



## Clinical trial results:

### Phase II Trial of CAP7.1 in adult patients with refractory malignancies Small cell lung carcinoma, Non-small cell lung carcinoma, Biliary carcinoma

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2012-002378-30 |
| Trial protocol           | DE             |
| Global end of trial date | 10 April 2017  |

#### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 29 August 2018 |
| First version publication date | 29 August 2018 |

#### Trial information

##### Trial identification

|                       |           |
|-----------------------|-----------|
| Sponsor protocol code | CPN710102 |
|-----------------------|-----------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02094560 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | CellAct Pharma GmbH   |
| Sponsor organisation address | Biomedizin Zentrum Dortmund, Otto-Hahn-Str. 15, Dortmund, Germany, 44227              |
| Public contact               | Nalân Utku, CellAct Pharma GmbH, 49 23197426350, n.utku@cellact.eu                    |
| Scientific contact           | Nalân Utku, CellAct Pharma GmbH, 49 23197426350, n.utku@cellact.eu                    |
| Sponsor organisation name    | Mundipharma EDO GmbH  |
| Sponsor organisation address | St. Alban-Rheinweg 74, Basel, Switzerland, CH-4020                                    |
| Public contact               | Thomas Mehrling, Mundipharma EDO GmbH, 41 61 205 1473, thomas.mehrling@edoncology.com |
| Scientific contact           | Thomas Mehrling, Mundipharma EDO GmbH, 41 61 205 1473, thomas.mehrling@edoncology.com |

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                       | 02 December 2015 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 10 April 2017    |
| Was the trial ended prematurely?                     | Yes              |

Notes:

## General information about the trial

Main objective of the trial:

The main objective of the study was to assess the antitumor activity of CAP7.1 based on the observed objective response rate and rate of disease stabilization using Response Evaluation Criteria in Solid Tumours (RECIST) 1.1.

Protection of trial subjects:

The study was conducted in agreement with the Declaration of Helsinki (Tokyo, Venice, Hong Kong, Somerset West and Edinburgh amendments) and the laws and regulations of the country, whichever provides the greatest protection of the subject.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 08 November 2011 |
| 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 | Germany: 43 |
| Worldwide total number of subjects   | 43          |
| EEA total number of subjects         | 43          |

Notes:

### Subjects enrolled per age group

|   |    |
|---|----|
| In utero                                  | 0  |
| Preterm newborn - gestational age < 37 wk | 0  |
| Newborns (0-27 days)                      | 0  |
| Infants and toddlers (28 days-23 months)  | 0  |
| Children (2-11 years)                     | 0  |
| Adolescents (12-17 years)                 | 0  |
| Adults (18-64 years)                      | 22 |

|                     |    |
|---------------------|----|
| From 65 to 84 years | 21 |
| 85 years and over   | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Overall 45 subjects were enrolled, Of them 43 subjects were treated.

### Period 1

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

### Arms

|                              |  |
|------------------------------|--|
| Are arms mutually exclusive? | Yes  |
| <b>Arm title</b>             | Non-Small Cell Lung Cancer (NSCLC): CAP7.1 |

Arm description:

Subjects with NSCLC who had progressed despite previous therapies received 60 minutes (min) intravenous infusion of 150 or 200 milligram per square meter (mg/m<sup>2</sup>) CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | CAP7.1                |
| Investigational medicinal product code | CAP7.1                |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

Subjects received 150 or 200 mg/m<sup>2</sup> (60 min intravenous infusion) of CAP7.1.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Non-Small Cell Lung Cancer (NSCLC): Best Supportive Care (BSC) |
|------------------|--|

Arm description:

Subjects with NSCLC who had progressed despite previous therapies received best support as per institutional standards. In case of progression, these subjects were allowed to cross over to CAP7.1 therapy at the dose of 150 or 200 mg/m<sup>2</sup> (60 min intravenous infusion) daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

|   |                      |
|---|----------------------|
| Arm type  | Best Supportive Care |
| No investigational medicinal product assigned in this arm |                      |

|                  |                                       |
|------------------|---------------------------------------|
| <b>Arm title</b> | Small Cell Lung Cancer (SCLC): CAP7.1 |
|------------------|---------------------------------------|

Arm description:

Subjects with SCLC who had progressed despite previous therapies received 60 min intravenous infusion of 150 or 200 mg/m<sup>2</sup> CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|   |                              |
|---|------------------------------|
| Investigational medicinal product name  | CAP7.1                       |
| Investigational medicinal product code  | CAP7.1                       |
| Other name  |                              |
| Pharmaceutical forms  | Solution for infusion        |
| Routes of administration  | Intravenous use              |
| Dosage and administration details:  |                              |
| Subjects received 150 or 200 mg/m <sup>2</sup> (60 min intravenous infusion) of CAP7.1. |                              |
| <b>Arm title</b>  | Biliary tract cancer: CAP7.1 |

**Arm description:**

Subjects with advanced biliary tract cancer who had progressed despite previous therapies received 60 min intravenous infusion of 150 or 200 mg/m<sup>2</sup> CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | CAP7.1                |
| Investigational medicinal product code | CAP7.1                |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

**Dosage and administration details:**

Subjects received 150 or 200 mg/m<sup>2</sup> (60 min intravenous infusion) of CAP7.1.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Biliary tract cancer: Best Supportive Care (BSC) |
|------------------|--|

**Arm description:**

Subjects with advanced biliary tract cancer who had progressed despite previous therapies received best support as per institutional standards. In case of progression, these subjects were allowed to cross over to CAP7.1 therapy at the dose of 150 or 200 mg/m<sup>2</sup> (60 min intravenous infusion) daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

|   |                      |
|---|----------------------|
| Arm type  | Best Supportive Care |
| No investigational medicinal product assigned in this arm |                      |

| Number of subjects in period 1 | Non-Small Cell Lung Cancer (NSCLC): CAP7.1 | Non-Small Cell Lung Cancer (NSCLC): Best Supportive Care (BSC) | Small Cell Lung Cancer (SCLC): CAP7.1 |
|--------------------------------|--|--|---------------------------------------|
|                                |  |  |                                       |
| Started                        | 4  | 4  | 8                                     |
| Completed                      | 2  | 0  | 4                                     |
| Not completed                  | 2  | 4  | 4                                     |
| Consent withdrawn by subject   | -  | 2  | -                                     |
| Physician decision             | -  | -  | -                                     |
| Removed Medically Warranted    | -  | 1  | -                                     |
| Other                          | -  | -  | -                                     |
| Progressive Disease            | 1  | 1  | 3                                     |
| Screening Failure              | -  | -  | -                                     |
| Adverse event                  | 1  | -  | 1                                     |

|                   |   |   |   |
|-------------------|---|---|---|
| Lost to follow-up | - | - | - |
|-------------------|---|---|---|

| Number of subjects in period 1 | Biliary tract cancer:<br>CAP7.1 | Biliary tract cancer:<br>Best Supportive Care<br>(BSC) |
|--------------------------------|---------------------------------|--|
|                                |                                 |  |
| Started                        | 14                              | 13   |
| Completed                      | 9                               | 5  |
| Not completed                  | 5                               | 8  |
| Consent withdrawn by subject   | -                               | 1  |
| Physician decision             | -                               | 1  |
| Removed Medically Warranted    | -                               | -  |
| Other                          | 1                               | 1  |
| Progressive Disease            | -                               | 1  |
| Screening Failure              | 1                               | -  |
| Adverse event                  | 3                               | 3  |
| Lost to follow-up              | -                               | 1  |

## Baseline characteristics

### Reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | Non-Small Cell Lung Cancer (NSCLC): CAP7.1 |
|-----------------------|--|

#### Reporting group description:

Subjects with NSCLC who had progressed despite previous therapies received 60 minutes (min) intravenous infusion of 150 or 200 milligram per square meter (mg/m<sup>2</sup>) CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

|                       |  |
|-----------------------|--|
| Reporting group title | Non-Small Cell Lung Cancer (NSCLC): Best Supportive Care (BSC) |
|-----------------------|--|

#### Reporting group description:

Subjects with NSCLC who had progressed despite previous therapies received best support as per institutional standards. In case of progression, these subjects were allowed to cross over to CAP7.1 therapy at the dose of 150 or 200 mg/m<sup>2</sup> (60 min intravenous infusion) daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | Small Cell Lung Cancer (SCLC): CAP7.1 |
|-----------------------|---------------------------------------|

#### Reporting group description:

Subjects with SCLC who had progressed despite previous therapies received 60 min intravenous infusion of 150 or 200 mg/m<sup>2</sup> CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Biliary tract cancer: CAP7.1 |
|-----------------------|------------------------------|

#### Reporting group description:

Subjects with advanced biliary tract cancer who had progressed despite previous therapies received 60 min intravenous infusion of 150 or 200 mg/m<sup>2</sup> CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

|                       |  |
|-----------------------|--|
| Reporting group title | Biliary tract cancer: Best Supportive Care (BSC) |
|-----------------------|--|

#### Reporting group description:

Subjects with advanced biliary tract cancer who had progressed despite previous therapies received best support as per institutional standards. In case of progression, these subjects were allowed to cross over to CAP7.1 therapy at the dose of 150 or 200 mg/m<sup>2</sup> (60 min intravenous infusion) daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

| Reporting group values | Non-Small Cell Lung Cancer (NSCLC): CAP7.1 | Non-Small Cell Lung Cancer (NSCLC): Best Supportive Care (BSC) | Small Cell Lung Cancer (SCLC): CAP7.1 |
|------------------------|--|--|---------------------------------------|
| Number of subjects     | 4  | 4  | 8                                     |
| Age categorical        |  |  |                                       |
| Units: Subjects        |  |  |                                       |
| Adults (18-64 years)   | 2  | 2  | 3                                     |
| From 65-84 years       | 2  | 2  | 5                                     |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 63.0<br>± 4.08 | 61.5<br>± 11.00 | 63.3<br>± 8.15 |
| Gender categorical<br>Units: Subjects                                   |                |                 |                |
| Female  | 2              | 1               | 1              |
| Male  | 2              | 3               | 7              |

| <b>Reporting group values</b>   | Biliary tract cancer:<br>CAP7.1 | Biliary tract cancer:<br>Best Supportive Care<br>(BSC) | Total |
|---|---------------------------------|--|-------|
| Number of subjects  | 14                              | 13   | 43    |
| Age categorical<br>Units: Subjects                                      |                                 |  |       |
| Adults (18-64 years)  | 9                               | 6  | 22    |
| From 65-84 years  | 5                               | 7  | 21    |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 60.3<br>± 10.54                 | 65.8<br>± 8.70   | -     |
| Gender categorical<br>Units: Subjects                                   |                                 |  |       |
| Female  | 6                               | 7  | 17    |
| Male  | 8                               | 6  | 26    |



## End points

### End points reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | Non-Small Cell Lung Cancer (NSCLC): CAP7.1 |
|-----------------------|--|

#### Reporting group description:

Subjects with NSCLC who had progressed despite previous therapies received 60 minutes (min) intravenous infusion of 150 or 200 milligram per square meter (mg/m<sup>2</sup>) CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

|                       |  |
|-----------------------|--|
| Reporting group title | Non-Small Cell Lung Cancer (NSCLC): Best Supportive Care (BSC) |
|-----------------------|--|

#### Reporting group description:

Subjects with NSCLC who had progressed despite previous therapies received best support as per institutional standards. In case of progression, these subjects were allowed to cross over to CAP7.1 therapy at the dose of 150 or 200 mg/m<sup>2</sup> (60 min intravenous infusion) daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | Small Cell Lung Cancer (SCLC): CAP7.1 |
|-----------------------|---------------------------------------|

#### Reporting group description:

Subjects with SCLC who had progressed despite previous therapies received 60 min intravenous infusion of 150 or 200 mg/m<sup>2</sup> CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Biliary tract cancer: CAP7.1 |
|-----------------------|------------------------------|

#### Reporting group description:

Subjects with advanced biliary tract cancer who had progressed despite previous therapies received 60 min intravenous infusion of 150 or 200 mg/m<sup>2</sup> CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

|                       |  |
|-----------------------|--|
| Reporting group title | Biliary tract cancer: Best Supportive Care (BSC) |
|-----------------------|--|

#### Reporting group description:

Subjects with advanced biliary tract cancer who had progressed despite previous therapies received best support as per institutional standards. In case of progression, these subjects were allowed to cross over to CAP7.1 therapy at the dose of 150 or 200 mg/m<sup>2</sup> (60 min intravenous infusion) daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

### Primary: Percentage of Subjects With Disease Control

|                 |   |
|-----------------|---|
| End point title | Percentage of Subjects With Disease Control |
|-----------------|---|

#### End point description:

The rate of disease control was defined as the percentage of subjects who have achieved complete, partial remission and stable disease (CR+PR+SD), according to RECIST 1.1. CR was defined as disappearance of all target lesions/ disappearance of all non-target lesions and normalization of tumor marker level. PR was defined as at least a 30% decrease in the sum of the limited-stage disease (LD) of target lesions, taking as reference the baseline sum LD. SD was defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (PD), taking as reference the smallest sum LD since the treatment started. PD was defined as at least a 20% increase in the sum of the LD of target lesions, taking as reference the smallest sum LD recorded since the treatment started or the appearance of one or more new lesions/appearance of one or more new lesions and/or

unequivocal progression of existing non-target lesions.

|   |         |
|---|---------|
| End point type  | Primary |
| End point timeframe:  |         |
| Start of study treatment until 30 days post-last study treatment (approximately 2 years and 9 months) |         |

| End point values                 | Non-Small Cell Lung Cancer (NSCLC): CAP7.1 | Non-Small Cell Lung Cancer (NSCLC): Best Supportive Care (BSC) | Small Cell Lung Cancer (SCLC): CAP7.1 | Biliary tract cancer: CAP7.1 |
|----------------------------------|--|--|---------------------------------------|------------------------------|
| Subject group type               | Reporting group                            | Reporting group  | Reporting group                       | Reporting group              |
| Number of subjects analysed      | 4 <sup>[1]</sup>                           | 3 <sup>[2]</sup>   | 8 <sup>[3]</sup>                      | 10 <sup>[4]</sup>            |
| Units: Percentage of subjects    |  |  |                                       |                              |
| number (confidence interval 95%) | 50.0 (6.8 to 93.2)                         | 0.0 (0.0 to 70.8)  | 25.0 (3.2 to 65.1)                    | 50.0 (18.7 to 81.3)          |

Notes:

[1] - Full analysis set (FAS) included all randomized subjects.

[2] - FAS with evaluable subjects for this end point.

[3] - FAS

[4] - FAS with evaluable subjects for this end point.

| End point values                 | Biliary tract cancer: Best Supportive Care (BSC) |  |  |  |
|----------------------------------|--|--|--|--|
| Subject group type               | Reporting group                                  |  |  |  |
| Number of subjects analysed      | 10 <sup>[5]</sup>                                |  |  |  |
| Units: Percentage of subjects    |  |  |  |  |
| number (confidence interval 95%) | 20.0 (2.5 to 55.6)                               |  |  |  |

Notes:

[5] - FAS with evaluable subjects for this end point.

## Statistical analyses

| Statistical analysis title              | Statistical analysis 1: NSCLC   |
|---|---|
| Comparison groups                       | Non-Small Cell Lung Cancer (NSCLC): CAP7.1 v Non-Small Cell Lung Cancer (NSCLC): Best Supportive Care (BSC) |
| Number of subjects included in analysis | 7   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority   |
| P-value                                 | = 0.286   |
| Method                                  | t-test, 1-sided   |
| Parameter estimate                      | Treatment difference  |
| Point estimate                          | 50  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -30.14  |
| upper limit                             | 93.24   |

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Statistical analysis 2: Biliary   |
| Comparison groups                       | Biliary tract cancer: CAP7.1 v Biliary tract cancer: Best Supportive Care (BSC) |
| Number of subjects included in analysis | 20  |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority   |
| P-value                                 | = 0.175   |
| Method                                  | t-test, 1-sided   |
| Parameter estimate                      | Treatment difference  |
| Point estimate                          | 30  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -18.44  |
| upper limit                             | 69.22   |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From start of study drug administration until 6 months post-therapy discontinuation/death

Adverse event reporting additional description:

The reporting groups "Biliary tract cancer: BSC before cross-over to CAP7.1" and "Biliary tract cancer: CAP7.1 after Best Supportive Care" were not mutually exclusive for the representation of adverse events.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

|                    |       |
|--------------------|-------|
| Dictionary version | 16.0E |
|--------------------|-------|

### Reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | Non-Small Cell Lung Cancer (NSCLC): CAP7.1 |
|-----------------------|--|

Reporting group description:

Subjects with NSCLC who had progressed despite previous therapies received 60 minutes (min) intravenous infusion of 150 or 200 milligram per square meter (mg/m<sup>2</sup>) CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

|                       |  |
|-----------------------|--|
| Reporting group title | Non-Small Cell Lung Cancer (NSCLC): Best Supportive Care |
|-----------------------|--|

Reporting group description:

Subjects with NSCLC who had progressed despite previous therapies received best support as per institutional standards. In case of progression, these subjects were allowed to cross over to CAP7.1 therapy at the dose of 150 or 200 mg/m<sup>2</sup> (60 min intravenous infusion) daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | Small Cell Lung Cancer (SCLC): CAP7.1 |
|-----------------------|---------------------------------------|

Reporting group description:

Subjects with SCLC who had progressed despite previous therapies received 60 min intravenous infusion of 150 or 200 mg/m<sup>2</sup> CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Biliary tract cancer: CAP7.1 |
|-----------------------|------------------------------|

Reporting group description:

Subjects with advanced biliary tract cancer who had progressed despite previous therapies received 60 min intravenous infusion of 150 or 200 mg/m<sup>2</sup> CAP7.1 daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

|                       |   |
|-----------------------|---|
| Reporting group title | Biliary tract cancer: BSC before cross-over to CAP7.1 |
|-----------------------|---|

Reporting group description:

Subjects with advanced biliary tract cancer who had progressed despite previous therapies received best support as per institutional standards. In case of progression, these subjects were allowed to cross over to CAP7.1 therapy at the dose of 150 or 200 mg/m<sup>2</sup> (60 min intravenous infusion) daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

|                       |   |
|-----------------------|---|
| Reporting group title | Biliary tract cancer: CAP7.1 after Best Supportive Care |
|-----------------------|---|

Reporting group description:

Subjects with advanced biliary tract cancer who had progressed despite previous therapies received best

support as per institutional standards. In case of progression, these subjects were allowed to cross over to CAP7.1 therapy at the dose of 150 or 200 mg/m<sup>2</sup> (60 min intravenous infusion) daily for 5 consecutive days, followed by a medication free interval of 23 days. The full 28-day treatment cycle (5 days on treatment and 23-day treatment-free interval) was repeated until disease progression, unmanageable toxicity or withdrawal of consent (whichever occurred first), if recovery from haematological and other toxicities was considered adequate.

| <b>Serious adverse events</b>                                       | Non-Small Cell Lung Cancer (NSCLC): CAP7.1 | Non-Small Cell Lung Cancer (NSCLC): Best Supportive Care | Small Cell Lung Cancer (SCLC): CAP7.1 |
|---|--|--|---------------------------------------|
| Total subjects affected by serious adverse events                   |  |  |                                       |
| subjects affected / exposed   | 2 / 4 (50.00%)                             | 1 / 2 (50.00%)   | 6 / 8 (75.00%)                        |
| number of deaths (all causes)                                       | 4  | 2  | 8                                     |
| number of deaths resulting from adverse events                      | 1  | 0  | 2                                     |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |  |                                       |
| Malignant neoplasm progression                                      |  |  |                                       |
| subjects affected / exposed   | 0 / 4 (0.00%)                              | 0 / 2 (0.00%)  | 0 / 8 (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   |  |  |                                       |
| Acute coronary syndrome   |  |  |                                       |
| subjects affected / exposed   | 0 / 4 (0.00%)                              | 0 / 2 (0.00%)  | 0 / 8 (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 arrest  |  |  |                                       |
| subjects affected / exposed   | 0 / 4 (0.00%)                              | 0 / 2 (0.00%)  | 0 / 8 (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 tamponade   |  |  |                                       |
| subjects affected / exposed   | 0 / 4 (0.00%)                              | 0 / 2 (0.00%)  | 1 / 8 (12.50%)                        |
| occurrences causally related to treatment / all                     | 0 / 0                                      | 0 / 0  | 0 / 1                                 |
| deaths causally related to treatment / all                          | 0 / 0                                      | 0 / 0  | 0 / 0                                 |
| Nervous system disorders  |  |  |                                       |
| Dizziness   |  |  |                                       |
| subjects affected / exposed   | 1 / 4 (25.00%)                             | 0 / 2 (0.00%)  | 0 / 8 (0.00%)                         |
| occurrences causally related to treatment / all                     | 2 / 2                                      | 0 / 0  | 0 / 0                                 |
| deaths causally related to treatment / all                          | 0 / 0                                      | 0 / 0  | 0 / 0                                 |
| Blood and lymphatic system disorders                                |  |  |                                       |

|  |                |               |                |
|--|----------------|---------------|----------------|
| Anaemia  |                |               |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 1 / 8 (12.50%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 1 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0          |
| Febrile neutropenia                                  |                |               |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 1 / 8 (12.50%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 1 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0          |
| Haematotoxicity                                      |                |               |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (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  |                |               |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 1 / 8 (12.50%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 1 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0          |
| Pancytopenia   |                |               |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 1 / 8 (12.50%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 1 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0          |
| Thrombocytopenia                                     |                |               |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 1 / 8 (12.50%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 1 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0          |
| General disorders and administration site conditions |                |               |                |
| Condition aggravated                                 |                |               |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (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          |
| Death  |                |               |                |
| subjects affected / exposed                          | 1 / 4 (25.00%) | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 1          | 0 / 0         | 0 / 0          |

|   |               |                |                |
|---|---------------|----------------|----------------|
| Device occlusion                                |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 2 (0.00%)  | 0 / 8 (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          |
| Disease progression                             |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 2 (0.00%)  | 2 / 8 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 2          |
| General physical health deterioration           |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 2 (0.00%)  | 1 / 8 (12.50%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Infusion site anaesthesia                       |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 2 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pain  |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 1 / 2 (50.00%) | 0 / 8 (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          |
| Pyrexia   |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 2 (0.00%)  | 0 / 8 (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                                  |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 2 (0.00%)  | 0 / 8 (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          |
| Ascites   |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 2 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                         |               |                |                |

|   |                |               |                |
|---|----------------|---------------|----------------|
| Cholangitis                                     |                |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (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          |
| Jaundice cholestatic                            |                |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (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, thoracic and mediastinal disorders |                |               |                |
| Cough   |                |               |                |
| subjects affected / exposed                     | 1 / 4 (25.00%) | 0 / 2 (0.00%) | 0 / 8 (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          |
| Psychiatric disorders                           |                |               |                |
| Confusional state                               |                |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (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                     |                |               |                |
| Renal impairment                                |                |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 1 / 8 (12.50%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Infections and infestations                     |                |               |                |
| Bronchitis                                      |                |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (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          |
| Febrile infection                               |                |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (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                              |                |               |                |



|   |                |               |                |
|---|----------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 1 / 8 (12.50%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Pneumonia                                       |                |               |                |
| subjects affected / exposed                     | 1 / 4 (25.00%) | 0 / 2 (0.00%) | 0 / 8 (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          |
| Urinary tract infection                         |                |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Metabolism and nutrition disorders              |                |               |                |
| Dehydration                                     |                |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (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          |
| Tumour lysis syndrome                           |                |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |

| <b>Serious adverse events</b>                                       | Biliary tract cancer:<br>CAP7.1 | Biliary tract cancer:<br>BSC before cross-<br>over to CAP7.1 | Biliary tract cancer:<br>CAP7.1 after Best<br>Supportive Care |
|---|---------------------------------|--|---|
| Total subjects affected by serious adverse events                   |                                 |  |   |
| subjects affected / exposed   | 7 / 13 (53.85%)                 | 2 / 10 (20.00%)  | 8 / 10 (80.00%)   |
| number of deaths (all causes)                                       | 12                              | 0  | 10  |
| number of deaths resulting from adverse events                      | 4                               | 0  | 4   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                 |  |   |
| Malignant neoplasm progression                                      |                                 |  |   |
| subjects affected / exposed   | 1 / 13 (7.69%)                  | 0 / 10 (0.00%)   | 0 / 10 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 1                           | 0 / 0  | 0 / 0   |
| deaths causally related to treatment / all                          | 0 / 1                           | 0 / 0  | 0 / 0   |
| Cardiac disorders   |                                 |  |   |
| Acute coronary syndrome   |                                 |  |   |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 13 (0.00%)  | 0 / 10 (0.00%) | 1 / 10 (10.00%) |
| 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 arrest                                  |                 |                |                 |
| subjects affected / exposed                     | 1 / 13 (7.69%)  | 0 / 10 (0.00%) | 0 / 10 (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           |
| Cardiac tamponade                               |                 |                |                 |
| subjects affected / exposed                     | 0 / 13 (0.00%)  | 0 / 10 (0.00%) | 0 / 10 (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                                       |                 |                |                 |
| subjects affected / exposed                     | 0 / 13 (0.00%)  | 0 / 10 (0.00%) | 0 / 10 (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   |                 |                |                 |
| subjects affected / exposed                     | 0 / 13 (0.00%)  | 0 / 10 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Febrile neutropenia                             |                 |                |                 |
| subjects affected / exposed                     | 1 / 13 (7.69%)  | 0 / 10 (0.00%) | 0 / 10 (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           |
| Haematotoxicity                                 |                 |                |                 |
| subjects affected / exposed                     | 0 / 13 (0.00%)  | 0 / 10 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Neutropenia                                     |                 |                |                 |
| subjects affected / exposed                     | 2 / 13 (15.38%) | 0 / 10 (0.00%) | 3 / 10 (30.00%) |
| occurrences causally related to treatment / all | 3 / 3           | 0 / 0          | 3 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Pancytopenia                                    |                 |                |                 |

|  |                |                |                 |
|--|----------------|----------------|-----------------|
| subjects affected / exposed                          | 0 / 13 (0.00%) | 0 / 10 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |
| Thrombocytopenia                                     |                |                |                 |
| subjects affected / exposed                          | 0 / 13 (0.00%) | 0 / 10 (0.00%) | 2 / 10 (20.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 2 / 2           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |
| General disorders and administration site conditions |                |                |                 |
| Condition aggravated                                 |                |                |                 |
| subjects affected / exposed                          | 1 / 13 (7.69%) | 0 / 10 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all      | 1 / 1          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 1           |
| Death  |                |                |                 |
| subjects affected / exposed                          | 0 / 13 (0.00%) | 0 / 10 (0.00%) | 0 / 10 (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           |
| Device occlusion                                     |                |                |                 |
| subjects affected / exposed                          | 0 / 13 (0.00%) | 0 / 10 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 4           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |
| Disease progression                                  |                |                |                 |
| subjects affected / exposed                          | 1 / 13 (7.69%) | 0 / 10 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 1          | 0 / 0          | 0 / 1           |
| General physical health deterioration                |                |                |                 |
| subjects affected / exposed                          | 1 / 13 (7.69%) | 0 / 10 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all           | 0 / 1          | 0 / 0          | 0 / 0           |
| Infusion site anaesthesia                            |                |                |                 |
| subjects affected / exposed                          | 1 / 13 (7.69%) | 0 / 10 (0.00%) | 0 / 10 (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           |
| Pain   |                |                |                 |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 13 (0.00%) | 0 / 10 (0.00%)  | 0 / 10 (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   |                |                 |                 |
| subjects affected / exposed                     | 0 / 13 (0.00%) | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Gastrointestinal disorders                      |                |                 |                 |
| Abdominal pain                                  |                |                 |                 |
| subjects affected / exposed                     | 0 / 13 (0.00%) | 1 / 10 (10.00%) | 2 / 10 (20.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           | 1 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Ascites   |                |                 |                 |
| subjects affected / exposed                     | 0 / 13 (0.00%) | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Hepatobiliary disorders                         |                |                 |                 |
| Cholangitis                                     |                |                 |                 |
| subjects affected / exposed                     | 1 / 13 (7.69%) | 1 / 10 (10.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 1           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Jaundice cholestatic                            |                |                 |                 |
| subjects affected / exposed                     | 0 / 13 (0.00%) | 1 / 10 (10.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders |                |                 |                 |
| Cough   |                |                 |                 |
| subjects affected / exposed                     | 0 / 13 (0.00%) | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Psychiatric disorders                           |                |                 |                 |
| Confusional state                               |                |                 |                 |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 1 / 13 (7.69%) | 0 / 10 (0.00%) | 0 / 10 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0           |
| Renal and urinary disorders                     |                |                |                 |
| Renal impairment                                |                |                |                 |
| subjects affected / exposed                     | 0 / 13 (0.00%) | 0 / 10 (0.00%) | 0 / 10 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Infections and infestations                     |                |                |                 |
| Bronchitis                                      |                |                |                 |
| subjects affected / exposed                     | 0 / 13 (0.00%) | 0 / 10 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 1 / 1           |
| Febrile infection                               |                |                |                 |
| subjects affected / exposed                     | 1 / 13 (7.69%) | 0 / 10 (0.00%) | 0 / 10 (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           |
| Neutropenic sepsis                              |                |                |                 |
| subjects affected / exposed                     | 0 / 13 (0.00%) | 0 / 10 (0.00%) | 0 / 10 (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                                       |                |                |                 |
| subjects affected / exposed                     | 0 / 13 (0.00%) | 0 / 10 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 1 / 1           |
| Urinary tract infection                         |                |                |                 |
| subjects affected / exposed                     | 0 / 13 (0.00%) | 0 / 10 (0.00%) | 1 / 10 (10.00%) |
| 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                                     |                |                |                 |
| subjects affected / exposed                     | 1 / 13 (7.69%) | 0 / 10 (0.00%) | 0 / 10 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0           |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Tumour lysis syndrome                           |                |                |                |
| subjects affected / exposed                     | 1 / 13 (7.69%) | 0 / 10 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 1 / 1          | 0 / 0          | 0 / 0          |

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

| <b>Non-serious adverse events</b>                     | Non-Small Cell Lung Cancer (NSCLC): CAP7.1 | Non-Small Cell Lung Cancer (NSCLC): Best Supportive Care | Small Cell Lung Cancer (SCLC): CAP7.1 |
|---|--|--|---------------------------------------|
| Total subjects affected by non-serious adverse events |  |  |                                       |
| subjects affected / exposed                           | 4 / 4 (100.00%)                            | 1 / 2 (50.00%)   | 8 / 8 (100.00%)                       |
| Vascular disorders                                    |  |  |                                       |
| Hypertension  |  |  |                                       |
| subjects affected / exposed                           | 0 / 4 (0.00%)                              | 0 / 2 (0.00%)  | 0 / 8 (0.00%)                         |
| occurrences (all)                                     | 0  | 0  | 0                                     |
| Hypertensive crisis                                   |  |  |                                       |
| subjects affected / exposed                           | 0 / 4 (0.00%)                              | 0 / 2 (0.00%)  | 0 / 8 (0.00%)                         |
| occurrences (all)                                     | 0  | 0  | 0                                     |
| Hypotension   |  |  |                                       |
| subjects affected / exposed                           | 0 / 4 (0.00%)                              | 0 / 2 (0.00%)  | 0 / 8 (0.00%)                         |
| occurrences (all)                                     | 0  | 0  | 0                                     |
| Microangiopathy                                       |  |  |                                       |
| subjects affected / exposed                           | 0 / 4 (0.00%)                              | 0 / 2 (0.00%)  | 0 / 8 (0.00%)                         |
| occurrences (all)                                     | 0  | 0  | 0                                     |
| Surgical and medical procedures                       |  |  |                                       |
| Central venous catheter removal                       |  |  |                                       |
| subjects affected / exposed                           | 0 / 4 (0.00%)                              | 0 / 2 (0.00%)  | 0 / 8 (0.00%)                         |
| occurrences (all)                                     | 0  | 0  | 0                                     |
| Resuscitation   |  |  |                                       |
| subjects affected / exposed                           | 0 / 4 (0.00%)                              | 0 / 2 (0.00%)  | 0 / 8 (0.00%)                         |
| occurrences (all)                                     | 0  | 0  | 0                                     |
| General disorders and administration site conditions  |  |  |                                       |
| Asthenia  |  |  |                                       |
| subjects affected / exposed                           | 0 / 4 (0.00%)                              | 0 / 2 (0.00%)  | 0 / 8 (0.00%)                         |
| occurrences (all)                                     | 0  | 0  | 0                                     |
| Chest discomfort                                      |  |  |                                       |

|                                       |                |               |                |
|---------------------------------------|----------------|---------------|----------------|
| subjects affected / exposed           | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                     | 0              | 0             | 0              |
| Chest pain                            |                |               |                |
| subjects affected / exposed           | 2 / 4 (50.00%) | 0 / 2 (0.00%) | 2 / 8 (25.00%) |
| occurrences (all)                     | 2              | 0             | 2              |
| Chills                                |                |               |                |
| subjects affected / exposed           | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                     | 0              | 0             | 0              |
| Fatigue                               |                |               |                |
| subjects affected / exposed           | 3 / 4 (75.00%) | 0 / 2 (0.00%) | 5 / 8 (62.50%) |
| occurrences (all)                     | 4              | 0             | 7              |
| Feeling abnormal                      |                |               |                |
| subjects affected / exposed           | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                     | 0              | 0             | 0              |
| General physical health deterioration |                |               |                |
| subjects affected / exposed           | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                     | 0              | 0             | 0              |
| Inflammation                          |                |               |                |
| subjects affected / exposed           | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all)                     | 0              | 0             | 1              |
| Infusion site anaesthesia             |                |               |                |
| subjects affected / exposed           | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                     | 0              | 0             | 0              |
| Infusion site extravasation           |                |               |                |
| subjects affected / exposed           | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all)                     | 0              | 0             | 1              |
| Mucosal inflammation                  |                |               |                |
| subjects affected / exposed           | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all)                     | 0              | 0             | 1              |
| Oedema                                |                |               |                |
| subjects affected / exposed           | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                     | 0              | 0             | 0              |
| Oedema peripheral                     |                |               |                |
| subjects affected / exposed           | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                     | 0              | 0             | 0              |
| Pain                                  |                |               |                |

|   |                     |                    |                     |
|---|---------------------|--------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 4 (25.00%)<br>1 | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Spinal pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 |
| Immune system disorders<br>Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Reproductive system and breast disorders<br>Breast swelling<br>subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Pruritus genital<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Vaginal haemorrhage<br>subjects affected / exposed<br>occurrences (all)   | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)    | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 2 / 8 (25.00%)<br>2 |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 5 / 8 (62.50%)<br>5 |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Pharyngeal oedema   |                     |                    |                     |



|   |                    |                    |                     |
|---|--------------------|--------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Pleural effusion<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 |
| Pulmonary embolism<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 4 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Psychiatric disorders<br>Agitation<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 4 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Depression<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 |
| Panic attack<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Stress<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Investigations<br>Blood lactate dehydrogenase increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 1 / 8 (12.50%)<br>2 |
| C-reactive protein increased<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 4 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 |
| Carbohydrate antigen 19-9 increased<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 4 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Carcinoembryonic antigen increased  |                    |                    |                     |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Coagulation time prolonged<br>subjects affected / exposed<br>occurrences (all)  | 1 / 4 (25.00%)<br>1 | 0 / 2 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Eastern Cooperative Oncology Group<br>performance status<br>subjects affected / exposed<br>occurrences (all)          | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Eastern Cooperative Oncology Group<br>performance status worsened<br>subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0  | 1 / 2 (50.00%)<br>1 | 0 / 8 (0.00%)<br>0  |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 |
| Injury, poisoning and procedural<br>complications   |                     |                     |                     |
| Fall<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Scratch<br>subjects affected / exposed<br>occurrences (all)   | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Cardiac disorders   |                     |                     |                     |
| Arrhythmia supraventricular<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)   | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 |
| Bradycardia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Nervous system disorders  |                     |                     |                     |
| Aphasia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |

|                                      |                |               |                |
|--------------------------------------|----------------|---------------|----------------|
| Dizziness                            |                |               |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Facial paresis                       |                |               |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Headache                             |                |               |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all)                    | 0              | 0             | 1              |
| Neuralgia                            |                |               |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Paraesthesia                         |                |               |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Tremor                               |                |               |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Blood and lymphatic system disorders |                |               |                |
| Anaemia                              |                |               |                |
| subjects affected / exposed          | 3 / 4 (75.00%) | 0 / 2 (0.00%) | 3 / 8 (37.50%) |
| occurrences (all)                    | 3              | 0             | 4              |
| Bicytopenia                          |                |               |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Eosinophilia                         |                |               |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Febrile neutropenia                  |                |               |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Leukocytosis                         |                |               |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Leukopenia                           |                |               |                |

|                             |                |               |                |
|-----------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 2 / 4 (50.00%) | 0 / 2 (0.00%) | 4 / 8 (50.00%) |
| occurrences (all)           | 2              | 0             | 7              |
| Lymphopenia                 |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Monocytopenia               |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Neutropenia                 |                |               |                |
| subjects affected / exposed | 2 / 4 (50.00%) | 0 / 2 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all)           | 2              | 0             | 1              |
| Reticulocytopenia           |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Thrombocytopenia            |                |               |                |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 1              | 0             | 0              |
| Ear and labyrinth disorders |                |               |                |
| Vertigo                     |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Eye disorders               |                |               |                |
| Eye irritation              |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Ocular icterus              |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Visual impairment           |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Gastrointestinal disorders  |                |               |                |
| Abdominal distension        |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Abdominal pain              |                |               |                |

|                             |                |               |                |
|-----------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 1              | 0             | 0              |
| Abdominal pain upper        |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Ascites                     |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Breath odour                |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Cheilitis                   |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Constipation                |                |               |                |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 2 (0.00%) | 3 / 8 (37.50%) |
| occurrences (all)           | 1              | 0             | 5              |
| Diarrhoea                   |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 3 / 8 (37.50%) |
| occurrences (all)           | 0              | 0             | 3              |
| Dysphagia                   |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Flatulence                  |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Hypoaesthesia oral          |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Nausea                      |                |               |                |
| subjects affected / exposed | 2 / 4 (50.00%) | 0 / 2 (0.00%) | 4 / 8 (50.00%) |
| occurrences (all)           | 2              | 0             | 6              |
| Stomatitis                  |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all)           | 0              | 0             | 1              |
| Vomiting                    |                |               |                |

|  |                     |                    |                     |
|--|---------------------|--------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 1 / 4 (25.00%)<br>1 | 0 / 2 (0.00%)<br>0 | 1 / 8 (12.50%)<br>2 |
| Hepatobiliary disorders                          |                     |                    |                     |
| Cholangitis                                      |                     |                    |                     |
| subjects affected / exposed                      | 0 / 4 (0.00%)       | 0 / 2 (0.00%)      | 0 / 8 (0.00%)       |
| occurrences (all)                                | 0                   | 0                  | 0                   |
| Hepatic pain                                     |                     |                    |                     |
| subjects affected / exposed                      | 0 / 4 (0.00%)       | 0 / 2 (0.00%)      | 0 / 8 (0.00%)       |
| occurrences (all)                                | 0                   | 0                  | 0                   |
| Hyperbilirubinaemia                              |                     |                    |                     |
| subjects affected / exposed                      | 0 / 4 (0.00%)       | 0 / 2 (0.00%)      | 0 / 8 (0.00%)       |
| occurrences (all)                                | 0                   | 0                  | 0                   |
| Hypertransaminaemia                              |                     |                    |                     |
| subjects affected / exposed                      | 0 / 4 (0.00%)       | 0 / 2 (0.00%)      | 0 / 8 (0.00%)       |
| occurrences (all)                                | 0                   | 0                  | 0                   |
| Jaundice   |                     |                    |                     |
| subjects affected / exposed                      | 0 / 4 (0.00%)       | 0 / 2 (0.00%)      | 0 / 8 (0.00%)       |
| occurrences (all)                                | 0                   | 0                  | 0                   |
| Skin and subcutaneous tissue disorders           |                     |                    |                     |
| Alopecia   |                     |                    |                     |
| subjects affected / exposed                      | 0 / 4 (0.00%)       | 0 / 2 (0.00%)      | 2 / 8 (25.00%)      |
| occurrences (all)                                | 0                   | 0                  | 2                   |
| Alopecia totalis                                 |                     |                    |                     |
| subjects affected / exposed                      | 0 / 4 (0.00%)       | 0 / 2 (0.00%)      | 0 / 8 (0.00%)       |
| occurrences (all)                                | 0                   | 0                  | 0                   |
| Decubitus ulcer                                  |                     |                    |                     |
| subjects affected / exposed                      | 0 / 4 (0.00%)       | 0 / 2 (0.00%)      | 0 / 8 (0.00%)       |
| occurrences (all)                                | 0                   | 0                  | 0                   |
| Dry skin   |                     |                    |                     |
| subjects affected / exposed                      | 0 / 4 (0.00%)       | 0 / 2 (0.00%)      | 0 / 8 (0.00%)       |
| occurrences (all)                                | 0                   | 0                  | 0                   |
| Erythema   |                     |                    |                     |
| subjects affected / exposed                      | 0 / 4 (0.00%)       | 0 / 2 (0.00%)      | 0 / 8 (0.00%)       |
| occurrences (all)                                | 0                   | 0                  | 0                   |
| Night sweats                                     |                     |                    |                     |

|                             |                |               |                |
|-----------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 1              | 0             | 0              |
| Pruritus                    |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Pruritus generalised        |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Rash                        |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Rash pruritic               |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all)           | 0              | 0             | 1              |
| Skin fissures               |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Skin hyperpigmentation      |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Skin lesion                 |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Renal and urinary disorders |                |               |                |
| Haematuria                  |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Leukocyturia                |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Proteinuria                 |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Renal failure acute         |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |

|  |                    |                    |                     |
|--|--------------------|--------------------|---------------------|
| Renal impairment<br>subjects affected / exposed<br>occurrences (all)     | 0 / 4 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 |
| Musculoskeletal and connective tissue disorders                          |                    |                    |                     |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)           | 0 / 4 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)            | 0 / 4 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Bone pain<br>subjects affected / exposed<br>occurrences (all)            | 0 / 4 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Bursitis<br>subjects affected / exposed<br>occurrences (all)             | 0 / 4 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Flank pain<br>subjects affected / exposed<br>occurrences (all)           | 0 / 4 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 |
| Muscle spasms<br>subjects affected / exposed<br>occurrences (all)        | 0 / 4 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 1 / 8 (12.50%)<br>2 |
| Muscle twitching<br>subjects affected / exposed<br>occurrences (all)     | 0 / 4 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Musculoskeletal pain<br>subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Myalgia<br>subjects affected / exposed<br>occurrences (all)              | 0 / 4 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 3 / 8 (37.50%)<br>5 |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)    | 0 / 4 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Infections and infestations  |                    |                    |                     |



|   |                     |                    |                     |
|---|---------------------|--------------------|---------------------|
| Administration site infection<br>subjects affected / exposed<br>occurrences (all)     | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Candidiasis<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 4 (25.00%)<br>1 | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Oral candidiasis<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 |
| Oral fungal infection<br>subjects affected / exposed<br>occurrences (all)             | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Periodontitis<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Pharyngitis<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Pneumonia<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 |
| Sepsis<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Vulvitis<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 4 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Metabolism and nutrition disorders<br>Decreased appetite                              |                     |                    |                     |

|                             |                |               |                |
|-----------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 2 / 4 (50.00%) | 0 / 2 (0.00%) | 5 / 8 (62.50%) |
| occurrences (all)           | 2              | 0             | 8              |
| Hyperkalaemia               |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Hyperphosphataemia          |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Hyperphosphatasaemia        |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Hyperuricaemia              |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Hypoalbuminaemia            |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all)           | 0              | 0             | 1              |
| Hypocalcaemia               |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Hyponatraemia               |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 2 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |

| <b>Non-serious adverse events</b>                        | Biliary tract cancer:<br>CAP7.1 | Biliary tract cancer:<br>BSC before cross-<br>over to CAP7.1 | Biliary tract cancer:<br>CAP7.1 after Best<br>Supportive Care |
|--|---------------------------------|--|---|
| Total subjects affected by non-serious<br>adverse events |                                 |  |   |
| subjects affected / exposed                              | 13 / 13 (100.00%)               | 8 / 10 (80.00%)  | 10 / 10 (100.00%)   |
| Vascular disorders                                       |                                 |  |   |
| Hypertension   |                                 |  |   |
| subjects affected / exposed                              | 1 / 13 (7.69%)                  | 0 / 10 (0.00%)   | 0 / 10 (0.00%)  |
| occurrences (all)  | 2                               | 0  | 0   |
| Hypertensive crisis                                      |                                 |  |   |
| subjects affected / exposed                              | 1 / 13 (7.69%)                  | 0 / 10 (0.00%)   | 0 / 10 (0.00%)  |
| occurrences (all)  | 1                               | 0  | 0   |
| Hypotension  |                                 |  |   |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed                          | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                                    | 1               | 0               | 0               |
| Microangiopathy                                      |                 |                 |                 |
| subjects affected / exposed                          | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                                    | 1               | 0               | 0               |
| Surgical and medical procedures                      |                 |                 |                 |
| Central venous catheter removal                      |                 |                 |                 |
| subjects affected / exposed                          | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                                    | 1               | 0               | 0               |
| Resuscitation  |                 |                 |                 |
| subjects affected / exposed                          | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                                    | 1               | 0               | 0               |
| General disorders and administration site conditions |                 |                 |                 |
| Asthenia   |                 |                 |                 |
| subjects affected / exposed                          | 1 / 13 (7.69%)  | 1 / 10 (10.00%) | 1 / 10 (10.00%) |
| occurrences (all)                                    | 1               | 1               | 1               |
| Chest discomfort                                     |                 |                 |                 |
| subjects affected / exposed                          | 0 / 13 (0.00%)  | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                                    | 0               | 0               | 1               |
| Chest pain   |                 |                 |                 |
| subjects affected / exposed                          | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                                    | 1               | 0               | 1               |
| Chills   |                 |                 |                 |
| subjects affected / exposed                          | 2 / 13 (15.38%) | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                                    | 2               | 0               | 1               |
| Fatigue  |                 |                 |                 |
| subjects affected / exposed                          | 4 / 13 (30.77%) | 0 / 10 (0.00%)  | 4 / 10 (40.00%) |
| occurrences (all)                                    | 6               | 0               | 4               |
| Feeling abnormal                                     |                 |                 |                 |
| subjects affected / exposed                          | 0 / 13 (0.00%)  | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                                    | 0               | 0               | 1               |
| General physical health deterioration                |                 |                 |                 |
| subjects affected / exposed                          | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                                    | 1               | 0               | 1               |
| Inflammation   |                 |                 |                 |

|   |                      |                      |                      |
|---|----------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 13 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Infusion site anaesthesia<br>subjects affected / exposed<br>occurrences (all)                                   | 1 / 13 (7.69%)<br>1  | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Infusion site extravasation<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 13 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Mucosal inflammation<br>subjects affected / exposed<br>occurrences (all)  | 1 / 13 (7.69%)<br>1  | 0 / 10 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 |
| Oedema<br>subjects affected / exposed<br>occurrences (all)  | 2 / 13 (15.38%)<br>2 | 0 / 10 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 |
| Oedema peripheral<br>subjects affected / exposed<br>occurrences (all)   | 1 / 13 (7.69%)<br>1  | 0 / 10 (0.00%)<br>0  | 2 / 10 (20.00%)<br>3 |
| Pain<br>subjects affected / exposed<br>occurrences (all)  | 2 / 13 (15.38%)<br>3 | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 13 (7.69%)<br>1  | 1 / 10 (10.00%)<br>1 | 1 / 10 (10.00%)<br>1 |
| Spinal pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 13 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Immune system disorders<br>Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 13 (7.69%)<br>1  | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Reproductive system and breast disorders<br>Breast swelling<br>subjects affected / exposed<br>occurrences (all) | 0 / 13 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 |
| Pruritus genital  |                      |                      |                      |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 13 (0.00%)  | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                               | 0               | 0               | 1               |
| Vaginal haemorrhage                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 13 (0.00%)  | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                               | 0               | 0               | 1               |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                 |
| Cough   |                 |                 |                 |
| subjects affected / exposed                     | 2 / 13 (15.38%) | 1 / 10 (10.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                               | 2               | 1               | 0               |
| Dyspnoea  |                 |                 |                 |
| subjects affected / exposed                     | 2 / 13 (15.38%) | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                               | 2               | 0               | 1               |
| Epistaxis                                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 13 (0.00%)  | 1 / 10 (10.00%) | 1 / 10 (10.00%) |
| occurrences (all)                               | 0               | 1               | 1               |
| Oropharyngeal pain                              |                 |                 |                 |
| subjects affected / exposed                     | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                               | 1               | 0               | 1               |
| Pharyngeal oedema                               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 13 (0.00%)  | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                               | 0               | 0               | 1               |
| Pleural effusion                                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 13 (0.00%)  | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Pulmonary embolism                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 13 (0.00%)  | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                               | 0               | 0               | 1               |
| Psychiatric disorders                           |                 |                 |                 |
| Agitation                                       |                 |                 |                 |
| subjects affected / exposed                     | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 1               | 0               | 0               |
| Depression                                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 13 (0.00%)  | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Insomnia  |                 |                 |                 |

|  |                |                |                 |
|--|----------------|----------------|-----------------|
| subjects affected / exposed                                    | 1 / 13 (7.69%) | 0 / 10 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)  | 1              | 0              | 1               |
| Panic attack   |                |                |                 |
| subjects affected / exposed                                    | 1 / 13 (7.69%) | 0 / 10 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)  | 1              | 0              | 0               |
| Stress   |                |                |                 |
| subjects affected / exposed                                    | 0 / 13 (0.00%) | 0 / 10 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)  | 0              | 0              | 1               |
| Investigations   |                |                |                 |
| Blood lactate dehydrogenase increased                          |                |                |                 |
| subjects affected / exposed                                    | 0 / 13 (0.00%) | 0 / 10 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)  | 0              | 0              | 0               |
| C-reactive protein increased                                   |                |                |                 |
| subjects affected / exposed                                    | 0 / 13 (0.00%) | 0 / 10 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)  | 0              | 0              | 0               |
| Carbohydrate antigen 19-9 increased                            |                |                |                 |
| subjects affected / exposed                                    | 1 / 13 (7.69%) | 0 / 10 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)  | 1              | 0              | 0               |
| Carcinoembryonic antigen increased                             |                |                |                 |
| subjects affected / exposed                                    | 1 / 13 (7.69%) | 0 / 10 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)  | 1              | 0              | 0               |
| Coagulation time prolonged                                     |                |                |                 |
| subjects affected / exposed                                    | 0 / 13 (0.00%) | 0 / 10 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)  | 0              | 0              | 0               |
| Eastern Cooperative Oncology Group performance status          |                |                |                 |
| subjects affected / exposed                                    | 0 / 13 (0.00%) | 0 / 10 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)  | 0              | 0              | 1               |
| Eastern Cooperative Oncology Group performance status worsened |                |                |                 |
| subjects affected / exposed                                    | 0 / 13 (0.00%) | 0 / 10 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)  | 0              | 0              | 0               |
| Weight decreased   |                |                |                 |
| subjects affected / exposed                                    | 0 / 13 (0.00%) | 0 / 10 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)  | 0              | 0              | 0               |
| Injury, poisoning and procedural complications                 |                |                |                 |

|                             |                |                 |                 |
|-----------------------------|----------------|-----------------|-----------------|
| Fall                        |                |                 |                 |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 2              | 0               | 0               |
| Scratch                     |                |                 |                 |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 1              | 0               | 0               |
| Cardiac disorders           |                |                 |                 |
| Arrhythmia supraventricular |                |                 |                 |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Atrial fibrillation         |                |                 |                 |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0              | 0               | 1               |
| Bradycardia                 |                |                 |                 |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 1              | 0               | 0               |
| Nervous system disorders    |                |                 |                 |
| Aphasia                     |                |                 |                 |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 1              | 0               | 0               |
| Dizziness                   |                |                 |                 |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 10 (10.00%) | 2 / 10 (20.00%) |
| occurrences (all)           | 1              | 1               | 2               |
| Facial paresis              |                |                 |                 |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 10 (10.00%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Headache                    |                |                 |                 |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 2              | 0               | 1               |
| Neuralgia                   |                |                 |                 |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 1              | 0               | 0               |
| Paraesthesia                |                |                 |                 |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0              | 0               | 1               |
| Tremor                      |                |                 |                 |

|  |                     |                     |                      |
|--|---------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 13 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0 | 1 / 10 (10.00%)<br>1 |
| Blood and lymphatic system disorders             |                     |                     |                      |
| Anaemia  |                     |                     |                      |
| subjects affected / exposed                      | 7 / 13 (53.85%)     | 1 / 10 (10.00%)     | 5 / 10 (50.00%)      |
| occurrences (all)                                | 20                  | 1                   | 13                   |
| Bicytopenia                                      |                     |                     |                      |
| subjects affected / exposed                      | 1 / 13 (7.69%)      | 0 / 10 (0.00%)      | 0 / 10 (0.00%)       |
| occurrences (all)                                | 1                   | 0                   | 0                    |
| Eosinophilia                                     |                     |                     |                      |
| subjects affected / exposed                      | 1 / 13 (7.69%)      | 0 / 10 (0.00%)      | 0 / 10 (0.00%)       |
| occurrences (all)                                | 1                   | 0                   | 0                    |
| Febrile neutropenia                              |                     |                     |                      |
| subjects affected / exposed                      | 2 / 13 (15.38%)     | 0 / 10 (0.00%)      | 0 / 10 (0.00%)       |
| occurrences (all)                                | 2                   | 0                   | 0                    |
| Leukocytosis                                     |                     |                     |                      |
| subjects affected / exposed                      | 1 / 13 (7.69%)      | 0 / 10 (0.00%)      | 1 / 10 (10.00%)      |
| occurrences (all)                                | 1                   | 0                   | 1                    |
| Leukopenia                                       |                     |                     |                      |
| subjects affected / exposed                      | 10 / 13 (76.92%)    | 0 / 10 (0.00%)      | 5 / 10 (50.00%)      |
| occurrences (all)                                | 25                  | 0                   | 7                    |
| Lymphopenia                                      |                     |                     |                      |
| subjects affected / exposed                      | 1 / 13 (7.69%)      | 0 / 10 (0.00%)      | 0 / 10 (0.00%)       |
| occurrences (all)                                | 1                   | 0                   | 0                    |
| Monocytopenia                                    |                     |                     |                      |
| subjects affected / exposed                      | 1 / 13 (7.69%)      | 0 / 10 (0.00%)      | 0 / 10 (0.00%)       |
| occurrences (all)                                | 1                   | 0                   | 0                    |
| Neutropenia                                      |                     |                     |                      |
| subjects affected / exposed                      | 7 / 13 (53.85%)     | 0 / 10 (0.00%)      | 7 / 10 (70.00%)      |
| occurrences (all)                                | 17                  | 0                   | 13                   |
| Reticulocytopenia                                |                     |                     |                      |
| subjects affected / exposed                      | 1 / 13 (7.69%)      | 0 / 10 (0.00%)      | 0 / 10 (0.00%)       |
| occurrences (all)                                | 1                   | 0                   | 0                    |
| Thrombocytopenia                                 |                     |                     |                      |
| subjects affected / exposed                      | 7 / 13 (53.85%)     | 0 / 10 (0.00%)      | 5 / 10 (50.00%)      |
| occurrences (all)                                | 21                  | 0                   | 7                    |



|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Ear and labyrinth disorders |                 |                 |                 |
| Vertigo                     |                 |                 |                 |
| subjects affected / exposed | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 2 / 10 (20.00%) |
| occurrences (all)           | 1               | 0               | 2               |
| Eye disorders               |                 |                 |                 |
| Eye irritation              |                 |                 |                 |
| subjects affected / exposed | 0 / 13 (0.00%)  | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0               | 0               | 1               |
| Ocular icterus              |                 |                 |                 |
| subjects affected / exposed | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0               |
| Visual impairment           |                 |                 |                 |
| subjects affected / exposed | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0               |
| Gastrointestinal disorders  |                 |                 |                 |
| Abdominal distension        |                 |                 |                 |
| subjects affected / exposed | 0 / 13 (0.00%)  | 1 / 10 (10.00%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Abdominal pain              |                 |                 |                 |
| subjects affected / exposed | 4 / 13 (30.77%) | 2 / 10 (20.00%) | 1 / 10 (10.00%) |
| occurrences (all)           | 5               | 2               | 1               |
| Abdominal pain upper        |                 |                 |                 |
| subjects affected / exposed | 2 / 13 (15.38%) | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 3               | 0               | 1               |
| Ascites                     |                 |                 |                 |
| subjects affected / exposed | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 2 / 10 (20.00%) |
| occurrences (all)           | 1               | 0               | 2               |
| Breath odour                |                 |                 |                 |
| subjects affected / exposed | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0               |
| Cheilitis                   |                 |                 |                 |
| subjects affected / exposed | 0 / 13 (0.00%)  | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0               | 0               | 1               |
| Constipation                |                 |                 |                 |
| subjects affected / exposed | 2 / 13 (15.38%) | 0 / 10 (0.00%)  | 4 / 10 (40.00%) |
| occurrences (all)           | 2               | 0               | 4               |
| Diarrhoea                   |                 |                 |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 5 / 13 (38.46%) | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 5               | 0               | 1               |
| Dysphagia                   |                 |                 |                 |
| subjects affected / exposed | 0 / 13 (0.00%)  | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0               | 0               | 1               |
| Flatulence                  |                 |                 |                 |
| subjects affected / exposed | 2 / 13 (15.38%) | 1 / 10 (10.00%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 2               | 1               | 0               |
| Hypoaesthesia oral          |                 |                 |                 |
| subjects affected / exposed | 0 / 13 (0.00%)  | 1 / 10 (10.00%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Nausea                      |                 |                 |                 |
| subjects affected / exposed | 4 / 13 (30.77%) | 1 / 10 (10.00%) | 2 / 10 (20.00%) |
| occurrences (all)           | 6               | 1               | 2               |
| Stomatitis                  |                 |                 |                 |
| subjects affected / exposed | 0 / 13 (0.00%)  | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0               | 0               | 1               |
| Vomiting                    |                 |                 |                 |
| subjects affected / exposed | 1 / 13 (7.69%)  | 1 / 10 (10.00%) | 2 / 10 (20.00%) |
| occurrences (all)           | 1               | 1               | 2               |
| Hepatobiliary disorders     |                 |                 |                 |
| Cholangitis                 |                 |                 |                 |
| subjects affected / exposed | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0               |
| Hepatic pain                |                 |                 |                 |
| subjects affected / exposed | 0 / 13 (0.00%)  | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0               | 0               | 1               |
| Hyperbilirubinaemia         |                 |                 |                 |
| subjects affected / exposed | 2 / 13 (15.38%) | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 3               | 0               | 1               |
| Hypertransaminaemia         |                 |                 |                 |
| subjects affected / exposed | 2 / 13 (15.38%) | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 5               | 0               | 0               |
| Jaundice                    |                 |                 |                 |
| subjects affected / exposed | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0               |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| Skin and subcutaneous tissue disorders |                 |                 |                 |
| Alopecia                               |                 |                 |                 |
| subjects affected / exposed            | 4 / 13 (30.77%) | 0 / 10 (0.00%)  | 4 / 10 (40.00%) |
| occurrences (all)                      | 4               | 0               | 4               |
| Alopecia totalis                       |                 |                 |                 |
| subjects affected / exposed            | 0 / 13 (0.00%)  | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                      | 0               | 0               | 1               |
| Decubitus ulcer                        |                 |                 |                 |
| subjects affected / exposed            | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                      | 1               | 0               | 0               |
| Dry skin                               |                 |                 |                 |
| subjects affected / exposed            | 0 / 13 (0.00%)  | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                      | 0               | 0               | 1               |
| Erythema                               |                 |                 |                 |
| subjects affected / exposed            | 0 / 13 (0.00%)  | 0 / 10 (0.00%)  | 2 / 10 (20.00%) |
| occurrences (all)                      | 0               | 0               | 2               |
| Night sweats                           |                 |                 |                 |
| subjects affected / exposed            | 0 / 13 (0.00%)  | 1 / 10 (10.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                      | 0               | 1               | 0               |
| Pruritus                               |                 |                 |                 |
| subjects affected / exposed            | 0 / 13 (0.00%)  | 0 / 10 (0.00%)  | 2 / 10 (20.00%) |
| occurrences (all)                      | 0               | 0               | 2               |
| Pruritus generalised                   |                 |                 |                 |
| subjects affected / exposed            | 0 / 13 (0.00%)  | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                      | 0               | 0               | 1               |
| Rash                                   |                 |                 |                 |
| subjects affected / exposed            | 0 / 13 (0.00%)  | 1 / 10 (10.00%) | 3 / 10 (30.00%) |
| occurrences (all)                      | 0               | 1               | 4               |
| Rash pruritic                          |                 |                 |                 |
| subjects affected / exposed            | 0 / 13 (0.00%)  | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                      | 0               | 0               | 0               |
| Skin fissures                          |                 |                 |                 |
| subjects affected / exposed            | 0 / 13 (0.00%)  | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                      | 0               | 0               | 1               |
| Skin hyperpigmentation                 |                 |                 |                 |

|   |                     |                      |                      |
|---|---------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                        | 0 / 13 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 |
| Skin lesion<br>subjects affected / exposed<br>occurrences (all)         | 0 / 13 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 |
| Renal and urinary disorders   |                     |                      |                      |
| Haematuria<br>subjects affected / exposed<br>occurrences (all)          | 1 / 13 (7.69%)<br>1 | 0 / 10 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 |
| Leukocyturia<br>subjects affected / exposed<br>occurrences (all)        | 1 / 13 (7.69%)<br>1 | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Proteinuria<br>subjects affected / exposed<br>occurrences (all)         | 1 / 13 (7.69%)<br>1 | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Renal failure acute<br>subjects affected / exposed<br>occurrences (all) | 0 / 13 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 |
| Renal impairment<br>subjects affected / exposed<br>occurrences (all)    | 0 / 13 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Musculoskeletal and connective tissue disorders                         |                     |                      |                      |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)          | 1 / 13 (7.69%)<br>1 | 1 / 10 (10.00%)<br>1 | 1 / 10 (10.00%)<br>2 |
| Back pain<br>subjects affected / exposed<br>occurrences (all)           | 1 / 13 (7.69%)<br>1 | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Bone pain<br>subjects affected / exposed<br>occurrences (all)           | 0 / 13 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 |
| Bursitis<br>subjects affected / exposed<br>occurrences (all)            | 1 / 13 (7.69%)<br>1 | 0 / 10 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Flank pain  |                     |                      |                      |

|                               |                |                 |                 |
|-------------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed   | 0 / 13 (0.00%) | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)             | 0              | 0               | 0               |
| Muscle spasms                 |                |                 |                 |
| subjects affected / exposed   | 0 / 13 (0.00%) | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)             | 0              | 0               | 1               |
| Muscle twitching              |                |                 |                 |
| subjects affected / exposed   | 0 / 13 (0.00%) | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)             | 0              | 0               | 1               |
| Musculoskeletal pain          |                |                 |                 |
| subjects affected / exposed   | 0 / 13 (0.00%) | 1 / 10 (10.00%) | 0 / 10 (0.00%)  |
| occurrences (all)             | 0              | 1               | 0               |
| Myalgia                       |                |                 |                 |
| subjects affected / exposed   | 0 / 13 (0.00%) | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)             | 0              | 0               | 0               |
| Pain in extremity             |                |                 |                 |
| subjects affected / exposed   | 0 / 13 (0.00%) | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)             | 0              | 0               | 1               |
| Infections and infestations   |                |                 |                 |
| Administration site infection |                |                 |                 |
| subjects affected / exposed   | 1 / 13 (7.69%) | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)             | 1              | 0               | 1               |
| Candidiasis                   |                |                 |                 |
| subjects affected / exposed   | 1 / 13 (7.69%) | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)             | 1              | 0               | 0               |
| Nasopharyngitis               |                |                 |                 |
| subjects affected / exposed   | 1 / 13 (7.69%) | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)             | 1              | 0               | 0               |
| Oral candidiasis              |                |                 |                 |
| subjects affected / exposed   | 0 / 13 (0.00%) | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)             | 0              | 0               | 1               |
| Oral fungal infection         |                |                 |                 |
| subjects affected / exposed   | 0 / 13 (0.00%) | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)             | 0              | 0               | 1               |
| Periodontitis                 |                |                 |                 |
| subjects affected / exposed   | 0 / 13 (0.00%) | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)             | 0              | 0               | 1               |

|                                    |                 |                 |                 |
|------------------------------------|-----------------|-----------------|-----------------|
| Pharyngitis                        |                 |                 |                 |
| subjects affected / exposed        | 0 / 13 (0.00%)  | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                  | 0               | 0               | 1               |
| Pneumonia                          |                 |                 |                 |
| subjects affected / exposed        | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                  | 1               | 0               | 0               |
| Sepsis                             |                 |                 |                 |
| subjects affected / exposed        | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                  | 1               | 0               | 0               |
| Upper respiratory tract infection  |                 |                 |                 |
| subjects affected / exposed        | 0 / 13 (0.00%)  | 1 / 10 (10.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                  | 0               | 1               | 0               |
| Vulvitis                           |                 |                 |                 |
| subjects affected / exposed        | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                  | 1               | 0               | 0               |
| Metabolism and nutrition disorders |                 |                 |                 |
| Decreased appetite                 |                 |                 |                 |
| subjects affected / exposed        | 3 / 13 (23.08%) | 1 / 10 (10.00%) | 1 / 10 (10.00%) |
| occurrences (all)                  | 3               | 1               | 1               |
| Hyperkalaemia                      |                 |                 |                 |
| subjects affected / exposed        | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                  | 1               | 0               | 0               |
| Hyperphosphataemia                 |                 |                 |                 |
| subjects affected / exposed        | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                  | 1               | 0               | 0               |
| Hyperphosphatasaemia               |                 |                 |                 |
| subjects affected / exposed        | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 2 / 10 (20.00%) |
| occurrences (all)                  | 1               | 0               | 2               |
| Hyperuricaemia                     |                 |                 |                 |
| subjects affected / exposed        | 1 / 13 (7.69%)  | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                  | 1               | 0               | 1               |
| Hypoalbuminaemia                   |                 |                 |                 |
| subjects affected / exposed        | 0 / 13 (0.00%)  | 0 / 10 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                  | 0               | 0               | 0               |
| Hypocalcaemia                      |                 |                 |                 |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 10 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Hyponatraemia               |                |                |                |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 10 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment   |
|------------------|---|
| 27 November 2013 | - Tissue sampling with MRT and Ultrasound was added.<br>- Dose adjustment |
| 27 February 2014 | - MRT removed   |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

The study was terminated to be redesigned for a trial according to EMA proposal.

Notes:

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28531881>