



## Clinical trial results:

### A Phase 1/2, First-in-Human, Open-Label, Dose-Escalation Study of MGC018 (Anti-B7-H3 Antibody Drug Conjugate) Alone and in Combination with MGA012 (Anti-PD-1 Antibody) in Patients with Advanced Solid Tumors

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2018-003555-38 |
| Trial protocol           | PL ES          |
| Global end of trial date | 18 March 2023  |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 07 December 2024 |
| First version publication date | 07 December 2024 |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | CP-MGC018-01 |
|-----------------------|--------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03729596 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | MacroGenics, Inc.  |
| Sponsor organisation address | 9704 Medical Center Drive, Rockville, MD, United States, 20850               |
| Public contact               | Global Trial Manager, MacroGenics, Inc., +1 3012515172, info@macrogenics.com |
| Scientific contact           | Global Trial Manager, MacroGenics, Inc., +1 3012515172, info@macrogenics.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                       | 08 December 2023 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 18 March 2023    |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 18 March 2023    |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To characterize the safety, tolerability, dose-limiting toxicities (DLTs), and maximum tolerated dose (MTD) or maximum administered dose (MAD) (if no MTD is defined) for MGC018 administered as monotherapy or in combination with MGA012, each administered intravenously (IV), in participants who have relapsed/refractory, unresectable locally advanced or metastatic solid tumors.

Protection of trial subjects:

This study was conducted under United States Investigational New Drug application, in compliance with Good Clinical Practice, as well as all applicable local and national laws and regulations of countries in which the trial was performed. At each trial site, an institutional review board (IRB) or independent ethics committee (IEC) reviewed and approved the clinical trial protocol, the current and previous versions of the Investigator's Brochure, and informed consent form(s), as applicable. The IRB/IEC subsequently approved protocol amendments and revisions. Investigators were responsible for obtaining and documenting written informed consent from each participant or legal representative. Written informed consent was obtained for all participants before any protocol-specific procedures or interventions were performed.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 21 November 2018 |
| 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 | Poland: 26        |
| Country: Number of subjects enrolled | Spain: 22         |
| Country: Number of subjects enrolled | Australia: 35     |
| Country: Number of subjects enrolled | United States: 60 |
| Worldwide total number of subjects   | 143               |
| EEA total number of subjects         | 48                |

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)                     | 66 |
| From 65 to 84 years                      | 76 |
| 85 years and over                        | 1  |

## Subject disposition

### Recruitment

Recruitment details:

Participants were enrolled from 19 investigational sites in 4 countries.

### Pre-assignment

Screening details:

Adult patients with metastatic or advanced solid tumors for who no approved therapy with demonstrated clinical benefit was available.

### Period 1

|                              |                                   |
|------------------------------|-----------------------------------|
| Period 1 title               | Treatment Period (overall period) |
| Is this the baseline period? | Yes                               |
| Allocation method            | Not applicable                    |
| Blinding used                | Not blinded                       |

### Arms

|                              |                     |
|------------------------------|---------------------|
| Are arms mutually exclusive? | Yes                 |
| <b>Arm title</b>             | Cohort 1: 0.5 mg/kg |

Arm description: -

|  |                           |
|--|---------------------------|
| Arm type                               | Experimental              |
| Investigational medicinal product name | vobramitamab duocarmazine |
| Investigational medicinal product code |                           |
| Other name                             | MGC018-01                 |
| Pharmaceutical forms                   | Infusion                  |
| Routes of administration               | Intravenous use           |

Dosage and administration details:

Intravenous infusion of 0.5 mg/kg every 3 weeks.

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | Cohort 2: 1.0 mg/kg |
|------------------|---------------------|

Arm description: -

|  |                           |
|--|---------------------------|
| Arm type                               | Experimental              |
| Investigational medicinal product name | vobramitamab duocarmazine |
| Investigational medicinal product code |                           |
| Other name                             | MGC018-01                 |
| Pharmaceutical forms                   | Infusion                  |
| Routes of administration               | Intravenous use           |

Dosage and administration details:

Intravenous infusion of 1.0 mg/kg every 3 weeks.

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | Cohort 3: 2.0 mg/kg |
|------------------|---------------------|

Arm description: -

|  |                           |
|--|---------------------------|
| Arm type                               | Experimental              |
| Investigational medicinal product name | vobramitamab duocarmazine |
| Investigational medicinal product code |                           |
| Other name                             | MGC018-01                 |
| Pharmaceutical forms                   | Infusion                  |
| Routes of administration               | Intravenous use           |

Dosage and administration details:

Intravenous infusion of 2.0 mg/kg every 3 weeks.

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | Cohort 4: 3.0 mg/kg |
|------------------|---------------------|

|  |                           |
|--|---------------------------|
| Arm description: -                     |                           |
| Arm type                               | Experimental              |
| Investigational medicinal product name | vobramitamab duocarmazine |
| Investigational medicinal product code |                           |
| Other name                             | MGC018-01                 |
| Pharmaceutical forms                   | Infusion                  |
| Routes of administration               | Intravenous use           |

Dosage and administration details:

Intravenous infusion of 3.0 mg/kg every 3 weeks.

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | Cohort 5: 4.0 mg/kg |
|------------------|---------------------|

|  |                           |
|--|---------------------------|
| Arm description: -                     |                           |
| Arm type                               | Experimental              |
| Investigational medicinal product name | vobramitamab duocarmazine |
| Investigational medicinal product code |                           |
| Other name                             | MGC018-01                 |
| Pharmaceutical forms                   | Infusion                  |
| Routes of administration               | Intravenous use           |

Dosage and administration details:

Intravenous infusion of 4.0 mg/kg every 3 weeks.

| <b>Number of subjects in period 1</b> | Cohort 1: 0.5 mg/kg | Cohort 2: 1.0 mg/kg | Cohort 3: 2.0 mg/kg |
|---------------------------------------|---------------------|---------------------|---------------------|
| Started                               | 3                   | 6                   | 7                   |
| Completed                             | 0                   | 0                   | 0                   |
| Not completed                         | 3                   | 6                   | 7                   |
| Consent withdrawn by subject          | -                   | -                   | -                   |
| Death                                 | 3                   | 5                   | 4                   |
| Protocol amendment                    | -                   | 1                   | 3                   |
| Study terminated by sponsor           | -                   | -                   | -                   |
| Lost to follow-up                     | -                   | -                   | -                   |

| <b>Number of subjects in period 1</b> | Cohort 4: 3.0 mg/kg | Cohort 5: 4.0 mg/kg |
|---------------------------------------|---------------------|---------------------|
| Started                               | 121                 | 6                   |
| Completed                             | 0                   | 0                   |
| Not completed                         | 121                 | 6                   |
| Consent withdrawn by subject          | 4                   | 1                   |
| Death                                 | 95                  | -                   |
| Protocol amendment                    | 6                   | 5                   |
| Study terminated by sponsor           | 14                  | -                   |
| Lost to follow-up                     | 2                   | -                   |

## Baseline characteristics

### Reporting groups

|                                |                     |
|--------------------------------|---------------------|
| Reporting group title          | Cohort 1: 0.5 mg/kg |
| Reporting group description: - |                     |
| Reporting group title          | Cohort 2: 1.0 mg/kg |
| Reporting group description: - |                     |
| Reporting group title          | Cohort 3: 2.0 mg/kg |
| Reporting group description: - |                     |
| Reporting group title          | Cohort 4: 3.0 mg/kg |
| Reporting group description: - |                     |
| Reporting group title          | Cohort 5: 4.0 mg/kg |
| Reporting group description: - |                     |

| Reporting group values | Cohort 1: 0.5 mg/kg | Cohort 2: 1.0 mg/kg | Cohort 3: 2.0 mg/kg |
|------------------------|---------------------|---------------------|---------------------|
| Number of subjects     | 3                   | 6                   | 7                   |
| Age categorical        |                     |                     |                     |
| Units: Subjects        |                     |                     |                     |
| Adults (18-64 years)   | 3                   | 4                   | 3                   |
| From 65-84 years       | 0                   | 2                   | 4                   |
| 85 years and over      | 0                   | 0                   | 0                   |
| Age continuous         |                     |                     |                     |
| Units: years           |                     |                     |                     |
| arithmetic mean        | 45.3                | 56.5                | 64.0                |
| standard deviation     | ± 12.42             | ± 11.98             | ± 11.72             |
| Gender categorical     |                     |                     |                     |
| Units: Subjects        |                     |                     |                     |
| Female                 | 1                   | 4                   | 2                   |
| Male                   | 2                   | 2                   | 5                   |

| Reporting group values | Cohort 4: 3.0 mg/kg | Cohort 5: 4.0 mg/kg | Total |
|------------------------|---------------------|---------------------|-------|
| Number of subjects     | 121                 | 6                   | 143   |
| Age categorical        |                     |                     |       |
| Units: Subjects        |                     |                     |       |
| Adults (18-64 years)   | 54                  | 2                   | 66    |
| From 65-84 years       | 66                  | 4                   | 76    |
| 85 years and over      | 1                   | 0                   | 1     |
| Age continuous         |                     |                     |       |
| Units: years           |                     |                     |       |
| arithmetic mean        | 62.9                | 65.3                | -     |
| standard deviation     | ± 12.22             | ± 8.09              | -     |
| Gender categorical     |                     |                     |       |
| Units: Subjects        |                     |                     |       |
| Female                 | 40                  | 1                   | 48    |
| Male                   | 81                  | 5                   | 95    |

## Subject analysis sets

|  |   |
|--|---|
| Subject analysis set title   | Response Evaluable Population                           |
| Subject analysis set type  | Modified intention-to-treat                             |
| Subject analysis set description:<br>All participants who received at least 1 dose of study drug, had baseline measurable disease, and had at least one post-baseline radiographic tumor assessment. |   |
| Subject analysis set title   | Safety population                                       |
| Subject analysis set type  | Safety analysis   |
| Subject analysis set description:<br>All participants who received at least 1 dose of study drug.  |   |
| Subject analysis set title   | Metastatic prostate cancer population                   |
| Subject analysis set type  | Sub-group analysis                                      |
| Subject analysis set description:<br>Participants with a diagnosis of metastatic prostate cancer who have received at least 1 dose of MGC018.  |   |
| Subject analysis set title   | Non-small cell lung cancer population                   |
| Subject analysis set type  | Sub-group analysis                                      |
| Subject analysis set description:<br>Participants with the diagnosis of non-small lung cancer who have received at least 1 dose of MGC018.   |   |
| Subject analysis set title   | Triple negative breast cancer population                |
| Subject analysis set type  | Sub-group analysis                                      |
| Subject analysis set description:<br>Participants with the diagnosis of triple negative breast cancer who have received at least 1 dose of MGC018.   |   |
| Subject analysis set title   | Melanoma population                                     |
| Subject analysis set type  | Sub-group analysis                                      |
| Subject analysis set description:<br>Participants with the diagnosis of melanoma who have received at least 1 dose of MGC018.  |   |
| Subject analysis set title   | Squamous cell carcinoma of the head and neck population |
| Subject analysis set type  | Sub-group analysis                                      |
| Subject analysis set description:<br>Participants with the diagnosis of squamous cell carcinoma of the head and neck who received at least 1 dose of MGC018.   |   |

| Reporting group values  | Response Evaluable Population | Safety population | Metastatic prostate cancer population |
|---|-------------------------------|-------------------|---------------------------------------|
| Number of subjects  | 139                           | 143               | 41                                    |
| Age categorical<br>Units: Subjects                                      |                               |                   |                                       |
| Adults (18-64 years)  | 63                            | 66                | 8                                     |
| From 65-84 years  | 75                            | 76                | 33                                    |
| 85 years and over   | 1                             | 1                 | 0                                     |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | ±                             | ±                 | ±                                     |
| Gender categorical<br>Units: Subjects                                   |                               |                   |                                       |
| Female  | 45                            | 48                | 0                                     |
| Male  | 94                            | 95                | 41                                    |

| Reporting group values | Non-small cell lung cancer population | Triple negative breast cancer population | Melanoma population |
|------------------------|---------------------------------------|--|---------------------|
|------------------------|---------------------------------------|--|---------------------|

|                      |    |    |    |
|----------------------|----|----|----|
| Number of subjects   | 20 | 16 | 21 |
| Age categorical      |    |    |    |
| Units: Subjects      |    |    |    |
| Adults (18-64 years) | 11 | 14 | 8  |
| From 65-84 years     | 9  | 2  | 12 |
| 85 years and over    | 0  | 0  | 1  |
| Age continuous       |    |    |    |
| Units: years         |    |    |    |
| arithmetic mean      |    |    |    |
| standard deviation   | ±  | ±  | ±  |
| Gender categorical   |    |    |    |
| Units: Subjects      |    |    |    |
| Female               | 11 | 16 | 5  |
| Male                 | 9  | 0  | 16 |

|                               |   |  |  |
|-------------------------------|---|--|--|
| <b>Reporting group values</b> | Squamous cell carcinoma of the head and neck population |  |  |
| Number of subjects            | 13  |  |  |
| Age categorical               |   |  |  |
| Units: Subjects               |   |  |  |
| Adults (18-64 years)          | 6   |  |  |
| From 65-84 years              | 7   |  |  |
| 85 years and over             | 0   |  |  |
| Age continuous                |   |  |  |
| Units: years                  |   |  |  |
| arithmetic mean               |   |  |  |
| standard deviation            | ±   |  |  |
| Gender categorical            |   |  |  |
| Units: Subjects               |   |  |  |
| Female                        | 4   |  |  |
| Male                          | 9   |  |  |



## End points

### End points reporting groups

|   |   |
|---|---|
| Reporting group title   | Cohort 1: 0.5 mg/kg                                     |
| Reporting group description: -  |   |
| Reporting group title   | Cohort 2: 1.0 mg/kg                                     |
| Reporting group description: -  |   |
| Reporting group title   | Cohort 3: 2.0 mg/kg                                     |
| Reporting group description: -  |   |
| Reporting group title   | Cohort 4: 3.0 mg/kg                                     |
| Reporting group description: -  |   |
| Reporting group title   | Cohort 5: 4.0 mg/kg                                     |
| Reporting group description: -  |   |
| Subject analysis set title  | Response Evaluable Population                           |
| Subject analysis set type   | Modified intention-to-treat                             |
| Subject analysis set description:   |   |
| All participants who received at least 1 dose of study drug, had baseline measurable disease, and had at least one post-baseline radiographic tumor assessment. |   |
| Subject analysis set title  | Safety population                                       |
| Subject analysis set type   | Safety analysis   |
| Subject analysis set description:   |   |
| All participants who received at least 1 dose of study drug.  |   |
| Subject analysis set title  | Metastatic prostate cancer population                   |
| Subject analysis set type   | Sub-group analysis                                      |
| Subject analysis set description:   |   |
| Participants with a diagnosis of metastatic prostate cancer who have received at least 1 dose of MGC018.  |   |
| Subject analysis set title  | Non-small cell lung cancer population                   |
| Subject analysis set type   | Sub-group analysis                                      |
| Subject analysis set description:   |   |
| Participants with the diagnosis of non-small lung cancer who have received at least 1 dose of MGC018.   |   |
| Subject analysis set title  | Triple negative breast cancer population                |
| Subject analysis set type   | Sub-group analysis                                      |
| Subject analysis set description:   |   |
| Participants with the diagnosis of triple negative breast cancer who have received at least 1 dose of MGC018.   |   |
| Subject analysis set title  | Melanoma population                                     |
| Subject analysis set type   | Sub-group analysis                                      |
| Subject analysis set description:   |   |
| Participants with the diagnosis of melanoma who have received at least 1 dose of MGC018.  |   |
| Subject analysis set title  | Squamous cell carcinoma of the head and neck population |
| Subject analysis set type   | Sub-group analysis                                      |
| Subject analysis set description:   |   |
| Participants with the diagnosis of squamous cell carcinoma of the head and neck who received at least 1 dose of MGC018.   |   |

### Primary: Type and number of adverse events

|                        |  |
|------------------------|--|
| End point title        | Type and number of adverse events <sup>[1]</sup> |
| End point description: |  |
| End point type         | Primary  |

End point timeframe:

Adverse events are recorded from the time of informed consent signature through 30 days of the last dose of study treatment.

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: Data displays were summary tables with the number and percent of participants who experience a given event. There is no active control or comparator to allow for statistical inferences.

| End point values                              | Cohort 1: 0.5 mg/kg | Cohort 2: 1.0 mg/kg | Cohort 3: 2.0 mg/kg | Cohort 4: 3.0 mg/kg |
|---|---------------------|---------------------|---------------------|---------------------|
| Subject group type                            | Reporting group     | Reporting group     | Reporting group     | Reporting group     |
| Number of subjects analysed                   | 3                   | 6                   | 7                   | 121                 |
| Units: participants with adverse events       |                     |                     |                     |                     |
| Study treatment related adverse event         | 3                   | 5                   | 6                   | 120                 |
| Severe adverse event                          | 3                   | 4                   | 7                   | 105                 |
| Severe treatment related adverse event        | 2                   | 2                   | 6                   | 79                  |
| Study treatment related serious adverse event | 1                   | 1                   | 2                   | 40                  |
| Fatal adverse event                           | 1                   | 0                   | 0                   | 4                   |

| End point values                              | Cohort 5: 4.0 mg/kg |  |  |  |
|---|---------------------|--|--|--|
| Subject group type                            | Reporting group     |  |  |  |
| Number of subjects analysed                   | 6                   |  |  |  |
| Units: participants with adverse events       |                     |  |  |  |
| Study treatment related adverse event         | 6                   |  |  |  |
| Severe adverse event                          | 5                   |  |  |  |
| Severe treatment related adverse event        | 4                   |  |  |  |
| Study treatment related serious adverse event | 2                   |  |  |  |
| Fatal adverse event                           | 0                   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Objective Response Rate

|                 |                         |
|-----------------|-------------------------|
| End point title | Objective Response Rate |
|-----------------|-------------------------|

End point description:

The percentage of patients who have a complete or partial response to study treatment.

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

End point timeframe:

From the first dose of study treatment throughout the study

| End point values            | Cohort 1: 0.5 mg/kg | Cohort 2: 1.0 mg/kg | Cohort 3: 2.0 mg/kg | Cohort 4: 3.0 mg/kg |
|-----------------------------|---------------------|---------------------|---------------------|---------------------|
| Subject group type          | Reporting group     | Reporting group     | Reporting group     | Reporting group     |
| Number of subjects analysed | 3                   | 6                   | 7                   | 118                 |
| Units: percentage           |                     |                     |                     |                     |
| number (not applicable)     | 0                   | 0                   | 0                   | 5.9                 |

| End point values            | Cohort 5: 4.0 mg/kg | Response Evaluable Population | Metastatic prostate cancer population | Non-small cell lung cancer population |
|-----------------------------|---------------------|-------------------------------|---------------------------------------|---------------------------------------|
| Subject group type          | Reporting group     | Subject analysis set          | Subject analysis set                  | Subject analysis set                  |
| Number of subjects analysed | 5                   | 139                           |                                       |                                       |
| Units: percentage           |                     |                               |                                       |                                       |
| number (not applicable)     | 20                  | 5.8                           | 4.9                                   | 15.0                                  |

| End point values            | Triple negative breast cancer population | Melanoma population  | Squamous cell carcinoma of the head and neck population |  |
|-----------------------------|--|----------------------|---|--|
| Subject group type          | Subject analysis set                     | Subject analysis set | Subject analysis set                                    |  |
| Number of subjects analysed |  |                      |   |  |
| Units: percentage           |  |                      |   |  |
| number (not applicable)     | 0  | 4.8                  | 7.7   |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Radiographic progression free survival in prostate cancer

|                 |   |
|-----------------|---|
| End point title | Radiographic progression free survival in prostate cancer |
|-----------------|---|

End point description:

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

End point timeframe:

From the first date of study treatment until first documented disease progression or death, whichever is earlier.

|                                  |                                       |  |  |  |
|----------------------------------|---------------------------------------|--|--|--|
| <b>End point values</b>          | Metastatic prostate cancer population |  |  |  |
| Subject group type               | Subject analysis set                  |  |  |  |
| Number of subjects analysed      | 41                                    |  |  |  |
| Units: Months                    |                                       |  |  |  |
| median (confidence interval 95%) | 5.5 (2.92 to 8.28)                    |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Prostate specific antigen response rate

|   |   |
|---|---|
| End point title   | Prostate specific antigen response rate |
| End point description:<br>The number of patients with metastatic prostate cancer who have greater than or equal to a 50% decline in PSA, with confirmation of the decline at least 3 weeks later. |   |
| End point type  | Secondary                               |
| End point timeframe:<br>From the date of first dose throughout the study.   |   |

|                                   |                                       |  |  |  |
|-----------------------------------|---------------------------------------|--|--|--|
| <b>End point values</b>           | Metastatic prostate cancer population |  |  |  |
| Subject group type                | Subject analysis set                  |  |  |  |
| Number of subjects analysed       | 41                                    |  |  |  |
| Units: patients with PSA response | 18                                    |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of PSA response

|  |                          |
|--|--------------------------|
| End point title                              | Duration of PSA response |
| End point description:                       |                          |
| End point type                               | Secondary                |
| End point timeframe:<br>Throughout the study |                          |

|                                  |                                       |  |  |  |
|----------------------------------|---------------------------------------|--|--|--|
| <b>End point values</b>          | Metastatic prostate cancer population |  |  |  |
| Subject group type               | Subject analysis set                  |  |  |  |
| Number of subjects analysed      | 41                                    |  |  |  |
| Units: Months                    |                                       |  |  |  |
| median (confidence interval 95%) | 6.2 (3.22 to 9.92)                    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Total exposure

|  |                |
|--|----------------|
| End point title  | Total exposure |
| End point description:   |                |
| Data were obtained from 143 study subjects, with , doses of 0.5, 1, 2, 3, and 4 mg/kg were administered to, respectively, 3, 6, 8, 120, and 6 subjects |                |
| End point type   | Secondary      |
| End point timeframe:   |                |
| Throughout the study from baseline through treatment discontinuation.  |                |

|                                      |                     |                     |                     |                     |
|--------------------------------------|---------------------|---------------------|---------------------|---------------------|
| <b>End point values</b>              | Cohort 1: 0.5 mg/kg | Cohort 2: 1.0 mg/kg | Cohort 3: 2.0 mg/kg | Cohort 4: 3.0 mg/kg |
| Subject group type                   | Reporting group     | Reporting group     | Reporting group     | Reporting group     |
| Number of subjects analysed          | 3                   | 6                   | 7                   | 120                 |
| Units: mcg/mL*day                    |                     |                     |                     |                     |
| arithmetic mean (standard deviation) |                     |                     |                     |                     |
| Antibody drug conjugate              | 10.6 (± 6.54)       | 51.5 (± 19.2)       | 119 (± 48.7)        | 140 (± 34.9)        |
| Duocarmycin                          | 0.0448 (± 0.023)    | 0.101 (± 0.0668)    | 0.0512 (± 0.0454)   | 0.0657 (± 0.0349)   |

|                                      |                     |  |  |  |
|--------------------------------------|---------------------|--|--|--|
| <b>End point values</b>              | Cohort 5: 4.0 mg/kg |  |  |  |
| Subject group type                   | Reporting group     |  |  |  |
| Number of subjects analysed          | 6                   |  |  |  |
| Units: mcg/mL*day                    |                     |  |  |  |
| arithmetic mean (standard deviation) |                     |  |  |  |
| Antibody drug conjugate              | 227 (± 105)         |  |  |  |
| Duocarmycin                          | 0.268 (± 0.061)     |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: PK parameters: peak and trough concentrations

End point title PK parameters: peak and trough concentrations

End point description:

End point type Secondary

End point timeframe:

Throughout the study from baseline through treatment discontinuation.

| End point values                     | Cohort 1: 0.5 mg/kg   | Cohort 2: 1.0 mg/kg  | Cohort 3: 2.0 mg/kg | Cohort 4: 3.0 mg/kg  |
|--------------------------------------|-----------------------|----------------------|---------------------|----------------------|
| Subject group type                   | Reporting group       | Reporting group      | Reporting group     | Reporting group      |
| Number of subjects analysed          | 3                     | 6                    | 7                   | 121                  |
| Units: mcg/mL                        |                       |                      |                     |                      |
| arithmetic mean (standard deviation) |                       |                      |                     |                      |
| ADC maximum concentration            | 7.69 (± 1.98)         | 23.4 (± 0.0408)      | 43.4 (± 14)         | 59 (± 11)            |
| ADC trough concentration             | 0.00928 (± 0.0129)    | 0.0415 (± 0.0415)    | 0.123 (± 0.652)     | 0.157 (± 0.119)      |
| Duocarmycin maximum concentration    | 0.0243 (± 0.0225)     | 0.0274 (± 0.016)     | 0.0512 (± 0.0454)   | 0.657 (± 0.0349)     |
| Duocarmycin trough concentration     | 0.000243 (± 0.000107) | 0.00074 (± 0.000532) | 0.00226 (± 0.00244) | 0.00185 (± 0.000658) |

| End point values                     | Cohort 5: 4.0 mg/kg  |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| Subject group type                   | Reporting group      |  |  |  |
| Number of subjects analysed          | 6                    |  |  |  |
| Units: mcg/mL                        |                      |  |  |  |
| arithmetic mean (standard deviation) |                      |  |  |  |
| ADC maximum concentration            | 78.6 (± 22.4)        |  |  |  |
| ADC trough concentration             | 0.313 (± 0.323)      |  |  |  |
| Duocarmycin maximum concentration    | 0.0571 (± 0.00757)   |  |  |  |
| Duocarmycin trough concentration     | 0.00194 (± 0.000973) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of Response

End point title Duration of Response

End point description:

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

End point timeframe:

The time from the first documented complete or partial response to the first documented disease progression or death, whichever comes first.

| End point values            | Cohort 1: 0.5 mg/kg | Cohort 2: 1.0 mg/kg | Cohort 3: 2.0 mg/kg | Cohort 4: 3.0 mg/kg |
|-----------------------------|---------------------|---------------------|---------------------|---------------------|
| Subject group type          | Reporting group     | Reporting group     | Reporting group     | Reporting group     |
| Number of subjects analysed | 0 <sup>[2]</sup>    | 0 <sup>[3]</sup>    | 0 <sup>[4]</sup>    | 7                   |
| Units: Months               |                     |                     |                     |                     |
| number (not applicable)     |                     |                     |                     |                     |
| Minimum duration            |                     |                     |                     | 1.41                |
| Maximum duration            |                     |                     |                     | 17.61               |

Notes:

[2] - There were no responses in this group.

[3] - There were no responses in this group.

[4] - There were no responses in this group.

| End point values            | Cohort 5: 4.0 mg/kg | Metastatic prostate cancer population | Non-small cell lung cancer population | Triple negative breast cancer population |
|-----------------------------|---------------------|---------------------------------------|---------------------------------------|--|
| Subject group type          | Reporting group     | Subject analysis set                  | Subject analysis set                  | Subject analysis set                     |
| Number of subjects analysed | 1                   | 41                                    | 20                                    | 0 <sup>[5]</sup>                         |
| Units: Months               |                     |                                       |                                       |  |
| number (not applicable)     |                     |                                       |                                       |  |
| Minimum duration            | 5.32                | 4.27                                  | 1.14                                  |  |
| Maximum duration            | 5.32                | 6.28                                  | 17.61                                 |  |

Notes:

[5] - There were no clinical responses in this group.

| End point values            | Melanoma population  | Squamous cell carcinoma of the head and neck population |  |  |
|-----------------------------|----------------------|---|--|--|
| Subject group type          | Subject analysis set | Subject analysis set                                    |  |  |
| Number of subjects analysed | 21                   | 13  |  |  |
| Units: Months               |                      |   |  |  |
| number (not applicable)     |                      |   |  |  |
| Minimum duration            | 10.28                | 2.10  |  |  |
| Maximum duration            | 10.28                | 2.10  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

AEs were collected from the time of first dose through 30 days after the last dose, average 6 months.  
All-cause mortality was collected from the first dose until the primary completion date, average 2 years.

Adverse event reporting additional description:

AEs are based on physical exam, patient reports, and significant abnormal laboratory values. AEs were not collected in survival follow up. Only SAEs were collected in survival follow up if related to study treatment.

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 25     |

### Reporting groups

|                                |                     |
|--------------------------------|---------------------|
| Reporting group title          | Cohort 1: 0.5 mg/kg |
| Reporting group description: - |                     |
| Reporting group title          | Cohort 2: 1.0 mg/kg |
| Reporting group description: - |                     |
| Reporting group title          | Cohort 3: 2.0 mg/kg |
| Reporting group description: - |                     |
| Reporting group title          | Cohort 4: 3.0 mg/kg |
| Reporting group description: - |                     |
| Reporting group title          | Cohort 5: 4.0 mg/kg |
| Reporting group description: - |                     |

| Serious adverse events                               | Cohort 1: 0.5 mg/kg | Cohort 2: 1.0 mg/kg | Cohort 3: 2.0 mg/kg |
|--|---------------------|---------------------|---------------------|
| Total subjects affected by serious adverse events    |                     |                     |                     |
| subjects affected / exposed                          | 1 / 3 (33.33%)      | 1 / 6 (16.67%)      | 3 / 7 (42.86%)      |
| number of deaths (all causes)                        | 3                   | 5                   | 4                   |
| number of deaths resulting from adverse events       | 1                   | 0                   | 0                   |
| General disorders and administration site conditions |                     |                     |                     |
| Pyrexia  |                     |                     |                     |
| subjects affected / exposed                          | 0 / 3 (0.00%)       | 0 / 6 (0.00%)       | 0 / 7 (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               |
| Asthenia   |                     |                     |                     |
| subjects affected / exposed                          | 0 / 3 (0.00%)       | 0 / 6 (0.00%)       | 0 / 7 (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               |
| Fatigue  |                     |                     |                     |



|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Oedema peripheral                               |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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         |
| Discomfort                                      |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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         |
| Face oedema                                     |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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         |
| Immune system disorders                         |               |               |               |
| Hypersensitivity                                |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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 |               |               |               |
| Dyspnoea exertional                             |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Investigations                                  |               |               |               |
| Neutrophil count decreased                      |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Platelet count decreased                        |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| White blood cell count decreased                |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Injury, poisoning and procedural complications  |               |               |               |
| Fall  |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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         |
| Thoracic vertebral fracture                     |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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                               |               |               |               |
| Cardiac arrest                                  |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Atrial fibrillation                             |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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         |
| Pericardial effusion                            |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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         |

|   |               |               |               |
|---|---------------|---------------|---------------|
| Angina pectoris                                 |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Supraventricular extrasystoles                  |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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         |
| Ventricular extrasystoles                       |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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                        |               |               |               |
| Ischaemic stroke                                |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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         |
| Lethargy  |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Peripheral sensory neuropathy                   |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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         |
| Disseminated intravascular coagulation          |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |

|   |               |               |               |
|---|---------------|---------------|---------------|
| Thrombocytopenia                                |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pancytopenia                                    |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Diarrhoea                                       |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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         |
| Colitis   |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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         |
| Duodenal ulcer                                  |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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         |
| Enterovesical fistula                           |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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 inflammation                   |               |               |               |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 6 (16.67%) | 0 / 7 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Nausea  |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Small intestinal obstruction                    |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%)  | 1 / 7 (14.29%) |
| 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                         |               |                |                |
| Hepatic failure                                 |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |               |                |                |
| Acute kidney injury                             |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (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          |
| Haematuria                                      |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue disorders |               |                |                |
| Flank pain                                      |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (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                     |               |                |                |
| COVID-19  |               |                |                |

|   |                |               |               |
|---|----------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (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 bacterial                             |                |               |               |
| subjects affected / exposed                     | 1 / 3 (33.33%) | 0 / 6 (0.00%) | 0 / 7 (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         |
| Sepsis pasteurella                              |                |               |               |
| subjects affected / exposed                     | 1 / 3 (33.33%) | 0 / 6 (0.00%) | 0 / 7 (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         |
| Urinary tract infection                         |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Cellulitis                                      |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Arthritis infective                             |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (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         |
| Catheter site infection                         |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (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         |
| Clostridium difficile infection                 |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 6 (0.00%) | 0 / 7 (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         |
| Coronavirus infection                           |                |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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 related infection                        |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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         |
| Herpes simplex                                  |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Lower respiratory tract infection               |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Oesophageal candidiasis                         |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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 aspiration                            |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Respiratory tract infection                     |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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         |
| Sepsis  |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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         |
| Subdural haematoma                              |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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              |               |               |               |
| Hypokalaemia                                    |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 6 (0.00%) | 0 / 7 (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>                        | Cohort 4: 3.0 mg/kg | Cohort 5: 4.0 mg/kg |  |
|--|---------------------|---------------------|--|
| Total subjects affected by serious adverse events    |                     |                     |  |
| subjects affected / exposed                          | 52 / 121 (42.98%)   | 2 / 6 (33.33%)      |  |
| number of deaths (all causes)                        | 95                  | 0                   |  |
| number of deaths resulting from adverse events       | 4                   | 0                   |  |
| General disorders and administration site conditions |                     |                     |  |
| Pyrexia  |                     |                     |  |
| subjects affected / exposed                          | 4 / 121 (3.31%)     | 0 / 6 (0.00%)       |  |
| occurrences causally related to treatment / all      | 4 / 4               | 0 / 0               |  |
| deaths causally related to treatment / all           | 0 / 0               | 0 / 0               |  |
| Asthenia   |                     |                     |  |
| subjects affected / exposed                          | 2 / 121 (1.65%)     | 0 / 6 (0.00%)       |  |
| occurrences causally related to treatment / all      | 1 / 2               | 0 / 0               |  |
| deaths causally related to treatment / all           | 0 / 0               | 0 / 0               |  |
| Fatigue  |                     |                     |  |
| subjects affected / exposed                          | 2 / 121 (1.65%)     | 0 / 6 (0.00%)       |  |
| occurrences causally related to treatment / all      | 2 / 2               | 0 / 0               |  |
| deaths causally related to treatment / all           | 0 / 0               | 0 / 0               |  |
| Oedema peripheral                                    |                     |                     |  |



|   |                 |               |  |
|---|-----------------|---------------|--|
| subjects affected / exposed                     | 2 / 121 (1.65%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Discomfort                                      |                 |               |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Face oedema                                     |                 |               |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Immune system disorders                         |                 |               |  |
| Hypersensitivity                                |                 |               |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Respiratory, thoracic and mediastinal disorders |                 |               |  |
| Dyspnoea exertional                             |                 |               |  |
| subjects affected / exposed                     | 2 / 121 (1.65%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Psychiatric disorders                           |                 |               |  |
| Confusional state                               |                 |               |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Investigations                                  |                 |               |  |
| Neutrophil count decreased                      |                 |               |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Platelet count decreased                        |                 |               |  |

|   |                 |               |  |
|---|-----------------|---------------|--|
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| White blood cell count decreased                |                 |               |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Injury, poisoning and procedural complications  |                 |               |  |
| Fall  |                 |               |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Thoracic vertebral fracture                     |                 |               |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Cardiac disorders                               |                 |               |  |
| Cardiac arrest                                  |                 |               |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 1 / 1           | 0 / 0         |  |
| Atrial fibrillation                             |                 |               |  |
| subjects affected / exposed                     | 5 / 121 (4.13%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 3 / 5           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Pericardial effusion                            |                 |               |  |
| subjects affected / exposed                     | 4 / 121 (3.31%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 4 / 4           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Angina pectoris                                 |                 |               |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| Supraventricular extrasystoles                  |                 |                |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Ventricular extrasystoles                       |                 |                |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Nervous system disorders                        |                 |                |  |
| Ischaemic stroke                                |                 |                |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Lethargy  |                 |                |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Peripheral sensory neuropathy                   |                 |                |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Blood and lymphatic system disorders            |                 |                |  |
| Anaemia   |                 |                |  |
| subjects affected / exposed                     | 5 / 121 (4.13%) | 0 / 6 (0.00%)  |  |
| occurrences causally related to treatment / all | 4 / 5           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Disseminated intravascular coagulation          |                 |                |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 1 / 1           | 0 / 0          |  |
| Thrombocytopenia                                |                 |                |  |
| subjects affected / exposed                     | 3 / 121 (2.48%) | 1 / 6 (16.67%) |  |
| occurrences causally related to treatment / all | 3 / 3           | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |

|   |                 |               |  |
|---|-----------------|---------------|--|
| Neutropenia                                     |                 |               |  |
| subjects affected / exposed                     | 2 / 121 (1.65%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Pancytopenia                                    |                 |               |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Gastrointestinal disorders                      |                 |               |  |
| Abdominal pain                                  |                 |               |  |
| subjects affected / exposed                     | 4 / 121 (3.31%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 2 / 5           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Diarrhoea                                       |                 |               |  |
| subjects affected / exposed                     | 3 / 121 (2.48%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 2 / 3           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Colitis   |                 |               |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Duodenal ulcer                                  |                 |               |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Enterovesical fistula                           |                 |               |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Gastrointestinal inflammation                   |                 |               |  |
| subjects affected / exposed                     | 0 / 121 (0.00%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Nausea  |                 |               |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Small intestinal obstruction                    |                 |                |  |
| subjects affected / exposed                     | 0 / 121 (0.00%) | 0 / 6 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Hepatobiliary disorders                         |                 |                |  |
| Hepatic failure                                 |                 |                |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 1 / 1           | 0 / 0          |  |
| Renal and urinary disorders                     |                 |                |  |
| Acute kidney injury                             |                 |                |  |
| subjects affected / exposed                     | 3 / 121 (2.48%) | 0 / 6 (0.00%)  |  |
| occurrences causally related to treatment / all | 3 / 3           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Haematuria                                      |                 |                |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 1 / 6 (16.67%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Musculoskeletal and connective tissue disorders |                 |                |  |
| Flank pain                                      |                 |                |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Infections and infestations                     |                 |                |  |
| COVID-19  |                 |                |  |
| subjects affected / exposed                     | 2 / 121 (1.65%) | 0 / 6 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| Pneumonia bacterial                             |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 0 / 121 (0.00%) | 0 / 6 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Sepsis pasteurella                              |                 |                |  |
| subjects affected / exposed                     | 0 / 121 (0.00%) | 0 / 6 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Urinary tract infection                         |                 |                |  |
| subjects affected / exposed                     | 3 / 121 (2.48%) | 0 / 6 (0.00%)  |  |
| occurrences causally related to treatment / all | 2 / 3           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Cellulitis                                      |                 |                |  |
| subjects affected / exposed                     | 2 / 121 (1.65%) | 0 / 6 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 3           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Arthritis infective                             |                 |                |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Catheter site infection                         |                 |                |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Clostridium difficile infection                 |                 |                |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Coronavirus infection                           |                 |                |  |
| subjects affected / exposed                     | 0 / 121 (0.00%) | 1 / 6 (16.67%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Device related infection                        |                 |                |  |

|   |                 |               |  |
|---|-----------------|---------------|--|
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Herpes simplex                                  |                 |               |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Lower respiratory tract infection               |                 |               |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Oesophageal candidiasis                         |                 |               |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Pneumonia                                       |                 |               |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Pneumonia aspiration                            |                 |               |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Respiratory tract infection                     |                 |               |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Sepsis  |                 |               |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Subdural haematoma                              |                 |               |  |

|   |                 |               |  |
|---|-----------------|---------------|--|
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Metabolism and nutrition disorders              |                 |               |  |
| Hypokalaemia                                    |                 |               |  |
| subjects affected / exposed                     | 1 / 121 (0.83%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |

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

| Non-serious adverse events                            | Cohort 1: 0.5 mg/kg | Cohort 2: 1.0 mg/kg | Cohort 3: 2.0 mg/kg |
|---|---------------------|---------------------|---------------------|
| Total subjects affected by non-serious adverse events |                     |                     |                     |
| subjects affected / exposed                           | 3 / 3 (100.00%)     | 6 / 6 (100.00%)     | 7 / 7 (100.00%)     |
| General disorders and administration site conditions  |                     |                     |                     |
| Nausea  |                     |                     |                     |
| subjects affected / exposed                           | 0 / 3 (0.00%)       | 3 / 6 (50.00%)      | 2 / 7 (28.57%)      |
| occurrences (all)                                     | 0                   | 4                   | 2                   |
| Asthenia  |                     |                     |                     |
| subjects affected / exposed                           | 0 / 3 (0.00%)       | 1 / 6 (16.67%)      | 0 / 7 (0.00%)       |
| occurrences (all)                                     | 0                   | 1                   | 0                   |
| Chills  |                     |                     |                     |
| subjects affected / exposed                           | 0 / 3 (0.00%)       | 1 / 6 (16.67%)      | 0 / 7 (0.00%)       |
| occurrences (all)                                     | 0                   | 1                   | 0                   |
| Fatigue   |                     |                     |                     |
| subjects affected / exposed                           | 1 / 3 (33.33%)      | 2 / 6 (33.33%)      | 2 / 7 (28.57%)      |
| occurrences (all)                                     | 1                   | 2                   | 2                   |
| Non-cardiac chest pain                                |                     |                     |                     |
| subjects affected / exposed                           | 0 / 3 (0.00%)       | 0 / 6 (0.00%)       | 0 / 7 (0.00%)       |
| occurrences (all)                                     | 0                   | 0                   | 0                   |
| Oedema peripheral                                     |                     |                     |                     |
| subjects affected / exposed                           | 0 / 3 (0.00%)       | 1 / 6 (16.67%)      | 1 / 7 (14.29%)      |
| occurrences (all)                                     | 0                   | 1                   | 1                   |
| Pyrexia   |                     |                     |                     |



|  |                     |                    |                     |
|--|---------------------|--------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 1 / 3 (33.33%)<br>1 | 0 / 6 (0.00%)<br>0 | 2 / 7 (28.57%)<br>2 |
| Respiratory, thoracic and mediastinal disorders  |                     |                    |                     |
| Cough  |                     |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)       | 1 / 6 (16.67%)     | 0 / 7 (0.00%)       |
| occurrences (all)                                | 0                   | 1                  | 0                   |
| Dyspnoea   |                     |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)       | 1 / 6 (16.67%)     | 1 / 7 (14.29%)      |
| occurrences (all)                                | 0                   | 2                  | 1                   |
| Pleural effusion                                 |                     |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)       | 0 / 6 (0.00%)      | 0 / 7 (0.00%)       |
| occurrences (all)                                | 0                   | 0                  | 0                   |
| Investigations                                   |                     |                    |                     |
| Aspartate aminotransferase increased             |                     |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)       | 1 / 6 (16.67%)     | 0 / 7 (0.00%)       |
| occurrences (all)                                | 0                   | 1                  | 0                   |
| Lymphocyte count decreased                       |                     |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)       | 1 / 6 (16.67%)     | 2 / 7 (28.57%)      |
| occurrences (all)                                | 0                   | 1                  | 2                   |
| Neutrophil count decreased                       |                     |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)       | 1 / 6 (16.67%)     | 1 / 7 (14.29%)      |
| occurrences (all)                                | 0                   | 3                  | 3                   |
| Platelet count decreased                         |                     |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)       | 0 / 6 (0.00%)      | 1 / 7 (14.29%)      |
| occurrences (all)                                | 0                   | 0                  | 1                   |
| Weight decreased                                 |                     |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)       | 1 / 6 (16.67%)     | 0 / 7 (0.00%)       |
| occurrences (all)                                | 0                   | 1                  | 0                   |
| White blood cell count decreased                 |                     |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)       | 1 / 6 (16.67%)     | 0 / 7 (0.00%)       |
| occurrences (all)                                | 0                   | 1                  | 0                   |
| Injury, poisoning and procedural complications   |                     |                    |                     |
| Infusion related reaction                        |                     |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)       | 0 / 6 (0.00%)      | 2 / 7 (28.57%)      |
| occurrences (all)                                | 0                   | 0                  | 3                   |

|                                      |                |                |                |
|--------------------------------------|----------------|----------------|----------------|
| Cardiac disorders                    |                |                |                |
| Atrial fibrillation                  |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 1 / 6 (16.67%) | 0 / 7 (0.00%)  |
| occurrences (all)                    | 0              | 1              | 0              |
| Pericardial effusion                 |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Nervous system disorders             |                |                |                |
| Dysgeusia                            |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Headache                             |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 1 / 6 (16.67%) | 1 / 7 (14.29%) |
| occurrences (all)                    | 0              | 1              | 1              |
| Neuropathy peripheral                |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Blood and lymphatic system disorders |                |                |                |
| Anaemia                              |                |                |                |
| subjects affected / exposed          | 1 / 3 (33.33%) | 1 / 6 (16.67%) | 2 / 7 (28.57%) |
| occurrences (all)                    | 1              | 1              | 2              |
| Neutropenia                          |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 1 / 6 (16.67%) | 2 / 7 (28.57%) |
| occurrences (all)                    | 0              | 1              | 2              |
| Thrombocytopenia                     |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Leukopenia                           |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Lymphopenia                          |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)                    | 0              | 0              | 1              |
| Eye disorders                        |                |                |                |
| Dry eye                              |                |                |                |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)                    | 0              | 0              | 1              |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Gastrointestinal disorders                  |                |                |                |
| Abdominal pain                              |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 2 / 6 (33.33%) | 0 / 7 (0.00%)  |
| occurrences (all)                           | 0              | 2              | 0              |
| Abdominal pain upper                        |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 2 / 6 (33.33%) | 1 / 7 (14.29%) |
| occurrences (all)                           | 0              | 2              | 1              |
| Constipation                                |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 1 / 6 (16.67%) | 1 / 7 (14.29%) |
| occurrences (all)                           | 0              | 1              | 1              |
| Diarrhoea                                   |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 1 / 6 (16.67%) | 1 / 7 (14.29%) |
| occurrences (all)                           | 0              | 1              | 1              |
| Dysphagia                                   |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 1 / 6 (16.67%) | 1 / 7 (14.29%) |
| occurrences (all)                           | 0              | 1              | 1              |
| Stomatitis                                  |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| Vomiting                                    |                |                |                |
| subjects affected / exposed                 | 1 / 3 (33.33%) | 3 / 6 (50.00%) | 2 / 7 (28.57%) |
| occurrences (all)                           | 1              | 4              | 2              |
| Skin and subcutaneous tissue disorders      |                |                |                |
| Dry skin                                    |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| Palmar-plantar erythrodysaesthesia syndrome |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  | 3 / 7 (42.86%) |
| occurrences (all)                           | 0              | 0              | 3              |
| Pruritus                                    |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 1 / 6 (16.67%) | 1 / 7 (14.29%) |
| occurrences (all)                           | 0              | 1              | 1              |
| Rash  |                |                |                |
| subjects affected / exposed                 | 0 / 3 (0.00%)  | 1 / 6 (16.67%) | 0 / 7 (0.00%)  |
| occurrences (all)                           | 0              | 2              | 0              |
| Skin hyperpigmentation                      |                |                |                |

|  |                    |                     |                     |
|--|--------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0 | 3 / 6 (50.00%)<br>3 | 1 / 7 (14.29%)<br>1 |
| Musculoskeletal and connective tissue disorders  |                    |                     |                     |
| Arthralgia                                       |                    |                     |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 6 (0.00%)       | 1 / 7 (14.29%)      |
| occurrences (all)                                | 0                  | 0                   | 1                   |
| Back pain  |                    |                     |                     |
| subjects affected / exposed                      | 1 / 3 (33.33%)     | 1 / 6 (16.67%)      | 0 / 7 (0.00%)       |
| occurrences (all)                                | 1                  | 1                   | 0                   |
| Myalgia  |                    |                     |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 6 (0.00%)       | 0 / 7 (0.00%)       |
| occurrences (all)                                | 0                  | 0                   | 0                   |
| Pain in extremity                                |                    |                     |                     |
| subjects affected / exposed                      | 1 / 3 (33.33%)     | 1 / 6 (16.67%)      | 0 / 7 (0.00%)       |
| occurrences (all)                                | 1                  | 1                   | 0                   |
| Infections and infestations                      |                    |                     |                     |
| Conjunctivitis                                   |                    |                     |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 6 (0.00%)       | 0 / 7 (0.00%)       |
| occurrences (all)                                | 0                  | 0                   | 0                   |
| Urinary tract infection                          |                    |                     |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 1 / 6 (16.67%)      | 0 / 7 (0.00%)       |
| occurrences (all)                                | 0                  | 1                   | 0                   |
| Metabolism and nutrition disorders               |                    |                     |                     |
| Decreased appetite                               |                    |                     |                     |
| subjects affected / exposed                      | 2 / 3 (66.67%)     | 0 / 6 (0.00%)       | 1 / 7 (14.29%)      |
| occurrences (all)                                | 2                  | 0                   | 1                   |
| Dehydration                                      |                    |                     |                     |
| subjects affected / exposed                      | 2 / 3 (66.67%)     | 3 / 6 (50.00%)      | 0 / 7 (0.00%)       |
| occurrences (all)                                | 3                  | 3                   | 0                   |
| Hypokalaemia                                     |                    |                     |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 6 (0.00%)       | 1 / 7 (14.29%)      |
| occurrences (all)                                | 0                  | 1                   | 1                   |

|   |                        |                     |  |
|---|------------------------|---------------------|--|
| <b>Non-serious adverse events</b>                     | Cohort 4: 3.0 mg/kg    | Cohort 5: 4.0 mg/kg |  |
| Total subjects affected by non-serious adverse events |                        |                     |  |
| subjects affected / exposed                           | 121 / 121<br>(100.00%) | 6 / 6 (100.00%)     |  |

|  |                   |                |  |
|--|-------------------|----------------|--|
| General disorders and administration site conditions |                   |                |  |
| Nausea   |                   |                |  |
| subjects affected / exposed                          | 42 / 121 (34.71%) | 3 / 6 (50.00%) |  |
| occurrences (all)                                    | 50                | 4              |  |
| Asthenia   |                   |                |  |
| subjects affected / exposed                          | 20 / 121 (16.53%) | 0 / 6 (0.00%)  |  |
| occurrences (all)                                    | 30                | 0              |  |
| Chills   |                   |                |  |
| subjects affected / exposed                          | 7 / 121 (5.79%)   | 2 / 6 (33.33%) |  |
| occurrences (all)                                    | 7                 | 2              |  |
| Fatigue  |                   |                |  |
| subjects affected / exposed                          | 61 / 121 (50.41%) | 3 / 6 (50.00%) |  |
| occurrences (all)                                    | 75                | 4              |  |
| Non-cardiac chest pain                               |                   |                |  |
| subjects affected / exposed                          | 9 / 121 (7.44%)   | 1 / 6 (16.67%) |  |
| occurrences (all)                                    | 9                 | 1              |  |
| Oedema peripheral                                    |                   |                |  |
| subjects affected / exposed                          | 35 / 121 (28.93%) | 0 / 6 (0.00%)  |  |
| occurrences (all)                                    | 47                | 0              |  |
| Pyrexia  |                   |                |  |
| subjects affected / exposed                          | 12 / 121 (9.92%)  | 4 / 6 (66.67%) |  |
| occurrences (all)                                    | 12                | 6              |  |
| Respiratory, thoracic and mediastinal disorders      |                   |                |  |
| Cough  |                   |                |  |
| subjects affected / exposed                          | 17 / 121 (14.05%) | 0 / 6 (0.00%)  |  |
| occurrences (all)                                    | 17                | 0              |  |
| Dyspnoea   |                   |                |  |
| subjects affected / exposed                          | 25 / 121 (20.66%) | 1 / 6 (16.67%) |  |
| occurrences (all)                                    | 25                | 3              |  |
| Pleural effusion                                     |                   |                |  |
| subjects affected / exposed                          | 35 / 121 (28.93%) | 1 / 6 (16.67%) |  |
| occurrences (all)                                    | 38                | 1              |  |
| Investigations                                       |                   |                |  |
| Aspartate aminotransferase increased                 |                   |                |  |

|  |                   |                |  |
|--|-------------------|----------------|--|
| subjects affected / exposed                    | 9 / 121 (7.44%)   | 0 / 6 (0.00%)  |  |
| occurrences (all)                              | 11                | 0              |  |
| Lymphocyte count decreased                     |                   |                |  |
| subjects affected / exposed                    | 17 / 121 (14.05%) | 0 / 6 (0.00%)  |  |
| occurrences (all)                              | 22                | 0              |  |
| Neutrophil count decreased                     |                   |                |  |
| subjects affected / exposed                    | 25 / 121 (20.66%) | 0 / 6 (0.00%)  |  |
| occurrences (all)                              | 44                | 0              |  |
| Platelet count decreased                       |                   |                |  |
| subjects affected / exposed                    | 16 / 121 (13.22%) | 1 / 6 (16.67%) |  |
| occurrences (all)                              | 22                | 1              |  |
| Weight decreased                               |                   |                |  |
| subjects affected / exposed                    | 19 / 121 (15.70%) | 1 / 6 (16.67%) |  |
| occurrences (all)                              | 19                | 1              |  |
| White blood cell count decreased               |                   |                |  |
| subjects affected / exposed                    | 16 / 121 (13.22%) | 1 / 6 (16.67%) |  |
| occurrences (all)                              | 18                | 2              |  |
| Injury, poisoning and procedural complications |                   |                |  |
| Infusion related reaction                      |                   |                |  |
| subjects affected / exposed                    | 17 / 121 (14.05%) | 2 / 6 (33.33%) |  |
| occurrences (all)                              | 29                | 2              |  |
| Cardiac disorders                              |                   |                |  |
| Atrial fibrillation                            |                   |                |  |
| subjects affected / exposed                    | 6 / 121 (4.96%)   | 1 / 6 (16.67%) |  |
| occurrences (all)                              | 9                 | 1              |  |
| Pericardial effusion                           |                   |                |  |
| subjects affected / exposed                    | 15 / 121 (12.40%) | 1 / 6 (16.67%) |  |
| occurrences (all)                              | 15                | 1              |  |
| Nervous system disorders                       |                   |                |  |
| Dysgeusia                                      |                   |                |  |
| subjects affected / exposed                    | 8 / 121 (6.61%)   | 0 / 6 (0.00%)  |  |
| occurrences (all)                              | 8                 | 0              |  |
| Headache                                       |                   |                |  |
| subjects affected / exposed                    | 25 / 121 (20.66%) | 1 / 6 (16.67%) |  |
| occurrences (all)                              | 29                | 1              |  |
| Neuropathy peripheral                          |                   |                |  |

|  |                       |                    |  |
|--|-----------------------|--------------------|--|
| subjects affected / exposed<br>occurrences (all) | 8 / 121 (6.61%)<br>10 | 0 / 6 (0.00%)<br>0 |  |
| Blood and lymphatic system disorders             |                       |                    |  |
| Anaemia  |                       |                    |  |
| subjects affected / exposed                      | 37 / 121 (30.58%)     | 2 / 6 (33.33%)     |  |
| occurrences (all)                                | 48                    | 2                  |  |
| Neutropenia                                      |                       |                    |  |
| subjects affected / exposed                      | 43 / 121 (35.54%)     | 3 / 6 (50.00%)     |  |
| occurrences (all)                                | 69                    | 3                  |  |
| Thrombocytopenia                                 |                       |                    |  |
| subjects affected / exposed                      | 17 / 121 (14.05%)     | 1 / 6 (16.67%)     |  |
| occurrences (all)                                | 25                    | 1                  |  |
| Leukopenia                                       |                       |                    |  |
| subjects affected / exposed                      | 8 / 121 (6.61%)       | 2 / 6 (33.33%)     |  |
| occurrences (all)                                | 10                    | 2                  |  |
| Lymphopenia                                      |                       |                    |  |
| subjects affected / exposed                      | 9 / 121 (7.44%)       | 1 / 6 (16.67%)     |  |
| occurrences (all)                                | 9                     | 1                  |  |
| Eye disorders                                    |                       |                    |  |
| Dry eye  |                       |                    |  |
| subjects affected / exposed                      | 12 / 121 (9.92%)      | 1 / 6 (16.67%)     |  |
| occurrences (all)                                | 13                    | 1                  |  |
| Gastrointestinal disorders                       |                       |                    |  |
| Abdominal pain                                   |                       |                    |  |
| subjects affected / exposed                      | 6 / 121 (4.96%)       | 0 / 6 (0.00%)      |  |
| occurrences (all)                                | 7                     | 0                  |  |
| Abdominal pain upper                             |                       |                    |  |
| subjects affected / exposed                      | 5 / 121 (4.13%)       | 0 / 6 (0.00%)      |  |
| occurrences (all)                                | 6                     | 0                  |  |
| Constipation                                     |                       |                    |  |
| subjects affected / exposed                      | 22 / 121 (18.18%)     | 1 / 6 (16.67%)     |  |
| occurrences (all)                                | 22                    | 1                  |  |
| Diarrhoea  |                       |                    |  |
| subjects affected / exposed                      | 17 / 121 (14.05%)     | 3 / 6 (50.00%)     |  |
| occurrences (all)                                | 21                    | 3                  |  |
| Dysphagia  |                       |                    |  |

|   |                   |                |  |
|---|-------------------|----------------|--|
| subjects affected / exposed                     | 8 / 121 (6.61%)   | 0 / 6 (0.00%)  |  |
| occurrences (all)                               | 12                | 0              |  |
| Stomatitis                                      |                   |                |  |
| subjects affected / exposed                     | 19 / 121 (15.70%) | 1 / 6 (16.67%) |  |
| occurrences (all)                               | 21                | 1              |  |
| Vomiting  |                   |                |  |
| subjects affected / exposed                     | 19 / 121 (15.70%) | 0 / 6 (0.00%)  |  |
| occurrences (all)                               | 22                | 0              |  |
| Skin and subcutaneous tissue disorders          |                   |                |  |
| Dry skin  |                   |                |  |
| subjects affected / exposed                     | 12 / 121 (9.92%)  | 0 / 6 (0.00%)  |  |
| occurrences (all)                               | 12                | 0              |  |
| Palmar-plantar erythrodysaesthesia syndrome     |                   |                |  |
| subjects affected / exposed                     | 50 / 121 (41.32%) | 2 / 6 (33.33%) |  |
| occurrences (all)                               | 64                | 2              |  |
| Pruritus  |                   |                |  |
| subjects affected / exposed                     | 19 / 121 (15.70%) | 0 / 6 (0.00%)  |  |
| occurrences (all)                               | 25                | 0              |  |
| Rash  |                   |                |  |
| subjects affected / exposed                     | 20 / 121 (16.53%) | 0 / 6 (0.00%)  |  |
| occurrences (all)                               | 22                | 0              |  |
| Skin hyperpigmentation                          |                   |                |  |
| subjects affected / exposed                     | 28 / 121 (23.14%) | 2 / 6 (33.33%) |  |
| occurrences (all)                               | 28                | 2              |  |
| Musculoskeletal and connective tissue disorders |                   |                |  |
| Arthralgia                                      |                   |                |  |
| subjects affected / exposed                     | 9 / 121 (7.44%)   | 1 / 6 (16.67%) |  |
| occurrences (all)                               | 10                | 1              |  |
| Back pain                                       |                   |                |  |
| subjects affected / exposed                     | 10 / 121 (8.26%)  | 0 / 6 (0.00%)  |  |
| occurrences (all)                               | 11                | 0              |  |
| Myalgia   |                   |                |  |
| subjects affected / exposed                     | 8 / 121 (6.61%)   | 2 / 6 (33.33%) |  |
| occurrences (all)                               | 8                 | 3              |  |
| Pain in extremity                               |                   |                |  |



|  |                      |                    |  |
|--|----------------------|--------------------|--|
| subjects affected / exposed<br>occurrences (all) | 6 / 121 (4.96%)<br>8 | 0 / 6 (0.00%)<br>0 |  |
| Infections and infestations                      |                      |                    |  |
| Conjunctivitis                                   |                      |                    |  |
| subjects affected / exposed                      | 10 / 121 (8.26%)     | 0 / 6 (0.00%)      |  |
| occurrences (all)                                | 12                   | 0                  |  |
| Urinary tract infection                          |                      |                    |  |
| subjects affected / exposed                      | 8 / 121 (6.61%)      | 1 / 6 (16.67%)     |  |
| occurrences (all)                                | 9                    | 1                  |  |
| Metabolism and nutrition disorders               |                      |                    |  |
| Decreased appetite                               |                      |                    |  |
| subjects affected / exposed                      | 40 / 121 (33.06%)    | 1 / 6 (16.67%)     |  |
| occurrences (all)                                | 44                   | 1                  |  |
| Dehydration                                      |                      |                    |  |
| subjects affected / exposed                      | 5 / 121 (4.13%)      | 1 / 6 (16.67%)     |  |
| occurrences (all)                                | 6                    | 1                  |  |
| Hypokalaemia                                     |                      |                    |  |
| subjects affected / exposed                      | 7 / 121 (5.79%)      | 2 / 6 (33.33%)     |  |
| occurrences (all)                                | 9                    | 4                  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 02 October 2018  | Added safety measures: sentinel dosing for first 2 dose levels, Independent Safety Monitor oversight, revised definition of non-hematologic dose limiting toxicity, revised inclusion criteria, added cardiac monitoring, added ophthalmological examinations, and amylase and lipase monitoring.  |
| 26 February 2019 | Modified entry criteria to require metastatic castration-resistant prostate cancer, and PSA testing for all participants with prostate cancer.   |
| 31 July 2020     | Added tumor types to expansion cohorts: metastatic castration-resistant prostate cancer, non-small cell lung cancer, and triple negative breast cancer. Relevant sections of the protocol were updated accordingly, including study design, sample size, objectives, eligibility, and medical history requirements. Added secondary objectives to describe the radiographic progression free survival, PSA response rate and best PSA percent change from baseline. Added exploratory objective for patient reported outcome using the brief pain inventory short form and symptomatic skeletal events . Provided guidance of study procedures during the COVID-19 pandemic. Revised toxicity management guidelines. |
| 17 March 2021    | Updated the study design to include additional expansion cohorts of squamous cell cancer of the head and neck and melanoma. Relevant sections of the protocol were updated accordingly, including study design, sample size, objectives, eligibility, and medical history requirements. Updated toxicity management guidelines   |
| 26 July 2021     | Revised toxicity management guidelines.  |
| 16 August 2021   | Revised toxicity management guidelines.  |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported