



## Clinical trial results:

### Randomised Phase II Pilot Study: Induction Chemotherapy with Docetaxel, Cisplatin und Cetuximab versus Docetaxel, Cisplatin und 5 FU followed by Radiotherapy with Cetuximab for locally advanced or not resectable Carcinoma of the Head and Neck

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2011-005540-99  |
| Trial protocol           | AT              |
| Global end of trial date | 28 January 2021 |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1              |
| This version publication date  | 29 January 2022 |
| First version publication date | 29 January 2022 |

#### Trial information

##### Trial identification

|                       |           |
|-----------------------|-----------|
| Sponsor protocol code | AGMT_HNO2 |
|-----------------------|-----------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01884259 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | AGMT  |
| Sponsor organisation address | Gentzgasse 60/21, Vienna, Austria, 1180   |
| Public contact               | Daniela Wolkersdorfer, AGMT gemeinnützige GmbH, +43 6626404412, d.wolkersdorfer@agmt.at |
| Scientific contact           | Felix Keil, AGMT gemeinnützige GmbH, +43 66264044112, felix.keil@oegk.at                |

Notes:

#### Paediatric regulatory details

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

Notes:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 08 December 2021 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 08 June 2018     |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 28 January 2021  |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

Response Rate (CR, PR) 3 months after end of therapy (RECIST)

Protection of trial subjects:

Safety assessments were done on a regular basis. All patients having received at least one dose of the study medication have been followed for adverse events for 28 days after discontinuing study treatment or completion of study treatment. In general, concomitant medications and therapies necessary for supportive care and safety of the patient were allowed and recommended.

Background therapy:

Arm A: Docetaxel 75mg/m<sup>2</sup> day 1; Cisplatin 75mg/m<sup>2</sup> day 1; 5FU 750 mg/m<sup>2</sup> day 1 -5

Arm B: Docetaxel 75 mg/m<sup>2</sup> day 1; Cisplatin 75mg/m<sup>2</sup> day 1

Evidence for comparator: -

|   |             |
|---|-------------|
| Actual start date of recruitment                          | 31 May 2013 |
| Long term follow-up planned                               | No          |
| Independent data monitoring committee (IDMC) involvement? | No          |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |              |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Austria: 100 |
| Worldwide total number of subjects   | 100          |
| EEA total number of subjects         | 100          |

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)                      | 75 |
| From 65 to 84 years                       | 25 |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

From March 2013 to January 2016, 102 patients were recruited in 8 sites in Austria.

### Pre-assignment

Screening details:

2 patients were ineligible for study participation and had to be replaced to reach the planned number of 100 eligible patients: 1 patient did not meet inclusion criteria, and 1 patient withdrew consent before treatment was initiated.

### Period 1

|                              |                         |
|------------------------------|-------------------------|
| Period 1 title               | Induction chemotherapy  |
| Is this the baseline period? | Yes                     |
| Allocation method            | Randomised - controlled |
| Blinding used                | Not blinded             |

### Arms

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes     |
| <b>Arm title</b>             | TPF-arm |

Arm description:

3 21-day cycles of induction chemotherapy consisting of docetaxel 75 mg/m<sup>2</sup> given as a 1-h infusion and cisplatin 75 mg/m<sup>2</sup> given as a 2-h infusion on day one, followed by 5FU 750 mg/m<sup>2</sup> administered as a continuous infusion for five consecutive days.

|  |                                       |
|--|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | Docetaxel                             |
| Investigational medicinal product code |                                       |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Infusion                              |

Dosage and administration details:

Docetaxel 75mg/m<sup>2</sup> day 1

|  |                                       |
|--|---------------------------------------|
| Investigational medicinal product name | Cisplatin                             |
| Investigational medicinal product code |                                       |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Infusion                              |

Dosage and administration details:

Cisplatin 75 mg/m<sup>2</sup> day 1

|  |                                       |
|--|---------------------------------------|
| Investigational medicinal product name | 5FU                                   |
| Investigational medicinal product code |                                       |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Infusion                              |

Dosage and administration details:

5FU 750mg/m<sup>2</sup> day 1-5

|                  |         |
|------------------|---------|
| <b>Arm title</b> | TPC-arm |
|------------------|---------|

Arm description:

3 21-day cycles of induction chemotherapy consisting of docetaxel 75 mg/m<sup>2</sup> given as a 1-h infusion and cisplatin 75 mg/m<sup>2</sup> cetuximab 400 mg/m<sup>2</sup> given as a 2-h infusion on day one as a loading dose, followed by cetuximab 250 mg/m<sup>2</sup> given as a 1-h infusion weekly (thrice per cycle).

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

|  |                       |
|--|-----------------------|
| Investigational medicinal product name | Cetuximab             |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Infusion              |

Dosage and administration details:

Cetuximab 400 mg/m<sup>2</sup> given as a 2-h infusion on day one as a loading dose, followed by cetuximab 250 mg/m<sup>2</sup> given as a 1-h infusion weekly (thrice per cycle).

|  |                                       |
|--|---------------------------------------|
| Investigational medicinal product name | Docetaxel                             |
| Investigational medicinal product code |                                       |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Infusion                              |

Dosage and administration details:

Docetaxel 75mg/m<sup>2</sup> day 1

|  |                                       |
|--|---------------------------------------|
| Investigational medicinal product name | Cisplatin                             |
| Investigational medicinal product code |                                       |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Infusion                              |

Dosage and administration details:

Cisplatin 75 mg/m<sup>2</sup> day 1

| Number of subjects in period 1 | TPF-arm | TPC-arm |
|--------------------------------|---------|---------|
| Started                        | 49      | 51      |
| Completed                      | 46      | 46      |
| Not completed                  | 3       | 5       |
| death                          | -       | 1       |
| drop-out                       | 3       | 4       |

## Period 2

|                              |                                  |
|------------------------------|----------------------------------|
| Period 2 title               | Radiation therapy plus Cetuximab |
| Is this the baseline period? | No                               |
| Allocation method            | Not applicable                   |
| Blinding used                | Not blinded                      |

## Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|  |                       |
|--|-----------------------|
| <b>Arm title</b>   | TPF-arm               |
| Arm description:   |                       |
| RT started maximum 6 weeks after the last administration of docetaxel and cisplatin. A loading dose of cetuximab 400 mg/m2 intravenously over 120 min was administered to the TPF arm one week before the start of concomitant boost RT. Followed by weekly infusions of cetuximab 250 mg/m2 during the whole course of RT (seven infusions in total). |                       |
| Arm type   | Experimental          |
| Investigational medicinal product name   | Cetuximab             |
| Investigational medicinal product code   |                       |
| Other name   |                       |
| Pharmaceutical forms   | Solution for infusion |
| Routes of administration   | Infusion              |
| Dosage and administration details:   |                       |
| Loading dose 400mg/m2; followed by weekly infusions with 250 mg/m2   |                       |
| <b>Arm title</b>   | TPC-arm               |

|   |                       |
|---|-----------------------|
| Arm description:  |                       |
| RT started maximum 6 weeks after the last administration of docetaxel and cisplatin. A dose of cetuximab 250mg/m2 intravenously over 120 min was administered to the TPC arm one week before the start of concomitant boost RT. Followed by weekly infusions of cetuximab 250 mg/m2 during the whole course of RT (seven infusions in total). |                       |
| Arm type  | Experimental          |
| Investigational medicinal product name  | Cetuximab             |
| Investigational medicinal product code  |                       |
| Other name  |                       |
| Pharmaceutical forms  | Solution for infusion |
| Routes of administration  | Infusion              |
| Dosage and administration details:  |                       |
| 250 mg/m2 one week before and during the whole course of RT (seven infusions in total).   |                       |

| <b>Number of subjects in period 2<sup>[1]</sup></b> | TPF-arm | TPC-arm |
|---|---------|---------|
| Started   | 44      | 45      |
| Completed   | 44      | 44      |
| Not completed                                       | 0       | 1       |
| death   | -       | 1       |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: TPF-arm: 2 patients did not start Radiotherapy+C: 1 patient due to PD, 1 patient due to protocol violation;

TPC-arm: 1 patient did not start Radiotherapy+C due to PD

## Baseline characteristics

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | TPF-arm |
|-----------------------|---------|

Reporting group description:

3 21-day cycles of induction chemotherapy consisting of docetaxel 75 mg/m<sup>2</sup> given as a 1-h infusion and cisplatin 75 mg/m<sup>2</sup> given as a 2-h infusion on day one, followed by 5FU 750 mg/m<sup>2</sup> administered as a continuous infusion for five consecutive days.

|                       |         |
|-----------------------|---------|
| Reporting group title | TPC-arm |
|-----------------------|---------|

Reporting group description:

3 21-day cycles of induction chemotherapy consisting of docetaxel 75 mg/m<sup>2</sup> given as a 1-h infusion and cisplatin 75 mg/m<sup>2</sup> cetuximab 400 mg/m<sup>2</sup> given as a 2-h infusion on day one as a loading dose, followed by cetuximab 250 mg/m<sup>2</sup> given as a 1-h infusion weekly (thrice per cycle).

| Reporting group values                                | TPF-arm  | TPC-arm  | Total |
|---|----------|----------|-------|
| Number of subjects                                    | 49       | 51       | 100   |
| Age categorical<br>Units: Subjects                    |          |          |       |
| In utero  |          |          | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) |          |          | 0     |
| Newborns (0-27 days)                                  |          |          | 0     |
| Infants and toddlers (28 days-23 months)              |          |          | 0     |
| Children (2-11 years)                                 |          |          | 0     |
| Adolescents (12-17 years)                             |          |          | 0     |
| Adults (18-64 years)                                  |          |          | 0     |
| From 65-84 years                                      |          |          | 0     |
| 85 years and over                                     |          |          | 0     |
| Age continuous<br>Units: years                        |          |          |       |
| geometric mean  | 58.3     | 58.2     |       |
| full range (min-max)                                  | 40 to 72 | 35 to 78 | -     |
| Gender categorical<br>Units: Subjects                 |          |          |       |
| Female  | 7        | 6        | 13    |
| Male  | 42       | 45       | 87    |

## End points

### End points reporting groups

|  |         |
|--|---------|
| Reporting group title  | TPF-arm |
| Reporting group description:<br>3 21-day cycles of induction chemotherapy consisting of docetaxel 75 mg/m <sup>2</sup> given as a 1-h infusion and cisplatin 75 mg/m <sup>2</sup> given as a 2-h infusion on day one, followed by 5FU 750 mg/m <sup>2</sup> administered as a continuous infusion for five consecutive days.   |         |
| Reporting group title  | TPC-arm |
| Reporting group description:<br>3 21-day cycles of induction chemotherapy consisting of docetaxel 75 mg/m <sup>2</sup> given as a 1-h infusion and cisplatin 75 mg/m <sup>2</sup> cetuximab 400 mg/m <sup>2</sup> given as a 2-h infusion on day one as a loading dose, followed by cetuximab 250 mg/m <sup>2</sup> given as a 1-h infusion weekly (thrice per cycle).   |         |
| Reporting group title  | TPF-arm |
| Reporting group description:<br>RT started maximum 6 weeks after the last administration of docetaxel and cisplatin. A loading dose of cetuximab 400 mg/m <sup>2</sup> intravenously over 120 min was administered to the TPF arm one week before the start of concomitant boost RT. Followed by weekly infusions of cetuximab 250 mg/m <sup>2</sup> during the whole course of RT (seven infusions in total). |         |
| Reporting group title  | TPC-arm |
| Reporting group description:<br>RT started maximum 6 weeks after the last administration of docetaxel and cisplatin. A dose of cetuximab 250mg/m <sup>2</sup> intravenously over 120 min was administered to the TPC arm one week before the start of concomitant boost RT. Followed by weekly infusions of cetuximab 250 mg/m <sup>2</sup> during the whole course of RT (seven infusions in total).          |         |

### Primary: Response three months after RT + C

|   |   |
|---|---|
| End point title   | Response three months after RT + C <sup>[1]</sup> |
| End point description:<br>The primary end-point of the study was overall response rate (ORR: complete remission [CR] + partial remission [PR]) three months after RT + C was finished, assessed on the basis of CT or MRI performance as per the RECIST criteria. |   |
| End point type  | Primary   |
| End point timeframe:<br>Three months after radiotherapie plus cetuximab   |   |
| Notes:  |   |

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

Justification: Although the ORR of TPC compared favourably with TPF (74.5% and 63.3%, respectively), the observed difference did not reach statistical significance.

| End point values            | TPF-arm         | TPC-arm         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 49              | 51              |  |  |
| Units: subjects             |                 |                 |  |  |
| Complete Remission (CR)     | 16              | 25              |  |  |
| Partial Remission (PR)      | 15              | 13              |  |  |
| Stable Disease (SD)         | 3               | 2               |  |  |
| Overall Response Rate (ORR) | 31              | 38              |  |  |

## Statistical analyses

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No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All patients having received at least one dose of the study medication were followed for adverse events for at least 28 days after discontinuing study treatment or completion of study treatment.

Adverse event reporting additional description:

Acute chemotherapy toxicity was collected after each cycle of chemotherapy until the start of radiation. Acute radiation toxicity was recorded once at the end of radiation or at toxicity-related pauses or discontinuation of radiation therapy. Acute toxicity was recorded 30 days and 3 months after the end of cetuximab and radiation.

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 21.0   |

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | Overall trial |
|-----------------------|---------------|

Reporting group description:

Relation to IMP cetuximab is given.

| Serious adverse events  | Overall trial     |  |  |
|---|-------------------|--|--|
| Total subjects affected by serious adverse events                   |                   |  |  |
| subjects affected / exposed   | 77 / 100 (77.00%) |  |  |
| number of deaths (all causes)                                       | 41                |  |  |
| number of deaths resulting from adverse events                      | 2                 |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                   |  |  |
| Adenoma benign  |                   |  |  |
| subjects affected / exposed   | 1 / 100 (1.00%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 1             |  |  |
| deaths causally related to treatment / all                          | 0 / 0             |  |  |
| Vascular disorders  |                   |  |  |
| Hypertension  |                   |  |  |
| subjects affected / exposed   | 1 / 100 (1.00%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 1             |  |  |
| deaths causally related to treatment / all                          | 0 / 0             |  |  |
| Thrombosis  |                   |  |  |
| subjects affected / exposed   | 1 / 100 (1.00%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 1             |  |  |
| deaths causally related to treatment / all                          | 0 / 0             |  |  |

|  |                   |  |  |
|--|-------------------|--|--|
| Hypotension  |                   |  |  |
| subjects affected / exposed                          | 1 / 100 (1.00%)   |  |  |
| occurrences causally related to treatment / all      | 0 / 1             |  |  |
| deaths causally related to treatment / all           | 0 / 0             |  |  |
| General disorders and administration site conditions |                   |  |  |
| Mucosal inflammation                                 |                   |  |  |
| subjects affected / exposed                          | 18 / 100 (18.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 27            |  |  |
| deaths causally related to treatment / all           | 0 / 0             |  |  |
| General physical health deterioration                |                   |  |  |
| subjects affected / exposed                          | 11 / 100 (11.00%) |  |  |
| occurrences causally related to treatment / all      | 2 / 17            |  |  |
| deaths causally related to treatment / all           | 0 / 0             |  |  |
| Pyrexia  |                   |  |  |
| subjects affected / exposed                          | 1 / 100 (1.00%)   |  |  |
| occurrences causally related to treatment / all      | 0 / 1             |  |  |
| deaths causally related to treatment / all           | 0 / 0             |  |  |
| Chest pain   |                   |  |  |
| subjects affected / exposed                          | 1 / 100 (1.00%)   |  |  |
| occurrences causally related to treatment / all      | 0 / 1             |  |  |
| deaths causally related to treatment / all           | 0 / 0             |  |  |
| Impaired healing                                     |                   |  |  |
| subjects affected / exposed                          | 1 / 100 (1.00%)   |  |  |
| occurrences causally related to treatment / all      | 0 / 1             |  |  |
| deaths causally related to treatment / all           | 0 / 0             |  |  |
| Extravasation  |                   |  |  |
| subjects affected / exposed                          | 1 / 100 (1.00%)   |  |  |
| occurrences causally related to treatment / all      | 1 / 1             |  |  |
| deaths causally related to treatment / all           | 0 / 0             |  |  |
| Pain   |                   |  |  |
| subjects affected / exposed                          | 1 / 100 (1.00%)   |  |  |
| occurrences causally related to treatment / all      | 0 / 1             |  |  |
| deaths causally related to treatment / all           | 0 / 0             |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Facial pain                                     |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Asthenia  |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Fatigue   |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Immune system disorders                         |                 |  |  |
| Anaphylactic reaction                           |                 |  |  |
| subjects affected / exposed                     | 2 / 100 (2.00%) |  |  |
| occurrences causally related to treatment / all | 2 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Respiratory, thoracic and mediastinal disorders |                 |  |  |
| Dyspnoea  |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Respiratory failure                             |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Epistaxis                                       |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pneumothorax                                    |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Pulmonary fibrosis                              |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Psychiatric disorders                           |                 |  |  |
| Insomnia  |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Delirium  |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Investigations                                  |                 |  |  |
| C-reactive protein increased                    |                 |  |  |
| subjects affected / exposed                     | 9 / 100 (9.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 9           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Blood creatine increased                        |                 |  |  |
| subjects affected / exposed                     | 5 / 100 (5.00%) |  |  |
| occurrences causally related to treatment / all | 1 / 5           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Weight decreased                                |                 |  |  |
| subjects affected / exposed                     | 2 / 100 (2.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| White blood cell count decreased                |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Inflammatory marker increased                   |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Creatinine renal clearance decreased            |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Injury, poisoning and procedural complications  |                 |  |  |
| Radiation skin injury                           |                 |  |  |
| subjects affected / exposed                     | 6 / 100 (6.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 6           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Infusion related reaction                       |                 |  |  |
| subjects affected / exposed                     | 2 / 100 (2.00%) |  |  |
| occurrences causally related to treatment / all | 2 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Laceration                                      |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cardiac disorders                               |                 |  |  |
| Atrial fibrillation                             |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Arteriospasm coronary                           |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Acute myocardial infarction                     |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Acute right ventricular failure                 |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Nervous system disorders                        |                 |  |  |
| Orthostatic intolerance                         |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Transient ischaemic attack                      |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Peroneal nerve palsy                            |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Dizziness                                       |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Aphasia   |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Neuropathy peripheral                           |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Blood and lymphatic system disorders            |                 |  |  |
| Leukopenia                                      |                 |  |  |
| subjects affected / exposed                     | 7 / 100 (7.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 9           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Neutropenia                                     |                 |  |  |
| subjects affected / exposed                     | 5 / 100 (5.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 5           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

|   |                   |  |  |
|---|-------------------|--|--|
| Febrile neutropenia                             |                   |  |  |
| subjects affected / exposed                     | 3 / 100 (3.00%)   |  |  |
| occurrences causally related to treatment / all | 0 / 3             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Thrombocytopenia                                |                   |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%)   |  |  |
| occurrences causally related to treatment / all | 0 / 1             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Anaemia   |                   |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%)   |  |  |
| occurrences causally related to treatment / all | 0 / 1             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Ear and labyrinth disorders                     |                   |  |  |
| Vertigo   |                   |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%)   |  |  |
| occurrences causally related to treatment / all | 0 / 1             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Gastrointestinal disorders                      |                   |  |  |
| Diarrhoea                                       |                   |  |  |
| subjects affected / exposed                     | 13 / 100 (13.00%) |  |  |
| occurrences causally related to treatment / all | 3 / 18            |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Dysphagia                                       |                   |  |  |
| subjects affected / exposed                     | 13 / 100 (13.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 13            |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Vomiting  |                   |  |  |
| subjects affected / exposed                     | 3 / 100 (3.00%)   |  |  |
| occurrences causally related to treatment / all | 0 / 3             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |
| Stomatitis                                      |                   |  |  |
| subjects affected / exposed                     | 3 / 100 (3.00%)   |  |  |
| occurrences causally related to treatment / all | 1 / 4             |  |  |
| deaths causally related to treatment / all      | 0 / 0             |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Gastrointestinal haemorrhage<br>subjects affected / exposed | 1 / 100 (1.00%) |  |  |
| occurrences causally related to<br>treatment / all          | 0 / 1           |  |  |
| deaths causally related to<br>treatment / all               | 0 / 0           |  |  |
| Abdominal pain upper<br>subjects affected / exposed         | 1 / 100 (1.00%) |  |  |
| occurrences causally related to<br>treatment / all          | 0 / 1           |  |  |
| deaths causally related to<br>treatment / all               | 0 / 0           |  |  |
| Cheilitis<br>subjects affected / exposed                    | 1 / 100 (1.00%) |  |  |
| occurrences causally related to<br>treatment / all          | 0 / 1           |  |  |
| deaths causally related to<br>treatment / all               | 0 / 0           |  |  |
| Abdominal pain<br>subjects affected / exposed               | 1 / 100 (1.00%) |  |  |
| occurrences causally related to<br>treatment / all          | 0 / 1           |  |  |
| deaths causally related to<br>treatment / all               | 0 / 0           |  |  |
| Nausea<br>subjects affected / exposed                       | 1 / 100 (1.00%) |  |  |
| occurrences causally related to<br>treatment / all          | 0 / 1           |  |  |
| deaths causally related to<br>treatment / all               | 0 / 0           |  |  |
| Rectal haemorrhage<br>subjects affected / exposed           | 1 / 100 (1.00%) |  |  |
| occurrences causally related to<br>treatment / all          | 0 / 1           |  |  |
| deaths causally related to<br>treatment / all               | 0 / 0           |  |  |
| Colitis<br>subjects affected / exposed                      | 1 / 100 (1.00%) |  |  |
| occurrences causally related to<br>treatment / all          | 0 / 1           |  |  |
| deaths causally related to<br>treatment / all               | 0 / 0           |  |  |
| Gastritis<br>subjects affected / exposed                    | 1 / 100 (1.00%) |  |  |
| occurrences causally related to<br>treatment / all          | 0 / 1           |  |  |
| deaths causally related to<br>treatment / all               | 0 / 0           |  |  |
| Hepatobiliary disorders                                     |                 |  |  |



|   |                 |  |  |
|---|-----------------|--|--|
| Hepatic necrosis                                |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cholelithiasis                                  |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Bile duct stone                                 |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Biliary colic                                   |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Skin and subcutaneous tissue disorders          |                 |  |  |
| Dermatitis                                      |                 |  |  |
| subjects affected / exposed                     | 9 / 100 (9.00%) |  |  |
| occurrences causally related to treatment / all | 1 / 11          |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Rash  |                 |  |  |
| subjects affected / exposed                     | 2 / 100 (2.00%) |  |  |
| occurrences causally related to treatment / all | 2 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Acne  |                 |  |  |
| subjects affected / exposed                     | 2 / 100 (2.00%) |  |  |
| occurrences causally related to treatment / all | 2 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Seborrhoeic dermatitis                          |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Skin lesion                                     |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Dermatitis acneiform                            |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Renal and urinary disorders                     |                 |  |  |
| Renal failure                                   |                 |  |  |
| subjects affected / exposed                     | 4 / 100 (4.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 4           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Acute kidney injury                             |                 |  |  |
| subjects affected / exposed                     | 3 / 100 (3.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 3           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Renal impairment                                |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Musculoskeletal and connective tissue disorders |                 |  |  |
| Pain in extremity                               |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Back pain                                       |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Infections and infestations                     |                 |  |  |
| Pneumonia                                       |                 |  |  |
| subjects affected / exposed                     | 8 / 100 (8.00%) |  |  |
| occurrences causally related to treatment / all | 1 / 11          |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| Infection                                       |                 |  |  |  |
| subjects affected / exposed                     | 6 / 100 (6.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 7           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Device related infection                        |                 |  |  |  |
| subjects affected / exposed                     | 3 / 100 (3.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 3           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Staphylococcal infection                        |                 |  |  |  |
| subjects affected / exposed                     | 3 / 100 (3.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 3           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Gastrointestinal infection                      |                 |  |  |  |
| subjects affected / exposed                     | 2 / 100 (2.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Wound infection                                 |                 |  |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Pseudomonal sepsis                              |                 |  |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Oral candidiasis                                |                 |  |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Brain abscess                                   |                 |  |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Respiratory tract infection                     |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Cystitis  |                 |  |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Sepsis  |                 |  |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Clostridial infection                           |                 |  |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Tracheitis                                      |                 |  |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Tracheostomy infection                          |                 |  |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Influenza                                       |                 |  |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Abscess   |                 |  |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Mastoiditis                                     |                 |  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Metabolism and nutrition disorders              |                 |  |  |
| Hypokalaemia                                    |                 |  |  |
| subjects affected / exposed                     | 2 / 100 (2.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 3           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hypophagia                                      |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Electrolyte imbalance                           |                 |  |  |
| subjects affected / exposed                     | 1 / 100 (1.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

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

| <b>Non-serious adverse events</b>                     | Overall trial     |  |  |
|---|-------------------|--|--|
| Total subjects affected by non-serious adverse events |                   |  |  |
| subjects affected / exposed                           | 99 / 100 (99.00%) |  |  |
| Investigations  |                   |  |  |
| Weight decreased                                      |                   |  |  |
| subjects affected / exposed                           | 74 / 100 (74.00%) |  |  |
| occurrences (all)                                     | 115               |  |  |
| C-reactive protein increased                          |                   |  |  |
| subjects affected / exposed                           | 10 / 100 (10.00%) |  |  |
| occurrences (all)                                     | 14                |  |  |
| Blood creatine increased                              |                   |  |  |
| subjects affected / exposed                           | 6 / 100 (6.00%)   |  |  |
| occurrences (all)                                     | 7                 |  |  |
| Injury, poisoning and procedural complications        |                   |  |  |

|  |   |  |  |
|--|---|--|--|
| Radiation skin injury<br>subjects affected / exposed<br>occurrences (all)  | 24 / 100 (24.00%)<br>24   |  |  |
| Vascular disorders<br>Lymphoedema<br>subjects affected / exposed<br>occurrences (all)  | 7 / 100 (7.00%)<br>7  |  |  |
| Nervous system disorders<br>Dysgeusia<br>subjects affected / exposed<br>occurrences (all)<br><br>Neuropathy peripheral<br>subjects affected / exposed<br>occurrences (all)   | 20 / 100 (20.00%)<br>23<br><br>6 / 100 (6.00%)<br>7   |  |  |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all)<br><br>Leukopenia<br>subjects affected / exposed<br>occurrences (all)<br><br>Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)<br><br>Neutropenia<br>subjects affected / exposed<br>occurrences (all) | 50 / 100 (50.00%)<br>122<br><br>33 / 100 (33.00%)<br>61<br><br>29 / 100 (29.00%)<br>50<br><br>24 / 100 (24.00%)<br>33 |  |  |
| General disorders and administration<br>site conditions<br>Mucosal inflammation<br>subjects affected / exposed<br>occurrences (all)<br><br>Fatigue<br>subjects affected / exposed<br>occurrences (all)<br><br>Pain   | 71 / 100 (71.00%)<br>123<br><br>35 / 100 (35.00%)<br>42   |  |  |

|  |                   |  |  |
|--|-------------------|--|--|
| subjects affected / exposed            | 19 / 100 (19.00%) |  |  |
| occurrences (all)                      | 20                |  |  |
| Application site oedema                |                   |  |  |
| subjects affected / exposed            | 10 / 100 (10.00%) |  |  |
| occurrences (all)                      | 11                |  |  |
| Pyrexia                                |                   |  |  |
| subjects affected / exposed            | 7 / 100 (7.00%)   |  |  |
| occurrences (all)                      | 7                 |  |  |
| Gastrointestinal disorders             |                   |  |  |
| Dry mouth                              |                   |  |  |
| subjects affected / exposed            | 53 / 100 (53.00%) |  |  |
| occurrences (all)                      | 65                |  |  |
| Dysphagia                              |                   |  |  |
| subjects affected / exposed            | 49 / 100 (49.00%) |  |  |
| occurrences (all)                      | 52                |  |  |
| Diarrhoea                              |                   |  |  |
| subjects affected / exposed            | 24 / 100 (24.00%) |  |  |
| occurrences (all)                      | 26                |  |  |
| Nausea                                 |                   |  |  |
| subjects affected / exposed            | 24 / 100 (24.00%) |  |  |
| occurrences (all)                      | 32                |  |  |
| Stomatitis                             |                   |  |  |
| subjects affected / exposed            | 14 / 100 (14.00%) |  |  |
| occurrences (all)                      | 17                |  |  |
| Skin and subcutaneous tissue disorders |                   |  |  |
| Dermatitis acneiform                   |                   |  |  |
| subjects affected / exposed            | 35 / 100 (35.00%) |  |  |
| occurrences (all)                      | 54                |  |  |
| Dermatitis                             |                   |  |  |
| subjects affected / exposed            | 31 / 100 (31.00%) |  |  |
| occurrences (all)                      | 39                |  |  |
| Rash                                   |                   |  |  |
| subjects affected / exposed            | 15 / 100 (15.00%) |  |  |
| occurrences (all)                      | 18                |  |  |
| Acne                                   |                   |  |  |

|  |                         |  |  |
|--|-------------------------|--|--|
| subjects affected / exposed<br>occurrences (all) | 14 / 100 (14.00%)<br>18 |  |  |
| Infections and infestations                      |                         |  |  |
| Candida infection                                |                         |  |  |
| subjects affected / exposed                      | 11 / 100 (11.00%)       |  |  |
| occurrences (all)                                | 11                      |  |  |
| Urinary tract infection                          |                         |  |  |
| subjects affected / exposed                      | 6 / 100 (6.00%)         |  |  |
| occurrences (all)                                | 6                       |  |  |
| Metabolism and nutrition disorders               |                         |  |  |
| Hypokalaemia                                     |                         |  |  |
| subjects affected / exposed                      | 33 / 100 (33.00%)       |  |  |
| occurrences (all)                                | 47                      |  |  |
| Hypomagnesaemia                                  |                         |  |  |
| subjects affected / exposed                      | 14 / 100 (14.00%)       |  |  |
| occurrences (all)                                | 21                      |  |  |
| Hypocalcaemia                                    |                         |  |  |
| subjects affected / exposed                      | 7 / 100 (7.00%)         |  |  |
| occurrences (all)                                | 10                      |  |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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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.

|      |
|------|
| None |
|------|

Notes:

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/34022697>