                         |                             |
|-----------------------------------------|-----------------------------|
|                                         | naive)                      |
| Number of subjects included in analysis | 153                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | superiority <sup>[58]</sup> |
| P-value                                 | = 0.597 <sup>[59]</sup>     |
| Method                                  | Logrank                     |
| Parameter estimate                      | Hazard ratio (HR)           |
| Point estimate                          | 1.134                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.746                       |
| upper limit                             | 1.724                       |

Notes:

[58] - Diarrhoea

[59] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

|                                         |                                                                                                                    |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 9                                                                                             |
| Statistical analysis description:       |                                                                                                                    |
| Financial difficulties                  |                                                                                                                    |
| Comparison groups                       | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) v Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) |
| Number of subjects included in analysis | 153                                                                                                                |
| Analysis specification                  | Pre-specified                                                                                                      |
| Analysis type                           | superiority <sup>[60]</sup>                                                                                        |
| P-value                                 | = 0.38 <sup>[61]</sup>                                                                                             |
| Method                                  | Logrank                                                                                                            |
| Parameter estimate                      | Hazard ratio (HR)                                                                                                  |
| Point estimate                          | 0.766                                                                                                              |
| Confidence interval                     |                                                                                                                    |
| level                                   | 95 %                                                                                                               |
| sides                                   | 2-sided                                                                                                            |
| lower limit                             | 0.425                                                                                                              |
| upper limit                             | 1.381                                                                                                              |

Notes:

[60] - Financial difficulties

[61] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

|                                         |                                                                                                                  |
|-----------------------------------------|------------------------------------------------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 10                                                                                          |
| Statistical analysis description:       |                                                                                                                  |
| Fatigue                                 |                                                                                                                  |
| Comparison groups                       | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) v Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab |
| Number of subjects included in analysis | 86                                                                                                               |
| Analysis specification                  | Pre-specified                                                                                                    |
| Analysis type                           | superiority <sup>[62]</sup>                                                                                      |
| P-value                                 | = 0.877 <sup>[63]</sup>                                                                                          |
| Method                                  | Logrank                                                                                                          |
| Parameter estimate                      | Hazard ratio (HR)                                                                                                |
| Point estimate                          | 1.046                                                                                                            |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.635   |
| upper limit         | 1.723   |

Notes:

[62] - Fatigue

[63] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

|                                         |                                                                                                                     |
|-----------------------------------------|---------------------------------------------------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 11                                                                                             |
| Statistical analysis description:       |                                                                                                                     |
| Nausea and vomiting                     |                                                                                                                     |
| Comparison groups                       | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) v<br>Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab |
| Number of subjects included in analysis | 86                                                                                                                  |
| Analysis specification                  | Pre-specified                                                                                                       |
| Analysis type                           | superiority <sup>[64]</sup>                                                                                         |
| P-value                                 | = 0.791 <sup>[65]</sup>                                                                                             |
| Method                                  | Logrank                                                                                                             |
| Parameter estimate                      | Hazard ratio (HR)                                                                                                   |
| Point estimate                          | 1.102                                                                                                               |
| Confidence interval                     |                                                                                                                     |
| level                                   | 95 %                                                                                                                |
| sides                                   | 2-sided                                                                                                             |
| lower limit                             | 0.568                                                                                                               |
| upper limit                             | 2.139                                                                                                               |

Notes:

[64] - Nausea and vomiting

[65] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

|                                         |                                                                                                                     |
|-----------------------------------------|---------------------------------------------------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 12                                                                                             |
| Statistical analysis description:       |                                                                                                                     |
| Pain                                    |                                                                                                                     |
| Comparison groups                       | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab pretreated) v<br>Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab |
| Number of subjects included in analysis | 86                                                                                                                  |
| Analysis specification                  | Pre-specified                                                                                                       |
| Analysis type                           | superiority <sup>[66]</sup>                                                                                         |
| P-value                                 | = 0.487 <sup>[67]</sup>                                                                                             |
| Method                                  | Logrank                                                                                                             |
| Parameter estimate                      | Hazard ratio (HR)                                                                                                   |
| Point estimate                          | 0.81                                                                                                                |
| Confidence interval                     |                                                                                                                     |
| level                                   | 95 %                                                                                                                |
| sides                                   | 2-sided                                                                                                             |
| lower limit                             | 0.454                                                                                                               |
| upper limit                             | 1.443                                                                                                               |

Notes:

[66] - Pain

[67] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

| Statistical analysis title              | Statistical analysis 13                                                                                          |
|-----------------------------------------|------------------------------------------------------------------------------------------------------------------|
| Statistical analysis description:       |                                                                                                                  |
| Dyspnoea                                |                                                                                                                  |
| Comparison groups                       | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) v Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab |
| Number of subjects included in analysis | 86                                                                                                               |
| Analysis specification                  | Pre-specified                                                                                                    |
| Analysis type                           | superiority <sup>[68]</sup>                                                                                      |
| P-value                                 | = 0.976 <sup>[69]</sup>                                                                                          |
| Method                                  | Logrank                                                                                                          |
| Parameter estimate                      | Hazard ratio (HR)                                                                                                |
| Point estimate                          | 1.014                                                                                                            |
| Confidence interval                     |                                                                                                                  |
| level                                   | 95 %                                                                                                             |
| sides                                   | 2-sided                                                                                                          |
| lower limit                             | 0.556                                                                                                            |
| upper limit                             | 1.85                                                                                                             |

Notes:

[68] - Dyspnoea

[69] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

| Statistical analysis title              | Statistical analysis 14                                                                                          |
|-----------------------------------------|------------------------------------------------------------------------------------------------------------------|
| Statistical analysis description:       |                                                                                                                  |
| Insomnia                                |                                                                                                                  |
| Comparison groups                       | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) v Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab |
| Number of subjects included in analysis | 86                                                                                                               |
| Analysis specification                  | Pre-specified                                                                                                    |
| Analysis type                           | superiority <sup>[70]</sup>                                                                                      |
| P-value                                 | = 0.111 <sup>[71]</sup>                                                                                          |
| Method                                  | Logrank                                                                                                          |
| Parameter estimate                      | Hazard ratio (HR)                                                                                                |
| Point estimate                          | 1.694                                                                                                            |
| Confidence interval                     |                                                                                                                  |
| level                                   | 95 %                                                                                                             |
| sides                                   | 2-sided                                                                                                          |
| lower limit                             | 0.882                                                                                                            |
| upper limit                             | 3.25                                                                                                             |

Notes:

[70] - Insomnia

[71] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

| Statistical analysis title        | Statistical analysis 15                                                                               |
|-----------------------------------|-------------------------------------------------------------------------------------------------------|
| Statistical analysis description: |                                                                                                       |
| Appetite loss                     |                                                                                                       |
| Comparison groups                 | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) v Phase2:Placebo+Gemcitabine+Docetaxel |

|                                         |                             |
|-----------------------------------------|-----------------------------|
|                                         | (Olaratumab pretreated)     |
| Number of subjects included in analysis | 86                          |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | superiority <sup>[72]</sup> |
| P-value                                 | = 0.76 <sup>[73]</sup>      |
| Method                                  | Logrank                     |
| Parameter estimate                      | Hazard ratio (HR)           |
| Point estimate                          | 1.108                       |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.62                        |
| upper limit                             | 1.979                       |

Notes:

[72] - Appetite loss

[73] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

|                                         |                                                                                                                     |
|-----------------------------------------|---------------------------------------------------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 16                                                                                             |
| Statistical analysis description:       |                                                                                                                     |
| Constipation                            |                                                                                                                     |
| Comparison groups                       | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) v<br>Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab |
| Number of subjects included in analysis | 86                                                                                                                  |
| Analysis specification                  | Pre-specified                                                                                                       |
| Analysis type                           | superiority <sup>[74]</sup>                                                                                         |
| P-value                                 | = 0.747 <sup>[75]</sup>                                                                                             |
| Method                                  | Logrank                                                                                                             |
| Parameter estimate                      | Hazard ratio (HR)                                                                                                   |
| Point estimate                          | 1.119                                                                                                               |
| Confidence interval                     |                                                                                                                     |
| level                                   | 95 %                                                                                                                |
| sides                                   | 2-sided                                                                                                             |
| lower limit                             | 0.586                                                                                                               |
| upper limit                             | 2.135                                                                                                               |

Notes:

[74] - Constipation

[75] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

|                                         |                                                                                                                     |
|-----------------------------------------|---------------------------------------------------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 17                                                                                             |
| Statistical analysis description:       |                                                                                                                     |
| Diarrhoea                               |                                                                                                                     |
| Comparison groups                       | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) v<br>Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab |
| Number of subjects included in analysis | 86                                                                                                                  |
| Analysis specification                  | Pre-specified                                                                                                       |
| Analysis type                           | superiority <sup>[76]</sup>                                                                                         |
| P-value                                 | = 0.33 <sup>[77]</sup>                                                                                              |
| Method                                  | Logrank                                                                                                             |
| Parameter estimate                      | Hazard ratio (HR)                                                                                                   |
| Point estimate                          | 1.367                                                                                                               |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.726   |
| upper limit         | 2.576   |

Notes:

[76] - Diarrhoea

[77] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

|                                         |                                                                                                                     |
|-----------------------------------------|---------------------------------------------------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 18                                                                                             |
| Statistical analysis description:       |                                                                                                                     |
| Financial difficulties                  |                                                                                                                     |
| Comparison groups                       | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) v<br>Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab |
| Number of subjects included in analysis | 86                                                                                                                  |
| Analysis specification                  | Pre-specified                                                                                                       |
| Analysis type                           | superiority <sup>[78]</sup>                                                                                         |
| P-value                                 | = 0.411 <sup>[79]</sup>                                                                                             |
| Method                                  | Logrank                                                                                                             |
| Parameter estimate                      | Hazard ratio (HR)                                                                                                   |
| Point estimate                          | 1.373                                                                                                               |
| Confidence interval                     |                                                                                                                     |
| level                                   | 95 %                                                                                                                |
| sides                                   | 2-sided                                                                                                             |
| lower limit                             | 0.636                                                                                                               |
| upper limit                             | 2.965                                                                                                               |

Notes:

[78] - Financial difficulties

[79] - Stratified by number of prior systemic therapies for locally advanced or metastatic disease (0 vs  $\geq 1$ ), histological tumor type (leiomyosarcoma vs non-leiomyosarcoma), and ECOG PS (0 vs1).

## Secondary: Phase 2: Health Status on the EuroQol 5-Dimension 5 Level (EQ-5D-5L)

|                 |                                                                                      |
|-----------------|--------------------------------------------------------------------------------------|
| End point title | Phase 2: Health Status on the EuroQol 5-Dimension 5 Level (EQ-5D-5L) <sup>[80]</sup> |
|-----------------|--------------------------------------------------------------------------------------|

End point description:

The EQ-5D-5L is a standardized instrument for use as a measure of self-reported health status. Five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) of health status are each assessed with 5 response options (1=no problem, 2=slight, 3=moderate, 4=severe, and 5=extreme problem) and scored as a composite index which were anchored on a scale of 0 to 1 with a higher score representing better health status. Additionally, current health status was assessed on a visual analogue scale (VAS) ranging from 0 to 100 with a higher score representing better health status.

Analysis Population Description: Phase 2: All randomized participants who completed EQ-5D-5L.

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

End point timeframe:

Cycle 1 (Day 1), Follow-up (Up to 38 Months)

Notes:

[80] - 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: Outcome reporting is only for Phase 2 participants.

| End point values                                    | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab pretreated) |
|-----------------------------------------------------|-----------------------------------------------------------|----------------------------------------------------------------|--------------------------------------------------------|-------------------------------------------------------------|
| Subject group type                                  | Reporting group                                           | Reporting group                                                | Reporting group                                        | Reporting group                                             |
| Number of subjects analysed                         | 71 <sup>[81]</sup>                                        | 42 <sup>[82]</sup>                                             | 75 <sup>[83]</sup>                                     | 35 <sup>[84]</sup>                                          |
| Units: score on a scale                             |                                                           |                                                                |                                                        |                                                             |
| arithmetic mean (standard deviation)                |                                                           |                                                                |                                                        |                                                             |
| EQ-5D-5L - Index Value [Cycle 1 (Day 1)]            | 0.80 (± 0.17)                                             | 0.83 (± 0.15)                                                  | 0.81 (± 0.17)                                          | 0.83 (± 0.22)                                               |
| EQ-5D-5L - VAS Score [Cycle 1 (Day 1)]              | 73.5 (± 18.9)                                             | 76.2 (± 19.6)                                                  | 72.7 (± 18.1)                                          | 70.3 (± 23.8)                                               |
| EQ-5D-5L - Index Value [Follow-up (Up to 38 Months) | 0.74 (± 0.21)                                             | 0.80 (± 0.20)                                                  | 0.71 (± 0.26)                                          | 0.76 (± 0.24)                                               |
| EQ-5D-5L - VAS Score [Follow-up (Up to 38 Months)]  | 68.7 (± 16.5)                                             | 74.8 (± 21.8)                                                  | 63.0 (± 21.6)                                          | 70.8 (± 24.2)                                               |

Notes:

[81] - EQ-5D-5L- Index Value, VAS Score Follow-up (Up to 38 Months) = 42 Participants

[82] - EQ-5D-5L- Index Value Cycle 1 (Day 1) = 39; Index Value, VAS Score Follow-up (Up to 38 Months) = 26

[83] - EQ-5D-5L- Index Value Cycle 1 (Day 1) = 74; Index Value, VAS Score Follow-up (Up to 38 Months) = 50

[84] - EQ-5D-5L- Index Value, VAS Score Follow-up (Up to 38 Months) = 25

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 2: Number of Participants With Treatment Emergent Anti-Olaratumab Antibodies

|                 |                                                                                                    |
|-----------------|----------------------------------------------------------------------------------------------------|
| End point title | Phase 2: Number of Participants With Treatment Emergent Anti-Olaratumab Antibodies <sup>[85]</sup> |
|-----------------|----------------------------------------------------------------------------------------------------|

End point description:

Phase 2: Analysis Population Description: All randomized participants who received at least one dose of Olaratumab and had evaluable immunogenicity data.

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

End point timeframe:

Baseline through Follow-Up (Up to 38 Months)

Notes:

[85] - 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: Outcome reporting is only for Phase 2 participants.

| End point values            | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) |  |  |
|-----------------------------|-----------------------------------------------------------|----------------------------------------------------------------|--|--|
| Subject group type          | Reporting group                                           | Reporting group                                                |  |  |
| Number of subjects analysed | 77                                                        | 43                                                             |  |  |
| Units: Participants         | 0                                                         | 0                                                              |  |  |

## Statistical analyses

---

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline to Follow-up (Up To 38 Months)

Adverse event reporting additional description:

Phase 1b/2: All participants who received at least one dose of study drug. Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 21.0 |
|--------------------|------|

### Reporting groups

|                       |                                                              |
|-----------------------|--------------------------------------------------------------|
| Reporting group title | Phase1b:Cohort1: 15mg/kg<br>Olaratumab+Gemcitabine+Docetaxel |
|-----------------------|--------------------------------------------------------------|

Reporting group description:

Participants received intravenous infusions of olaratumab 15 milligrams per kilogram (mg/kg) on days 1, 8 plus gemcitabine 900 milligrams per meter square (mg/m<sup>2</sup>) on days 1, 8 plus docetaxel 75 mg/m<sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

|                       |                                                                  |
|-----------------------|------------------------------------------------------------------|
| Reporting group title | Phase1b:Cohort2Expand:20mg/kgOlaratumab+Gemcitabine+D<br>ocetaxe |
|-----------------------|------------------------------------------------------------------|

Reporting group description:

Following a protocol amendment, additional participants were enrolled into this group to confirm the safety of the 20 mg/kg dose level prior to opening the Phase 2. Participants received intravenous infusions of olaratumab 20 milligrams per kilogram (mg/kg) on days 1, 8 plus gemcitabine 900 milligrams per meter square (mg/m<sup>2</sup>) on days 1, 8 plus docetaxel 75 mg/m<sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

|                       |                                                              |
|-----------------------|--------------------------------------------------------------|
| Reporting group title | Phase1b:Cohort2: 20mg/kg<br>Olaratumab+Gemcitabine+Docetaxel |
|-----------------------|--------------------------------------------------------------|

Reporting group description:

Participants received intravenous infusions of olaratumab 20 mg/kg on days 1, 8 in combination with gemcitabine 900 mg/m<sup>2</sup> on days 1, 8 and docetaxel 75 mg/m<sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

|                       |                                                               |
|-----------------------|---------------------------------------------------------------|
| Reporting group title | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-<br>naive) |
|-----------------------|---------------------------------------------------------------|

Reporting group description:

This cohort included participants who never received olaratumab prior to enrollment. Participants received intravenous infusions of olaratumab loading dose 20 mg/kg on days 1, 8 of cycle 1 followed by 15 mg/kg on days 1, 8 of all subsequent cycles in combination with gemcitabine 900 mg/m<sup>2</sup> on days 1, 8 and docetaxel 75 mg/m<sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

|                       |                                                                   |
|-----------------------|-------------------------------------------------------------------|
| Reporting group title | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab<br>Pretreated) |
|-----------------------|-------------------------------------------------------------------|

Reporting group description:

This cohort included participants who received commercially available olaratumab prior to enrollment. Participants received intravenous infusions of olaratumab loading dose 20 mg/kg on days 1, 8 of cycle 1 followed by 15 mg/kg on days 1, 8 of all subsequent cycles in combination with gemcitabine 900 mg/m<sup>2</sup> on days 1, 8 and docetaxel 75 mg/m<sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

|                       |                                                        |
|-----------------------|--------------------------------------------------------|
| Reporting group title | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) |
|-----------------------|--------------------------------------------------------|

Reporting group description:

This cohort included participants who never received olaratumab prior to enrollment. Participants received intravenous infusions of placebo on days 1, 8 in combination with gemcitabine 900 mg/m<sup>2</sup> on days 1, 8 and docetaxel 75 mg/m<sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

|                       |                                                 |
|-----------------------|-------------------------------------------------|
| Reporting group title | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab |
|-----------------------|-------------------------------------------------|

## Reporting group description:

This cohort included participants who received commercially available olaratumab prior to enrollment. Participants received intravenous infusions of placebo on days 1, 8 in combination with gemcitabine 900 mg/m<sup>2</sup> on days 1, 8 and docetaxel 75 mg/m<sup>2</sup> on day 8 of a 21-day cycle until disease progression, unacceptable toxicity, death, or other discontinuation criteria were met.

| <b>Serious adverse events</b>                                       | Phase1b:Cohort1:<br>15mg/kg<br>Olaratumab+Gemcitabine+Docetaxel | Phase1b:Cohort2Exp<br>and:20mg/kgOlaratumab+Gemcitabine+Docetaxel | Phase1b:Cohort2:<br>20mg/kg<br>Olaratumab+Gemcitabine+Docetaxel |
|---------------------------------------------------------------------|-----------------------------------------------------------------|-------------------------------------------------------------------|-----------------------------------------------------------------|
| Total subjects affected by serious adverse events                   |                                                                 |                                                                   |                                                                 |
| subjects affected / exposed                                         | 6 / 21 (28.57%)                                                 | 9 / 15 (60.00%)                                                   | 9 / 18 (50.00%)                                                 |
| number of deaths (all causes)                                       | 15                                                              | 12                                                                | 11                                                              |
| number of deaths resulting from adverse events                      | 0                                                               | 0                                                                 | 0                                                               |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                                 |                                                                   |                                                                 |
| tumour haemorrhage                                                  |                                                                 |                                                                   |                                                                 |
| alternative dictionary used: MedDRA 21.0                            |                                                                 |                                                                   |                                                                 |
| subjects affected / exposed                                         | 0 / 21 (0.00%)                                                  | 0 / 15 (0.00%)                                                    | 0 / 18 (0.00%)                                                  |
| occurrences causally related to treatment / all                     | 0 / 0                                                           | 0 / 0                                                             | 0 / 0                                                           |
| deaths causally related to treatment / all                          | 0 / 0                                                           | 0 / 0                                                             | 0 / 0                                                           |
| Vascular disorders                                                  |                                                                 |                                                                   |                                                                 |
| capillary leak syndrome                                             |                                                                 |                                                                   |                                                                 |
| alternative dictionary used: MedDRA 21.0                            |                                                                 |                                                                   |                                                                 |
| subjects affected / exposed                                         | 0 / 21 (0.00%)                                                  | 0 / 15 (0.00%)                                                    | 0 / 18 (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                                                           |
| deep vein thrombosis                                                |                                                                 |                                                                   |                                                                 |
| alternative dictionary used: MedDRA 21.0                            |                                                                 |                                                                   |                                                                 |
| subjects affected / exposed                                         | 0 / 21 (0.00%)                                                  | 0 / 15 (0.00%)                                                    | 0 / 18 (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                                                           |
| embolism                                                            |                                                                 |                                                                   |                                                                 |
| alternative dictionary used: MedDRA 21.0                            |                                                                 |                                                                   |                                                                 |
| subjects affected / exposed                                         | 0 / 21 (0.00%)                                                  | 0 / 15 (0.00%)                                                    | 0 / 18 (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                                                           |

|                                                         |                |                |                |  |
|---------------------------------------------------------|----------------|----------------|----------------|--|
| haematoma                                               |                |                |                |  |
| alternative dictionary used:<br>MedDRA 21.0             |                |                |                |  |
| subjects affected / exposed                             | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |  |
| haemorrhage                                             |                |                |                |  |
| alternative dictionary used:<br>MedDRA 21.0             |                |                |                |  |
| subjects affected / exposed                             | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |  |
| hypotension                                             |                |                |                |  |
| alternative dictionary used:<br>MedDRA 21.0             |                |                |                |  |
| subjects affected / exposed                             | 1 / 21 (4.76%) | 0 / 15 (0.00%) | 0 / 18 (0.00%) |  |
| occurrences causally related to<br>treatment / all      | 0 / 1          | 0 / 0          | 0 / 0          |  |
| deaths causally related to<br>treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |  |
| peripheral artery stenosis                              |                |                |                |  |
| alternative dictionary used:<br>MedDRA 21.0             |                |                |                |  |
| subjects affected / exposed                             | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |  |
| General disorders and administration<br>site conditions |                |                |                |  |
| chest pain                                              |                |                |                |  |
| alternative dictionary used:<br>MedDRA 21.0             |                |                |                |  |
| subjects affected / exposed                             | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |  |
| fatigue                                                 |                |                |                |  |
| alternative dictionary used:<br>MedDRA 21.0             |                |                |                |  |
| subjects affected / exposed                             | 0 / 21 (0.00%) | 1 / 15 (6.67%) | 0 / 18 (0.00%) |  |
| occurrences causally related to<br>treatment / all      | 0 / 0          | 1 / 1          | 0 / 0          |  |
| deaths causally related to<br>treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |  |
| influenza like illness                                  |                |                |                |  |
| alternative dictionary used:<br>MedDRA 21.0             |                |                |                |  |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| mucosal inflammation                            |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| non-cardiac chest pain                          |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| oedema                                          |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| oedema peripheral                               |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| peripheral swelling                             |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| pyrexia                                         |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |

|                                                    |                |                |                |
|----------------------------------------------------|----------------|----------------|----------------|
| sudden death                                       |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 1 / 18 (5.56%) |
| 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 / 1          |
| Immune system disorders                            |                |                |                |
| anaphylactic reaction                              |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| anaphylactic shock                                 |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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 |                |                |                |
| cough                                              |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| dyspnoea                                           |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 1 / 18 (5.56%) |
| 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          |
| epistaxis                                          |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 1 / 15 (6.67%) | 0 / 18 (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          |
| hypoxia                                            |                |                |                |

|                                                    |                |                |                |
|----------------------------------------------------|----------------|----------------|----------------|
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| interstitial lung disease                          |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| pneumonitis                                        |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 1 / 15 (6.67%) | 0 / 18 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 1 / 1          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| pneumothorax                                       |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| pulmonary embolism                                 |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| pulmonary haemorrhage                              |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 1 / 15 (6.67%) | 0 / 18 (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          |
| pulmonary oedema                                   |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |

|                                                                                                     |                |                |                |
|-----------------------------------------------------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                                                                         | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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 failure<br>alternative dictionary used:<br>MedDRA 21.0                                  |                |                |                |
| subjects affected / exposed                                                                         | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all                                                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                                                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Psychiatric disorders<br>confusional state<br>alternative dictionary used:<br>MedDRA 21.0           |                |                |                |
| subjects affected / exposed                                                                         | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| Investigations<br>alanine aminotransferase increased<br>alternative dictionary used:<br>MedDRA 21.0 |                |                |                |
| subjects affected / exposed                                                                         | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| international normalised ratio increased<br>alternative dictionary used:<br>MedDRA 21.0             |                |                |                |
| subjects affected / exposed                                                                         | 0 / 21 (0.00%) | 1 / 15 (6.67%) | 0 / 18 (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          |
| neutrophil count decreased<br>alternative dictionary used:<br>MedDRA 21.0                           |                |                |                |
| subjects affected / exposed                                                                         | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| platelet count decreased<br>alternative dictionary used:<br>MedDRA 21.0                             |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| troponin increased                              |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| white blood cell count decreased                |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| Injury, poisoning and procedural complications  |                |                |                |
| arterial bypass occlusion                       |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 1 / 21 (4.76%) | 0 / 15 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 5          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| fall                                            |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 1 / 15 (6.67%) | 0 / 18 (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          |
| femoral neck fracture                           |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| femur fracture                                  |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| hip fracture                                    |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| infusion related reaction                       |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 1 / 21 (4.76%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| skull fracture                                  |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| Cardiac disorders                               |                |                |                |
| atrial fibrillation                             |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| atrial tachycardia                              |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 1 / 15 (6.67%) | 0 / 18 (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 failure                                 |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| myocardial infarction                           |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1          |
| pericardial effusion                            |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| supraventricular tachycardia                    |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| Nervous system disorders                        |                |                |                |
| dizziness                                       |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| epilepsy                                        |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| facial paralysis                                |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| headache                                        |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| nervous system disorder                         |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| polyneuropathy                                  |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| seizure                                         |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 1 / 21 (4.76%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| spinal cord compression                         |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| syncope                                         |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |

|                                                    |                |                |                |
|----------------------------------------------------|----------------|----------------|----------------|
| Blood and lymphatic system disorders               |                |                |                |
| anaemia                                            |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 1 / 18 (5.56%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| bandaemia                                          |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 1 / 18 (5.56%) |
| 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          |
| febrile neutropenia                                |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 1 / 15 (6.67%) | 1 / 18 (5.56%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 1 / 1          | 1 / 1          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| haemolytic uraemic syndrome                        |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| hypochromic anaemia                                |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| neutropenia                                        |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 1 / 18 (5.56%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| neutrophilia                                       |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| normocytic anaemia                              |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| pancytopenia                                    |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| thrombocytopenia                                |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 1 / 15 (6.67%) | 0 / 18 (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          |
| thrombotic microangiopathy                      |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| Ear and labyrinth disorders                     |                |                |                |
| hypoacusis                                      |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| Gastrointestinal disorders                      |                |                |                |
| abdominal pain                                  |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| constipation                                    |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| diarrhoea                                       |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| enterocolitis                                   |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| gastritis                                       |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| haemorrhoidal haemorrhage                       |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| nausea                                          |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |

|                                                    |                |                |                |
|----------------------------------------------------|----------------|----------------|----------------|
| oesophageal ulcer                                  |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| rectal haemorrhage                                 |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| small intestinal obstruction                       |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 1 / 15 (6.67%) | 0 / 18 (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          |
| stomatitis                                         |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| vomiting                                           |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| Hepatobiliary disorders                            |                |                |                |
| hepatic failure                                    |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| jaundice cholestatic                               |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| Skin and subcutaneous tissue disorders          |                |                |                |
| eczema                                          |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| petechiae                                       |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| Renal and urinary disorders                     |                |                |                |
| acute kidney injury                             |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| renal failure                                   |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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 retention                               |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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 21.0        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| arthritis                                       |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| back pain                                       |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| muscular weakness                               |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| myalgia                                         |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| myositis                                        |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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                     |                |                |                |
| anorectal infection                             |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| appendicitis                                    |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| arthritis infective                             |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| bacteraemia                                     |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| bronchitis                                      |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| campylobacter infection                         |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| cellulitis                                      |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 1 / 21 (4.76%) | 1 / 15 (6.67%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 2 / 4          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|                                                    |                |                |                |  |
|----------------------------------------------------|----------------|----------------|----------------|--|
| clostridium difficile colitis                      |                |                |                |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |  |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |  |
| cystitis                                           |                |                |                |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |  |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |  |
| device related infection                           |                |                |                |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |  |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 1 / 18 (5.56%) |  |
| 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          |  |
| diverticulitis                                     |                |                |                |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |  |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |  |
| erysipelas                                         |                |                |                |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |  |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |  |
| gastrointestinal infection                         |                |                |                |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |  |
| subjects affected / exposed                        | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |  |
| influenza                                          |                |                |                |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |  |

|                                                                                  |                |                |                |
|----------------------------------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                                                      | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| lower respiratory tract infection<br>alternative dictionary used:<br>MedDRA 21.0 |                |                |                |
| subjects affected / exposed                                                      | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| neutropenic sepsis<br>alternative dictionary used:<br>MedDRA 21.0                |                |                |                |
| subjects affected / exposed                                                      | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| pneumonia<br>alternative dictionary used:<br>MedDRA 21.0                         |                |                |                |
| subjects affected / exposed                                                      | 2 / 21 (9.52%) | 0 / 15 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all                                  | 0 / 3          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                                       | 0 / 1          | 0 / 0          | 0 / 0          |
| pneumonia bacterial<br>alternative dictionary used:<br>MedDRA 21.0               |                |                |                |
| subjects affected / exposed                                                      | 1 / 21 (4.76%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| pneumonia viral<br>alternative dictionary used:<br>MedDRA 21.0                   |                |                |                |
| subjects affected / exposed                                                      | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| rectal abscess<br>alternative dictionary used:<br>MedDRA 21.0                    |                |                |                |
| subjects affected / exposed                                                      | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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<br>alternative dictionary used:<br>MedDRA 21.0 |                |                |                |  |
| subjects affected / exposed                                                | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |  |
| sepsis<br>alternative dictionary used:<br>MedDRA 21.0                      |                |                |                |  |
| subjects affected / exposed                                                | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 1 / 18 (5.56%) |  |
| occurrences causally related to<br>treatment / all                         | 0 / 0          | 0 / 0          | 1 / 1          |  |
| deaths causally related to<br>treatment / all                              | 0 / 0          | 0 / 0          | 0 / 0          |  |
| septic shock<br>alternative dictionary used:<br>MedDRA 21.0                |                |                |                |  |
| subjects affected / exposed                                                | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |  |
| skin infection<br>alternative dictionary used:<br>MedDRA 21.0              |                |                |                |  |
| subjects affected / exposed                                                | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |  |
| staphylococcal bacteraemia<br>alternative dictionary used:<br>MedDRA 21.0  |                |                |                |  |
| subjects affected / exposed                                                | 0 / 21 (0.00%) | 1 / 15 (6.67%) | 0 / 18 (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          |  |
| urinary tract infection<br>alternative dictionary used:<br>MedDRA 21.0     |                |                |                |  |
| subjects affected / exposed                                                | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |  |
| viral infection<br>alternative dictionary used:<br>MedDRA 21.0             |                |                |                |  |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders              |                |                |                |
| dehydration                                     |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 0 / 18 (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          |
| hypokalaemia                                    |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>                                       | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab-naive) | Phase2:Olaratumab+Gemcitabine+Docetaxel(Olaratumab Pretreated) | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) |
|---------------------------------------------------------------------|-----------------------------------------------------------|----------------------------------------------------------------|--------------------------------------------------------|
| Total subjects affected by serious adverse events                   |                                                           |                                                                |                                                        |
| subjects affected / exposed                                         | 44 / 81 (54.32%)                                          | 21 / 45 (46.67%)                                               | 38 / 86 (44.19%)                                       |
| number of deaths (all causes)                                       | 54                                                        | 28                                                             | 58                                                     |
| number of deaths resulting from adverse events                      | 0                                                         | 1                                                              | 0                                                      |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                           |                                                                |                                                        |
| tumour haemorrhage                                                  |                                                           |                                                                |                                                        |
| alternative dictionary used: MedDRA 21.0                            |                                                           |                                                                |                                                        |
| subjects affected / exposed                                         | 0 / 81 (0.00%)                                            | 0 / 45 (0.00%)                                                 | 1 / 86 (1.16%)                                         |
| occurrences causally related to treatment / all                     | 0 / 0                                                     | 0 / 0                                                          | 2 / 2                                                  |
| deaths causally related to treatment / all                          | 0 / 0                                                     | 0 / 0                                                          | 0 / 0                                                  |
| Vascular disorders                                                  |                                                           |                                                                |                                                        |
| capillary leak syndrome                                             |                                                           |                                                                |                                                        |
| alternative dictionary used: MedDRA 21.0                            |                                                           |                                                                |                                                        |
| subjects affected / exposed                                         | 0 / 81 (0.00%)                                            | 0 / 45 (0.00%)                                                 | 1 / 86 (1.16%)                                         |
| occurrences causally related to treatment / all                     | 0 / 0                                                     | 0 / 0                                                          | 1 / 1                                                  |
| deaths causally related to treatment / all                          | 0 / 0                                                     | 0 / 0                                                          | 0 / 0                                                  |
| deep vein thrombosis                                                |                                                           |                                                                |                                                        |

|                                                         |                |                |                |
|---------------------------------------------------------|----------------|----------------|----------------|
| alternative dictionary used:<br>MedDRA 21.0             |                |                |                |
| subjects affected / exposed                             | 1 / 81 (1.23%) | 2 / 45 (4.44%) | 1 / 86 (1.16%) |
| occurrences causally related to<br>treatment / all      | 0 / 1          | 0 / 3          | 1 / 1          |
| deaths causally related to<br>treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| embolism                                                |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0             |                |                |                |
| subjects affected / exposed                             | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 1 / 86 (1.16%) |
| occurrences causally related to<br>treatment / all      | 0 / 0          | 0 / 1          | 1 / 1          |
| deaths causally related to<br>treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| haematoma                                               |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0             |                |                |                |
| subjects affected / exposed                             | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to<br>treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| haemorrhage                                             |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0             |                |                |                |
| subjects affected / exposed                             | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to<br>treatment / all      | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| hypotension                                             |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0             |                |                |                |
| subjects affected / exposed                             | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| peripheral artery stenosis                              |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0             |                |                |                |
| subjects affected / exposed                             | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| 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          |
| General disorders and administration<br>site conditions |                |                |                |
| chest pain                                              |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0             |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| fatigue                                         |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 3 / 81 (3.70%) | 1 / 45 (2.22%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all | 3 / 3          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| influenza like illness                          |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| mucosal inflammation                            |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| non-cardiac chest pain                          |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| oedema                                          |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| oedema peripheral                               |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 2 / 81 (2.47%) | 2 / 45 (4.44%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2          | 2 / 2          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|                                                    |                |                |                |
|----------------------------------------------------|----------------|----------------|----------------|
| peripheral swelling                                |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| pyrexia                                            |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 7 / 81 (8.64%) | 2 / 45 (4.44%) | 7 / 86 (8.14%) |
| occurrences causally related to<br>treatment / all | 7 / 10         | 1 / 2          | 4 / 8          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| sudden death                                       |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| Immune system disorders                            |                |                |                |
| anaphylactic reaction                              |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| anaphylactic shock                                 |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| 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, thoracic and mediastinal disorders    |                |                |                |
| cough                                              |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to<br>treatment / all | 1 / 1          | 0 / 0          | 1 / 1          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| dyspnoea                                           |                |                |                |

|                                                    |                |                |                |
|----------------------------------------------------|----------------|----------------|----------------|
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 3 / 81 (3.70%) | 2 / 45 (4.44%) | 4 / 86 (4.65%) |
| occurrences causally related to<br>treatment / all | 2 / 4          | 1 / 2          | 2 / 4          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| epistaxis                                          |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 2 / 86 (2.33%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 1 / 2          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| hypoxia                                            |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| 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          |
| interstitial lung disease                          |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| pneumonitis                                        |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 1 / 81 (1.23%) | 1 / 45 (2.22%) | 2 / 86 (2.33%) |
| occurrences causally related to<br>treatment / all | 1 / 1          | 1 / 1          | 2 / 2          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| pneumothorax                                       |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 3          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| pulmonary embolism                                 |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |

|                                                                                                     |                |                |                |
|-----------------------------------------------------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                                                                         | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all                                                     | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all                                                          | 0 / 0          | 0 / 0          | 0 / 0          |
| pulmonary haemorrhage<br>alternative dictionary used:<br>MedDRA 21.0                                |                |                |                |
| subjects affected / exposed                                                                         | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| pulmonary oedema<br>alternative dictionary used:<br>MedDRA 21.0                                     |                |                |                |
| subjects affected / exposed                                                                         | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| respiratory failure<br>alternative dictionary used:<br>MedDRA 21.0                                  |                |                |                |
| subjects affected / exposed                                                                         | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all                                                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                                                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Psychiatric disorders<br>confusional state<br>alternative dictionary used:<br>MedDRA 21.0           |                |                |                |
| subjects affected / exposed                                                                         | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| Investigations<br>alanine aminotransferase increased<br>alternative dictionary used:<br>MedDRA 21.0 |                |                |                |
| subjects affected / exposed                                                                         | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| international normalised ratio increased<br>alternative dictionary used:<br>MedDRA 21.0             |                |                |                |

|                                                                                 |                |                |                |
|---------------------------------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                                                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| neutrophil count decreased<br>alternative dictionary used:<br>MedDRA 21.0       |                |                |                |
| subjects affected / exposed                                                     | 1 / 81 (1.23%) | 1 / 45 (2.22%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all                                 | 1 / 1          | 1 / 1          | 1 / 1          |
| deaths causally related to treatment / all                                      | 0 / 0          | 0 / 0          | 0 / 0          |
| platelet count decreased<br>alternative dictionary used:<br>MedDRA 21.0         |                |                |                |
| subjects affected / exposed                                                     | 2 / 81 (2.47%) | 1 / 45 (2.22%) | 2 / 86 (2.33%) |
| occurrences causally related to treatment / all                                 | 2 / 2          | 2 / 2          | 2 / 2          |
| deaths causally related to treatment / all                                      | 0 / 0          | 0 / 0          | 0 / 0          |
| troponin increased<br>alternative dictionary used:<br>MedDRA 21.0               |                |                |                |
| subjects affected / exposed                                                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| white blood cell count decreased<br>alternative dictionary used:<br>MedDRA 21.0 |                |                |                |
| subjects affected / exposed                                                     | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 0 / 86 (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          |
| Injury, poisoning and procedural complications                                  |                |                |                |
| arterial bypass occlusion<br>alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                                                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| fall<br>alternative dictionary used:<br>MedDRA 21.0                             |                |                |                |

|                                                                                         |                |                |                |
|-----------------------------------------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                                                             | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all                                         | 0 / 0          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all                                              | 0 / 0          | 0 / 0          | 0 / 0          |
| femoral neck fracture<br>alternative dictionary used:<br>MedDRA 21.0                    |                |                |                |
| subjects affected / exposed                                                             | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 0 / 86 (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          |
| femur fracture<br>alternative dictionary used:<br>MedDRA 21.0                           |                |                |                |
| subjects affected / exposed                                                             | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 0 / 86 (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          |
| hip fracture<br>alternative dictionary used:<br>MedDRA 21.0                             |                |                |                |
| subjects affected / exposed                                                             | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 0 / 86 (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          |
| infusion related reaction<br>alternative dictionary used:<br>MedDRA 21.0                |                |                |                |
| subjects affected / exposed                                                             | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| skull fracture<br>alternative dictionary used:<br>MedDRA 21.0                           |                |                |                |
| subjects affected / exposed                                                             | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all                                         | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all                                              | 0 / 0          | 0 / 0          | 0 / 1          |
| Cardiac disorders<br>atrial fibrillation<br>alternative dictionary used:<br>MedDRA 21.0 |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| atrial tachycardia                              |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| cardiac failure                                 |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| myocardial infarction                           |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1          |
| pericardial effusion                            |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| supraventricular tachycardia                    |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| Nervous system disorders                        |                |                |                |
| dizziness                                       |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| epilepsy                                        |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| facial paralysis                                |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| headache                                        |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| nervous system disorder                         |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 0 / 86 (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          |
| polyneuropathy                                  |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| seizure                                         |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 0 / 86 (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          |

|                                                                            |                |                |                |
|----------------------------------------------------------------------------|----------------|----------------|----------------|
| spinal cord compression<br>alternative dictionary used:<br>MedDRA 21.0     |                |                |                |
| subjects affected / exposed                                                | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to<br>treatment / all                         | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all                              | 0 / 0          | 0 / 0          | 0 / 0          |
| syncope<br>alternative dictionary used:<br>MedDRA 21.0                     |                |                |                |
| subjects affected / exposed                                                | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 0 / 86 (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          |
| Blood and lymphatic system disorders                                       |                |                |                |
| anaemia<br>alternative dictionary used:<br>MedDRA 21.0                     |                |                |                |
| subjects affected / exposed                                                | 4 / 81 (4.94%) | 2 / 45 (4.44%) | 4 / 86 (4.65%) |
| occurrences causally related to<br>treatment / all                         | 4 / 7          | 2 / 2          | 4 / 5          |
| deaths causally related to<br>treatment / all                              | 0 / 0          | 0 / 0          | 0 / 0          |
| bandaemia<br>alternative dictionary used:<br>MedDRA 21.0                   |                |                |                |
| subjects affected / exposed                                                | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| febrile neutropenia<br>alternative dictionary used:<br>MedDRA 21.0         |                |                |                |
| subjects affected / exposed                                                | 6 / 81 (7.41%) | 1 / 45 (2.22%) | 3 / 86 (3.49%) |
| occurrences causally related to<br>treatment / all                         | 6 / 6          | 1 / 1          | 3 / 3          |
| deaths causally related to<br>treatment / all                              | 0 / 0          | 0 / 0          | 0 / 0          |
| haemolytic uraemic syndrome<br>alternative dictionary used:<br>MedDRA 21.0 |                |                |                |
| subjects affected / exposed                                                | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0          | 0 / 0          | 2 / 2          |
| deaths causally related to<br>treatment / all                              | 0 / 0          | 0 / 0          | 0 / 0          |
| hypochromic anaemia<br>alternative dictionary used:<br>MedDRA 21.0         |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| neutropenia                                     |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 2 / 45 (4.44%) | 2 / 86 (2.33%) |
| occurrences causally related to treatment / all | 1 / 1          | 2 / 2          | 2 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| neutrophilia                                    |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| normocytic anaemia                              |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| pancytopenia                                    |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 2 / 86 (2.33%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 1 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| thrombocytopenia                                |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 2 / 81 (2.47%) | 3 / 45 (6.67%) | 3 / 86 (3.49%) |
| occurrences causally related to treatment / all | 3 / 3          | 5 / 5          | 5 / 5          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| thrombotic microangiopathy                      |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 0 / 86 (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          |

|                                                                                                                                                                                                                                   |                                          |                                          |                                          |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------|------------------------------------------|------------------------------------------|
| Ear and labyrinth disorders<br>hypoacusis<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all    | <br><br>0 / 81 (0.00%)<br>0 / 0<br>0 / 0 | <br><br>0 / 45 (0.00%)<br>0 / 0<br>0 / 0 | <br><br>1 / 86 (1.16%)<br>0 / 1<br>0 / 0 |
| Gastrointestinal disorders<br>abdominal pain<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | <br><br>1 / 81 (1.23%)<br>1 / 1<br>0 / 0 | <br><br>0 / 45 (0.00%)<br>0 / 0<br>0 / 0 | <br><br>0 / 86 (0.00%)<br>0 / 0<br>0 / 0 |
| constipation<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                 | <br><br>0 / 81 (0.00%)<br>0 / 0<br>0 / 0 | <br><br>1 / 45 (2.22%)<br>1 / 1<br>0 / 0 | <br><br>0 / 86 (0.00%)<br>0 / 0<br>0 / 0 |
| diarrhoea<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                    | <br><br>2 / 81 (2.47%)<br>2 / 2<br>0 / 0 | <br><br>1 / 45 (2.22%)<br>0 / 1<br>0 / 0 | <br><br>1 / 86 (1.16%)<br>1 / 1<br>0 / 0 |
| enterocolitis<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                | <br><br>1 / 81 (1.23%)<br>1 / 1<br>0 / 0 | <br><br>0 / 45 (0.00%)<br>0 / 0<br>0 / 0 | <br><br>0 / 86 (0.00%)<br>0 / 0<br>0 / 0 |
| gastritis<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                    | <br><br>0 / 81 (0.00%)<br>0 / 0<br>0 / 0 | <br><br>0 / 45 (0.00%)<br>0 / 0<br>0 / 0 | <br><br>1 / 86 (1.16%)<br>1 / 1<br>0 / 0 |
| haemorrhoidal haemorrhage<br>alternative dictionary used:<br>MedDRA 21.0                                                                                                                                                          |                                          |                                          |                                          |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| nausea                                          |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 2 / 81 (2.47%) | 0 / 45 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all | 2 / 3          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| oesophageal ulcer                               |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| rectal haemorrhage                              |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 0 / 86 (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          |
| small intestinal obstruction                    |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| stomatitis                                      |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 3 / 3          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| vomiting                                        |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 2 / 81 (2.47%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 1 / 2          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Hepatobiliary disorders                         |                |                |                |
| hepatic failure                                 |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 1 / 1          | 0 / 0          |
| jaundice cholestatic                            |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| Skin and subcutaneous tissue disorders          |                |                |                |
| eczema                                          |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| petechiae                                       |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| Renal and urinary disorders                     |                |                |                |
| acute kidney injury                             |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 2 / 86 (2.33%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 1 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| renal failure                                   |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 2 / 81 (2.47%) | 0 / 45 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| urinary retention                               |                |                |                |

|                                                    |                |                |                |
|----------------------------------------------------|----------------|----------------|----------------|
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 0 / 86 (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          |
| Musculoskeletal and connective tissue disorders    |                |                |                |
| arthralgia                                         |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| arthritis                                          |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| back pain                                          |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 0 / 86 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| muscular weakness                                  |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| myalgia                                            |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 0 / 86 (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          |
| myositis                                           |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 0 / 86 (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          |
| Infections and infestations                     |                |                |                |
| anorectal infection                             |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 0 / 86 (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          |
| appendicitis                                    |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| arthritis infective                             |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| bacteraemia                                     |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| bronchitis                                      |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 0 / 86 (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          |
| campylobacter infection                         |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 0 / 86 (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          |
| cellulitis                                      |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 2 / 81 (2.47%) | 1 / 45 (2.22%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 1 / 2          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| clostridium difficile colitis                   |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| cystitis                                        |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 2 / 86 (2.33%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| device related infection                        |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| diverticulitis                                  |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 2 / 81 (2.47%) | 1 / 45 (2.22%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| erysipelas                                      |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 0 / 86 (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          |

|                                                    |                |                |                |  |
|----------------------------------------------------|----------------|----------------|----------------|--|
| gastrointestinal infection                         |                |                |                |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |  |
| subjects affected / exposed                        | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 0 / 86 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 1 / 1          | 0 / 0          |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |  |
| influenza                                          |                |                |                |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |  |
| subjects affected / exposed                        | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 1 / 86 (1.16%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 1          | 0 / 1          |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |  |
| lower respiratory tract infection                  |                |                |                |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |  |
| subjects affected / exposed                        | 2 / 81 (2.47%) | 1 / 45 (2.22%) | 1 / 86 (1.16%) |  |
| occurrences causally related to<br>treatment / all | 1 / 2          | 1 / 1          | 1 / 1          |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |  |
| neutropenic sepsis                                 |                |                |                |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |  |
| subjects affected / exposed                        | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |  |
| pneumonia                                          |                |                |                |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |  |
| subjects affected / exposed                        | 5 / 81 (6.17%) | 3 / 45 (6.67%) | 6 / 86 (6.98%) |  |
| occurrences causally related to<br>treatment / all | 4 / 5          | 2 / 3          | 2 / 6          |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |  |
| pneumonia bacterial                                |                |                |                |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |  |
| subjects affected / exposed                        | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |  |
| pneumonia viral                                    |                |                |                |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |  |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 0 / 86 (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          |
| rectal abscess                                  |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 45 (2.22%) | 0 / 86 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| respiratory tract infection                     |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| sepsis                                          |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 2 / 81 (2.47%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to treatment / all | 1 / 2          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| septic shock                                    |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| skin infection                                  |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| staphylococcal bacteraemia                      |                |                |                |
| alternative dictionary used: MedDRA 21.0        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 0 / 86 (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:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 4 / 81 (4.94%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to<br>treatment / all | 3 / 4          | 0 / 0          | 1 / 1          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| viral infection                                    |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 0 / 86 (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          |
| Metabolism and nutrition disorders                 |                |                |                |
| dehydration                                        |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 2 / 81 (2.47%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| occurrences causally related to<br>treatment / all | 2 / 2          | 0 / 0          | 0 / 1          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| hypokalaemia                                       |                |                |                |
| alternative dictionary used:<br>MedDRA 21.0        |                |                |                |
| subjects affected / exposed                        | 0 / 81 (0.00%) | 0 / 45 (0.00%) | 1 / 86 (1.16%) |
| 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          |

|                                                                     |                                                             |  |  |
|---------------------------------------------------------------------|-------------------------------------------------------------|--|--|
| <b>Serious adverse events</b>                                       | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab pretreated) |  |  |
| Total subjects affected by serious adverse events                   |                                                             |  |  |
| subjects affected / exposed                                         | 23 / 43 (53.49%)                                            |  |  |
| number of deaths (all causes)                                       | 28                                                          |  |  |
| number of deaths resulting from adverse events                      | 1                                                           |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                             |  |  |
| tumour haemorrhage                                                  |                                                             |  |  |
| alternative dictionary used:<br>MedDRA 21.0                         |                                                             |  |  |
| subjects affected / exposed                                         | 0 / 43 (0.00%)                                              |  |  |
| occurrences causally related to<br>treatment / all                  | 0 / 0                                                       |  |  |
| deaths causally related to<br>treatment / all                       | 0 / 0                                                       |  |  |

|                                                    |                |  |  |  |
|----------------------------------------------------|----------------|--|--|--|
| Vascular disorders                                 |                |  |  |  |
| capillary leak syndrome                            |                |  |  |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                        | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0          |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0          |  |  |  |
| deep vein thrombosis                               |                |  |  |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                        | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0          |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0          |  |  |  |
| embolism                                           |                |  |  |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                        | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0          |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0          |  |  |  |
| haematoma                                          |                |  |  |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                        | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0          |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0          |  |  |  |
| haemorrhage                                        |                |  |  |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                        | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0          |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0          |  |  |  |
| hypotension                                        |                |  |  |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                        | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0          |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0          |  |  |  |
| peripheral artery stenosis                         |                |  |  |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |  |  |  |

|                                                      |                |  |  |
|------------------------------------------------------|----------------|--|--|
| subjects affected / exposed                          | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| General disorders and administration site conditions |                |  |  |
| chest pain                                           |                |  |  |
| alternative dictionary used: MedDRA 21.0             |                |  |  |
| subjects affected / exposed                          | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| fatigue                                              |                |  |  |
| alternative dictionary used: MedDRA 21.0             |                |  |  |
| subjects affected / exposed                          | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| influenza like illness                               |                |  |  |
| alternative dictionary used: MedDRA 21.0             |                |  |  |
| subjects affected / exposed                          | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| mucosal inflammation                                 |                |  |  |
| alternative dictionary used: MedDRA 21.0             |                |  |  |
| subjects affected / exposed                          | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| non-cardiac chest pain                               |                |  |  |
| alternative dictionary used: MedDRA 21.0             |                |  |  |
| subjects affected / exposed                          | 1 / 43 (2.33%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| oedema                                               |                |  |  |
| alternative dictionary used: MedDRA 21.0             |                |  |  |

|                                                 |                 |  |  |
|-------------------------------------------------|-----------------|--|--|
| subjects affected / exposed                     | 1 / 43 (2.33%)  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| oedema peripheral                               |                 |  |  |
| alternative dictionary used: MedDRA 21.0        |                 |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%)  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| peripheral swelling                             |                 |  |  |
| alternative dictionary used: MedDRA 21.0        |                 |  |  |
| subjects affected / exposed                     | 1 / 43 (2.33%)  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| pyrexia                                         |                 |  |  |
| alternative dictionary used: MedDRA 21.0        |                 |  |  |
| subjects affected / exposed                     | 6 / 43 (13.95%) |  |  |
| occurrences causally related to treatment / all | 2 / 6           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| sudden death                                    |                 |  |  |
| alternative dictionary used: MedDRA 21.0        |                 |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%)  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Immune system disorders                         |                 |  |  |
| anaphylactic reaction                           |                 |  |  |
| alternative dictionary used: MedDRA 21.0        |                 |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%)  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| anaphylactic shock                              |                 |  |  |
| alternative dictionary used: MedDRA 21.0        |                 |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Respiratory, thoracic and mediastinal disorders |                |  |  |
| cough                                           |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| dyspnoea                                        |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 1 / 43 (2.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| epistaxis                                       |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 1 / 43 (2.33%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| hypoxia                                         |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| interstitial lung disease                       |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| pneumonitis                                     |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 4 / 43 (9.30%) |  |  |
| occurrences causally related to treatment / all | 4 / 4          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| pneumothorax                                    |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 1 / 43 (2.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| pulmonary embolism                              |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 1 / 43 (2.33%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| pulmonary haemorrhage                           |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| pulmonary oedema                                |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| respiratory failure                             |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 2 / 43 (4.65%) |  |  |
| occurrences causally related to treatment / all | 2 / 2          |  |  |
| deaths causally related to treatment / all      | 1 / 1          |  |  |
| Psychiatric disorders                           |                |  |  |
| confusional state                               |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Investigations                                  |                |  |  |
| alanine aminotransferase increased              |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| international normalised ratio increased        |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| neutrophil count decreased                      |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| platelet count decreased                        |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 1 / 43 (2.33%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| troponin increased                              |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 1 / 43 (2.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| white blood cell count decreased                |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Injury, poisoning and procedural complications  |                |  |  |
| arterial bypass occlusion                       |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| fall                                            |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| femoral neck fracture                           |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| femur fracture                                  |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| hip fracture                                    |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 1 / 43 (2.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| infusion related reaction                       |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| skull fracture                                  |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cardiac disorders                               |                |  |  |
| atrial fibrillation                             |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 1 / 43 (2.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| atrial tachycardia                              |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| cardiac failure                                 |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| myocardial infarction                           |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| pericardial effusion                            |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| supraventricular tachycardia                    |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Nervous system disorders                        |                |  |  |
| dizziness                                       |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| epilepsy                                        |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| facial paralysis                                |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| headache                                        |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| nervous system disorder                         |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| polyneuropathy                                  |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| seizure                                         |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| spinal cord compression                         |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| syncope                                         |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Blood and lymphatic system disorders            |                |  |  |
| anaemia                                         |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| bandaemia                                       |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |

|                                                 |                |  |  |  |
|-------------------------------------------------|----------------|--|--|--|
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| febrile neutropenia                             |                |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                     | 1 / 43 (2.33%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| haemolytic uraemic syndrome                     |                |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| hypochromic anaemia                             |                |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                     | 1 / 43 (2.33%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| neutropenia                                     |                |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                     | 1 / 43 (2.33%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| neutrophilia                                    |                |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                     | 1 / 43 (2.33%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| normocytic anaemia                              |                |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |

|                                                                                                                                                                                                                                   |                                  |  |  |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|--|--|
| pancytopenia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                 | 0 / 43 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| thrombocytopenia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                             | 2 / 43 (4.65%)<br>2 / 2<br>0 / 0 |  |  |
| thrombotic microangiopathy<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                   | 0 / 43 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| Ear and labyrinth disorders<br>hypoacusis<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all    | 0 / 43 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| Gastrointestinal disorders<br>abdominal pain<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 1 / 43 (2.33%)<br>0 / 1<br>0 / 0 |  |  |
| constipation<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                 | 1 / 43 (2.33%)<br>0 / 1<br>0 / 0 |  |  |
| diarrhoea<br>alternative dictionary used:<br>MedDRA 21.0                                                                                                                                                                          |                                  |  |  |

|                                                 |                |  |  |  |
|-------------------------------------------------|----------------|--|--|--|
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| enterocolitis                                   |                |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| gastritis                                       |                |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| haemorrhoidal haemorrhage                       |                |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| nausea                                          |                |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| oesophageal ulcer                               |                |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                     | 1 / 43 (2.33%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| rectal haemorrhage                              |                |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |

|                                                                                                                                                                                                                                       |                                  |  |  |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|--|--|
| small intestinal obstruction<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                     | 0 / 43 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| stomatitis<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                       | 0 / 43 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| vomiting<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                         | 0 / 43 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| Hepatobiliary disorders<br>hepatic failure<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all       | 0 / 43 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| jaundice cholestatic<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                             | 1 / 43 (2.33%)<br>0 / 1<br>0 / 0 |  |  |
| Skin and subcutaneous tissue disorders<br>eczema<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 0 / 43 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| petechiae<br>alternative dictionary used:<br>MedDRA 21.0                                                                                                                                                                              |                                  |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Renal and urinary disorders                     |                |  |  |
| acute kidney injury                             |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| renal failure                                   |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| urinary retention                               |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Musculoskeletal and connective tissue disorders |                |  |  |
| arthralgia                                      |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| arthritis                                       |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| back pain                                       |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 1 / 43 (2.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| muscular weakness                               |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| myalgia                                         |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| myositis                                        |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Infections and infestations                     |                |  |  |
| anorectal infection                             |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| appendicitis                                    |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| arthritis infective                             |                |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |

|                                                 |                |  |  |  |
|-------------------------------------------------|----------------|--|--|--|
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| bacteraemia                                     |                |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| bronchitis                                      |                |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                     | 1 / 43 (2.33%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| campylobacter infection                         |                |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| cellulitis                                      |                |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| clostridium difficile colitis                   |                |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| cystitis                                        |                |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |

|                                                    |                |  |  |  |
|----------------------------------------------------|----------------|--|--|--|
| device related infection                           |                |  |  |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                        | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0          |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0          |  |  |  |
| diverticulitis                                     |                |  |  |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                        | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0          |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0          |  |  |  |
| erysipelas                                         |                |  |  |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                        | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0          |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0          |  |  |  |
| gastrointestinal infection                         |                |  |  |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                        | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0          |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0          |  |  |  |
| influenza                                          |                |  |  |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                        | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0          |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0          |  |  |  |
| lower respiratory tract infection                  |                |  |  |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |  |  |  |
| subjects affected / exposed                        | 0 / 43 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0          |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0          |  |  |  |
| neutropenic sepsis                                 |                |  |  |  |
| alternative dictionary used:<br>MedDRA 21.0        |                |  |  |  |

|                                                 |                 |  |  |  |
|-------------------------------------------------|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 43 (0.00%)  |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| pneumonia                                       |                 |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                 |  |  |  |
| subjects affected / exposed                     | 5 / 43 (11.63%) |  |  |  |
| occurrences causally related to treatment / all | 3 / 5           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| pneumonia bacterial                             |                 |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%)  |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| pneumonia viral                                 |                 |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%)  |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| rectal abscess                                  |                 |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%)  |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| respiratory tract infection                     |                 |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%)  |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| sepsis                                          |                 |  |  |  |
| alternative dictionary used: MedDRA 21.0        |                 |  |  |  |
| subjects affected / exposed                     | 2 / 43 (4.65%)  |  |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|                                                                                                                                                                                                                                                                                                       |                                  |  |  |  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|--|--|--|
| septic shock<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                                                                                     | 1 / 43 (2.33%)<br>1 / 1<br>0 / 0 |  |  |  |
| skin infection<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                                                                                   | 1 / 43 (2.33%)<br>0 / 1<br>0 / 0 |  |  |  |
| staphylococcal bacteraemia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                                                                       | 0 / 43 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| urinary tract infection<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                                                                          | 0 / 43 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| viral infection<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                                                                                  | 0 / 43 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| Metabolism and nutrition disorders<br>dehydration<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all<br>hypokalaemia<br>alternative dictionary used:<br>MedDRA 21.0 | 0 / 43 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 43 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

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

| <b>Non-serious adverse events</b>                                                                                                                                                     | Phase1b:Cohort1:<br>15mg/kg<br>Olaratumab+Gemcitabine+Docetaxel | Phase1b:Cohort2Exp<br>and:20mg/kgOlaratumab+Gemcitabine+Docetaxe | Phase1b:Cohort2:<br>20mg/kg<br>Olaratumab+Gemcitabine+Docetaxel |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------|------------------------------------------------------------------|-----------------------------------------------------------------|
| Total subjects affected by non-serious adverse events                                                                                                                                 |                                                                 |                                                                  |                                                                 |
| subjects affected / exposed                                                                                                                                                           | 21 / 21 (100.00%)                                               | 15 / 15 (100.00%)                                                | 18 / 18 (100.00%)                                               |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps)<br>tumour pain<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all) | 2 / 21 (9.52%)<br>4                                             | 0 / 15 (0.00%)<br>0                                              | 0 / 18 (0.00%)<br>0                                             |
| Vascular disorders<br>embolism<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                                     | 0 / 21 (0.00%)<br>0                                             | 1 / 15 (6.67%)<br>1                                              | 0 / 18 (0.00%)<br>0                                             |
| embolism venous<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                                                    | 0 / 21 (0.00%)<br>0                                             | 1 / 15 (6.67%)<br>1                                              | 0 / 18 (0.00%)<br>0                                             |
| flushing<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                                                           | 0 / 21 (0.00%)<br>0                                             | 0 / 15 (0.00%)<br>0                                              | 2 / 18 (11.11%)<br>2                                            |
| hot flush<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                                                          | 1 / 21 (4.76%)<br>1                                             | 0 / 15 (0.00%)<br>0                                              | 0 / 18 (0.00%)<br>0                                             |
| hypertension<br>alternative dictionary used:<br>MedDRA 21.0                                                                                                                           |                                                                 |                                                                  |                                                                 |

|                                                                                                                                                                                                 |                                  |                                 |                                 |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|---------------------------------|---------------------------------|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                     | <p>3 / 21 (14.29%)</p> <p>3</p>  | <p>2 / 15 (13.33%)</p> <p>2</p> | <p>0 / 18 (0.00%)</p> <p>0</p>  |
| <p>hypotension</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                              | <p>2 / 21 (9.52%)</p> <p>2</p>   | <p>2 / 15 (13.33%)</p> <p>2</p> | <p>0 / 18 (0.00%)</p> <p>0</p>  |
| <p>peripheral venous disease</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                | <p>0 / 21 (0.00%)</p> <p>0</p>   | <p>0 / 15 (0.00%)</p> <p>0</p>  | <p>1 / 18 (5.56%)</p> <p>1</p>  |
| <p>phlebitis</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                | <p>0 / 21 (0.00%)</p> <p>0</p>   | <p>0 / 15 (0.00%)</p> <p>0</p>  | <p>1 / 18 (5.56%)</p> <p>1</p>  |
| <p>Surgical and medical procedures</p> <p>orchidectomy</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed<sup>[1]</sup></p> <p>occurrences (all)</p>        | <p>0 / 10 (0.00%)</p> <p>0</p>   | <p>1 / 8 (12.50%)</p> <p>1</p>  | <p>0 / 10 (0.00%)</p> <p>0</p>  |
| <p>General disorders and administration<br/>site conditions</p> <p>asthenia</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>4 / 21 (19.05%)</p> <p>21</p> | <p>0 / 15 (0.00%)</p> <p>0</p>  | <p>2 / 18 (11.11%)</p> <p>8</p> |
| <p>catheter site pain</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                       | <p>0 / 21 (0.00%)</p> <p>0</p>   | <p>1 / 15 (6.67%)</p> <p>1</p>  | <p>0 / 18 (0.00%)</p> <p>0</p>  |
| <p>chills</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                   | <p>1 / 21 (4.76%)</p> <p>1</p>   | <p>1 / 15 (6.67%)</p> <p>1</p>  | <p>2 / 18 (11.11%)</p> <p>3</p> |
| <p>device related thrombosis</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p>                                                                                                            |                                  |                                 |                                 |

|                                             |                  |                  |                  |
|---------------------------------------------|------------------|------------------|------------------|
| subjects affected / exposed                 | 0 / 21 (0.00%)   | 0 / 15 (0.00%)   | 1 / 18 (5.56%)   |
| occurrences (all)                           | 0                | 0                | 1                |
| face oedema                                 |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 0 / 21 (0.00%)   | 0 / 15 (0.00%)   | 0 / 18 (0.00%)   |
| occurrences (all)                           | 0                | 0                | 0                |
| fatigue                                     |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 13 / 21 (61.90%) | 12 / 15 (80.00%) | 14 / 18 (77.78%) |
| occurrences (all)                           | 32               | 21               | 35               |
| influenza like illness                      |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 1 / 21 (4.76%)   | 0 / 15 (0.00%)   | 2 / 18 (11.11%)  |
| occurrences (all)                           | 1                | 0                | 2                |
| infusion site extravasation                 |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 0 / 21 (0.00%)   | 0 / 15 (0.00%)   | 1 / 18 (5.56%)   |
| occurrences (all)                           | 0                | 0                | 1                |
| localised oedema                            |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 0 / 21 (0.00%)   | 0 / 15 (0.00%)   | 1 / 18 (5.56%)   |
| occurrences (all)                           | 0                | 0                | 1                |
| malaise                                     |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 1 / 21 (4.76%)   | 0 / 15 (0.00%)   | 1 / 18 (5.56%)   |
| occurrences (all)                           | 1                | 0                | 1                |
| non-cardiac chest pain                      |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 2 / 21 (9.52%)   | 1 / 15 (6.67%)   | 1 / 18 (5.56%)   |
| occurrences (all)                           | 2                | 1                | 1                |
| non-pitting oedema                          |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 0 / 21 (0.00%)   | 0 / 15 (0.00%)   | 1 / 18 (5.56%)   |
| occurrences (all)                           | 0                | 0                | 1                |

|                                                                                                                                                             |                       |                      |                       |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|----------------------|-----------------------|
| oedema peripheral<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                        | 8 / 21 (38.10%)<br>13 | 5 / 15 (33.33%)<br>8 | 5 / 18 (27.78%)<br>9  |
| pain<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                                     | 1 / 21 (4.76%)<br>1   | 0 / 15 (0.00%)<br>0  | 2 / 18 (11.11%)<br>2  |
| peripheral swelling<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 21 (0.00%)<br>0   | 1 / 15 (6.67%)<br>1  | 0 / 18 (0.00%)<br>0   |
| pyrexia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                                  | 6 / 21 (28.57%)<br>8  | 2 / 15 (13.33%)<br>2 | 8 / 18 (44.44%)<br>11 |
| Respiratory, thoracic and mediastinal disorders<br>cough<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all) | 3 / 21 (14.29%)<br>3  | 1 / 15 (6.67%)<br>3  | 6 / 18 (33.33%)<br>9  |
| dyspnoea<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                                 | 3 / 21 (14.29%)<br>4  | 5 / 15 (33.33%)<br>9 | 7 / 18 (38.89%)<br>11 |
| dyspnoea exertional<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 21 (0.00%)<br>0   | 0 / 15 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0   |
| epistaxis<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                                | 4 / 21 (19.05%)<br>4  | 2 / 15 (13.33%)<br>5 | 1 / 18 (5.56%)<br>1   |
| haemoptysis<br>alternative dictionary used:                                                                                                                 |                       |                      |                       |

|                                             |                 |                 |                 |
|---------------------------------------------|-----------------|-----------------|-----------------|
| MedDRA 21.0                                 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 1 / 15 (6.67%)  | 0 / 18 (0.00%)  |
| occurrences (all)                           | 0               | 1               | 0               |
| hiccups                                     |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 1 / 15 (6.67%)  | 3 / 18 (16.67%) |
| occurrences (all)                           | 0               | 1               | 3               |
| hypoxia                                     |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 2 / 15 (13.33%) | 0 / 18 (0.00%)  |
| occurrences (all)                           | 0               | 2               | 0               |
| laryngeal haemorrhage                       |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                           | 0               | 0               | 1               |
| lower respiratory tract congestion          |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                           | 0               | 0               | 1               |
| nasal congestion                            |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 3 / 21 (14.29%) | 1 / 15 (6.67%)  | 2 / 18 (11.11%) |
| occurrences (all)                           | 3               | 2               | 3               |
| nasal dryness                               |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                           | 0               | 0               | 1               |
| oropharyngeal pain                          |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  | 0 / 18 (0.00%)  |
| occurrences (all)                           | 0               | 0               | 0               |
| pleural effusion                            |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |

|                                             |                |                 |                 |
|---------------------------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed                 | 0 / 21 (0.00%) | 1 / 15 (6.67%)  | 2 / 18 (11.11%) |
| occurrences (all)                           | 0              | 1               | 2               |
| pneumonitis                                 |                |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%) | 1 / 15 (6.67%)  | 0 / 18 (0.00%)  |
| occurrences (all)                           | 0              | 1               | 0               |
| productive cough                            |                |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                |                 |                 |
| subjects affected / exposed                 | 1 / 21 (4.76%) | 0 / 15 (0.00%)  | 0 / 18 (0.00%)  |
| occurrences (all)                           | 2              | 0               | 0               |
| pulmonary embolism                          |                |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%) | 2 / 15 (13.33%) | 0 / 18 (0.00%)  |
| occurrences (all)                           | 0              | 2               | 0               |
| upper-airway cough syndrome                 |                |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%) | 0 / 15 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                           | 0              | 0               | 1               |
| Psychiatric disorders                       |                |                 |                 |
| anxiety                                     |                |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%) | 2 / 15 (13.33%) | 3 / 18 (16.67%) |
| occurrences (all)                           | 0              | 2               | 5               |
| depression                                  |                |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%) | 0 / 15 (0.00%)  | 2 / 18 (11.11%) |
| occurrences (all)                           | 0              | 0               | 2               |
| insomnia                                    |                |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%) | 1 / 15 (6.67%)  | 1 / 18 (5.56%)  |
| occurrences (all)                           | 0              | 1               | 1               |
| nightmare                                   |                |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                |                 |                 |

|                                             |                 |                 |                 |
|---------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                           | 0               | 0               | 1               |
| Investigations                              |                 |                 |                 |
| alanine aminotransferase increased          |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 5 / 21 (23.81%) | 2 / 15 (13.33%) | 6 / 18 (33.33%) |
| occurrences (all)                           | 7               | 2               | 13              |
| aspartate aminotransferase increased        |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 4 / 21 (19.05%) | 2 / 15 (13.33%) | 4 / 18 (22.22%) |
| occurrences (all)                           | 4               | 2               | 7               |
| blood alkaline phosphatase increased        |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 4 / 21 (19.05%) | 2 / 15 (13.33%) | 3 / 18 (16.67%) |
| occurrences (all)                           | 4               | 2               | 6               |
| blood bilirubin increased                   |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  | 3 / 18 (16.67%) |
| occurrences (all)                           | 0               | 0               | 4               |
| blood creatinine increased                  |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  | 2 / 18 (11.11%) |
| occurrences (all)                           | 0               | 0               | 2               |
| blood thyroid stimulating hormone increased |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 1 / 15 (6.67%)  | 0 / 18 (0.00%)  |
| occurrences (all)                           | 0               | 1               | 0               |
| gamma-glutamyltransferase increased         |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 4 / 21 (19.05%) | 0 / 15 (0.00%)  | 3 / 18 (16.67%) |
| occurrences (all)                           | 5               | 0               | 5               |
| haemoglobin decreased                       |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |

|                                          |                 |                 |                 |
|------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed              | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                        | 0               | 0               | 1               |
| international normalised ratio increased |                 |                 |                 |
| alternative dictionary used: MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed              | 0 / 21 (0.00%)  | 2 / 15 (13.33%) | 3 / 18 (16.67%) |
| occurrences (all)                        | 0               | 2               | 3               |
| lymphocyte count decreased               |                 |                 |                 |
| alternative dictionary used: MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed              | 1 / 21 (4.76%)  | 0 / 15 (0.00%)  | 4 / 18 (22.22%) |
| occurrences (all)                        | 3               | 0               | 15              |
| neutrophil count decreased               |                 |                 |                 |
| alternative dictionary used: MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed              | 1 / 21 (4.76%)  | 0 / 15 (0.00%)  | 5 / 18 (27.78%) |
| occurrences (all)                        | 3               | 0               | 7               |
| platelet count decreased                 |                 |                 |                 |
| alternative dictionary used: MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed              | 2 / 21 (9.52%)  | 2 / 15 (13.33%) | 7 / 18 (38.89%) |
| occurrences (all)                        | 2               | 2               | 15              |
| transaminases increased                  |                 |                 |                 |
| alternative dictionary used: MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed              | 0 / 21 (0.00%)  | 1 / 15 (6.67%)  | 0 / 18 (0.00%)  |
| occurrences (all)                        | 0               | 3               | 0               |
| weight decreased                         |                 |                 |                 |
| alternative dictionary used: MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed              | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  | 4 / 18 (22.22%) |
| occurrences (all)                        | 0               | 0               | 6               |
| weight increased                         |                 |                 |                 |
| alternative dictionary used: MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed              | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                        | 0               | 0               | 1               |
| white blood cell count decreased         |                 |                 |                 |
| alternative dictionary used: MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed              | 3 / 21 (14.29%) | 0 / 15 (0.00%)  | 4 / 18 (22.22%) |
| occurrences (all)                        | 3               | 0               | 11              |

|                                                                                                                                                        |                      |                      |                      |
|--------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|----------------------|----------------------|
| Injury, poisoning and procedural complications<br>fall<br>alternative dictionary used: MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all) | 0 / 21 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 0 / 18 (0.00%)<br>0  |
| infusion related reaction<br>alternative dictionary used: MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                              | 3 / 21 (14.29%)<br>3 | 2 / 15 (13.33%)<br>2 | 0 / 18 (0.00%)<br>0  |
| meniscus injury<br>alternative dictionary used: MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                        | 0 / 21 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 0 / 18 (0.00%)<br>0  |
| wound complication<br>alternative dictionary used: MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 21 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1  |
| Cardiac disorders<br>atrial fibrillation<br>alternative dictionary used: MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)               | 0 / 21 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 0 / 18 (0.00%)<br>0  |
| sinus tachycardia<br>alternative dictionary used: MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 21 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 0 / 18 (0.00%)<br>0  |
| tachycardia<br>alternative dictionary used: MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                            | 0 / 21 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 0 / 18 (0.00%)<br>0  |
| Nervous system disorders<br>dizziness<br>alternative dictionary used: MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 21 (0.00%)<br>0  | 2 / 15 (13.33%)<br>4 | 2 / 18 (11.11%)<br>2 |

|                                             |                 |                |                 |
|---------------------------------------------|-----------------|----------------|-----------------|
| dysgeusia                                   |                 |                |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                |                 |
| subjects affected / exposed                 | 3 / 21 (14.29%) | 0 / 15 (0.00%) | 7 / 18 (38.89%) |
| occurrences (all)                           | 7               | 0              | 7               |
| headache                                    |                 |                |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                |                 |
| subjects affected / exposed                 | 5 / 21 (23.81%) | 1 / 15 (6.67%) | 5 / 18 (27.78%) |
| occurrences (all)                           | 6               | 1              | 5               |
| memory impairment                           |                 |                |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 0 / 15 (0.00%) | 1 / 18 (5.56%)  |
| occurrences (all)                           | 0               | 0              | 2               |
| neuropathy peripheral                       |                 |                |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                |                 |
| subjects affected / exposed                 | 1 / 21 (4.76%)  | 1 / 15 (6.67%) | 1 / 18 (5.56%)  |
| occurrences (all)                           | 1               | 1              | 1               |
| paraesthesia                                |                 |                |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                |                 |
| subjects affected / exposed                 | 1 / 21 (4.76%)  | 1 / 15 (6.67%) | 0 / 18 (0.00%)  |
| occurrences (all)                           | 2               | 1              | 0               |
| peripheral motor neuropathy                 |                 |                |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 0 / 15 (0.00%) | 1 / 18 (5.56%)  |
| occurrences (all)                           | 0               | 0              | 2               |
| peripheral sensory neuropathy               |                 |                |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 1 / 15 (6.67%) | 3 / 18 (16.67%) |
| occurrences (all)                           | 0               | 1              | 4               |
| sciatica                                    |                 |                |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 1 / 15 (6.67%) | 0 / 18 (0.00%)  |
| occurrences (all)                           | 0               | 1              | 0               |
| syncope                                     |                 |                |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                |                 |

|                                                                                                                                                           |                        |                       |                        |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|-----------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)                                                                                                          | 0 / 21 (0.00%)<br>0    | 0 / 15 (0.00%)<br>0   | 0 / 18 (0.00%)<br>0    |
| taste disorder<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                         | 0 / 21 (0.00%)<br>0    | 0 / 15 (0.00%)<br>0   | 0 / 18 (0.00%)<br>0    |
| <b>Blood and lymphatic system disorders</b><br>anaemia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all) | 13 / 21 (61.90%)<br>42 | 9 / 15 (60.00%)<br>24 | 12 / 18 (66.67%)<br>54 |
| leukopenia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 21 (0.00%)<br>0    | 0 / 15 (0.00%)<br>0   | 0 / 18 (0.00%)<br>0    |
| neutropenia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                            | 3 / 21 (14.29%)<br>4   | 2 / 15 (13.33%)<br>5  | 3 / 18 (16.67%)<br>4   |
| neutrophilia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                           | 0 / 21 (0.00%)<br>0    | 1 / 15 (6.67%)<br>1   | 0 / 18 (0.00%)<br>0    |
| thrombocytopenia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                       | 2 / 21 (9.52%)<br>8    | 4 / 15 (26.67%)<br>12 | 3 / 18 (16.67%)<br>3   |
| <b>Ear and labyrinth disorders</b><br>ear pain<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)         | 0 / 21 (0.00%)<br>0    | 1 / 15 (6.67%)<br>1   | 1 / 18 (5.56%)<br>1    |
| <b>Eye disorders</b><br>dry eye<br>alternative dictionary used:<br>MedDRA 21.0                                                                            |                        |                       |                        |

|                                             |                 |                |                |
|---------------------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed                 | 1 / 21 (4.76%)  | 1 / 15 (6.67%) | 0 / 18 (0.00%) |
| occurrences (all)                           | 2               | 1              | 0              |
| lacrimation increased                       |                 |                |                |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                |                |
| subjects affected / exposed                 | 1 / 21 (4.76%)  | 0 / 15 (0.00%) | 0 / 18 (0.00%) |
| occurrences (all)                           | 1               | 0              | 0              |
| photopsia                                   |                 |                |                |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                |                |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 0 / 15 (0.00%) | 1 / 18 (5.56%) |
| occurrences (all)                           | 0               | 0              | 1              |
| vision blurred                              |                 |                |                |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                |                |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 1 / 15 (6.67%) | 0 / 18 (0.00%) |
| occurrences (all)                           | 0               | 1              | 0              |
| Gastrointestinal disorders                  |                 |                |                |
| abdominal distension                        |                 |                |                |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                |                |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 0 / 15 (0.00%) | 0 / 18 (0.00%) |
| occurrences (all)                           | 0               | 0              | 0              |
| abdominal pain                              |                 |                |                |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                |                |
| subjects affected / exposed                 | 2 / 21 (9.52%)  | 0 / 15 (0.00%) | 0 / 18 (0.00%) |
| occurrences (all)                           | 4               | 0              | 0              |
| abdominal pain upper                        |                 |                |                |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                |                |
| subjects affected / exposed                 | 3 / 21 (14.29%) | 0 / 15 (0.00%) | 0 / 18 (0.00%) |
| occurrences (all)                           | 3               | 0              | 0              |
| anorectal discomfort                        |                 |                |                |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                |                |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 0 / 15 (0.00%) | 1 / 18 (5.56%) |
| occurrences (all)                           | 0               | 0              | 1              |
| aphthous ulcer                              |                 |                |                |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                |                |

|                                             |                 |                 |                 |
|---------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                           | 0               | 0               | 1               |
| constipation                                |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 6 / 21 (28.57%) | 4 / 15 (26.67%) | 3 / 18 (16.67%) |
| occurrences (all)                           | 8               | 6               | 7               |
| diarrhoea                                   |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 7 / 21 (33.33%) | 5 / 15 (33.33%) | 8 / 18 (44.44%) |
| occurrences (all)                           | 22              | 8               | 14              |
| dry mouth                                   |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  | 0 / 18 (0.00%)  |
| occurrences (all)                           | 0               | 0               | 0               |
| dyspepsia                                   |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 1 / 15 (6.67%)  | 3 / 18 (16.67%) |
| occurrences (all)                           | 0               | 2               | 3               |
| gastrooesophageal reflux disease            |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 2 / 21 (9.52%)  | 1 / 15 (6.67%)  | 0 / 18 (0.00%)  |
| occurrences (all)                           | 2               | 2               | 0               |
| haemorrhoids                                |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 1 / 21 (4.76%)  | 0 / 15 (0.00%)  | 0 / 18 (0.00%)  |
| occurrences (all)                           | 1               | 0               | 0               |
| intestinal fistula                          |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 1 / 15 (6.67%)  | 0 / 18 (0.00%)  |
| occurrences (all)                           | 0               | 1               | 0               |
| nausea                                      |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 5 / 21 (23.81%) | 3 / 15 (20.00%) | 9 / 18 (50.00%) |
| occurrences (all)                           | 8               | 4               | 15              |

|                                                                                                                            |                      |                     |                       |
|----------------------------------------------------------------------------------------------------------------------------|----------------------|---------------------|-----------------------|
| oral pain<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)               | 0 / 21 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 2 / 18 (11.11%)<br>3  |
| proctalgia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)              | 0 / 21 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1   |
| salivary hypersecretion<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all) | 0 / 21 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1   |
| stomatitis<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)              | 4 / 21 (19.05%)<br>8 | 0 / 15 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1   |
| toothache<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)               | 1 / 21 (4.76%)<br>1  | 1 / 15 (6.67%)<br>1 | 0 / 18 (0.00%)<br>0   |
| vomiting<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                | 3 / 21 (14.29%)<br>5 | 1 / 15 (6.67%)<br>1 | 2 / 18 (11.11%)<br>2  |
| Skin and subcutaneous tissue disorders                                                                                     |                      |                     |                       |
| alopecia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                | 8 / 21 (38.10%)<br>8 | 1 / 15 (6.67%)<br>1 | 5 / 18 (27.78%)<br>10 |
| dermatitis acneiform<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)    | 1 / 21 (4.76%)<br>1  | 0 / 15 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1   |
| dry skin<br>alternative dictionary used:<br>MedDRA 21.0                                                                    |                      |                     |                       |

|                                                |                 |                |                 |
|------------------------------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed                    | 0 / 21 (0.00%)  | 0 / 15 (0.00%) | 2 / 18 (11.11%) |
| occurrences (all)                              | 0               | 0              | 2               |
| eczema                                         |                 |                |                 |
| alternative dictionary used:<br>MedDRA 21.0    |                 |                |                 |
| subjects affected / exposed                    | 0 / 21 (0.00%)  | 1 / 15 (6.67%) | 0 / 18 (0.00%)  |
| occurrences (all)                              | 0               | 1              | 0               |
| erythema                                       |                 |                |                 |
| alternative dictionary used:<br>MedDRA 21.0    |                 |                |                 |
| subjects affected / exposed                    | 0 / 21 (0.00%)  | 0 / 15 (0.00%) | 0 / 18 (0.00%)  |
| occurrences (all)                              | 0               | 0              | 0               |
| nail discolouration                            |                 |                |                 |
| alternative dictionary used:<br>MedDRA 21.0    |                 |                |                 |
| subjects affected / exposed                    | 0 / 21 (0.00%)  | 0 / 15 (0.00%) | 1 / 18 (5.56%)  |
| occurrences (all)                              | 0               | 0              | 1               |
| nail dystrophy                                 |                 |                |                 |
| alternative dictionary used:<br>MedDRA 21.0    |                 |                |                 |
| subjects affected / exposed                    | 3 / 21 (14.29%) | 0 / 15 (0.00%) | 1 / 18 (5.56%)  |
| occurrences (all)                              | 3               | 0              | 1               |
| onychomadesis                                  |                 |                |                 |
| alternative dictionary used:<br>MedDRA 21.0    |                 |                |                 |
| subjects affected / exposed                    | 0 / 21 (0.00%)  | 0 / 15 (0.00%) | 0 / 18 (0.00%)  |
| occurrences (all)                              | 0               | 0              | 0               |
| palmar-plantar erythrodysaesthesia<br>syndrome |                 |                |                 |
| alternative dictionary used:<br>MedDRA 21.0    |                 |                |                 |
| subjects affected / exposed                    | 0 / 21 (0.00%)  | 0 / 15 (0.00%) | 1 / 18 (5.56%)  |
| occurrences (all)                              | 0               | 0              | 2               |
| pruritus                                       |                 |                |                 |
| alternative dictionary used:<br>MedDRA 21.0    |                 |                |                 |
| subjects affected / exposed                    | 0 / 21 (0.00%)  | 0 / 15 (0.00%) | 1 / 18 (5.56%)  |
| occurrences (all)                              | 0               | 0              | 1               |
| rash                                           |                 |                |                 |
| alternative dictionary used:<br>MedDRA 21.0    |                 |                |                 |
| subjects affected / exposed                    | 0 / 21 (0.00%)  | 1 / 15 (6.67%) | 0 / 18 (0.00%)  |
| occurrences (all)                              | 0               | 1              | 0               |

|                                                                                                                           |                     |                      |                      |
|---------------------------------------------------------------------------------------------------------------------------|---------------------|----------------------|----------------------|
| rash maculo-papular<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)    | 1 / 21 (4.76%)<br>1 | 2 / 15 (13.33%)<br>2 | 2 / 18 (11.11%)<br>2 |
| rash pruritic<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)          | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1  |
| skin hyperpigmentation<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all) | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  |
| Renal and urinary disorders                                                                                               |                     |                      |                      |
| chromaturia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)            | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1  |
| haematuria<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)             | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  |
| micturition urgency<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)    | 0 / 21 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  | 0 / 18 (0.00%)<br>0  |
| proteinuria<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)            | 2 / 21 (9.52%)<br>2 | 0 / 15 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  |
| Endocrine disorders                                                                                                       |                     |                      |                      |
| adrenal insufficiency<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)  | 0 / 21 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  | 0 / 18 (0.00%)<br>0  |
| hypothyroidism                                                                                                            |                     |                      |                      |

|                                                                                                                               |                      |                      |                      |
|-------------------------------------------------------------------------------------------------------------------------------|----------------------|----------------------|----------------------|
| alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 21 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 2 / 18 (11.11%)<br>2 |
| Musculoskeletal and connective tissue disorders                                                                               |                      |                      |                      |
| arthralgia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                 | 2 / 21 (9.52%)<br>3  | 2 / 15 (13.33%)<br>3 | 3 / 18 (16.67%)<br>4 |
| back pain<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                  | 4 / 21 (19.05%)<br>6 | 6 / 15 (40.00%)<br>7 | 5 / 18 (27.78%)<br>7 |
| bone pain<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                  | 3 / 21 (14.29%)<br>3 | 0 / 15 (0.00%)<br>0  | 3 / 18 (16.67%)<br>3 |
| coccydynia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 21 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 0 / 18 (0.00%)<br>0  |
| muscle spasms<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)              | 0 / 21 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  |
| muscular weakness<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)          | 0 / 21 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 2 / 18 (11.11%)<br>2 |
| musculoskeletal chest pain<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all) | 0 / 21 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 2 / 18 (11.11%)<br>5 |
| musculoskeletal pain<br>alternative dictionary used:<br>MedDRA 21.0                                                           |                      |                      |                      |

|                                             |                 |                 |                 |
|---------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                 | 2 / 21 (9.52%)  | 1 / 15 (6.67%)  | 1 / 18 (5.56%)  |
| occurrences (all)                           | 2               | 1               | 1               |
| myalgia                                     |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 7 / 21 (33.33%) | 4 / 15 (26.67%) | 6 / 18 (33.33%) |
| occurrences (all)                           | 9               | 4               | 6               |
| pain in extremity                           |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 1 / 15 (6.67%)  | 2 / 18 (11.11%) |
| occurrences (all)                           | 0               | 1               | 4               |
| Infections and infestations                 |                 |                 |                 |
| bronchitis                                  |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                           | 0               | 0               | 1               |
| cellulitis                                  |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 2 / 15 (13.33%) | 0 / 18 (0.00%)  |
| occurrences (all)                           | 0               | 2               | 0               |
| cystitis                                    |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                           | 0               | 0               | 1               |
| folliculitis                                |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 1 / 15 (6.67%)  | 0 / 18 (0.00%)  |
| occurrences (all)                           | 0               | 1               | 0               |
| oral candidiasis                            |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                           | 0               | 0               | 1               |
| oral herpes                                 |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                 |

|                                             |                |                 |                 |
|---------------------------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed                 | 0 / 21 (0.00%) | 1 / 15 (6.67%)  | 0 / 18 (0.00%)  |
| occurrences (all)                           | 0              | 1               | 0               |
| paronychia                                  |                |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%) | 0 / 15 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                           | 0              | 0               | 1               |
| pneumonia                                   |                |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                |                 |                 |
| subjects affected / exposed                 | 1 / 21 (4.76%) | 0 / 15 (0.00%)  | 0 / 18 (0.00%)  |
| occurrences (all)                           | 1              | 0               | 0               |
| rash pustular                               |                |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%) | 1 / 15 (6.67%)  | 0 / 18 (0.00%)  |
| occurrences (all)                           | 0              | 1               | 0               |
| respiratory tract infection                 |                |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%) | 0 / 15 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                           | 0              | 0               | 1               |
| sinusitis                                   |                |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%) | 1 / 15 (6.67%)  | 0 / 18 (0.00%)  |
| occurrences (all)                           | 0              | 1               | 0               |
| skin infection                              |                |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                |                 |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%) | 1 / 15 (6.67%)  | 0 / 18 (0.00%)  |
| occurrences (all)                           | 0              | 1               | 0               |
| upper respiratory tract infection           |                |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                |                 |                 |
| subjects affected / exposed                 | 2 / 21 (9.52%) | 3 / 15 (20.00%) | 2 / 18 (11.11%) |
| occurrences (all)                           | 2              | 3               | 2               |
| urinary tract infection                     |                |                 |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                |                 |                 |
| subjects affected / exposed                 | 1 / 21 (4.76%) | 0 / 15 (0.00%)  | 2 / 18 (11.11%) |
| occurrences (all)                           | 1              | 0               | 2               |

|                                                                                                                                                             |                      |                     |                      |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|---------------------|----------------------|
| vaginal infection<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed <sup>[2]</sup><br>occurrences (all)                         | 0 / 11 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 | 0 / 8 (0.00%)<br>0   |
| Metabolism and nutrition disorders<br>decreased appetite<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all) | 5 / 21 (23.81%)<br>6 | 0 / 15 (0.00%)<br>0 | 6 / 18 (33.33%)<br>8 |
| dehydration<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                              | 1 / 21 (4.76%)<br>1  | 1 / 15 (6.67%)<br>1 | 0 / 18 (0.00%)<br>0  |
| failure to thrive<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                        | 0 / 21 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1 | 0 / 18 (0.00%)<br>0  |
| hypercalcaemia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                           | 2 / 21 (9.52%)<br>2  | 0 / 15 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1  |
| hyperglycaemia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                           | 4 / 21 (19.05%)<br>4 | 0 / 15 (0.00%)<br>0 | 4 / 18 (22.22%)<br>5 |
| hyperkalaemia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                            | 1 / 21 (4.76%)<br>1  | 0 / 15 (0.00%)<br>0 | 1 / 18 (5.56%)<br>2  |
| hypernatraemia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                           | 0 / 21 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1  |
| hyperuricaemia<br>alternative dictionary used:<br>MedDRA 21.0                                                                                               |                      |                     |                      |

|                                             |                |                |                 |
|---------------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed                 | 2 / 21 (9.52%) | 0 / 15 (0.00%) | 1 / 18 (5.56%)  |
| occurrences (all)                           | 2              | 0              | 1               |
| hypoalbuminaemia                            |                |                |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                |                |                 |
| subjects affected / exposed                 | 1 / 21 (4.76%) | 0 / 15 (0.00%) | 3 / 18 (16.67%) |
| occurrences (all)                           | 1              | 0              | 4               |
| hypocalcaemia                               |                |                |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                |                |                 |
| subjects affected / exposed                 | 0 / 21 (0.00%) | 0 / 15 (0.00%) | 4 / 18 (22.22%) |
| occurrences (all)                           | 0              | 0              | 4               |
| hypokalaemia                                |                |                |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                |                |                 |
| subjects affected / exposed                 | 2 / 21 (9.52%) | 1 / 15 (6.67%) | 5 / 18 (27.78%) |
| occurrences (all)                           | 2              | 1              | 10              |
| hypomagnesaemia                             |                |                |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                |                |                 |
| subjects affected / exposed                 | 1 / 21 (4.76%) | 0 / 15 (0.00%) | 1 / 18 (5.56%)  |
| occurrences (all)                           | 1              | 0              | 1               |
| hyponatraemia                               |                |                |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                |                |                 |
| subjects affected / exposed                 | 1 / 21 (4.76%) | 0 / 15 (0.00%) | 3 / 18 (16.67%) |
| occurrences (all)                           | 8              | 0              | 4               |
| hypophosphataemia                           |                |                |                 |
| alternative dictionary used:<br>MedDRA 21.0 |                |                |                 |
| subjects affected / exposed                 | 2 / 21 (9.52%) | 0 / 15 (0.00%) | 1 / 18 (5.56%)  |
| occurrences (all)                           | 2              | 0              | 1               |

| <b>Non-serious adverse events</b>                                   | Phase2:Olaratumab<br>+Gemcitabine+Docetaxel(Olaratumab-naive) | Phase2:Olaratumab<br>+Gemcitabine+Docetaxel(Olaratumab Pretreated) | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab-naive) |
|---------------------------------------------------------------------|---------------------------------------------------------------|--------------------------------------------------------------------|--------------------------------------------------------|
| Total subjects affected by non-serious adverse events               |                                                               |                                                                    |                                                        |
| subjects affected / exposed                                         | 78 / 81 (96.30%)                                              | 45 / 45 (100.00%)                                                  | 81 / 86 (94.19%)                                       |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                               |                                                                    |                                                        |
| tumour pain                                                         |                                                               |                                                                    |                                                        |
| alternative dictionary used:<br>MedDRA 21.0                         |                                                               |                                                                    |                                                        |

|                                                  |                     |                     |                     |
|--------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 1 / 81 (1.23%)<br>1 | 1 / 45 (2.22%)<br>1 | 2 / 86 (2.33%)<br>4 |
| Vascular disorders                               |                     |                     |                     |
| embolism                                         |                     |                     |                     |
| alternative dictionary used:<br>MedDRA 21.0      |                     |                     |                     |
| subjects affected / exposed                      | 1 / 81 (1.23%)      | 2 / 45 (4.44%)      | 6 / 86 (6.98%)      |
| occurrences (all)                                | 1                   | 2                   | 6                   |
| embolism venous                                  |                     |                     |                     |
| alternative dictionary used:<br>MedDRA 21.0      |                     |                     |                     |
| subjects affected / exposed                      | 0 / 81 (0.00%)      | 0 / 45 (0.00%)      | 0 / 86 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| flushing                                         |                     |                     |                     |
| alternative dictionary used:<br>MedDRA 21.0      |                     |                     |                     |
| subjects affected / exposed                      | 10 / 81 (12.35%)    | 2 / 45 (4.44%)      | 4 / 86 (4.65%)      |
| occurrences (all)                                | 13                  | 2                   | 7                   |
| hot flush                                        |                     |                     |                     |
| alternative dictionary used:<br>MedDRA 21.0      |                     |                     |                     |
| subjects affected / exposed                      | 4 / 81 (4.94%)      | 1 / 45 (2.22%)      | 5 / 86 (5.81%)      |
| occurrences (all)                                | 5                   | 1                   | 9                   |
| hypertension                                     |                     |                     |                     |
| alternative dictionary used:<br>MedDRA 21.0      |                     |                     |                     |
| subjects affected / exposed                      | 5 / 81 (6.17%)      | 6 / 45 (13.33%)     | 7 / 86 (8.14%)      |
| occurrences (all)                                | 20                  | 6                   | 23                  |
| hypotension                                      |                     |                     |                     |
| alternative dictionary used:<br>MedDRA 21.0      |                     |                     |                     |
| subjects affected / exposed                      | 4 / 81 (4.94%)      | 8 / 45 (17.78%)     | 5 / 86 (5.81%)      |
| occurrences (all)                                | 4                   | 8                   | 5                   |
| peripheral venous disease                        |                     |                     |                     |
| alternative dictionary used:<br>MedDRA 21.0      |                     |                     |                     |
| subjects affected / exposed                      | 0 / 81 (0.00%)      | 0 / 45 (0.00%)      | 0 / 86 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| phlebitis                                        |                     |                     |                     |
| alternative dictionary used:<br>MedDRA 21.0      |                     |                     |                     |

|                                                                                                                                                                        |                         |                        |                         |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|------------------------|-------------------------|
| subjects affected / exposed<br>occurrences (all)                                                                                                                       | 1 / 81 (1.23%)<br>1     | 0 / 45 (0.00%)<br>0    | 1 / 86 (1.16%)<br>1     |
| Surgical and medical procedures<br>orchidectomy<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed <sup>[1]</sup><br>occurrences (all)      | 0 / 33 (0.00%)<br>0     | 0 / 17 (0.00%)<br>0    | 0 / 28 (0.00%)<br>0     |
| General disorders and administration<br>site conditions<br>asthenia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all) | 12 / 81 (14.81%)<br>59  | 1 / 45 (2.22%)<br>1    | 14 / 86 (16.28%)<br>58  |
| catheter site pain<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                                  | 1 / 81 (1.23%)<br>1     | 0 / 45 (0.00%)<br>0    | 0 / 86 (0.00%)<br>0     |
| chills<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                                              | 8 / 81 (9.88%)<br>13    | 5 / 45 (11.11%)<br>5   | 4 / 86 (4.65%)<br>5     |
| device related thrombosis<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                           | 1 / 81 (1.23%)<br>1     | 0 / 45 (0.00%)<br>0    | 0 / 86 (0.00%)<br>0     |
| face oedema<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                                         | 5 / 81 (6.17%)<br>8     | 2 / 45 (4.44%)<br>2    | 0 / 86 (0.00%)<br>0     |
| fatigue<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                                             | 49 / 81 (60.49%)<br>126 | 34 / 45 (75.56%)<br>76 | 45 / 86 (52.33%)<br>110 |
| influenza like illness<br>alternative dictionary used:<br>MedDRA 21.0                                                                                                  |                         |                        |                         |

|                                             |                  |                  |                  |
|---------------------------------------------|------------------|------------------|------------------|
| subjects affected / exposed                 | 5 / 81 (6.17%)   | 3 / 45 (6.67%)   | 3 / 86 (3.49%)   |
| occurrences (all)                           | 5                | 3                | 6                |
| infusion site extravasation                 |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 2 / 81 (2.47%)   | 0 / 45 (0.00%)   | 0 / 86 (0.00%)   |
| occurrences (all)                           | 2                | 0                | 0                |
| localised oedema                            |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 1 / 81 (1.23%)   | 3 / 45 (6.67%)   | 0 / 86 (0.00%)   |
| occurrences (all)                           | 1                | 3                | 0                |
| malaise                                     |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 2 / 81 (2.47%)   | 1 / 45 (2.22%)   | 2 / 86 (2.33%)   |
| occurrences (all)                           | 3                | 1                | 2                |
| non-cardiac chest pain                      |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 7 / 81 (8.64%)   | 3 / 45 (6.67%)   | 8 / 86 (9.30%)   |
| occurrences (all)                           | 9                | 4                | 8                |
| non-pitting oedema                          |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 0 / 81 (0.00%)   | 0 / 45 (0.00%)   | 0 / 86 (0.00%)   |
| occurrences (all)                           | 0                | 0                | 0                |
| oedema peripheral                           |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 37 / 81 (45.68%) | 21 / 45 (46.67%) | 23 / 86 (26.74%) |
| occurrences (all)                           | 67               | 36               | 33               |
| pain                                        |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 3 / 81 (3.70%)   | 1 / 45 (2.22%)   | 1 / 86 (1.16%)   |
| occurrences (all)                           | 3                | 1                | 1                |
| peripheral swelling                         |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 6 / 81 (7.41%)   | 1 / 45 (2.22%)   | 8 / 86 (9.30%)   |
| occurrences (all)                           | 6                | 2                | 11               |

|                                                                                                                                                             |                        |                        |                        |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|------------------------|------------------------|
| pyrexia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                                  | 23 / 81 (28.40%)<br>51 | 10 / 45 (22.22%)<br>12 | 26 / 86 (30.23%)<br>49 |
| Respiratory, thoracic and mediastinal disorders<br>cough<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all) | 16 / 81 (19.75%)<br>22 | 13 / 45 (28.89%)<br>21 | 21 / 86 (24.42%)<br>27 |
| dyspnoea<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                                 | 19 / 81 (23.46%)<br>30 | 15 / 45 (33.33%)<br>30 | 18 / 86 (20.93%)<br>25 |
| dyspnoea exertional<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 81 (0.00%)<br>0    | 2 / 45 (4.44%)<br>4    | 5 / 86 (5.81%)<br>7    |
| epistaxis<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                                | 16 / 81 (19.75%)<br>19 | 5 / 45 (11.11%)<br>6   | 17 / 86 (19.77%)<br>22 |
| haemoptysis<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                              | 1 / 81 (1.23%)<br>1    | 0 / 45 (0.00%)<br>0    | 1 / 86 (1.16%)<br>2    |
| hiccups<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                                  | 0 / 81 (0.00%)<br>0    | 0 / 45 (0.00%)<br>0    | 1 / 86 (1.16%)<br>1    |
| hypoxia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                                  | 3 / 81 (3.70%)<br>3    | 2 / 45 (4.44%)<br>2    | 0 / 86 (0.00%)<br>0    |
| laryngeal haemorrhage<br>alternative dictionary used:                                                                                                       |                        |                        |                        |

|                                             |                 |                 |                |
|---------------------------------------------|-----------------|-----------------|----------------|
| MedDRA 21.0                                 |                 |                 |                |
| subjects affected / exposed                 | 0 / 81 (0.00%)  | 0 / 45 (0.00%)  | 0 / 86 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0              |
| lower respiratory tract congestion          |                 |                 |                |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                |
| subjects affected / exposed                 | 0 / 81 (0.00%)  | 0 / 45 (0.00%)  | 0 / 86 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0              |
| nasal congestion                            |                 |                 |                |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                |
| subjects affected / exposed                 | 2 / 81 (2.47%)  | 1 / 45 (2.22%)  | 0 / 86 (0.00%) |
| occurrences (all)                           | 2               | 1               | 0              |
| nasal dryness                               |                 |                 |                |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                |
| subjects affected / exposed                 | 0 / 81 (0.00%)  | 0 / 45 (0.00%)  | 0 / 86 (0.00%) |
| occurrences (all)                           | 0               | 0               | 0              |
| oropharyngeal pain                          |                 |                 |                |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                |
| subjects affected / exposed                 | 9 / 81 (11.11%) | 4 / 45 (8.89%)  | 6 / 86 (6.98%) |
| occurrences (all)                           | 11              | 4               | 6              |
| pleural effusion                            |                 |                 |                |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                |
| subjects affected / exposed                 | 2 / 81 (2.47%)  | 6 / 45 (13.33%) | 1 / 86 (1.16%) |
| occurrences (all)                           | 4               | 7               | 1              |
| pneumonitis                                 |                 |                 |                |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                |
| subjects affected / exposed                 | 7 / 81 (8.64%)  | 3 / 45 (6.67%)  | 1 / 86 (1.16%) |
| occurrences (all)                           | 8               | 3               | 1              |
| productive cough                            |                 |                 |                |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                |
| subjects affected / exposed                 | 3 / 81 (3.70%)  | 4 / 45 (8.89%)  | 5 / 86 (5.81%) |
| occurrences (all)                           | 3               | 6               | 6              |
| pulmonary embolism                          |                 |                 |                |
| alternative dictionary used:<br>MedDRA 21.0 |                 |                 |                |

|                                                                                                                                                         |                        |                       |                        |
|---------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|-----------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)                                                                                                        | 0 / 81 (0.00%)<br>0    | 1 / 45 (2.22%)<br>1   | 1 / 86 (1.16%)<br>1    |
| upper-airway cough syndrome<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                          | 2 / 81 (2.47%)<br>3    | 3 / 45 (6.67%)<br>3   | 2 / 86 (2.33%)<br>2    |
| Psychiatric disorders<br>anxiety<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                     | 5 / 81 (6.17%)<br>5    | 2 / 45 (4.44%)<br>2   | 5 / 86 (5.81%)<br>5    |
| depression<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                           | 1 / 81 (1.23%)<br>2    | 0 / 45 (0.00%)<br>0   | 2 / 86 (2.33%)<br>2    |
| insomnia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                             | 15 / 81 (18.52%)<br>17 | 6 / 45 (13.33%)<br>7  | 7 / 86 (8.14%)<br>8    |
| nightmare<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                            | 0 / 81 (0.00%)<br>0    | 0 / 45 (0.00%)<br>0   | 0 / 86 (0.00%)<br>0    |
| Investigations<br>alanine aminotransferase increased<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all) | 13 / 81 (16.05%)<br>36 | 8 / 45 (17.78%)<br>19 | 16 / 86 (18.60%)<br>33 |
| aspartate aminotransferase increased<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                 | 10 / 81 (12.35%)<br>22 | 6 / 45 (13.33%)<br>15 | 11 / 86 (12.79%)<br>14 |
| blood alkaline phosphatase increased<br>alternative dictionary used:<br>MedDRA 21.0                                                                     |                        |                       |                        |

|                                                |                |                  |                 |
|------------------------------------------------|----------------|------------------|-----------------|
| subjects affected / exposed                    | 7 / 81 (8.64%) | 11 / 45 (24.44%) | 4 / 86 (4.65%)  |
| occurrences (all)                              | 15             | 22               | 6               |
| blood bilirubin increased                      |                |                  |                 |
| alternative dictionary used:<br>MedDRA 21.0    |                |                  |                 |
| subjects affected / exposed                    | 2 / 81 (2.47%) | 1 / 45 (2.22%)   | 0 / 86 (0.00%)  |
| occurrences (all)                              | 2              | 1                | 0               |
| blood creatinine increased                     |                |                  |                 |
| alternative dictionary used:<br>MedDRA 21.0    |                |                  |                 |
| subjects affected / exposed                    | 2 / 81 (2.47%) | 3 / 45 (6.67%)   | 4 / 86 (4.65%)  |
| occurrences (all)                              | 6              | 3                | 4               |
| blood thyroid stimulating hormone<br>increased |                |                  |                 |
| alternative dictionary used:<br>MedDRA 21.0    |                |                  |                 |
| subjects affected / exposed                    | 1 / 81 (1.23%) | 0 / 45 (0.00%)   | 0 / 86 (0.00%)  |
| occurrences (all)                              | 2              | 0                | 0               |
| gamma-glutamyltransferase<br>increased         |                |                  |                 |
| alternative dictionary used:<br>MedDRA 21.0    |                |                  |                 |
| subjects affected / exposed                    | 4 / 81 (4.94%) | 4 / 45 (8.89%)   | 1 / 86 (1.16%)  |
| occurrences (all)                              | 5              | 4                | 4               |
| haemoglobin decreased                          |                |                  |                 |
| alternative dictionary used:<br>MedDRA 21.0    |                |                  |                 |
| subjects affected / exposed                    | 1 / 81 (1.23%) | 0 / 45 (0.00%)   | 0 / 86 (0.00%)  |
| occurrences (all)                              | 2              | 0                | 0               |
| international normalised ratio<br>increased    |                |                  |                 |
| alternative dictionary used:<br>MedDRA 21.0    |                |                  |                 |
| subjects affected / exposed                    | 0 / 81 (0.00%) | 2 / 45 (4.44%)   | 0 / 86 (0.00%)  |
| occurrences (all)                              | 0              | 2                | 0               |
| lymphocyte count decreased                     |                |                  |                 |
| alternative dictionary used:<br>MedDRA 21.0    |                |                  |                 |
| subjects affected / exposed                    | 8 / 81 (9.88%) | 5 / 45 (11.11%)  | 9 / 86 (10.47%) |
| occurrences (all)                              | 31             | 32               | 33              |
| neutrophil count decreased                     |                |                  |                 |
| alternative dictionary used:<br>MedDRA 21.0    |                |                  |                 |

|                                                |                  |                  |                  |
|------------------------------------------------|------------------|------------------|------------------|
| subjects affected / exposed                    | 16 / 81 (19.75%) | 20 / 45 (44.44%) | 14 / 86 (16.28%) |
| occurrences (all)                              | 44               | 72               | 32               |
| platelet count decreased                       |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0    |                  |                  |                  |
| subjects affected / exposed                    | 19 / 81 (23.46%) | 15 / 45 (33.33%) | 16 / 86 (18.60%) |
| occurrences (all)                              | 50               | 44               | 46               |
| transaminases increased                        |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0    |                  |                  |                  |
| subjects affected / exposed                    | 0 / 81 (0.00%)   | 0 / 45 (0.00%)   | 1 / 86 (1.16%)   |
| occurrences (all)                              | 0                | 0                | 1                |
| weight decreased                               |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0    |                  |                  |                  |
| subjects affected / exposed                    | 5 / 81 (6.17%)   | 3 / 45 (6.67%)   | 6 / 86 (6.98%)   |
| occurrences (all)                              | 9                | 4                | 14               |
| weight increased                               |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0    |                  |                  |                  |
| subjects affected / exposed                    | 7 / 81 (8.64%)   | 0 / 45 (0.00%)   | 1 / 86 (1.16%)   |
| occurrences (all)                              | 11               | 0                | 1                |
| white blood cell count decreased               |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0    |                  |                  |                  |
| subjects affected / exposed                    | 12 / 81 (14.81%) | 12 / 45 (26.67%) | 12 / 86 (13.95%) |
| occurrences (all)                              | 50               | 63               | 43               |
| Injury, poisoning and procedural complications |                  |                  |                  |
| fall                                           |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0    |                  |                  |                  |
| subjects affected / exposed                    | 1 / 81 (1.23%)   | 2 / 45 (4.44%)   | 2 / 86 (2.33%)   |
| occurrences (all)                              | 1                | 4                | 3                |
| infusion related reaction                      |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0    |                  |                  |                  |
| subjects affected / exposed                    | 2 / 81 (2.47%)   | 0 / 45 (0.00%)   | 2 / 86 (2.33%)   |
| occurrences (all)                              | 2                | 0                | 2                |
| meniscus injury                                |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0    |                  |                  |                  |

|                                             |                  |                  |                  |
|---------------------------------------------|------------------|------------------|------------------|
| subjects affected / exposed                 | 0 / 81 (0.00%)   | 0 / 45 (0.00%)   | 0 / 86 (0.00%)   |
| occurrences (all)                           | 0                | 0                | 0                |
| wound complication                          |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 0 / 81 (0.00%)   | 0 / 45 (0.00%)   | 0 / 86 (0.00%)   |
| occurrences (all)                           | 0                | 0                | 0                |
| Cardiac disorders                           |                  |                  |                  |
| atrial fibrillation                         |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 0 / 81 (0.00%)   | 0 / 45 (0.00%)   | 1 / 86 (1.16%)   |
| occurrences (all)                           | 0                | 0                | 1                |
| sinus tachycardia                           |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 3 / 81 (3.70%)   | 3 / 45 (6.67%)   | 5 / 86 (5.81%)   |
| occurrences (all)                           | 5                | 3                | 8                |
| tachycardia                                 |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 3 / 81 (3.70%)   | 2 / 45 (4.44%)   | 3 / 86 (3.49%)   |
| occurrences (all)                           | 3                | 2                | 3                |
| Nervous system disorders                    |                  |                  |                  |
| dizziness                                   |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 11 / 81 (13.58%) | 3 / 45 (6.67%)   | 9 / 86 (10.47%)  |
| occurrences (all)                           | 26               | 4                | 12               |
| dysgeusia                                   |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 12 / 81 (14.81%) | 13 / 45 (28.89%) | 11 / 86 (12.79%) |
| occurrences (all)                           | 20               | 21               | 11               |
| headache                                    |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 15 / 81 (18.52%) | 6 / 45 (13.33%)  | 13 / 86 (15.12%) |
| occurrences (all)                           | 23               | 7                | 15               |
| memory impairment                           |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |

|                                             |                  |                  |                  |
|---------------------------------------------|------------------|------------------|------------------|
| subjects affected / exposed                 | 1 / 81 (1.23%)   | 1 / 45 (2.22%)   | 0 / 86 (0.00%)   |
| occurrences (all)                           | 1                | 1                | 0                |
| neuropathy peripheral                       |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 7 / 81 (8.64%)   | 0 / 45 (0.00%)   | 5 / 86 (5.81%)   |
| occurrences (all)                           | 10               | 0                | 5                |
| paraesthesia                                |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 3 / 81 (3.70%)   | 4 / 45 (8.89%)   | 4 / 86 (4.65%)   |
| occurrences (all)                           | 4                | 5                | 4                |
| peripheral motor neuropathy                 |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 3 / 81 (3.70%)   | 1 / 45 (2.22%)   | 3 / 86 (3.49%)   |
| occurrences (all)                           | 6                | 2                | 8                |
| peripheral sensory neuropathy               |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 10 / 81 (12.35%) | 10 / 45 (22.22%) | 13 / 86 (15.12%) |
| occurrences (all)                           | 15               | 20               | 31               |
| sciatica                                    |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 0 / 81 (0.00%)   | 1 / 45 (2.22%)   | 1 / 86 (1.16%)   |
| occurrences (all)                           | 0                | 1                | 1                |
| syncope                                     |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 3 / 81 (3.70%)   | 2 / 45 (4.44%)   | 2 / 86 (2.33%)   |
| occurrences (all)                           | 4                | 2                | 6                |
| taste disorder                              |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 4 / 81 (4.94%)   | 0 / 45 (0.00%)   | 1 / 86 (1.16%)   |
| occurrences (all)                           | 5                | 0                | 1                |
| Blood and lymphatic system disorders        |                  |                  |                  |
| anaemia                                     |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |

|                                                                                                                                                                                                                                                                                                                                                                       |                                                               |                                                               |                                                               |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------|---------------------------------------------------------------|---------------------------------------------------------------|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                                                                                                           | <p>43 / 81 (53.09%)</p> <p>168</p>                            | <p>33 / 45 (73.33%)</p> <p>145</p>                            | <p>47 / 86 (54.65%)</p> <p>147</p>                            |
| <p>leukopenia</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                                     | <p>7 / 81 (8.64%)</p> <p>13</p>                               | <p>1 / 45 (2.22%)</p> <p>4</p>                                | <p>3 / 86 (3.49%)</p> <p>6</p>                                |
| <p>neutropenia</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                                    | <p>20 / 81 (24.69%)</p> <p>55</p>                             | <p>6 / 45 (13.33%)</p> <p>6</p>                               | <p>24 / 86 (27.91%)</p> <p>43</p>                             |
| <p>neutrophilia</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                                   | <p>0 / 81 (0.00%)</p> <p>0</p>                                | <p>0 / 45 (0.00%)</p> <p>0</p>                                | <p>0 / 86 (0.00%)</p> <p>0</p>                                |
| <p>thrombocytopenia</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                               | <p>10 / 81 (12.35%)</p> <p>21</p>                             | <p>9 / 45 (20.00%)</p> <p>18</p>                              | <p>13 / 86 (15.12%)</p> <p>21</p>                             |
| <p>Ear and labyrinth disorders</p> <p>ear pain</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                    | <p>1 / 81 (1.23%)</p> <p>1</p>                                | <p>1 / 45 (2.22%)</p> <p>2</p>                                | <p>0 / 86 (0.00%)</p> <p>0</p>                                |
| <p>Eye disorders</p> <p>dry eye</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>lacrimation increased</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>photopsia</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> | <p>2 / 81 (2.47%)</p> <p>2</p> <p>4 / 81 (4.94%)</p> <p>4</p> | <p>2 / 45 (4.44%)</p> <p>2</p> <p>3 / 45 (6.67%)</p> <p>3</p> | <p>0 / 86 (0.00%)</p> <p>0</p> <p>3 / 86 (3.49%)</p> <p>3</p> |

|                                             |                  |                  |                  |
|---------------------------------------------|------------------|------------------|------------------|
| subjects affected / exposed                 | 0 / 81 (0.00%)   | 0 / 45 (0.00%)   | 0 / 86 (0.00%)   |
| occurrences (all)                           | 0                | 0                | 0                |
| vision blurred                              |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 4 / 81 (4.94%)   | 3 / 45 (6.67%)   | 2 / 86 (2.33%)   |
| occurrences (all)                           | 5                | 3                | 2                |
| Gastrointestinal disorders                  |                  |                  |                  |
| abdominal distension                        |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 3 / 81 (3.70%)   | 5 / 45 (11.11%)  | 1 / 86 (1.16%)   |
| occurrences (all)                           | 3                | 5                | 1                |
| abdominal pain                              |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 9 / 81 (11.11%)  | 7 / 45 (15.56%)  | 10 / 86 (11.63%) |
| occurrences (all)                           | 11               | 12               | 10               |
| abdominal pain upper                        |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 3 / 81 (3.70%)   | 0 / 45 (0.00%)   | 2 / 86 (2.33%)   |
| occurrences (all)                           | 5                | 0                | 2                |
| anorectal discomfort                        |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 0 / 81 (0.00%)   | 1 / 45 (2.22%)   | 0 / 86 (0.00%)   |
| occurrences (all)                           | 0                | 1                | 0                |
| aphthous ulcer                              |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 0 / 81 (0.00%)   | 0 / 45 (0.00%)   | 0 / 86 (0.00%)   |
| occurrences (all)                           | 0                | 0                | 0                |
| constipation                                |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 21 / 81 (25.93%) | 12 / 45 (26.67%) | 20 / 86 (23.26%) |
| occurrences (all)                           | 29               | 14               | 24               |
| diarrhoea                                   |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |

|                                             |                  |                  |                  |
|---------------------------------------------|------------------|------------------|------------------|
| subjects affected / exposed                 | 36 / 81 (44.44%) | 21 / 45 (46.67%) | 30 / 86 (34.88%) |
| occurrences (all)                           | 84               | 42               | 50               |
| dry mouth                                   |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 5 / 81 (6.17%)   | 6 / 45 (13.33%)  | 3 / 86 (3.49%)   |
| occurrences (all)                           | 5                | 6                | 3                |
| dyspepsia                                   |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 6 / 81 (7.41%)   | 2 / 45 (4.44%)   | 8 / 86 (9.30%)   |
| occurrences (all)                           | 9                | 2                | 9                |
| gastrooesophageal reflux disease            |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 0 / 81 (0.00%)   | 6 / 45 (13.33%)  | 5 / 86 (5.81%)   |
| occurrences (all)                           | 0                | 7                | 5                |
| haemorrhoids                                |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 1 / 81 (1.23%)   | 3 / 45 (6.67%)   | 4 / 86 (4.65%)   |
| occurrences (all)                           | 1                | 3                | 4                |
| intestinal fistula                          |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 0 / 81 (0.00%)   | 0 / 45 (0.00%)   | 0 / 86 (0.00%)   |
| occurrences (all)                           | 0                | 0                | 0                |
| nausea                                      |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 38 / 81 (46.91%) | 20 / 45 (44.44%) | 40 / 86 (46.51%) |
| occurrences (all)                           | 59               | 31               | 73               |
| oral pain                                   |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 1 / 81 (1.23%)   | 1 / 45 (2.22%)   | 3 / 86 (3.49%)   |
| occurrences (all)                           | 1                | 1                | 3                |
| proctalgia                                  |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 0 / 81 (0.00%)   | 1 / 45 (2.22%)   | 2 / 86 (2.33%)   |
| occurrences (all)                           | 0                | 1                | 2                |

|                                                                                                                            |                        |                       |                        |
|----------------------------------------------------------------------------------------------------------------------------|------------------------|-----------------------|------------------------|
| salivary hypersecretion<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all) | 0 / 81 (0.00%)<br>0    | 0 / 45 (0.00%)<br>0   | 0 / 86 (0.00%)<br>0    |
| stomatitis<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)              | 17 / 81 (20.99%)<br>34 | 7 / 45 (15.56%)<br>18 | 15 / 86 (17.44%)<br>26 |
| toothache<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)               | 2 / 81 (2.47%)<br>2    | 0 / 45 (0.00%)<br>0   | 0 / 86 (0.00%)<br>0    |
| vomiting<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                | 25 / 81 (30.86%)<br>30 | 7 / 45 (15.56%)<br>8  | 13 / 86 (15.12%)<br>17 |
| Skin and subcutaneous tissue disorders                                                                                     |                        |                       |                        |
| alopecia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                | 29 / 81 (35.80%)<br>35 | 5 / 45 (11.11%)<br>5  | 32 / 86 (37.21%)<br>44 |
| dermatitis acneiform<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)    | 3 / 81 (3.70%)<br>4    | 4 / 45 (8.89%)<br>5   | 2 / 86 (2.33%)<br>3    |
| dry skin<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                | 3 / 81 (3.70%)<br>4    | 5 / 45 (11.11%)<br>5  | 5 / 86 (5.81%)<br>6    |
| eczema<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 81 (1.23%)<br>1    | 0 / 45 (0.00%)<br>0   | 1 / 86 (1.16%)<br>2    |
| erythema<br>alternative dictionary used:<br>MedDRA 21.0                                                                    |                        |                       |                        |

|                                                |                  |                 |                  |
|------------------------------------------------|------------------|-----------------|------------------|
| subjects affected / exposed                    | 5 / 81 (6.17%)   | 0 / 45 (0.00%)  | 5 / 86 (5.81%)   |
| occurrences (all)                              | 5                | 0               | 6                |
| nail discolouration                            |                  |                 |                  |
| alternative dictionary used:<br>MedDRA 21.0    |                  |                 |                  |
| subjects affected / exposed                    | 5 / 81 (6.17%)   | 3 / 45 (6.67%)  | 4 / 86 (4.65%)   |
| occurrences (all)                              | 5                | 3               | 4                |
| nail dystrophy                                 |                  |                 |                  |
| alternative dictionary used:<br>MedDRA 21.0    |                  |                 |                  |
| subjects affected / exposed                    | 0 / 81 (0.00%)   | 0 / 45 (0.00%)  | 2 / 86 (2.33%)   |
| occurrences (all)                              | 0                | 0               | 5                |
| onychomadesis                                  |                  |                 |                  |
| alternative dictionary used:<br>MedDRA 21.0    |                  |                 |                  |
| subjects affected / exposed                    | 1 / 81 (1.23%)   | 7 / 45 (15.56%) | 3 / 86 (3.49%)   |
| occurrences (all)                              | 1                | 8               | 3                |
| palmar-plantar erythrodysaesthesia<br>syndrome |                  |                 |                  |
| alternative dictionary used:<br>MedDRA 21.0    |                  |                 |                  |
| subjects affected / exposed                    | 6 / 81 (7.41%)   | 3 / 45 (6.67%)  | 4 / 86 (4.65%)   |
| occurrences (all)                              | 16               | 8               | 7                |
| pruritus                                       |                  |                 |                  |
| alternative dictionary used:<br>MedDRA 21.0    |                  |                 |                  |
| subjects affected / exposed                    | 8 / 81 (9.88%)   | 2 / 45 (4.44%)  | 6 / 86 (6.98%)   |
| occurrences (all)                              | 8                | 3               | 8                |
| rash                                           |                  |                 |                  |
| alternative dictionary used:<br>MedDRA 21.0    |                  |                 |                  |
| subjects affected / exposed                    | 15 / 81 (18.52%) | 1 / 45 (2.22%)  | 11 / 86 (12.79%) |
| occurrences (all)                              | 17               | 1               | 17               |
| rash maculo-papular                            |                  |                 |                  |
| alternative dictionary used:<br>MedDRA 21.0    |                  |                 |                  |
| subjects affected / exposed                    | 10 / 81 (12.35%) | 6 / 45 (13.33%) | 6 / 86 (6.98%)   |
| occurrences (all)                              | 17               | 7               | 7                |
| rash pruritic                                  |                  |                 |                  |
| alternative dictionary used:<br>MedDRA 21.0    |                  |                 |                  |
| subjects affected / exposed                    | 1 / 81 (1.23%)   | 1 / 45 (2.22%)  | 0 / 86 (0.00%)   |
| occurrences (all)                              | 1                | 1               | 0                |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                             |                                                                                                                             |                                                                                                                             |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|
| <p>skin hyperpigmentation</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                                                                                                                                                                                                                                         | <p>3 / 81 (3.70%)</p> <p>6</p>                                                                                              | <p>3 / 45 (6.67%)</p> <p>3</p>                                                                                              | <p>4 / 86 (4.65%)</p> <p>4</p>                                                                                              |
| <p>Renal and urinary disorders</p> <p>chromaturia</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>haematuria</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>micturition urgency</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>proteinuria</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 81 (0.00%)</p> <p>0</p> <p>5 / 81 (6.17%)</p> <p>6</p> <p>0 / 81 (0.00%)</p> <p>0</p> <p>3 / 81 (3.70%)</p> <p>3</p> | <p>0 / 45 (0.00%)</p> <p>0</p> <p>0 / 45 (0.00%)</p> <p>0</p> <p>0 / 45 (0.00%)</p> <p>0</p> <p>0 / 45 (0.00%)</p> <p>0</p> | <p>0 / 86 (0.00%)</p> <p>0</p> <p>1 / 86 (1.16%)</p> <p>3</p> <p>0 / 86 (0.00%)</p> <p>0</p> <p>0 / 86 (0.00%)</p> <p>0</p> |
| <p>Endocrine disorders</p> <p>adrenal insufficiency</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>hypothyroidism</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                                                                         | <p>0 / 81 (0.00%)</p> <p>0</p> <p>3 / 81 (3.70%)</p> <p>5</p>                                                               | <p>0 / 45 (0.00%)</p> <p>0</p> <p>3 / 45 (6.67%)</p> <p>3</p>                                                               | <p>0 / 86 (0.00%)</p> <p>0</p> <p>0 / 86 (0.00%)</p> <p>0</p>                                                               |
| <p>Musculoskeletal and connective tissue disorders</p> <p>arthralgia</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                                                                                                                                                                                              | <p>13 / 81 (16.05%)</p> <p>24</p>                                                                                           | <p>6 / 45 (13.33%)</p> <p>8</p>                                                                                             | <p>14 / 86 (16.28%)</p> <p>18</p>                                                                                           |

|                                             |                  |                  |                  |
|---------------------------------------------|------------------|------------------|------------------|
| back pain                                   |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 10 / 81 (12.35%) | 7 / 45 (15.56%)  | 7 / 86 (8.14%)   |
| occurrences (all)                           | 16               | 8                | 10               |
| bone pain                                   |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 9 / 81 (11.11%)  | 5 / 45 (11.11%)  | 7 / 86 (8.14%)   |
| occurrences (all)                           | 10               | 5                | 7                |
| coccydynia                                  |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 1 / 81 (1.23%)   | 0 / 45 (0.00%)   | 0 / 86 (0.00%)   |
| occurrences (all)                           | 1                | 0                | 0                |
| muscle spasms                               |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 6 / 81 (7.41%)   | 3 / 45 (6.67%)   | 1 / 86 (1.16%)   |
| occurrences (all)                           | 8                | 4                | 1                |
| muscular weakness                           |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 6 / 81 (7.41%)   | 7 / 45 (15.56%)  | 5 / 86 (5.81%)   |
| occurrences (all)                           | 9                | 8                | 10               |
| musculoskeletal chest pain                  |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 2 / 81 (2.47%)   | 0 / 45 (0.00%)   | 0 / 86 (0.00%)   |
| occurrences (all)                           | 2                | 0                | 0                |
| musculoskeletal pain                        |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 1 / 81 (1.23%)   | 2 / 45 (4.44%)   | 3 / 86 (3.49%)   |
| occurrences (all)                           | 1                | 2                | 6                |
| myalgia                                     |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 16 / 81 (19.75%) | 13 / 45 (28.89%) | 11 / 86 (12.79%) |
| occurrences (all)                           | 27               | 16               | 18               |
| pain in extremity                           |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |

|                                                  |                        |                      |                     |
|--------------------------------------------------|------------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 13 / 81 (16.05%)<br>16 | 5 / 45 (11.11%)<br>7 | 8 / 86 (9.30%)<br>9 |
| Infections and infestations                      |                        |                      |                     |
| bronchitis                                       |                        |                      |                     |
| alternative dictionary used:<br>MedDRA 21.0      |                        |                      |                     |
| subjects affected / exposed                      | 2 / 81 (2.47%)         | 1 / 45 (2.22%)       | 1 / 86 (1.16%)      |
| occurrences (all)                                | 3                      | 2                    | 1                   |
| cellulitis                                       |                        |                      |                     |
| alternative dictionary used:<br>MedDRA 21.0      |                        |                      |                     |
| subjects affected / exposed                      | 4 / 81 (4.94%)         | 2 / 45 (4.44%)       | 2 / 86 (2.33%)      |
| occurrences (all)                                | 5                      | 2                    | 2                   |
| cystitis                                         |                        |                      |                     |
| alternative dictionary used:<br>MedDRA 21.0      |                        |                      |                     |
| subjects affected / exposed                      | 0 / 81 (0.00%)         | 0 / 45 (0.00%)       | 2 / 86 (2.33%)      |
| occurrences (all)                                | 0                      | 0                    | 2                   |
| folliculitis                                     |                        |                      |                     |
| alternative dictionary used:<br>MedDRA 21.0      |                        |                      |                     |
| subjects affected / exposed                      | 1 / 81 (1.23%)         | 0 / 45 (0.00%)       | 0 / 86 (0.00%)      |
| occurrences (all)                                | 1                      | 0                    | 0                   |
| oral candidiasis                                 |                        |                      |                     |
| alternative dictionary used:<br>MedDRA 21.0      |                        |                      |                     |
| subjects affected / exposed                      | 1 / 81 (1.23%)         | 3 / 45 (6.67%)       | 3 / 86 (3.49%)      |
| occurrences (all)                                | 1                      | 5                    | 4                   |
| oral herpes                                      |                        |                      |                     |
| alternative dictionary used:<br>MedDRA 21.0      |                        |                      |                     |
| subjects affected / exposed                      | 3 / 81 (3.70%)         | 0 / 45 (0.00%)       | 0 / 86 (0.00%)      |
| occurrences (all)                                | 3                      | 0                    | 0                   |
| paronychia                                       |                        |                      |                     |
| alternative dictionary used:<br>MedDRA 21.0      |                        |                      |                     |
| subjects affected / exposed                      | 2 / 81 (2.47%)         | 1 / 45 (2.22%)       | 1 / 86 (1.16%)      |
| occurrences (all)                                | 2                      | 1                    | 1                   |
| pneumonia                                        |                        |                      |                     |
| alternative dictionary used:<br>MedDRA 21.0      |                        |                      |                     |

|                                             |                  |                 |                  |
|---------------------------------------------|------------------|-----------------|------------------|
| subjects affected / exposed                 | 5 / 81 (6.17%)   | 5 / 45 (11.11%) | 2 / 86 (2.33%)   |
| occurrences (all)                           | 5                | 6               | 2                |
| rash pustular                               |                  |                 |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                 |                  |
| subjects affected / exposed                 | 2 / 81 (2.47%)   | 0 / 45 (0.00%)  | 1 / 86 (1.16%)   |
| occurrences (all)                           | 4                | 0               | 1                |
| respiratory tract infection                 |                  |                 |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                 |                  |
| subjects affected / exposed                 | 1 / 81 (1.23%)   | 1 / 45 (2.22%)  | 1 / 86 (1.16%)   |
| occurrences (all)                           | 1                | 1               | 1                |
| sinusitis                                   |                  |                 |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                 |                  |
| subjects affected / exposed                 | 5 / 81 (6.17%)   | 2 / 45 (4.44%)  | 1 / 86 (1.16%)   |
| occurrences (all)                           | 5                | 2               | 1                |
| skin infection                              |                  |                 |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                 |                  |
| subjects affected / exposed                 | 3 / 81 (3.70%)   | 4 / 45 (8.89%)  | 1 / 86 (1.16%)   |
| occurrences (all)                           | 4                | 4               | 1                |
| upper respiratory tract infection           |                  |                 |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                 |                  |
| subjects affected / exposed                 | 7 / 81 (8.64%)   | 3 / 45 (6.67%)  | 14 / 86 (16.28%) |
| occurrences (all)                           | 9                | 4               | 19               |
| urinary tract infection                     |                  |                 |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                 |                  |
| subjects affected / exposed                 | 15 / 81 (18.52%) | 3 / 45 (6.67%)  | 8 / 86 (9.30%)   |
| occurrences (all)                           | 18               | 4               | 8                |
| vaginal infection                           |                  |                 |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                 |                  |
| subjects affected / exposed <sup>[2]</sup>  | 0 / 48 (0.00%)   | 0 / 28 (0.00%)  | 0 / 58 (0.00%)   |
| occurrences (all)                           | 0                | 0               | 0                |
| Metabolism and nutrition disorders          |                  |                 |                  |
| decreased appetite                          |                  |                 |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                 |                  |

|                                             |                  |                  |                  |
|---------------------------------------------|------------------|------------------|------------------|
| subjects affected / exposed                 | 21 / 81 (25.93%) | 11 / 45 (24.44%) | 15 / 86 (17.44%) |
| occurrences (all)                           | 33               | 14               | 30               |
| dehydration                                 |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 4 / 81 (4.94%)   | 3 / 45 (6.67%)   | 2 / 86 (2.33%)   |
| occurrences (all)                           | 4                | 4                | 2                |
| failure to thrive                           |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 0 / 81 (0.00%)   | 0 / 45 (0.00%)   | 0 / 86 (0.00%)   |
| occurrences (all)                           | 0                | 0                | 0                |
| hypercalcaemia                              |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 0 / 81 (0.00%)   | 1 / 45 (2.22%)   | 0 / 86 (0.00%)   |
| occurrences (all)                           | 0                | 2                | 0                |
| hyperglycaemia                              |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 6 / 81 (7.41%)   | 10 / 45 (22.22%) | 4 / 86 (4.65%)   |
| occurrences (all)                           | 7                | 16               | 4                |
| hyperkalaemia                               |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 2 / 81 (2.47%)   | 0 / 45 (0.00%)   | 0 / 86 (0.00%)   |
| occurrences (all)                           | 4                | 0                | 0                |
| hypernatraemia                              |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 0 / 81 (0.00%)   | 0 / 45 (0.00%)   | 1 / 86 (1.16%)   |
| occurrences (all)                           | 0                | 0                | 1                |
| hyperuricaemia                              |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 0 / 81 (0.00%)   | 1 / 45 (2.22%)   | 2 / 86 (2.33%)   |
| occurrences (all)                           | 0                | 3                | 4                |
| hypoalbuminaemia                            |                  |                  |                  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |                  |                  |
| subjects affected / exposed                 | 8 / 81 (9.88%)   | 4 / 45 (8.89%)   | 2 / 86 (2.33%)   |
| occurrences (all)                           | 9                | 6                | 3                |

|                                                                                                                      |                      |                       |                        |
|----------------------------------------------------------------------------------------------------------------------|----------------------|-----------------------|------------------------|
| hypocalcaemia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)     | 5 / 81 (6.17%)<br>6  | 4 / 45 (8.89%)<br>5   | 1 / 86 (1.16%)<br>1    |
| hypokalaemia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)      | 6 / 81 (7.41%)<br>10 | 9 / 45 (20.00%)<br>16 | 10 / 86 (11.63%)<br>24 |
| hypomagnesaemia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)   | 1 / 81 (1.23%)<br>1  | 3 / 45 (6.67%)<br>5   | 3 / 86 (3.49%)<br>5    |
| hyponatraemia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)     | 4 / 81 (4.94%)<br>7  | 2 / 45 (4.44%)<br>2   | 2 / 86 (2.33%)<br>7    |
| hypophosphataemia<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all) | 2 / 81 (2.47%)<br>6  | 1 / 45 (2.22%)<br>1   | 4 / 86 (4.65%)<br>8    |

|                                                                                                                                                                                       |                                                             |  |  |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------|--|--|
| <b>Non-serious adverse events</b>                                                                                                                                                     | Phase2:Placebo+Gemcitabine+Docetaxel(Olaratumab pretreated) |  |  |
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed                                                                                                  | 42 / 43 (97.67%)                                            |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps)<br>tumour pain<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all) | 0 / 43 (0.00%)<br>0                                         |  |  |
| Vascular disorders<br>embolism<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                                     | 2 / 43 (4.65%)<br>2                                         |  |  |

|                                                                                                                                                                                                                         |  |  |  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|
| <p>embolism venous</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>0 / 43 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>                                                   |  |  |  |
| <p>flushing</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>5 / 43 (11.63%)</p> <p>occurrences (all)</p> <p>6</p>                                                         |  |  |  |
| <p>hot flush</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>3 / 43 (6.98%)</p> <p>occurrences (all)</p> <p>3</p>                                                         |  |  |  |
| <p>hypertension</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>6 / 43 (13.95%)</p> <p>occurrences (all)</p> <p>7</p>                                                     |  |  |  |
| <p>hypotension</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>2 / 43 (4.65%)</p> <p>occurrences (all)</p> <p>2</p>                                                       |  |  |  |
| <p>peripheral venous disease</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>0 / 43 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>                                         |  |  |  |
| <p>phlebitis</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>0 / 43 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>                                                         |  |  |  |
| <p>Surgical and medical procedures</p> <p>orchidectomy</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed<sup>[1]</sup></p> <p>0 / 15 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> |  |  |  |
| <p>General disorders and administration<br/>site conditions</p>                                                                                                                                                         |  |  |  |

|                                             |                  |  |  |
|---------------------------------------------|------------------|--|--|
| asthenia                                    |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 3 / 43 (6.98%)   |  |  |
| occurrences (all)                           | 9                |  |  |
| catheter site pain                          |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%)   |  |  |
| occurrences (all)                           | 0                |  |  |
| chills                                      |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 7 / 43 (16.28%)  |  |  |
| occurrences (all)                           | 8                |  |  |
| device related thrombosis                   |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%)   |  |  |
| occurrences (all)                           | 0                |  |  |
| face oedema                                 |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 1 / 43 (2.33%)   |  |  |
| occurrences (all)                           | 1                |  |  |
| fatigue                                     |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 23 / 43 (53.49%) |  |  |
| occurrences (all)                           | 44               |  |  |
| influenza like illness                      |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 1 / 43 (2.33%)   |  |  |
| occurrences (all)                           | 1                |  |  |
| infusion site extravasation                 |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%)   |  |  |
| occurrences (all)                           | 0                |  |  |
| localised oedema                            |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |

|                                                 |                  |  |  |
|-------------------------------------------------|------------------|--|--|
| subjects affected / exposed                     | 2 / 43 (4.65%)   |  |  |
| occurrences (all)                               | 2                |  |  |
| malaise                                         |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0     |                  |  |  |
| subjects affected / exposed                     | 1 / 43 (2.33%)   |  |  |
| occurrences (all)                               | 1                |  |  |
| non-cardiac chest pain                          |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0     |                  |  |  |
| subjects affected / exposed                     | 3 / 43 (6.98%)   |  |  |
| occurrences (all)                               | 3                |  |  |
| non-pitting oedema                              |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0     |                  |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%)   |  |  |
| occurrences (all)                               | 0                |  |  |
| oedema peripheral                               |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0     |                  |  |  |
| subjects affected / exposed                     | 14 / 43 (32.56%) |  |  |
| occurrences (all)                               | 21               |  |  |
| pain                                            |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0     |                  |  |  |
| subjects affected / exposed                     | 1 / 43 (2.33%)   |  |  |
| occurrences (all)                               | 1                |  |  |
| peripheral swelling                             |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0     |                  |  |  |
| subjects affected / exposed                     | 0 / 43 (0.00%)   |  |  |
| occurrences (all)                               | 0                |  |  |
| pyrexia                                         |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0     |                  |  |  |
| subjects affected / exposed                     | 11 / 43 (25.58%) |  |  |
| occurrences (all)                               | 17               |  |  |
| Respiratory, thoracic and mediastinal disorders |                  |  |  |
| cough                                           |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0     |                  |  |  |

|                                             |                  |  |  |
|---------------------------------------------|------------------|--|--|
| subjects affected / exposed                 | 9 / 43 (20.93%)  |  |  |
| occurrences (all)                           | 10               |  |  |
| dyspnoea                                    |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 12 / 43 (27.91%) |  |  |
| occurrences (all)                           | 19               |  |  |
| dyspnoea exertional                         |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 1 / 43 (2.33%)   |  |  |
| occurrences (all)                           | 1                |  |  |
| epistaxis                                   |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 9 / 43 (20.93%)  |  |  |
| occurrences (all)                           | 11               |  |  |
| haemoptysis                                 |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%)   |  |  |
| occurrences (all)                           | 0                |  |  |
| hiccups                                     |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 1 / 43 (2.33%)   |  |  |
| occurrences (all)                           | 1                |  |  |
| hypoxia                                     |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 1 / 43 (2.33%)   |  |  |
| occurrences (all)                           | 3                |  |  |
| laryngeal haemorrhage                       |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%)   |  |  |
| occurrences (all)                           | 0                |  |  |
| lower respiratory tract congestion          |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%)   |  |  |
| occurrences (all)                           | 0                |  |  |

|                                             |                |  |  |
|---------------------------------------------|----------------|--|--|
| nasal congestion                            |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                |  |  |
| subjects affected / exposed                 | 2 / 43 (4.65%) |  |  |
| occurrences (all)                           | 2              |  |  |
| nasal dryness                               |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%) |  |  |
| occurrences (all)                           | 0              |  |  |
| oropharyngeal pain                          |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%) |  |  |
| occurrences (all)                           | 0              |  |  |
| pleural effusion                            |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                |  |  |
| subjects affected / exposed                 | 4 / 43 (9.30%) |  |  |
| occurrences (all)                           | 4              |  |  |
| pneumonitis                                 |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                |  |  |
| subjects affected / exposed                 | 3 / 43 (6.98%) |  |  |
| occurrences (all)                           | 3              |  |  |
| productive cough                            |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                |  |  |
| subjects affected / exposed                 | 3 / 43 (6.98%) |  |  |
| occurrences (all)                           | 4              |  |  |
| pulmonary embolism                          |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                |  |  |
| subjects affected / exposed                 | 1 / 43 (2.33%) |  |  |
| occurrences (all)                           | 1              |  |  |
| upper-airway cough syndrome                 |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                |  |  |
| subjects affected / exposed                 | 1 / 43 (2.33%) |  |  |
| occurrences (all)                           | 1              |  |  |
| Psychiatric disorders                       |                |  |  |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                               |  |  |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|--|--|
| <p>anxiety</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | <p>3 / 43 (6.98%)</p> <p>4</p>                                                                                                |  |  |
| <p>depression</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | <p>2 / 43 (4.65%)</p> <p>2</p>                                                                                                |  |  |
| <p>insomnia</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | <p>10 / 43 (23.26%)</p> <p>11</p>                                                                                             |  |  |
| <p>nightmare</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | <p>0 / 43 (0.00%)</p> <p>0</p>                                                                                                |  |  |
| <p>Investigations</p> <p>alanine aminotransferase increased</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>aspartate aminotransferase increased</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>blood alkaline phosphatase increased</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>blood bilirubin increased</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>blood creatinine increased</p> <p>alternative dictionary used:</p> | <p>7 / 43 (16.28%)</p> <p>20</p> <p>3 / 43 (6.98%)</p> <p>7</p> <p>3 / 43 (6.98%)</p> <p>6</p> <p>0 / 43 (0.00%)</p> <p>0</p> |  |  |

|                                             |                 |  |  |
|---------------------------------------------|-----------------|--|--|
| MedDRA 21.0                                 |                 |  |  |
| subjects affected / exposed                 | 2 / 43 (4.65%)  |  |  |
| occurrences (all)                           | 9               |  |  |
| blood thyroid stimulating hormone increased |                 |  |  |
| alternative dictionary used: MedDRA 21.0    |                 |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%)  |  |  |
| occurrences (all)                           | 0               |  |  |
| gamma-glutamyltransferase increased         |                 |  |  |
| alternative dictionary used: MedDRA 21.0    |                 |  |  |
| subjects affected / exposed                 | 3 / 43 (6.98%)  |  |  |
| occurrences (all)                           | 5               |  |  |
| haemoglobin decreased                       |                 |  |  |
| alternative dictionary used: MedDRA 21.0    |                 |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%)  |  |  |
| occurrences (all)                           | 0               |  |  |
| international normalised ratio increased    |                 |  |  |
| alternative dictionary used: MedDRA 21.0    |                 |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%)  |  |  |
| occurrences (all)                           | 0               |  |  |
| lymphocyte count decreased                  |                 |  |  |
| alternative dictionary used: MedDRA 21.0    |                 |  |  |
| subjects affected / exposed                 | 3 / 43 (6.98%)  |  |  |
| occurrences (all)                           | 4               |  |  |
| neutrophil count decreased                  |                 |  |  |
| alternative dictionary used: MedDRA 21.0    |                 |  |  |
| subjects affected / exposed                 | 4 / 43 (9.30%)  |  |  |
| occurrences (all)                           | 4               |  |  |
| platelet count decreased                    |                 |  |  |
| alternative dictionary used: MedDRA 21.0    |                 |  |  |
| subjects affected / exposed                 | 7 / 43 (16.28%) |  |  |
| occurrences (all)                           | 10              |  |  |
| transaminases increased                     |                 |  |  |
| alternative dictionary used: MedDRA 21.0    |                 |  |  |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |  |  |  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|
| <p>subjects affected / exposed</p> <p>0 / 43 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>weight decreased</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>5 / 43 (11.63%)</p> <p>occurrences (all)</p> <p>7</p> <p>weight increased</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>1 / 43 (2.33%)</p> <p>occurrences (all)</p> <p>2</p> <p>white blood cell count decreased</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>4 / 43 (9.30%)</p> <p>occurrences (all)</p> <p>6</p>                                                                                                                |  |  |  |
| <p>Injury, poisoning and procedural complications</p> <p>fall</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>2 / 43 (4.65%)</p> <p>occurrences (all)</p> <p>2</p> <p>infusion related reaction</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>0 / 43 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>meniscus injury</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>0 / 43 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>wound complication</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>0 / 43 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> |  |  |  |
| <p>Cardiac disorders</p> <p>atrial fibrillation</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |  |  |  |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |  |  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|
| <p>subjects affected / exposed</p> <p>0 / 43 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |  |  |  |
| <p>sinus tachycardia</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>2 / 43 (4.65%)</p> <p>occurrences (all)</p> <p>4</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |  |  |  |
| <p>tachycardia</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>1 / 43 (2.33%)</p> <p>occurrences (all)</p> <p>2</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |  |  |  |
| <p>Nervous system disorders</p> <p>dizziness</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>4 / 43 (9.30%)</p> <p>occurrences (all)</p> <p>4</p> <p>dysgeusia</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>14 / 43 (32.56%)</p> <p>occurrences (all)</p> <p>18</p> <p>headache</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>5 / 43 (11.63%)</p> <p>occurrences (all)</p> <p>5</p> <p>memory impairment</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>0 / 43 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>neuropathy peripheral</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>1 / 43 (2.33%)</p> <p>occurrences (all)</p> <p>1</p> <p>paraesthesia</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> |  |  |  |

|                                             |                  |  |  |
|---------------------------------------------|------------------|--|--|
| subjects affected / exposed                 | 3 / 43 (6.98%)   |  |  |
| occurrences (all)                           | 3                |  |  |
| peripheral motor neuropathy                 |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%)   |  |  |
| occurrences (all)                           | 0                |  |  |
| peripheral sensory neuropathy               |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 9 / 43 (20.93%)  |  |  |
| occurrences (all)                           | 14               |  |  |
| sciatica                                    |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%)   |  |  |
| occurrences (all)                           | 0                |  |  |
| syncope                                     |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 3 / 43 (6.98%)   |  |  |
| occurrences (all)                           | 3                |  |  |
| taste disorder                              |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 3 / 43 (6.98%)   |  |  |
| occurrences (all)                           | 3                |  |  |
| Blood and lymphatic system disorders        |                  |  |  |
| anaemia                                     |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 20 / 43 (46.51%) |  |  |
| occurrences (all)                           | 57               |  |  |
| leukopenia                                  |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 1 / 43 (2.33%)   |  |  |
| occurrences (all)                           | 4                |  |  |
| neutropenia                                 |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |  |  |  |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|
| <p>subjects affected / exposed</p> <p>4 / 43 (9.30%)</p> <p>occurrences (all)</p> <p>10</p> <p>neutrophilia</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>0 / 43 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>thrombocytopenia</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>6 / 43 (13.95%)</p> <p>occurrences (all)</p> <p>12</p>                                                                                                                                                                                                                                                             |  |  |  |
| <p>Ear and labyrinth disorders</p> <p>ear pain</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>0 / 43 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |  |  |  |
| <p>Eye disorders</p> <p>dry eye</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>0 / 43 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>lacrimation increased</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>3 / 43 (6.98%)</p> <p>occurrences (all)</p> <p>3</p> <p>photopsia</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>0 / 43 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>vision blurred</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>1 / 43 (2.33%)</p> <p>occurrences (all)</p> <p>1</p> |  |  |  |
| <p>Gastrointestinal disorders</p> <p>abdominal distension</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |  |  |  |

|                                             |                  |  |  |
|---------------------------------------------|------------------|--|--|
| subjects affected / exposed                 | 0 / 43 (0.00%)   |  |  |
| occurrences (all)                           | 0                |  |  |
| abdominal pain                              |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 6 / 43 (13.95%)  |  |  |
| occurrences (all)                           | 7                |  |  |
| abdominal pain upper                        |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 2 / 43 (4.65%)   |  |  |
| occurrences (all)                           | 2                |  |  |
| anorectal discomfort                        |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%)   |  |  |
| occurrences (all)                           | 0                |  |  |
| aphthous ulcer                              |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%)   |  |  |
| occurrences (all)                           | 0                |  |  |
| constipation                                |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 12 / 43 (27.91%) |  |  |
| occurrences (all)                           | 13               |  |  |
| diarrhoea                                   |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 14 / 43 (32.56%) |  |  |
| occurrences (all)                           | 21               |  |  |
| dry mouth                                   |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 4 / 43 (9.30%)   |  |  |
| occurrences (all)                           | 4                |  |  |
| dyspepsia                                   |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 3 / 43 (6.98%)   |  |  |
| occurrences (all)                           | 3                |  |  |

|                                             |                  |  |  |
|---------------------------------------------|------------------|--|--|
| gastrooesophageal reflux disease            |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 1 / 43 (2.33%)   |  |  |
| occurrences (all)                           | 1                |  |  |
| haemorrhoids                                |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 1 / 43 (2.33%)   |  |  |
| occurrences (all)                           | 1                |  |  |
| intestinal fistula                          |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%)   |  |  |
| occurrences (all)                           | 0                |  |  |
| nausea                                      |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 12 / 43 (27.91%) |  |  |
| occurrences (all)                           | 22               |  |  |
| oral pain                                   |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 4 / 43 (9.30%)   |  |  |
| occurrences (all)                           | 4                |  |  |
| proctalgia                                  |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 1 / 43 (2.33%)   |  |  |
| occurrences (all)                           | 1                |  |  |
| salivary hypersecretion                     |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%)   |  |  |
| occurrences (all)                           | 0                |  |  |
| stomatitis                                  |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 11 / 43 (25.58%) |  |  |
| occurrences (all)                           | 20               |  |  |
| toothache                                   |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |  |  |  |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|
| <p>subjects affected / exposed</p> <p>0 / 43 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>vomiting</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>7 / 43 (16.28%)</p> <p>occurrences (all)</p> <p>13</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |  |  |  |
| <p>Skin and subcutaneous tissue disorders</p> <p>alopecia</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>5 / 43 (11.63%)</p> <p>occurrences (all)</p> <p>5</p> <p>dermatitis acneiform</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>2 / 43 (4.65%)</p> <p>occurrences (all)</p> <p>5</p> <p>dry skin</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>5 / 43 (11.63%)</p> <p>occurrences (all)</p> <p>5</p> <p>eczema</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>0 / 43 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>erythema</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>1 / 43 (2.33%)</p> <p>occurrences (all)</p> <p>1</p> <p>nail discolouration</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>2 / 43 (4.65%)</p> <p>occurrences (all)</p> <p>3</p> <p>nail dystrophy</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> |  |  |  |

|                                                |                |  |  |
|------------------------------------------------|----------------|--|--|
| subjects affected / exposed                    | 0 / 43 (0.00%) |  |  |
| occurrences (all)                              | 0              |  |  |
| onychomadesis                                  |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0    |                |  |  |
| subjects affected / exposed                    | 2 / 43 (4.65%) |  |  |
| occurrences (all)                              | 4              |  |  |
| palmar-plantar erythrodysaesthesia<br>syndrome |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0    |                |  |  |
| subjects affected / exposed                    | 2 / 43 (4.65%) |  |  |
| occurrences (all)                              | 5              |  |  |
| pruritus                                       |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0    |                |  |  |
| subjects affected / exposed                    | 3 / 43 (6.98%) |  |  |
| occurrences (all)                              | 3              |  |  |
| rash                                           |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0    |                |  |  |
| subjects affected / exposed                    | 2 / 43 (4.65%) |  |  |
| occurrences (all)                              | 3              |  |  |
| rash maculo-papular                            |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0    |                |  |  |
| subjects affected / exposed                    | 3 / 43 (6.98%) |  |  |
| occurrences (all)                              | 3              |  |  |
| rash pruritic                                  |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0    |                |  |  |
| subjects affected / exposed                    | 0 / 43 (0.00%) |  |  |
| occurrences (all)                              | 0              |  |  |
| skin hyperpigmentation                         |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0    |                |  |  |
| subjects affected / exposed                    | 0 / 43 (0.00%) |  |  |
| occurrences (all)                              | 0              |  |  |
| Renal and urinary disorders                    |                |  |  |
| chromaturia                                    |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0    |                |  |  |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |  |  |  |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|
| <p>subjects affected / exposed</p> <p>0 / 43 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>haematuria</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>0 / 43 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>micturition urgency</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>0 / 43 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>proteinuria</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>1 / 43 (2.33%)</p> <p>occurrences (all)</p> <p>2</p> |  |  |  |
| <p>Endocrine disorders</p> <p>adrenal insufficiency</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>0 / 43 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>hypothyroidism</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>0 / 43 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>                                                                                                                                                                                                                             |  |  |  |
| <p>Musculoskeletal and connective tissue disorders</p> <p>arthralgia</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>5 / 43 (11.63%)</p> <p>occurrences (all)</p> <p>8</p> <p>back pain</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p> <p>subjects affected / exposed</p> <p>3 / 43 (6.98%)</p> <p>occurrences (all)</p> <p>4</p> <p>bone pain</p> <p>alternative dictionary used:<br/>MedDRA 21.0</p>                                                                                                                                           |  |  |  |

|                                             |                  |  |  |
|---------------------------------------------|------------------|--|--|
| subjects affected / exposed                 | 6 / 43 (13.95%)  |  |  |
| occurrences (all)                           | 6                |  |  |
| coccydynia                                  |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%)   |  |  |
| occurrences (all)                           | 0                |  |  |
| muscle spasms                               |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 1 / 43 (2.33%)   |  |  |
| occurrences (all)                           | 1                |  |  |
| muscular weakness                           |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 5 / 43 (11.63%)  |  |  |
| occurrences (all)                           | 5                |  |  |
| musculoskeletal chest pain                  |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 1 / 43 (2.33%)   |  |  |
| occurrences (all)                           | 1                |  |  |
| musculoskeletal pain                        |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 2 / 43 (4.65%)   |  |  |
| occurrences (all)                           | 3                |  |  |
| myalgia                                     |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 11 / 43 (25.58%) |  |  |
| occurrences (all)                           | 19               |  |  |
| pain in extremity                           |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |
| subjects affected / exposed                 | 4 / 43 (9.30%)   |  |  |
| occurrences (all)                           | 4                |  |  |
| Infections and infestations                 |                  |  |  |
| bronchitis                                  |                  |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                  |  |  |

|                                             |                |  |  |
|---------------------------------------------|----------------|--|--|
| subjects affected / exposed                 | 0 / 43 (0.00%) |  |  |
| occurrences (all)                           | 0              |  |  |
| cellulitis                                  |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                |  |  |
| subjects affected / exposed                 | 1 / 43 (2.33%) |  |  |
| occurrences (all)                           | 1              |  |  |
| cystitis                                    |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                |  |  |
| subjects affected / exposed                 | 1 / 43 (2.33%) |  |  |
| occurrences (all)                           | 1              |  |  |
| folliculitis                                |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                |  |  |
| subjects affected / exposed                 | 1 / 43 (2.33%) |  |  |
| occurrences (all)                           | 1              |  |  |
| oral candidiasis                            |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                |  |  |
| subjects affected / exposed                 | 3 / 43 (6.98%) |  |  |
| occurrences (all)                           | 4              |  |  |
| oral herpes                                 |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%) |  |  |
| occurrences (all)                           | 0              |  |  |
| paronychia                                  |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                |  |  |
| subjects affected / exposed                 | 1 / 43 (2.33%) |  |  |
| occurrences (all)                           | 2              |  |  |
| pneumonia                                   |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                |  |  |
| subjects affected / exposed                 | 3 / 43 (6.98%) |  |  |
| occurrences (all)                           | 4              |  |  |
| rash pustular                               |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%) |  |  |
| occurrences (all)                           | 0              |  |  |

|                                                                                                                                                             |                        |  |  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|--|--|
| respiratory tract infection<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 43 (0.00%)<br>0    |  |  |
| sinusitis<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                                | 1 / 43 (2.33%)<br>1    |  |  |
| skin infection<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                           | 1 / 43 (2.33%)<br>3    |  |  |
| upper respiratory tract infection<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                        | 3 / 43 (6.98%)<br>4    |  |  |
| urinary tract infection<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                  | 1 / 43 (2.33%)<br>1    |  |  |
| vaginal infection<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed <sup>[2]</sup><br>occurrences (all)                         | 0 / 28 (0.00%)<br>0    |  |  |
| Metabolism and nutrition disorders<br>decreased appetite<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all) | 14 / 43 (32.56%)<br>14 |  |  |
| dehydration<br>alternative dictionary used:<br>MedDRA 21.0<br>subjects affected / exposed<br>occurrences (all)                                              | 3 / 43 (6.98%)<br>3    |  |  |
| failure to thrive<br>alternative dictionary used:<br>MedDRA 21.0                                                                                            |                        |  |  |

|                                             |                 |  |  |
|---------------------------------------------|-----------------|--|--|
| subjects affected / exposed                 | 0 / 43 (0.00%)  |  |  |
| occurrences (all)                           | 0               |  |  |
| hypercalcaemia                              |                 |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                 |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%)  |  |  |
| occurrences (all)                           | 0               |  |  |
| hyperglycaemia                              |                 |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                 |  |  |
| subjects affected / exposed                 | 2 / 43 (4.65%)  |  |  |
| occurrences (all)                           | 4               |  |  |
| hyperkalaemia                               |                 |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                 |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%)  |  |  |
| occurrences (all)                           | 0               |  |  |
| hypernatraemia                              |                 |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                 |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%)  |  |  |
| occurrences (all)                           | 0               |  |  |
| hyperuricaemia                              |                 |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                 |  |  |
| subjects affected / exposed                 | 0 / 43 (0.00%)  |  |  |
| occurrences (all)                           | 0               |  |  |
| hypoalbuminaemia                            |                 |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                 |  |  |
| subjects affected / exposed                 | 5 / 43 (11.63%) |  |  |
| occurrences (all)                           | 7               |  |  |
| hypocalcaemia                               |                 |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                 |  |  |
| subjects affected / exposed                 | 3 / 43 (6.98%)  |  |  |
| occurrences (all)                           | 5               |  |  |
| hypokalaemia                                |                 |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                 |  |  |
| subjects affected / exposed                 | 7 / 43 (16.28%) |  |  |
| occurrences (all)                           | 14              |  |  |

|                                             |                |  |  |
|---------------------------------------------|----------------|--|--|
| hypomagnesaemia                             |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                |  |  |
| subjects affected / exposed                 | 3 / 43 (6.98%) |  |  |
| occurrences (all)                           | 7              |  |  |
| hyponatraemia                               |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                |  |  |
| subjects affected / exposed                 | 1 / 43 (2.33%) |  |  |
| occurrences (all)                           | 1              |  |  |
| hypophosphataemia                           |                |  |  |
| alternative dictionary used:<br>MedDRA 21.0 |                |  |  |
| subjects affected / exposed                 | 2 / 43 (4.65%) |  |  |
| occurrences (all)                           | 4              |  |  |

---

Notes:

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

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

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

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

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 15 June 2016    | The rationale for amendment (a) was based on feedback received from global regulatory authorities and compliance with local regulatory requirements for submissions. Major changes for amendment (a) included the following: new descriptive language on premedication prior to olaratumab/placebo doses on Days 1 and 8 of Cycle 1 and in subsequent cycles. Clarification was also added related to the olaratumab observation period.                       |
| 05 January 2017 | Amendment (b): The protocol was amended to allow for expansion of the olaratumab 20 mg/kg dose level (Cohort 2) by enrolling approximately 15 additional patients. The rationale for adding an additional 15 patients to Cohort 2 is to confirm the safety of the 20 mg/kg dose level prior to opening the Phase 2 randomized double-blinded portion of the trial.                                                                                             |
| 19 July 2017    | Amendment (c): The protocol was amended to enroll an additional cohort of 90 patients previously treated with olaratumab in combination with doxorubicin, in order to evaluate, as secondary objective, the effect of olaratumab as continuation therapy with regimens such as gemcitabine/docetaxel that are customarily administered after maximal doxorubicin dosing. The protocol amendment also added an interim efficacy analysis of all study outcomes. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported