



## Clinical trial results:

### A Phase 2, Open-label, Randomized Controlled Trial of BMS-986218 or BMS-986218 Plus Nivolumab in Combination with Docetaxel in Participants with Metastatic Castration-resistant Prostate Cancer

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2021-003990-74   |
| Trial protocol           | ES GR            |
| Global end of trial date | 13 December 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 | CA022-009 |
|-----------------------|-----------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |                                                                                                 |
|------------------------------|-------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Bristol Myers Squibb                                                                            |
| Sponsor organisation address | Chaussée de la Hulpe 185, Brussels, Belgium, 1170                                               |
| Public contact               | EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com |
| Scientific contact           | Bristol-Myers Squibb Study Director, Bristol Myers Squibb, Clinical.Trials@bms.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                       | 13 December 2023 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 13 December 2023 |
| Was the trial ended prematurely?                     | Yes              |

Notes:

## General information about the trial

Main objective of the trial:

To assess the safety, tolerability, and DLTs of docetaxel in combination with BMS-986218 or in combination with BMS-986218 plus nivolumab in participants with mCRPC

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 14 February 2022 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | Yes              |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | United States: 10 |
| Worldwide total number of subjects   | 10                |
| EEA total number of subjects         | 0                 |

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)                      | 4 |
| From 65 to 84 years                       | 6 |
| 85 years and over                         | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

10 Participants Enrolled and Treated

### Period 1

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

### Arms

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

|                  |             |
|------------------|-------------|
| <b>Arm title</b> | Treatment 1 |
|------------------|-------------|

Arm description:

BMS-986218 30mg Q3W + Docetaxel 75 mg/m<sup>2</sup> Q3W

|                                        |                       |
|----------------------------------------|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | Docetaxel             |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravascular use     |

Dosage and administration details:

75 mg/m<sup>2</sup> Q3W

|                                        |                       |
|----------------------------------------|-----------------------|
| Investigational medicinal product name | BMS-986218            |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravascular use     |

Dosage and administration details:

30mg Q3W

|                  |             |
|------------------|-------------|
| <b>Arm title</b> | Treatment 2 |
|------------------|-------------|

Arm description:

BMS-986218 50mg Q3W + Docetaxel 75 mg/m<sup>2</sup> Q3W

|                                        |                       |
|----------------------------------------|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | Docetaxel             |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravascular use     |

Dosage and administration details:

75 mg/m<sup>2</sup> Q3W

|                                        |                       |
|----------------------------------------|-----------------------|
| Investigational medicinal product name | BMS-986218            |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravascular use     |

| <b>Number of subjects in period 1</b>        | Treatment 1 | Treatment 2 |
|----------------------------------------------|-------------|-------------|
| Started                                      | 3           | 7           |
| Completed                                    | 1           | 0           |
| Not completed                                | 2           | 7           |
| Participant request to discontinue treatment | -           | 1           |
| Physician decision                           | -           | 1           |
| Adverse event, non-fatal                     | 1           | 3           |
| Progressive Disease                          | 1           | 1           |
| Other Reason                                 | -           | 1           |

## Baseline characteristics

### Reporting groups

|                                                                                          |             |
|------------------------------------------------------------------------------------------|-------------|
| Reporting group title                                                                    | Treatment 1 |
| Reporting group description:<br>BMS-986218 30mg Q3W + Docetaxel 75 mg/m <sup>2</sup> Q3W |             |
| Reporting group title                                                                    | Treatment 2 |
| Reporting group description:<br>BMS-986218 50mg Q3W + Docetaxel 75 mg/m <sup>2</sup> Q3W |             |

| Reporting group values                    | Treatment 1 | Treatment 2 | Total |
|-------------------------------------------|-------------|-------------|-------|
| Number of subjects                        | 3           | 7           | 10    |
| Age categorical                           |             |             |       |
| Units: Subjects                           |             |             |       |
| Adults (18-64 years)                      | 1           | 3           | 4     |
| From 65-84 years                          | 2           | 4           | 6     |
| Age Continuous                            |             |             |       |
| Units: Years                              |             |             |       |
| arithmetic mean                           | 68.3        | 65.7        |       |
| standard deviation                        | ± 6.11      | ± 9.14      | -     |
| Sex: Female, Male                         |             |             |       |
| Units: Participants                       |             |             |       |
| Female                                    | 0           | 0           | 0     |
| Male                                      | 3           | 7           | 10    |
| Race (NIH/OMB)                            |             |             |       |
| Units: Subjects                           |             |             |       |
| American Indian or Alaska Native          | 0           | 0           | 0     |
| Asian                                     | 0           | 0           | 0     |
| Native Hawaiian or Other Pacific Islander | 0           | 0           | 0     |
| Black or African American                 | 0           | 0           | 0     |
| White                                     | 3           | 6           | 9     |
| More than one race                        | 0           | 0           | 0     |
| Unknown or Not Reported                   | 0           | 1           | 1     |
| Ethnicity (NIH/OMB)                       |             |             |       |
| Units: Subjects                           |             |             |       |
| Hispanic or Latino                        | 1           | 0           | 1     |
| Not Hispanic or Latino                    | 2           | 6           | 8     |
| Unknown or Not Reported                   | 0           | 1           | 1     |

## End points

### End points reporting groups

|                                                                                          |             |
|------------------------------------------------------------------------------------------|-------------|
| Reporting group title                                                                    | Treatment 1 |
| Reporting group description:<br>BMS-986218 30mg Q3W + Docetaxel 75 mg/m <sup>2</sup> Q3W |             |
| Reporting group title                                                                    | Treatment 2 |
| Reporting group description:<br>BMS-986218 50mg Q3W + Docetaxel 75 mg/m <sup>2</sup> Q3W |             |

### Primary: Number of Participants with Treatment related Adverse Events

|                                                                                                                                                                                                                                                |                                                       |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|
| End point title                                                                                                                                                                                                                                | Number of Participants with Treatment related Adverse |
| End point description:<br>Adverse events will be prespecified using National Cancer Institute Common Terminology Criteria for Adverse Events version 5 (NCI CTCAE v5).                                                                         |                                                       |
| End point type                                                                                                                                                                                                                                 | Primary                                               |
| End point timeframe:<br>From first dose to 100 days follow up to last dose (Approximately 22 months)                                                                                                                                           |                                                       |
| Notes:<br>[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.<br>Justification: No statistical analysis done for this endpoint |                                                       |

| End point values            | Treatment 1     | Treatment 2     |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 3               | 7               |  |  |
| Units: Participants         | 3               | 7               |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Number of Participants with Treatment related Serious Adverse Events

|                                                                                                                                                                                                                                                |                                                                                     |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                | Number of Participants with Treatment related Serious Adverse Events <sup>[2]</sup> |
| End point description:<br>Adverse events will be prespecified using National Cancer Institute Common Terminology Criteria for Adverse Events version 5 (NCI CTCAE v5).                                                                         |                                                                                     |
| End point type                                                                                                                                                                                                                                 | Primary                                                                             |
| End point timeframe:<br>From first dose to 100 days follow up to last dose (Approximately 22 months)                                                                                                                                           |                                                                                     |
| Notes:<br>[2] - 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.<br>Justification: No statistical analysis done for this endpoint |                                                                                     |

| End point values            | Treatment 1     | Treatment 2     |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 3               | 7               |  |  |
| Units: Participants         | 1               | 4               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of Participants with Dose Limiting Toxicities

|                 |                                                                     |
|-----------------|---------------------------------------------------------------------|
| End point title | Number of Participants with Dose Limiting Toxicities <sup>[3]</sup> |
|-----------------|---------------------------------------------------------------------|

End point description:

DLTs will be defined as:

Any treatment-related AEs for which a participant permanently discontinues a study treatment (other than daily prednisone) and that occurs during the first 2 cycles of treatment.

Any death not clearly due to the underlying disease or extraneous causes and that occurs during the first 2 cycles of treatment

Greater than or equal to Grade 2 pneumonitis lasting greater than 5 days despite appropriate medical therapy and that occurs during the first 2 cycles of treatment

Any neutropenic fever as well as Grade 4 neutropenia or thrombocytopenia for > 7 days that occurs during the first 2 cycles of treatment

Any treatment-related AE that delays initiation of Cycle 2 or Cycle 3 of treatment by greater than 2 consecutive weeks.

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

End point timeframe:

From first dose to 100 days follow up to last dose (Approximately 22 months)

Notes:

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

Justification: No statistical analysis done for this endpoint

| End point values            | Treatment 1     | Treatment 2     |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 3               | 7               |  |  |
| Units: Participants         | 1               | 0               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of Participants with AEs leading to discontinuation

|                 |                                                                           |
|-----------------|---------------------------------------------------------------------------|
| End point title | Number of Participants with AEs leading to discontinuation <sup>[4]</sup> |
|-----------------|---------------------------------------------------------------------------|

End point description:

Adverse events will be prespecified using National Cancer Institute Common Terminology Criteria for Adverse Events version 5 (NCI CTCAE v5).

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

End point timeframe:

From first dose to 100 days follow up to last dose (Approximately 22 months)

Notes:

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

Justification: No statistical analysis done for this endpoint

| End point values            | Treatment 1     | Treatment 2     |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 3               | 7               |  |  |
| Units: Participants         | 2               | 4               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of Participants who died

|                                                                              |                                                |
|------------------------------------------------------------------------------|------------------------------------------------|
| End point title                                                              | Number of Participants who died <sup>[5]</sup> |
| End point description:                                                       |                                                |
| Number of participant deaths                                                 |                                                |
| End point type                                                               | Primary                                        |
| End point timeframe:                                                         |                                                |
| From first dose to 100 days follow up to last dose (Approximately 22 months) |                                                |

Notes:

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

Justification: No statistical analysis done for this endpoint

| End point values            | Treatment 1     | Treatment 2     |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 3               | 7               |  |  |
| Units: Participants         | 2               | 2               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Objective Response Rate

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                         |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Objective Response Rate |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                         |
| Objective response rate per PCWG3 (ORR-PCWG3) is the proportion of participants who have a confirmed complete or partial best overall response (BOR) per PCWG3 among randomized participants who have measurable disease at baseline. The BOR is defined as the best response designation, as determined by the BICR, recorded between the date of randomization and the date of objectively documented radiographic progression, or last tumor measurement, whichever occurs first. |                         |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Secondary               |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                         |
| From first dose to 100 days follow up to last dose (Approximately 22 months)                                                                                                                                                                                                                                                                                                                                                                                                         |                         |

| End point values                  | Treatment 1      | Treatment 2      |  |  |
|-----------------------------------|------------------|------------------|--|--|
| Subject group type                | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed       | 0 <sup>[6]</sup> | 0 <sup>[7]</sup> |  |  |
| Units: Percentage of Participants |                  |                  |  |  |
| number (confidence interval 95%)  | ( to )           | ( to )           |  |  |

Notes:

[6] - No subjects Analyzed for this endpoint

[7] - No subjects Analyzed for this endpoint

## Statistical analyses

No statistical analyses for this end point

## Secondary: Prostate Specific Antigen Response Rate (PSA-RR)

|                                                                                                                                                                                                                                             |                                                  |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|
| End point title                                                                                                                                                                                                                             | Prostate Specific Antigen Response Rate (PSA-RR) |
| End point description:                                                                                                                                                                                                                      |                                                  |
| PSA-RR is the proportion of randomized participants with a 50% or greater decrease in PSA from baseline to any post-baseline PSA result. A second consecutive value obtained 3 or more weeks later is required to confirm the PSA response. |                                                  |
| End point type                                                                                                                                                                                                                              | Secondary                                        |
| End point timeframe:                                                                                                                                                                                                                        |                                                  |
| From first dose to 100 days follow up to last dose (Approximately 22 months)                                                                                                                                                                |                                                  |

| End point values                        | Treatment 1        | Treatment 2         |  |  |
|-----------------------------------------|--------------------|---------------------|--|--|
| Subject group type                      | Reporting group    | Reporting group     |  |  |
| Number of subjects analysed             | 3                  | 7                   |  |  |
| Units: Percentage of Participants       |                    |                     |  |  |
| number (confidence interval 95%)        |                    |                     |  |  |
| Unconfirmed or Confirmed PSA responders | 33.3 (0.8 to 90.6) | 57.1 (18.4 to 90.1) |  |  |
| Confirmed PSA responders                | 33.3 (0.8 to 90.6) | 57.1 (18.4 to 90.1) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Duration of Response

|                                                                                                                                                                                                                                    |                      |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|
| End point title                                                                                                                                                                                                                    | Duration of Response |
| End point description:                                                                                                                                                                                                             |                      |
| Duration of response per PCWG3 (DOR-PCWG3) is the time between the date of first response (CR/PR per PCWG3) to the date of first documented radiographic progression per PCWG3 (as determined by BICR), or death due to any cause. |                      |
| End point type                                                                                                                                                                                                                     | Secondary            |

End point timeframe:

From first dose to 100 days follow up to last dose (Approximately 22 months)

| End point values              | Treatment 1      | Treatment 2      |  |  |
|-------------------------------|------------------|------------------|--|--|
| Subject group type            | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed   | 0 <sup>[8]</sup> | 0 <sup>[9]</sup> |  |  |
| Units: Months                 |                  |                  |  |  |
| median (full range (min-max)) | ( to )           | ( to )           |  |  |

Notes:

[8] - No subjects Analyzed for this endpoint

[9] - No subjects Analyzed for this endpoint

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Response

|                 |                  |
|-----------------|------------------|
| End point title | Time to Response |
|-----------------|------------------|

End point description:

Time to response per PCWG3 (TTR-PCWG3) is the time from randomization date to the date of the first documented CR or PR per PCWG3, as determined by BICR.

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

End point timeframe:

From first dose to 100 days follow up to last dose (Approximately 22 months)

| End point values              | Treatment 1       | Treatment 2       |  |  |
|-------------------------------|-------------------|-------------------|--|--|
| Subject group type            | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed   | 0 <sup>[10]</sup> | 0 <sup>[11]</sup> |  |  |
| Units: Months                 |                   |                   |  |  |
| median (full range (min-max)) | ( to )            | ( to )            |  |  |

Notes:

[10] - No subjects Analyzed for this endpoint

[11] - No subjects Analyzed for this endpoint

### Statistical analyses

No statistical analyses for this end point

### Secondary: Overall Survival

|                 |                  |
|-----------------|------------------|
| End point title | Overall Survival |
|-----------------|------------------|

End point description:

OS for all randomized participants is the time between randomization date and the date of death from any cause.

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

End point timeframe:

From first dose to 100 days follow up to last dose (Approximately 22 months)

| <b>End point values</b>           | Treatment 1       | Treatment 2       |  |  |
|-----------------------------------|-------------------|-------------------|--|--|
| Subject group type                | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed       | 0 <sup>[12]</sup> | 0 <sup>[13]</sup> |  |  |
| Units: Percentage of Participants |                   |                   |  |  |
| number (confidence interval 95%)  | ( to )            | ( to )            |  |  |

Notes:

[12] - No subjects Analyzed for this endpoint

[13] - No subjects Analyzed for this endpoint

### **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse Events and Serious Adverse Events: (From first dose to last dose + 100 days): Approximately 22 Months

All-Cause mortality (From randomization to end of study): Approximately 22 Months.

Adverse event reporting additional description:

The number at Risk for All-Cause Mortality represents all Randomized Participants. The number at Risk for Serious Adverse Events and Other (Not Including Serious) Adverse Events represents all participants that received at least 1 dose of study medication

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 26.1   |

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Treatment 1 |
|-----------------------|-------------|

Reporting group description:

BMS-986218 30mg Q3W + Docetaxel 75 mg/m<sup>2</sup> Q3W

|                       |             |
|-----------------------|-------------|
| Reporting group title | Treatment 2 |
|-----------------------|-------------|

Reporting group description:

BMS-986218 50mg Q3W + Docetaxel 75 mg/m<sup>2</sup> Q3W

| Serious adverse events                                              | Treatment 1    | Treatment 2    |  |
|---------------------------------------------------------------------|----------------|----------------|--|
| Total subjects affected by serious adverse events                   |                |                |  |
| subjects affected / exposed                                         | 1 / 3 (33.33%) | 6 / 7 (85.71%) |  |
| number of deaths (all causes)                                       | 2              | 2              |  |
| number of deaths resulting from adverse events                      |                |                |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |                |  |
| Malignant neoplasm progression                                      |                |                |  |
| subjects affected / exposed                                         | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 1          |  |
| Injury, poisoning and procedural complications                      |                |                |  |
| Fall                                                                |                |                |  |
| subjects affected / exposed                                         | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          |  |
| Vascular disorders                                                  |                |                |  |
| Vasculitis                                                          |                |                |  |

|                                                      |                |                |  |
|------------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                          | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Hypotension                                          |                |                |  |
| subjects affected / exposed                          | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Shock haemorrhagic                                   |                |                |  |
| subjects affected / exposed                          | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Nervous system disorders                             |                |                |  |
| Metabolic encephalopathy                             |                |                |  |
| subjects affected / exposed                          | 1 / 3 (33.33%) | 0 / 7 (0.00%)  |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Syncope                                              |                |                |  |
| subjects affected / exposed                          | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Blood and lymphatic system disorders                 |                |                |  |
| Anaemia                                              |                |                |  |
| subjects affected / exposed                          | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| General disorders and administration site conditions |                |                |  |
| Pyrexia                                              |                |                |  |
| subjects affected / exposed                          | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 2          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Gastrointestinal disorders                           |                |                |  |
| Diarrhoea                                            |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastrointestinal haemorrhage                    |                |                |  |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 2 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Enterocolitis                                   |                |                |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) | 0 / 7 (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 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Small intestinal haemorrhage                    |                |                |  |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Respiratory, thoracic and mediastinal disorders |                |                |  |
| Pulmonary embolism                              |                |                |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) | 0 / 7 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Renal and urinary disorders                     |                |                |  |
| Acute kidney injury                             |                |                |  |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Infections and infestations                     |                |                |  |
| Rectal abscess                                  |                |                |  |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| Enterocolitis infectious                        |                |                |  |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Sepsis                                          |                |                |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) | 3 / 7 (42.86%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 3          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

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

| <b>Non-serious adverse events</b>                     | Treatment 1     | Treatment 2     |  |
|-------------------------------------------------------|-----------------|-----------------|--|
| Total subjects affected by non-serious adverse events |                 |                 |  |
| subjects affected / exposed                           | 3 / 3 (100.00%) | 7 / 7 (100.00%) |  |
| Vascular disorders                                    |                 |                 |  |
| Orthostatic hypotension                               |                 |                 |  |
| subjects affected / exposed                           | 0 / 3 (0.00%)   | 1 / 7 (14.29%)  |  |
| occurrences (all)                                     | 0               | 1               |  |
| Hypotension                                           |                 |                 |  |
| subjects affected / exposed                           | 0 / 3 (0.00%)   | 5 / 7 (71.43%)  |  |
| occurrences (all)                                     | 0               | 11              |  |
| Hypertension                                          |                 |                 |  |
| subjects affected / exposed                           | 1 / 3 (33.33%)  | 1 / 7 (14.29%)  |  |
| occurrences (all)                                     | 1               | 1               |  |
| Hot flush                                             |                 |                 |  |
| subjects affected / exposed                           | 0 / 3 (0.00%)   | 2 / 7 (28.57%)  |  |
| occurrences (all)                                     | 0               | 2               |  |
| Flushing                                              |                 |                 |  |
| subjects affected / exposed                           | 0 / 3 (0.00%)   | 1 / 7 (14.29%)  |  |
| occurrences (all)                                     | 0               | 1               |  |
| General disorders and administration site conditions  |                 |                 |  |
| Asthenia                                              |                 |                 |  |
| subjects affected / exposed                           | 1 / 3 (33.33%)  | 1 / 7 (14.29%)  |  |
| occurrences (all)                                     | 1               | 1               |  |
| Chills                                                |                 |                 |  |

|                             |                 |                |
|-----------------------------|-----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%)   | 1 / 7 (14.29%) |
| occurrences (all)           | 0               | 2              |
| Face oedema                 |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)   | 1 / 7 (14.29%) |
| occurrences (all)           | 0               | 1              |
| Fatigue                     |                 |                |
| subjects affected / exposed | 3 / 3 (100.00%) | 4 / 7 (57.14%) |
| occurrences (all)           | 3               | 4              |
| Generalised oedema          |                 |                |
| subjects affected / exposed | 1 / 3 (33.33%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 1               | 0              |
| Influenza like illness      |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)   | 1 / 7 (14.29%) |
| occurrences (all)           | 0               | 2              |
| Pyrexia                     |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)   | 4 / 7 (57.14%) |
| occurrences (all)           | 0               | 5              |
| Oedema peripheral           |                 |                |
| subjects affected / exposed | 1 / 3 (33.33%)  | 3 / 7 (42.86%) |
| occurrences (all)           | 1               | 3              |
| Mucosal inflammation        |                 |                |
| subjects affected / exposed | 1 / 3 (33.33%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 6               | 0              |
| Malaise                     |                 |                |
| subjects affected / exposed | 1 / 3 (33.33%)  | 1 / 7 (14.29%) |
| occurrences (all)           | 1               | 1              |
| Localised oedema            |                 |                |
| subjects affected / exposed | 1 / 3 (33.33%)  | 1 / 7 (14.29%) |
| occurrences (all)           | 1               | 1              |
| Injection site reaction     |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)   | 1 / 7 (14.29%) |
| occurrences (all)           | 0               | 1              |
| Swelling face               |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)   | 1 / 7 (14.29%) |
| occurrences (all)           | 0               | 1              |
| Terminal agitation          |                 |                |

|                                                  |                     |                    |  |
|--------------------------------------------------|---------------------|--------------------|--|
| subjects affected / exposed<br>occurrences (all) | 1 / 3 (33.33%)<br>1 | 0 / 7 (0.00%)<br>0 |  |
| Immune system disorders                          |                     |                    |  |
| Drug hypersensitivity                            |                     |                    |  |
| subjects affected / exposed                      | 1 / 3 (33.33%)      | 0 / 7 (0.00%)      |  |
| occurrences (all)                                | 4                   | 0                  |  |
| Hypersensitivity                                 |                     |                    |  |
| subjects affected / exposed                      | 0 / 3 (0.00%)       | 1 / 7 (14.29%)     |  |
| occurrences (all)                                | 0                   | 2                  |  |
| Respiratory, thoracic and mediastinal disorders  |                     |                    |  |
| Pulmonary oedema                                 |                     |                    |  |
| subjects affected / exposed                      | 1 / 3 (33.33%)      | 0 / 7 (0.00%)      |  |
| occurrences (all)                                | 1                   | 0                  |  |
| Pleural effusion                                 |                     |                    |  |
| subjects affected / exposed                      | 0 / 3 (0.00%)       | 1 / 7 (14.29%)     |  |
| occurrences (all)                                | 0                   | 1                  |  |
| Oropharyngeal pain                               |                     |                    |  |
| subjects affected / exposed                      | 0 / 3 (0.00%)       | 1 / 7 (14.29%)     |  |
| occurrences (all)                                | 0                   | 1                  |  |
| Laryngeal inflammation                           |                     |                    |  |
| subjects affected / exposed                      | 0 / 3 (0.00%)       | 1 / 7 (14.29%)     |  |
| occurrences (all)                                | 0                   | 1                  |  |
| Epistaxis                                        |                     |                    |  |
| subjects affected / exposed                      | 1 / 3 (33.33%)      | 0 / 7 (0.00%)      |  |
| occurrences (all)                                | 1                   | 0                  |  |
| Dyspnoea exertional                              |                     |                    |  |
| subjects affected / exposed                      | 0 / 3 (0.00%)       | 1 / 7 (14.29%)     |  |
| occurrences (all)                                | 0                   | 1                  |  |
| Dyspnoea                                         |                     |                    |  |
| subjects affected / exposed                      | 1 / 3 (33.33%)      | 2 / 7 (28.57%)     |  |
| occurrences (all)                                | 1                   | 2                  |  |
| Cough                                            |                     |                    |  |
| subjects affected / exposed                      | 1 / 3 (33.33%)      | 2 / 7 (28.57%)     |  |
| occurrences (all)                                | 2                   | 2                  |  |
| Sleep apnoea syndrome                            |                     |                    |  |

|                                                                                                    |                     |                     |  |
|----------------------------------------------------------------------------------------------------|---------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all)                                                   | 0 / 3 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |  |
| Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 3 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |  |
| Respiratory failure<br>subjects affected / exposed<br>occurrences (all)                            | 1 / 3 (33.33%)<br>1 | 0 / 7 (0.00%)<br>0  |  |
| Psychiatric disorders<br>Insomnia<br>subjects affected / exposed<br>occurrences (all)              | 1 / 3 (33.33%)<br>1 | 0 / 7 (0.00%)<br>0  |  |
| Depression<br>subjects affected / exposed<br>occurrences (all)                                     | 1 / 3 (33.33%)<br>1 | 0 / 7 (0.00%)<br>0  |  |
| Confusional state<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 3 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |  |
| Investigations<br>Lymphocyte count decreased<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |  |
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)             | 0 / 3 (0.00%)<br>0  | 1 / 7 (14.29%)<br>3 |  |
| Influenza A virus test positive<br>subjects affected / exposed<br>occurrences (all)                | 0 / 3 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |  |
| Blood thyroid stimulating hormone<br>increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 3 (33.33%)<br>1 | 0 / 7 (0.00%)<br>0  |  |
| Blood lactate dehydrogenase<br>increased<br>subjects affected / exposed<br>occurrences (all)       | 1 / 3 (33.33%)<br>1 | 2 / 7 (28.57%)<br>2 |  |
| Blood creatinine increased                                                                         |                     |                     |  |

|                                                  |                |                |  |
|--------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                      | 1 / 3 (33.33%) | 1 / 7 (14.29%) |  |
| occurrences (all)                                | 2              | 2              |  |
| Blood alkaline phosphatase increased             |                |                |  |
| subjects affected / exposed                      | 1 / 3 (33.33%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                                | 1              | 0              |  |
| Aspartate aminotransferase increased             |                |                |  |
| subjects affected / exposed                      | 1 / 3 (33.33%) | 2 / 7 (28.57%) |  |
| occurrences (all)                                | 1              | 2              |  |
| Mycobacterium tuberculosis complex test positive |                |                |  |
| subjects affected / exposed                      | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                                | 0              | 1              |  |
| Neutrophil count decreased                       |                |                |  |
| subjects affected / exposed                      | 0 / 3 (0.00%)  | 2 / 7 (28.57%) |  |
| occurrences (all)                                | 0              | 2              |  |
| Nitrite urine present                            |                |                |  |
| subjects affected / exposed                      | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                                | 0              | 1              |  |
| Platelet count decreased                         |                |                |  |
| subjects affected / exposed                      | 2 / 3 (66.67%) | 1 / 7 (14.29%) |  |
| occurrences (all)                                | 2              | 2              |  |
| Prostatic specific antigen increased             |                |                |  |
| subjects affected / exposed                      | 1 / 3 (33.33%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                                | 1              | 0              |  |
| Weight increased                                 |                |                |  |
| subjects affected / exposed                      | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                                | 0              | 2              |  |
| White blood cell count decreased                 |                |                |  |
| subjects affected / exposed                      | 1 / 3 (33.33%) | 1 / 7 (14.29%) |  |
| occurrences (all)                                | 1              | 2              |  |
| Injury, poisoning and procedural complications   |                |                |  |
| Fall                                             |                |                |  |
| subjects affected / exposed                      | 1 / 3 (33.33%) | 1 / 7 (14.29%) |  |
| occurrences (all)                                | 1              | 1              |  |
| Infusion related reaction                        |                |                |  |

|                                      |                |                |  |
|--------------------------------------|----------------|----------------|--|
| subjects affected / exposed          | 1 / 3 (33.33%) | 1 / 7 (14.29%) |  |
| occurrences (all)                    | 1              | 1              |  |
| Procedural pain                      |                |                |  |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                    | 0              | 1              |  |
| Nervous system disorders             |                |                |  |
| Dizziness                            |                |                |  |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 3 / 7 (42.86%) |  |
| occurrences (all)                    | 0              | 3              |  |
| Dysgeusia                            |                |                |  |
| subjects affected / exposed          | 1 / 3 (33.33%) | 3 / 7 (42.86%) |  |
| occurrences (all)                    | 1              | 3              |  |
| Syncope                              |                |                |  |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                    | 0              | 2              |  |
| Somnolence                           |                |                |  |
| subjects affected / exposed          | 1 / 3 (33.33%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                    | 1              | 0              |  |
| Presyncope                           |                |                |  |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                    | 0              | 1              |  |
| Headache                             |                |                |  |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                    | 0              | 1              |  |
| Neuropathy peripheral                |                |                |  |
| subjects affected / exposed          | 1 / 3 (33.33%) | 1 / 7 (14.29%) |  |
| occurrences (all)                    | 1              | 1              |  |
| Paraesthesia                         |                |                |  |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                    | 0              | 1              |  |
| Peripheral sensory neuropathy        |                |                |  |
| subjects affected / exposed          | 1 / 3 (33.33%) | 2 / 7 (28.57%) |  |
| occurrences (all)                    | 1              | 2              |  |
| Blood and lymphatic system disorders |                |                |  |
| Blood loss anaemia                   |                |                |  |

|                                                                                                        |                     |                     |  |
|--------------------------------------------------------------------------------------------------------|---------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all)                                                       | 1 / 3 (33.33%)<br>1 | 0 / 7 (0.00%)<br>0  |  |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)                                            | 1 / 3 (33.33%)<br>1 | 4 / 7 (57.14%)<br>4 |  |
| Ear and labyrinth disorders<br>Tinnitus<br>subjects affected / exposed<br>occurrences (all)            | 1 / 3 (33.33%)<br>1 | 0 / 7 (0.00%)<br>0  |  |
| Eye disorders<br>Eye disorder<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 3 (33.33%)<br>1 | 0 / 7 (0.00%)<br>0  |  |
| Gastrointestinal disorders<br>Abdominal distension<br>subjects affected / exposed<br>occurrences (all) | 1 / 3 (33.33%)<br>1 | 0 / 7 (0.00%)<br>0  |  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)                                       | 1 / 3 (33.33%)<br>1 | 2 / 7 (28.57%)<br>3 |  |
| Colitis<br>subjects affected / exposed<br>occurrences (all)                                            | 1 / 3 (33.33%)<br>1 | 4 / 7 (57.14%)<br>5 |  |
| Bowel movement irregularity<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 3 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |  |
| Ascites<br>subjects affected / exposed<br>occurrences (all)                                            | 0 / 3 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 3 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                                           | 0 / 3 (0.00%)<br>0  | 3 / 7 (42.86%)<br>4 |  |
| Proctitis                                                                                              |                     |                     |  |

|                                        |                 |                |  |
|----------------------------------------|-----------------|----------------|--|
| subjects affected / exposed            | 0 / 3 (0.00%)   | 2 / 7 (28.57%) |  |
| occurrences (all)                      | 0               | 2              |  |
| Oral pain                              |                 |                |  |
| subjects affected / exposed            | 0 / 3 (0.00%)   | 1 / 7 (14.29%) |  |
| occurrences (all)                      | 0               | 1              |  |
| Nausea                                 |                 |                |  |
| subjects affected / exposed            | 1 / 3 (33.33%)  | 5 / 7 (71.43%) |  |
| occurrences (all)                      | 1               | 8              |  |
| Mouth ulceration                       |                 |                |  |
| subjects affected / exposed            | 0 / 3 (0.00%)   | 1 / 7 (14.29%) |  |
| occurrences (all)                      | 0               | 1              |  |
| Lower gastrointestinal haemorrhage     |                 |                |  |
| subjects affected / exposed            | 1 / 3 (33.33%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)                      | 1               | 0              |  |
| Haemorrhoids                           |                 |                |  |
| subjects affected / exposed            | 0 / 3 (0.00%)   | 1 / 7 (14.29%) |  |
| occurrences (all)                      | 0               | 1              |  |
| Haemorrhoidal haemorrhage              |                 |                |  |
| subjects affected / exposed            | 0 / 3 (0.00%)   | 2 / 7 (28.57%) |  |
| occurrences (all)                      | 0               | 2              |  |
| Haematochezia                          |                 |                |  |
| subjects affected / exposed            | 1 / 3 (33.33%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                      | 1               | 1              |  |
| Gastrointestinal haemorrhage           |                 |                |  |
| subjects affected / exposed            | 1 / 3 (33.33%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)                      | 1               | 0              |  |
| Enterocolitis                          |                 |                |  |
| subjects affected / exposed            | 1 / 3 (33.33%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)                      | 1               | 0              |  |
| Dysphagia                              |                 |                |  |
| subjects affected / exposed            | 1 / 3 (33.33%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)                      | 1               | 0              |  |
| Diarrhoea                              |                 |                |  |
| subjects affected / exposed            | 3 / 3 (100.00%) | 4 / 7 (57.14%) |  |
| occurrences (all)                      | 3               | 11             |  |
| Skin and subcutaneous tissue disorders |                 |                |  |

|                             |                |                |
|-----------------------------|----------------|----------------|
| Skin ulcer                  |                |                |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 7 (14.29%) |
| occurrences (all)           | 1              | 1              |
| Skin exfoliation            |                |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)           | 0              | 1              |
| Skin disorder               |                |                |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 7 (0.00%)  |
| occurrences (all)           | 1              | 0              |
| Rash maculo-papular         |                |                |
| subjects affected / exposed | 1 / 3 (33.33%) | 3 / 7 (42.86%) |
| occurrences (all)           | 1              | 3              |
| Rash macular                |                |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)           | 0              | 1              |
| Rash                        |                |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)           | 0              | 1              |
| Pruritus                    |                |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)           | 0              | 1              |
| Night sweats                |                |                |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 7 (0.00%)  |
| occurrences (all)           | 1              | 0              |
| Nail discolouration         |                |                |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 7 (0.00%)  |
| occurrences (all)           | 1              | 0              |
| Erythema                    |                |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)           | 0              | 1              |
| Alopecia                    |                |                |
| subjects affected / exposed | 2 / 3 (66.67%) | 3 / 7 (42.86%) |
| occurrences (all)           | 2              | 3              |
| Skin hyperpigmentation      |                |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)           | 0              | 1              |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| Renal and urinary disorders                     |                |                |  |
| Urethral pain                                   |                |                |  |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                               | 0              | 1              |  |
| Proteinuria                                     |                |                |  |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                               | 0              | 1              |  |
| Haematuria                                      |                |                |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                               | 1              | 0              |  |
| Cystitis noninfective                           |                |                |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                               | 1              | 0              |  |
| Acute kidney injury                             |                |                |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                               | 1              | 0              |  |
| Endocrine disorders                             |                |                |  |
| Hypothyroidism                                  |                |                |  |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                               | 0              | 2              |  |
| Adrenal insufficiency                           |                |                |  |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                               | 0              | 1              |  |
| Musculoskeletal and connective tissue disorders |                |                |  |
| Arthralgia                                      |                |                |  |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 3 / 7 (42.86%) |  |
| occurrences (all)                               | 0              | 3              |  |
| Back pain                                       |                |                |  |
| subjects affected / exposed                     | 2 / 3 (66.67%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                               | 2              | 0              |  |
| Bone pain                                       |                |                |  |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                               | 0              | 1              |  |
| Muscular weakness                               |                |                |  |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 2 / 7 (28.57%) |  |
| occurrences (all)                               | 0              | 2              |  |

|                                   |                |                |  |
|-----------------------------------|----------------|----------------|--|
| Neck pain                         |                |                |  |
| subjects affected / exposed       | 1 / 3 (33.33%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                 | 1              | 0              |  |
| Pain in extremity                 |                |                |  |
| subjects affected / exposed       | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                 | 0              | 1              |  |
| Sacral pain                       |                |                |  |
| subjects affected / exposed       | 1 / 3 (33.33%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                 | 1              | 0              |  |
| Infections and infestations       |                |                |  |
| COVID-19                          |                |                |  |
| subjects affected / exposed       | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                 | 0              | 1              |  |
| Candida infection                 |                |                |  |
| subjects affected / exposed       | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                 | 0              | 5              |  |
| Cellulitis                        |                |                |  |
| subjects affected / exposed       | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                 | 0              | 1              |  |
| Rectal abscess                    |                |                |  |
| subjects affected / exposed       | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                 | 0              | 1              |  |
| Sinusitis                         |                |                |  |
| subjects affected / exposed       | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                 | 0              | 1              |  |
| Staphylococcal skin infection     |                |                |  |
| subjects affected / exposed       | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                 | 0              | 1              |  |
| Submandibular abscess             |                |                |  |
| subjects affected / exposed       | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                 | 0              | 2              |  |
| Tooth infection                   |                |                |  |
| subjects affected / exposed       | 1 / 3 (33.33%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                 | 1              | 0              |  |
| Upper respiratory tract infection |                |                |  |

|                                    |                |                |  |
|------------------------------------|----------------|----------------|--|
| subjects affected / exposed        | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                  | 0              | 1              |  |
| Urinary tract infection            |                |                |  |
| subjects affected / exposed        | 1 / 3 (33.33%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                  | 1              | 0              |  |
| Metabolism and nutrition disorders |                |                |  |
| Decreased appetite                 |                |                |  |
| subjects affected / exposed        | 1 / 3 (33.33%) | 2 / 7 (28.57%) |  |
| occurrences (all)                  | 1              | 3              |  |
| Dehydration                        |                |                |  |
| subjects affected / exposed        | 1 / 3 (33.33%) | 1 / 7 (14.29%) |  |
| occurrences (all)                  | 2              | 1              |  |
| Hypercalcaemia                     |                |                |  |
| subjects affected / exposed        | 1 / 3 (33.33%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                  | 1              | 0              |  |
| Hyperglycaemia                     |                |                |  |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                  | 0              | 1              |  |
| Hypermagnesaemia                   |                |                |  |
| subjects affected / exposed        | 1 / 3 (33.33%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                  | 1              | 0              |  |
| Hyperphosphataemia                 |                |                |  |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                  | 0              | 1              |  |
| Hypoalbuminaemia                   |                |                |  |
| subjects affected / exposed        | 1 / 3 (33.33%) | 2 / 7 (28.57%) |  |
| occurrences (all)                  | 1              | 2              |  |
| Hypocalcaemia                      |                |                |  |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 2 / 7 (28.57%) |  |
| occurrences (all)                  | 0              | 3              |  |
| Hypokalaemia                       |                |                |  |
| subjects affected / exposed        | 1 / 3 (33.33%) | 3 / 7 (42.86%) |  |
| occurrences (all)                  | 1              | 8              |  |
| Hypomagnesaemia                    |                |                |  |
| subjects affected / exposed        | 1 / 3 (33.33%) | 1 / 7 (14.29%) |  |
| occurrences (all)                  | 1              | 3              |  |

|                             |               |                |  |
|-----------------------------|---------------|----------------|--|
| Hyponatraemia               |               |                |  |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 7 (28.57%) |  |
| occurrences (all)           | 0             | 3              |  |
| Hypophosphataemia           |               |                |  |
| subjects affected / exposed | 0 / 3 (0.00%) | 4 / 7 (57.14%) |  |
| occurrences (all)           | 0             | 6              |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 18 February 2022 | <p>The overall purpose for Protocol Amendment 02 is to introduce information regarding BMS-986288, an additional "next-generation" anti-cytotoxic T-lymphocyte-associated protein 4 (anti-CTLA-4) monoclonal antibody (mAb). BMS-986288 may be incorporated into the study design via future protocol amendment to test further the central study hypothesis that addition of nextgeneration anti-CTLA-4 agents, with or without nivolumab, will improve outcomes compared to docetaxel alone. BMS-986288 is another non-fucosylated next-generation anti-CTLA-4 that shares the Fcγ receptor (FcγR)-dependent mechanisms of BMS-986218. BMS-986288 is identical to BMS-986218 except for an additional "Probody" design element that could decrease toxicity by preventing binding to sites outside of the tumor, and thus further improve the benefit/risk profile as compared to BMS-986218.</p> <p>An update was also made to the Bayesian Optimal Interval (BOIN) table that eliminated criteria for 1 or 2 participants, as enrollment will be in groups of 3 to 4 participants at a time in Part 1a and Part 1b.</p> |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

This study was terminated early after the safety lead-in portion (Part 1).

Notes: