



## Clinical trial results:

### A Phase 1/2, Open-Label, Dose-Escalation/Dose-Expansion, Safety and Tolerability Study of INCB057643 in Subjects With Advanced Malignancies

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2017-002641-29   |
| Trial protocol           | FR               |
| Global end of trial date | 13 February 2019 |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 23 February 2020 |
| First version publication date | 23 February 2020 |

#### Trial information

##### Trial identification

|                       |               |
|-----------------------|---------------|
| Sponsor protocol code | INCB57643-101 |
|-----------------------|---------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02711137 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Incyte Corporation  |
| Sponsor organisation address | 1801 Augustine Cut-Off, Delaware, United States, 19803  |
| Public contact               | Incyte Corporation Call Centre, Incyte Corporation, +1 +80000027423, globalmedinfo@incyte.com |
| Scientific contact           | Incyte Corporation Call Centre, Incyte Corporation, +1 +80000027423, globalmedinfo@incyte.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:

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**Results analysis stage**

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 01 May 2019      |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 13 February 2019 |
| Was the trial ended prematurely?                     | Yes              |

Notes:

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**General information about the trial**

Main objective of the trial:

To assess the safety and tolerability of INCB057643 as monotherapy and in combination with standard of care (SOC) agents in subjects with advanced malignancies.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

|   |             |
|---|-------------|
| Actual start date of recruitment                          | 18 May 2016 |
| Long term follow-up planned                               | No          |
| Independent data monitoring committee (IDMC) involvement? | No          |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United States: 137 |
| Worldwide total number of subjects   | 137                |
| EEA total number of subjects         | 0                  |

Notes:

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**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)                      | 61 |
| From 65 to 84 years                       | 76 |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

A total of 137 subjects enrolled at 19 different sites in USA.

### Pre-assignment

Screening details:

Subjects were assigned to either dose escalation/dose-expansion study of INCB057643 as monotherapy or in combination with SOC agents in subjects with relapsing or refractory malignancies.

### Period 1

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

### Arms

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

|                  |   |
|------------------|---|
| <b>Arm title</b> | Part1/Treatment Group A : 8mg QD INCB057643 |
|------------------|---|

Arm description: -

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | INCB057643   |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Initial cohort dose of INCB057643 monotherapy at the protocol specified starting dose in the TGA.  
Treatment Group A included solid tumors and lymphoma

|                  |  |
|------------------|--|
| <b>Arm title</b> | Part1/Treatment Group A : 12mg QD INCB057643 |
|------------------|--|

Arm description: -

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | INCB057643   |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Initial cohort dose of INCB057643 monotherapy at the protocol specified starting dose in the TGA.  
Treatment Group A included solid tumors and lymphoma

|                  |  |
|------------------|--|
| <b>Arm title</b> | Part1/Treatment Group A : 16mg QD INCB057643 |
|------------------|--|

Arm description: -

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | INCB057643   |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Initial cohort dose of INCB057643 monotherapy at the protocol specified starting dose in the TGA.  
Treatment Group A included solid tumors and lymphoma

|   |   |
|---|---|
| <b>Arm title</b>  | Part1/Treatment Group B : 8mg QD INCB057643                 |
| Arm description: -  |   |
| Arm type  | Experimental  |
| Investigational medicinal product name  | INCB057643  |
| Investigational medicinal product code  |   |
| Other name  |   |
| Pharmaceutical forms  | Tablet  |
| Routes of administration  | Oral use  |
| Dosage and administration details:  |   |
| Initial cohort dose of INCB054763 monotherapy at the protocol-specified cohort escalation treatment group B (TGB), based on protocol-specific criteria. Treatment Group B included any acute leukemia, HR-MDS,MDS/MPN, or MF.   |   |
| <b>Arm title</b>  | Part1/Treatment Group B : 12mg QD INCB057643                |
| Arm description: -  |   |
| Arm type  | Experimental  |
| Investigational medicinal product name  | INCB057643  |
| Investigational medicinal product code  |   |
| Other name  |   |
| Pharmaceutical forms  | Tablet  |
| Routes of administration  | Oral use  |
| Dosage and administration details:  |   |
| Initial cohort dose of INCB054763 monotherapy at the protocol-specified cohort escalation treatment group B (TGB), based on protocol-specific criteria. Treatment Group B included any acute leukemia, HR-MDS,MDS/MPN, or MF.   |   |
| <b>Arm title</b>  | Part1/Treatment Group C : 8mg QD INCB057643                 |
| Arm description: -  |   |
| Arm type  | Experimental  |
| Investigational medicinal product name  | INCB057643  |
| Investigational medicinal product code  |   |
| Other name  |   |
| Pharmaceutical forms  | Tablet  |
| Routes of administration  | Oral use  |
| Dosage and administration details:  |   |
| Initial cohort dose of INCB054763 monotherapy at the protocol-specified cohort escalation treatment group C (TGC), based on protocol-specific criteria. Treatment Group C includes subjects with MM   |   |
| <b>Arm title</b>  | Part2/Treatment Group A : 12 mg INCB057643 Expansion Cohort |
| Arm description: -  |   |
| Arm type  | Experimental  |
| Investigational medicinal product name  | INCB057643  |
| Investigational medicinal product code  |   |
| Other name  |   |
| Pharmaceutical forms  | Tablet  |
| Routes of administration  | Oral use  |
| Dosage and administration details:  |   |
| Initial cohort dose of INCB054763 monotherapy at the specified RP2D dose selected in Part 1 cohort escalation treatment group A (TGA), based on protocol-specific criteria. Part 2 Treatment Group A expansion included pancreatic adenocarcinoma, castration-resistant prostate cancer, breast cancer, high grade serous ovarian cancer, glioblastoma multiform, non-hodgkin's lymphoma, ewing's sarcoma, and solid tumor or lymphoma. |   |
| <b>Arm title</b>  | Part2/Treatment Group B : 12 mg INCB057643 Expansion Cohort |
| Arm description: -  |   |
| Arm type  | Experimental  |

|   |  |
|---|--|
| Investigational medicinal product name  | INCB057643   |
| Investigational medicinal product code  |  |
| Other name  |  |
| Pharmaceutical forms  | Tablet   |
| Routes of administration  | Oral use   |
| Dosage and administration details:  |  |
| Initial cohort dose of INCB057643 monotherapy at the specified RP2D dose selected in Part 1 cohort escalation treatment group B (TGB), based on protocol-specific criteria. Part 2 Treatment Group B expansion included pancreatic adenocarcinoma, castration-resistant prostate cancer, breast cancer, high grade serous ovarian cancer, glioblastoma multiform, non-hodgkin's lymphoma, ewing's sarcoma, and solid tumor or lymphoma. |  |
| <b>Arm title</b>  | Part3/Treatment Group A : 8 mg INCB057643 + Gemcitabine 1000mg |
| Arm description: -  |  |
| Arm type  | Experimental   |
| Investigational medicinal product name  | INCB057643   |
| Investigational medicinal product code  |  |
| Other name  |  |
| Pharmaceutical forms  | Tablet   |
| Routes of administration  | Oral use   |
| Dosage and administration details:  |  |
| Initial cohort dose of INCB057643 monotherapy based on protocol-specific criteria. Part 3 will determine the MTD and/or a tolerated dose of the combination of INCB057643 and one of the SOC agents (Gemcitabine) in relapsed or refractory advanced or metastatic solid tumors and hematologic malignancies where Gemcitabine is relevant  |  |
| <b>Arm title</b>  | Part3/Treatment Group B : 8 mg INCB057643 + Paclitaxel 80mg    |
| Arm description: -  |  |
| Arm type  | Experimental   |
| Investigational medicinal product name  | INCB057643   |
| Investigational medicinal product code  |  |
| Other name  |  |
| Pharmaceutical forms  | Tablet   |
| Routes of administration  | Oral use   |
| Dosage and administration details:  |  |
| Initial cohort dose of INCB057643 monotherapy based on protocol-specific criteria. Part 3 will determine the MTD and/or a tolerated dose of the combination of INCB057643 and one of the SOC agents (Paclitaxel) in relapsed or refractory advanced or metastatic solid tumors and hematologic malignancies.  |  |
| <b>Arm title</b>  | Part3/Treatment Group C : 8 mg INCB057643 + Rucaparib 600mg    |
| Arm description: -  |  |
| Arm type  | Experimental   |
| Investigational medicinal product name  | INCB057643   |
| Investigational medicinal product code  |  |
| Other name  |  |
| Pharmaceutical forms  | Tablet   |
| Routes of administration  | Oral use   |
| Dosage and administration details:  |  |
| Initial cohort dose of INCB057643 monotherapy based on protocol-specific criteria. Part 3 will determine the MTD and/or a tolerated dose of the combination of INCB057643 and one of the SOC agents (Rucaparib) in relapsed or refractory advanced or metastatic solid tumors and hematologic malignancies.   |  |
| <b>Arm title</b>  | Part3/Treatment Group D : 8 mg INCB057643 + Abir +Predni       |
| Arm description: -  |  |
| Arm type  | Experimental   |

|   |  |
|---|--|
| Investigational medicinal product name  | INCB057643   |
| Investigational medicinal product code  |  |
| Other name  |  |
| Pharmaceutical forms  | Tablet   |
| Routes of administration  | Oral use   |
| Dosage and administration details:  |  |
| Initial cohort dose of INCB054763 monotherapy based on protocol-specific criteria. Part 3 will determine the MTD and/or a tolerated dose of the combination of INCB057643 and one of the SOC agents (Abiraterone + Prednisone) in Castration Resistant Prostrate Cancer . |  |
| <b>Arm title</b>  | Part3/Treatment Group E : 8 mg INCB057643 + Ruxolitinib 20mg |
| Arm description: -  |  |
| Arm type  | Experimental   |
| Investigational medicinal product name  | INCB057643   |
| Investigational medicinal product code  |  |
| Other name  |  |
| Pharmaceutical forms  | Tablet   |
| Routes of administration  | Oral use   |
| Dosage and administration details:  |  |
| Initial cohort dose of INCB054763 monotherapy based on protocol-specific criteria. Part 3 will determine the MTD and/or a tolerated dose of the combination of INCB057643 and one of the SOC agents (Ruxolitinib) in Myelofibrosis.                                       |  |
| <b>Arm title</b>  | Part3/Treatment Group F : 8 mg INCB057643 + Azacitidine 75mg |
| Arm description: -  |  |
| Arm type  | Experimental   |
| Investigational medicinal product name  | INCB057643   |
| Investigational medicinal product code  |  |
| Other name  |  |
| Pharmaceutical forms  | Tablet   |
| Routes of administration  | Oral use   |
| Dosage and administration details:  |  |
| Initial cohort dose of INCB054763 monotherapy based on protocol-specific criteria. Part 3 will determine the MTD and/or a tolerated dose of the combination of INCB057643 and one of the SOC agents (Azacitidine) in Acute Myeloid Leukemia and Myelodysplastic Syndrome  |  |
| <b>Arm title</b>  | Enrolled but not dosed                                       |
| Arm description:  |  |
| Subjects enrolled in the study but not dosed  |  |
| Arm type  | No intervention  |
| No investigational medicinal product assigned in this arm   |  |

| <b>Number of subjects in period 1</b> | Part1/Treatment Group A : 8mg QD INCB057643 | Part1/Treatment Group A : 12mg QD INCB057643 | Part1/Treatment Group A : 16mg QD INCB057643 |
|---------------------------------------|---|--|--|
| Started                               | 4   | 5  | 8  |
| Completed                             | 0   | 0  | 0  |
| Not completed                         | 4   | 5  | 8  |
| Physician decision                    | 1   | -  | 2  |
| withdrawal by subject                 | 1   | -  | -  |
| Death                                 | 1   | 4  | 5  |

|                             |   |   |   |
|-----------------------------|---|---|---|
| Unknown                     | - | 1 | - |
| study terminated by sponsor | - | - | 1 |
| Lost to follow-up           | 1 | - | - |

| Number of subjects in period 1 | Part1/Treatment<br>Group B : 8mg QD<br>INCB057643 | Part1/Treatment<br>Group B : 12mg QD<br>INCB057643 | Part1/Treatment<br>Group C : 8mg QD<br>INCB057643 |
|--------------------------------|---|--|---|
| Started                        | 7   | 5  | 1   |
| Completed                      | 0   | 0  | 0   |
| Not completed                  | 7   | 5  | 1   |
| Physician decision             | 1   | 1  | -   |
| withdrawal by subject          | 1   | 1  | -   |
| Death                          | 5   | 3  | 1   |
| Unknown                        | -   | -  | -   |
| study terminated by sponsor    | -   | -  | -   |
| Lost to follow-up              | -   | -  | -   |

| Number of subjects in period 1 | Part2/Treatment<br>Group A : 12 mg<br>INCB057643<br>Expansion Cohort | Part2/Treatment<br>Group B : 12 mg<br>INCB057643<br>Expansion Cohort | Part3/Treatment<br>Group A : 8 mg<br>INCB057643 +<br>Gemcitabine<br>1000mg |
|--------------------------------|--|--|--|
|                                |  |  |  |
| Started                        | 86   | 5  | 1  |
| Completed                      | 0  | 0  | 0  |
| Not completed                  | 86   | 5  | 1  |
| Physician decision             | 12   | 2  | 1  |
| withdrawal by subject          | 7  | -  | -  |
| Death                          | 61   | 3  | -  |
| Unknown                        | 3  | -  | -  |
| study terminated by sponsor    | 1  | -  | -  |
| Lost to follow-up              | 2  | -  | -  |

| Number of subjects in period 1 | Part3/Treatment<br>Group B : 8 mg<br>INCB057643 +<br>Paclitaxel 80mg | Part3/Treatment<br>Group C : 8 mg<br>INCB057643 +<br>Rucaparib 600mg | Part3/Treatment<br>Group D : 8 mg<br>INCB057643 + Abir<br>+Predni |
|--------------------------------|--|--|---|
| Started                        | 2  | 4  | 3   |
| Completed                      | 0  | 0  | 0   |
| Not completed                  | 2  | 4  | 3   |
| Physician decision             | 1  | 3  | 2   |
| withdrawal by subject          | -  | -  | -   |
| Death                          | 1  | 1  | 1   |
| Unknown                        | -  | -  | -   |
| study terminated by sponsor    | -  | -  | -   |
| Lost to follow-up              | -  | -  | -   |

| Number of subjects in period 1 | Part3/Treatment<br>Group E : 8 mg | Part3/Treatment<br>Group F : 8 mg | Enrolled but not<br>dosed |
|--------------------------------|-----------------------------------|-----------------------------------|---------------------------|
|--------------------------------|-----------------------------------|-----------------------------------|---------------------------|

|                             | INCB057643 +<br>Ruxolitinib 20mg | INCB057643 +<br>Azacitidine 75mg |   |
|-----------------------------|----------------------------------|----------------------------------|---|
| Started                     | 1                                | 2                                | 3 |
| Completed                   | 0                                | 0                                | 0 |
| Not completed               | 1                                | 2                                | 3 |
| Physician decision          | 1                                | 1                                | 2 |
| withdrawal by subject       | -                                | 1                                | - |
| Death                       | -                                | -                                | - |
| Unknown                     | -                                | -                                | 1 |
| study terminated by sponsor | -                                | -                                | - |
| Lost to follow-up           | -                                | -                                | - |



## Baseline characteristics

| Reporting groups                             |  |
|--|--|
| Reporting group title                        | Part1/Treatment Group A : 8mg QD INCB057643                    |
| Reporting group description: -               |  |
| Reporting group title                        | Part1/Treatment Group A : 12mg QD INCB057643                   |
| Reporting group description: -               |  |
| Reporting group title                        | Part1/Treatment Group A : 16mg QD INCB057643                   |
| Reporting group description: -               |  |
| Reporting group title                        | Part1/Treatment Group B : 8mg QD INCB057643                    |
| Reporting group description: -               |  |
| Reporting group title                        | Part1/Treatment Group B : 12mg QD INCB057643                   |
| Reporting group description: -               |  |
| Reporting group title                        | Part1/Treatment Group C : 8mg QD INCB057643                    |
| Reporting group description: -               |  |
| Reporting group title                        | Part2/Treatment Group A : 12 mg INCB057643 Expansion Cohort    |
| Reporting group description: -               |  |
| Reporting group title                        | Part2/Treatment Group B : 12 mg INCB057643 Expansion Cohort    |
| Reporting group description: -               |  |
| Reporting group title                        | Part3/Treatment Group A : 8 mg INCB057643 + Gemcitabine 1000mg |
| Reporting group description: -               |  |
| Reporting group title                        | Part3/Treatment Group B : 8 mg INCB057643 + Paclitaxel 80mg    |
| Reporting group description: -               |  |
| Reporting group title                        | Part3/Treatment Group C : 8 mg INCB057643 + Rucaparib 600mg    |
| Reporting group description: -               |  |
| Reporting group title                        | Part3/Treatment Group D : 8 mg INCB057643 + Abir +Predni       |
| Reporting group description: -               |  |
| Reporting group title                        | Part3/Treatment Group E : 8 mg INCB057643 + Ruxolitinib 20mg   |
| Reporting group description: -               |  |
| Reporting group title                        | Part3/Treatment Group F : 8 mg INCB057643 + Azacitidine 75mg   |
| Reporting group description: -               |  |
| Reporting group title                        | Enrolled but not dosed   |
| Reporting group description:                 |  |
| Subjects enrolled in the study but not dosed |  |

| Reporting group values                             | Part1/Treatment Group A : 8mg QD INCB057643 | Part1/Treatment Group A : 12mg QD INCB057643 | Part1/Treatment Group A : 16mg QD INCB057643 |
|--|---|--|--|
| Number of subjects                                 | 4   | 5  | 8  |
| Age categorical                                    |   |  |  |
| Units: Subjects                                    |   |  |  |
| In utero   | 0   | 0  | 0  |
| Preterm newborn infants (gestational age < 37 wks) | 0   | 0  | 0  |
| Newborns (0-27 days)                               | 0   | 0  | 0  |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Infants and toddlers (28 days-23 months)                                | 0               | 0               | 0               |
| Children (2-11 years)   | 0               | 0               | 0               |
| Adolescents (12-17 years)   | 0               | 0               | 0               |
| Adults (18-64 years)  | 2               | 3               | 5               |
| From 65-84 years  | 2               | 2               | 3               |
| 85 years and over   | 0               | 0               | 0               |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 64.3<br>± 10.21 | 60.2<br>± 12.26 | 60.5<br>± 11.44 |
| Gender categorical<br>Units: Subjects                                   |                 |                 |                 |
| Female  | 2               | 2               | 5               |
| Male  | 2               | 3               | 3               |
| Race<br>Units: Subjects   |                 |                 |                 |
| White/Caucasian   | 3               | 3               | 5               |
| Black/African-American  | 1               | 0               | 2               |
| Asian   | 0               | 0               | 0               |
| American-Indian/Alaska Native   | 0               | 0               | 0               |
| Native Hawaiian/Pacific Islander  | 0               | 1               | 0               |
| Other   | 0               | 1               | 1               |
| Missing   | 0               | 0               | 0               |

| <b>Reporting group values</b>   | Part1/Treatment<br>Group B : 8mg QD<br>INCB057643 | Part1/Treatment<br>Group B : 12mg QD<br>INCB057643 | Part1/Treatment<br>Group C : 8mg QD<br>INCB057643 |
|---|---|--|---|
| Number of subjects  | 7   | 5  | 1   |
| Age categorical<br>Units: Subjects                                      |   |  |   |
| In utero  | 0   | 0  | 0   |
| Preterm newborn infants<br>(gestational age < 37 wks)                   | 0   | 0  | 0   |
| Newborns (0-27 days)  | 0   | 0  | 0   |
| Infants and toddlers (28 days-23 months)                                | 0   | 0  | 0   |
| Children (2-11 years)   | 0   | 0  | 0   |
| Adolescents (12-17 years)   | 0   | 0  | 0   |
| Adults (18-64 years)  | 2   | 0  | 0   |
| From 65-84 years  | 5   | 5  | 1   |
| 85 years and over   | 0   | 0  | 0   |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 68.9<br>± 5.81                                    | 75.8<br>± 7.33                                     | 70.0<br>± 0                                       |
| Gender categorical<br>Units: Subjects                                   |   |  |   |
| Female  | 3   | 1  | 0   |
| Male  | 4   | 4  | 1   |
| Race<br>Units: Subjects   |   |  |   |
| White/Caucasian   | 6   | 4  | 0   |

|                                  |   |   |   |
|----------------------------------|---|---|---|
| Black/African-American           | 1 | 0 | 0 |
| Asian                            | 0 | 0 | 0 |
| American-Indian/Alaska Native    | 0 | 0 | 0 |
| Native Hawaiian/Pacific Islander | 0 | 0 | 0 |
| Other                            | 0 | 1 | 1 |
| Missing                          | 0 | 0 | 0 |

| <b>Reporting group values</b>                      | Part2/Treatment Group A : 12 mg INCB057643 Expansion Cohort | Part2/Treatment Group B : 12 mg INCB057643 Expansion Cohort | Part3/Treatment Group A : 8 mg INCB057643 + Gemcitabine 1000mg |
|--|---|---|--|
| Number of subjects                                 | 86  | 5   | 1  |
| Age categorical<br>Units: Subjects                 |   |   |  |
| In utero   | 0   | 0   | 0  |
| Preterm newborn infants (gestational age < 37 wks) | 0   | 0   | 0  |
| Newborns (0-27 days)                               | 0   | 0   | 0  |
| Infants and toddlers (28 days-23 months)           | 0   | 0   | 0  |
| Children (2-11 years)                              | 0   | 0   | 0  |
| Adolescents (12-17 years)                          | 0   | 0   | 0  |
| Adults (18-64 years)                               | 44  | 1   | 0  |
| From 65-84 years                                   | 42  | 4   | 1  |
| 85 years and over                                  | 0   | 0   | 0  |
| Age continuous<br>Units: years                     |   |   |  |
| arithmetic mean                                    | 60.6  | 72.6  | 72.0   |
| standard deviation                                 | ± 13.80   | ± 10.92   | ± 0  |
| Gender categorical<br>Units: Subjects              |   |   |  |
| Female   | 48  | 0   | 1  |
| Male   | 38  | 5   | 0  |
| Race<br>Units: Subjects                            |   |   |  |
| White/Caucasian                                    | 72  | 5   | 0  |
| Black/African-American                             | 10  | 0   | 1  |
| Asian  | 0   | 0   | 0  |
| American-Indian/Alaska Native                      | 1   | 0   | 0  |
| Native Hawaiian/Pacific Islander                   | 0   | 0   | 0  |
| Other  | 2   | 0   | 0  |
| Missing  | 1   | 0   | 0  |

| <b>Reporting group values</b>                      | Part3/Treatment Group B : 8 mg INCB057643 + Paclitaxel 80mg | Part3/Treatment Group C : 8 mg INCB057643 + Rucaparib 600mg | Part3/Treatment Group D : 8 mg INCB057643 + Abir +Predni |
|--|---|---|--|
| Number of subjects                                 | 2   | 4   | 3  |
| Age categorical<br>Units: Subjects                 |   |   |  |
| In utero   | 0   | 0   | 0  |
| Preterm newborn infants (gestational age < 37 wks) | 0   | 0   | 0  |
| Newborns (0-27 days)                               | 0   | 0   | 0  |

|  |         |        |        |
|--|---------|--------|--------|
| Infants and toddlers (28 days-23 months) | 0       | 0      | 0      |
| Children (2-11 years)                    | 0       | 0      | 0      |
| Adolescents (12-17 years)                | 0       | 0      | 0      |
| Adults (18-64 years)                     | 1       | 1      | 1      |
| From 65-84 years                         | 1       | 3      | 2      |
| 85 years and over                        | 0       | 0      | 0      |
| Age continuous<br>Units: years           |         |        |        |
| arithmetic mean                          | 56.0    | 66.0   | 67.7   |
| standard deviation                       | ± 12.73 | ± 6.16 | ± 4.04 |
| Gender categorical<br>Units: Subjects    |         |        |        |
| Female                                   | 1       | 4      | 0      |
| Male                                     | 1       | 0      | 3      |
| Race<br>Units: Subjects                  |         |        |        |
| White/Caucasian                          | 1       | 4      | 3      |
| Black/African-American                   | 1       | 0      | 0      |
| Asian                                    | 0       | 0      | 0      |
| American-Indian/Alaska Native            | 0       | 0      | 0      |
| Native Hawaiian/Pacific Islander         | 0       | 0      | 0      |
| Other                                    | 0       | 0      | 0      |
| Missing                                  | 0       | 0      | 0      |

| <b>Reporting group values</b>                      | Part3/Treatment Group E : 8 mg INCB057643 + Ruxolitinib 20mg | Part3/Treatment Group F : 8 mg INCB057643 + Azacitidine 75mg | Enrolled but not dosed |
|--|--|--|------------------------|
| Number of subjects                                 | 1  | 2  | 3                      |
| Age categorical<br>Units: Subjects                 |  |  |                        |
| In utero   | 0  | 0  | 0                      |
| Preterm newborn infants (gestational age < 37 wks) | 0  | 0  | 0                      |
| Newborns (0-27 days)                               | 0  | 0  | 0                      |
| Infants and toddlers (28 days-23 months)           | 0  | 0  | 0                      |
| Children (2-11 years)                              | 0  | 0  | 0                      |
| Adolescents (12-17 years)                          | 0  | 0  | 0                      |
| Adults (18-64 years)                               | 0  | 0  | 1                      |
| From 65-84 years                                   | 1  | 2  | 2                      |
| 85 years and over                                  | 0  | 0  | 0                      |
| Age continuous<br>Units: years                     |  |  |                        |
| arithmetic mean                                    | 75.0   | 76.5   | 66.0                   |
| standard deviation                                 | ± 0  | ± 2.12   | ± 6.24                 |
| Gender categorical<br>Units: Subjects              |  |  |                        |
| Female   | 0  | 0  | 1                      |
| Male   | 1  | 2  | 2                      |

|                                  |   |   |   |
|----------------------------------|---|---|---|
| Race                             |   |   |   |
| Units: Subjects                  |   |   |   |
| White/Caucasian                  | 1 | 2 | 3 |
| Black/African-American           | 0 | 0 | 0 |
| Asian                            | 0 | 0 | 0 |
| American-Indian/Alaska Native    | 0 | 0 | 0 |
| Native Hawaiian/Pacific Islander | 0 | 0 | 0 |
| Other                            | 0 | 0 | 0 |
| Missing                          | 0 | 0 | 0 |

|   |       |  |  |
|---|-------|--|--|
| <b>Reporting group values</b>                         | Total |  |  |
| Number of subjects                                    | 137   |  |  |
| Age categorical                                       |       |  |  |
| Units: Subjects                                       |       |  |  |
| In utero  | 0     |  |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0     |  |  |
| Newborns (0-27 days)                                  | 0     |  |  |
| Infants and toddlers (28 days-23<br>months)           | 0     |  |  |
| Children (2-11 years)                                 | 0     |  |  |
| Adolescents (12-17 years)                             | 0     |  |  |
| Adults (18-64 years)                                  | 61    |  |  |
| From 65-84 years                                      | 76    |  |  |
| 85 years and over                                     | 0     |  |  |
| Age continuous  |       |  |  |
| Units: years  |       |  |  |
| arithmetic mean                                       |       |  |  |
| standard deviation                                    | -     |  |  |
| Gender categorical                                    |       |  |  |
| Units: Subjects                                       |       |  |  |
| Female  | 68    |  |  |
| Male  | 69    |  |  |
| Race  |       |  |  |
| Units: Subjects                                       |       |  |  |
| White/Caucasian                                       | 112   |  |  |
| Black/African-American                                | 16    |  |  |
| Asian   | 0     |  |  |
| American-Indian/Alaska Native                         | 1     |  |  |
| Native Hawaiian/Pacific Islander                      | 1     |  |  |
| Other   | 6     |  |  |
| Missing   | 1     |  |  |

## End points

### End points reporting groups

|  |  |
|--|--|
| Reporting group title  | Part1/Treatment Group A : 8mg QD INCB057643                    |
| Reporting group description: -   |  |
| Reporting group title  | Part1/Treatment Group A : 12mg QD INCB057643                   |
| Reporting group description: -   |  |
| Reporting group title  | Part1/Treatment Group A : 16mg QD INCB057643                   |
| Reporting group description: -   |  |
| Reporting group title  | Part1/Treatment Group B : 8mg QD INCB057643                    |
| Reporting group description: -   |  |
| Reporting group title  | Part1/Treatment Group B : 12mg QD INCB057643                   |
| Reporting group description: -   |  |
| Reporting group title  | Part1/Treatment Group C : 8mg QD INCB057643                    |
| Reporting group description: -   |  |
| Reporting group title  | Part2/Treatment Group A : 12 mg INCB057643 Expansion Cohort    |
| Reporting group description: -   |  |
| Reporting group title  | Part2/Treatment Group B : 12 mg INCB057643 Expansion Cohort    |
| Reporting group description: -   |  |
| Reporting group title  | Part3/Treatment Group A : 8 mg INCB057643 + Gemcitabine 1000mg |
| Reporting group description: -   |  |
| Reporting group title  | Part3/Treatment Group B : 8 mg INCB057643 + Paclitaxel 80mg    |
| Reporting group description: -   |  |
| Reporting group title  | Part3/Treatment Group C : 8 mg INCB057643 + Rucaparib 600mg    |
| Reporting group description: -   |  |
| Reporting group title  | Part3/Treatment Group D : 8 mg INCB057643 + Abir +Predni       |
| Reporting group description: -   |  |
| Reporting group title  | Part3/Treatment Group E : 8 mg INCB057643 + Ruxolitinib 20mg   |
| Reporting group description: -   |  |
| Reporting group title  | Part3/Treatment Group F : 8 mg INCB057643 + Azacitidine 75mg   |
| Reporting group description: -   |  |
| Reporting group title  | Enrolled but not dosed   |
| Reporting group description:   |  |
| Subjects enrolled in the study but not dosed   |  |
| Subject analysis set title   | Part 1 and 2 : 8mg QD INCB057643                               |
| Subject analysis set type  | Sub-group analysis   |
| Subject analysis set description:  |  |
| PK Analysis was done on subjects by dosage irrelevant of the Part 1 or Part 2 assignment |  |
| Subject analysis set title   | Part 1 and 2 : 12 mg QD INCB057643                             |
| Subject analysis set type  | Sub-group analysis   |
| Subject analysis set description:  |  |
| PK Analysis was done on subjects by dosage irrelevant of the Part 1 or Part 2 assignment |  |
| Subject analysis set title   | Part 1 and 2 : 16 mg QD INCB057643                             |
| Subject analysis set type  | Sub-group analysis   |
| Subject analysis set description:  |  |
| PK Analysis was done on subjects by dosage irrelevant of the Part 1 or Part 2 assignment |  |

**Primary: Safety and tolerability of INCB057643 as monotherapy and in combination with standard of care (SOC) agents in patients with advanced malignancies; assessed by clinical laboratory assessments, physical examinations, 12 lead ECGs, and adverse events (AEs)**

|                 |  |
|-----------------|--|
| End point title | Safety and tolerability of INCB057643 as monotherapy and in combination with standard of care (SOC) agents in patients with advanced malignancies; assessed by clinical laboratory assessments, physical examinations, 12 lead ECGs, and adverse events (AEs) <sup>[1]</sup> |
|-----------------|--|

End point description:

Descriptive statistics for clinical laboratory assessments, physical examinations, 12 lead ECGs are provided.

Tabulation of adverse events are provided.

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

End point timeframe:

From screening through at least 30 days after end of treatment, up to approximately 24 months

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: There is no hypothesis testing for this endpoint , descriptive analysis is provided.

| End point values            | Part1/Treatment Group A : 8mg QD INCB057643 | Part1/Treatment Group A : 12mg QD INCB057643 | Part1/Treatment Group A : 16mg QD INCB057643 | Part1/Treatment Group B : 8mg QD INCB057643 |
|-----------------------------|---|--|--|---|
| Subject group type          | Reporting group                             | Reporting group                              | Reporting group                              | Reporting group                             |
| Number of subjects analysed | 4   | 5  | 8  | 7   |
| Units: Subjects             | 4   | 5  | 8  | 7   |

| End point values            | Part1/Treatment Group B : 12mg QD INCB057643 | Part1/Treatment Group C : 8mg QD INCB057643 | Part2/Treatment Group A : 12 mg INCB057643 Expansion Cohort | Part2/Treatment Group B : 12 mg INCB057643 Expansion Cohort |
|-----------------------------|--|---|---|---|
| Subject group type          | Reporting group                              | Reporting group                             | Reporting group   | Reporting group   |
| Number of subjects analysed | 5  | 1   | 86  | 5   |
| Units: Subjects             | 5  | 1   | 86  | 5   |

| End point values            | Part3/Treatment Group A : 8 mg INCB057643 + Gemcitabine 1000mg | Part3/Treatment Group B : 8 mg INCB057643 + Paclitaxel 80mg | Part3/Treatment Group C : 8 mg INCB057643 + Rucaparib 600mg | Part3/Treatment Group D : 8 mg INCB057643 + Abir +Predni |
|-----------------------------|--|---|---|--|
| Subject group type          | Reporting group  | Reporting group   | Reporting group   | Reporting group  |
| Number of subjects analysed | 1  | 2   | 4   | 3  |
| Units: Subjects             | 1  | 2   | 4   | 3  |

|                             |  |  |                        |  |
|-----------------------------|--|--|------------------------|--|
| <b>End point values</b>     | Part3/Treatment Group E : 8 mg<br>INCB057643 + Ruxolitinib<br>20mg | Part3/Treatment Group F : 8 mg<br>INCB057643 + Azacitidine<br>75mg | Enrolled but not dosed |  |
| Subject group type          | Reporting group  | Reporting group  | Reporting group        |  |
| Number of subjects analysed | 1  | 2  | 0 <sup>[2]</sup>       |  |
| Units: Subjects             | 1  | 2  |                        |  |

Notes:

[2] - No Participants were treated

## Statistical analyses

No statistical analyses for this end point

### Secondary: AUC0-24 Analysis of INCB057643

|                 |                                |
|-----------------|--------------------------------|
| End point title | AUC0-24 Analysis of INCB057643 |
|-----------------|--------------------------------|

End point description:

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

End point timeframe:

AUC0-24 is the area under the plasma or serum concentration-time curve from time = 0 to the last measurable concentration at time = 24 measured at steady state (Day 8)

|   |  |  |  |  |
|---|--|--|--|--|
| <b>End point values</b>                             | Part 1 and 2 :<br>8mg QD<br>INCB057643 | Part 1 and 2 :<br>12 mg QD<br>INCB057643 | Part 1 and 2 :<br>16 mg QD<br>INCB057643 |  |
| Subject group type                                  | Subject analysis set                   | Subject analysis set                     | Subject analysis set                     |  |
| Number of subjects analysed                         | 10                                     | 89                                       | 7  |  |
| Units: hours*nM                                     |  |  |  |  |
| geometric mean (geometric coefficient of variation) | 1940 (± 45.1)                          | 2740 (± 43.2)                            | 3610 (± 71.9)                            |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: T1/2: Terminal Half-life of INCB057643

|                 |  |
|-----------------|--|
| End point title | T1/2: Terminal Half-life of INCB057643 |
|-----------------|--|

End point description:

The apparent terminal half-life is the time required for plasma concentration to decrease by 50% after pseudo-equilibrium of distribution has been reached, and calculated as the natural logarithm of 2 (0.693) / Apparent terminal rate constant (λ<sub>z</sub>).

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

End point timeframe:

Day 8



| End point values                                    | Part 1 and 2 :<br>8mg QD<br>INCB057643 | Part 1 and 2 :<br>12 mg QD<br>INCB057643 | Part 1 and 2 :<br>16 mg QD<br>INCB057643 |  |
|---|--|--|--|--|
| Subject group type                                  | Subject analysis set                   | Subject analysis set                     | Subject analysis set                     |  |
| Number of subjects analysed                         | 10                                     | 89                                       | 7  |  |
| Units: hours  |  |  |  |  |
| geometric mean (geometric coefficient of variation) | 9.67 ( $\pm$ 50.8)                     | 9.17 ( $\pm$ 49.7)                       | 12.8 ( $\pm$ 71.4)                       |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: VzF: Apparent Volume of Distribution of INCB057643

|                 |  |
|-----------------|--|
| End point title | VzF: Apparent Volume of Distribution of INCB057643 |
|-----------------|--|

End point description:

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

End point timeframe:

Apparent volume of distribution of INCB057643

| End point values                                    | Part 1 and 2 :<br>8mg QD<br>INCB057643 | Part 1 and 2 :<br>12 mg QD<br>INCB057643 | Part 1 and 2 :<br>16 mg QD<br>INCB057643 |  |
|---|--|--|--|--|
| Subject group type                                  | Subject analysis set                   | Subject analysis set                     | Subject analysis set                     |  |
| Number of subjects analysed                         | 10                                     | 89                                       | 7  |  |
| Units: Liters                                       |  |  |  |  |
| geometric mean (geometric coefficient of variation) | 138 ( $\pm$ 46.1)                      | 139 ( $\pm$ 51.2)                        | 197 ( $\pm$ 42.9)                        |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Objective Response Rate (ORR) With INCB057643 in Solid Tumors

|                 |  |
|-----------------|--|
| End point title | Objective Response Rate (ORR) With INCB057643 in Solid Tumors <sup>[3]</sup> |
|-----------------|--|

End point description:

Objective response rate is defined as the proportion of subjects who have an objective response using the applicable disease assessment criteria.

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

End point timeframe:

Efficacy measures from screening through end of treatment and follow-up (every 9 weeks), up to approximately 24 months

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.  
Justification: ORR is summarized by tumor type.

| End point values            | Part1/Treatment Group A : 8mg QD INCB057643 | Part1/Treatment Group A : 12mg QD INCB057643 | Part1/Treatment Group A : 16mg QD INCB057643 | Part2/Treatment Group A : 12 mg INCB057643 Expansion Cohort |
|-----------------------------|---|--|--|---|
| Subject group type          | Reporting group                             | Reporting group                              | Reporting group                              | Reporting group   |
| Number of subjects analysed | 3 <sup>[4]</sup>                            | 4 <sup>[5]</sup>                             | 6 <sup>[6]</sup>                             | 63 <sup>[7]</sup>   |
| Units: Subjects             | 0   | 0  | 0  | 0   |

Notes:

[4] - Efficacy Evaluable Population

[5] - Efficacy Evaluable Population

[6] - Efficacy Evaluable Population

[7] - Efficacy Evaluable Population

| End point values            | Part3/Treatment Group A : 8 mg INCB057643 + Gemcitabine 1000mg | Part3/Treatment Group B : 8 mg INCB057643 + Paclitaxel 80mg | Part3/Treatment Group C : 8 mg INCB057643 + Rucaparib 600mg | Part3/Treatment Group D : 8 mg INCB057643 + Abir +Predni |
|-----------------------------|--|---|---|--|
| Subject group type          | Reporting group  | Reporting group   | Reporting group   | Reporting group  |
| Number of subjects analysed | 1 <sup>[8]</sup>   | 2 <sup>[9]</sup>  | 4 <sup>[10]</sup>   | 3 <sup>[11]</sup>  |
| Units: Subjects             | 0  | 1   | 0   | 0  |

Notes:

[8] - Efficacy Evaluable Population

[9] - Efficacy Evaluable Population

[10] - Efficacy Evaluable Population

[11] - Efficacy Evaluable Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cmax: Maximum Observed Plasma Concentration of INCB057643

|                 |   |
|-----------------|---|
| End point title | Cmax: Maximum Observed Plasma Concentration of INCB057643 |
|-----------------|---|

End point description:

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

End point timeframe:

Predose, 0.5, 1, 2, 4, 6, 8 hours of C1D8

| End point values                                    | Part 1 and 2 :<br>8mg QD<br>INCB057643 | Part 1 and 2 :<br>12 mg QD<br>INCB057643 | Part 1 and 2 :<br>16 mg QD<br>INCB057643 |  |
|---|--|--|--|--|
| Subject group type                                  | Subject analysis set                   | Subject analysis set                     | Subject analysis set                     |  |
| Number of subjects analysed                         | 10                                     | 89                                       | 7  |  |
| Units: nM   |  |  |  |  |
| geometric mean (geometric coefficient of variation) | 191 (± 50.3)                           | 272 (± 40.9)                             | 310 (± 47.5)                             |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Cmin: Minimum Observed Plasma Concentration Over the Dose Interval Analysis of INCB057643

|                 |   |
|-----------------|---|
| End point title | Cmin: Minimum Observed Plasma Concentration Over the Dose Interval Analysis of INCB057643 |
|-----------------|---|

End point description:

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

End point timeframe:

Predose, 0.5, 1, 2, 4, 6, 8 hours of C1D8

| End point values                                    | Part 1 and 2 :<br>8mg QD<br>INCB057643 | Part 1 and 2 :<br>12 mg QD<br>INCB057643 | Part 1 and 2 :<br>16 mg QD<br>INCB057643 |  |
|---|--|--|--|--|
| Subject group type                                  | Subject analysis set                   | Subject analysis set                     | Subject analysis set                     |  |
| Number of subjects analysed                         | 10                                     | 89                                       | 7  |  |
| Units: nM   |  |  |  |  |
| geometric mean (geometric coefficient of variation) | 27.1 (± 92.9)                          | 39.1 (± 82.5)                            | 63.7 (± 163)                             |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Cl/F Analysis of INCB0557643

|                 |                              |
|-----------------|------------------------------|
| End point title | Cl/F Analysis of INCB0557643 |
|-----------------|------------------------------|

End point description:

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

End point timeframe:

Predose, 0.5, 1, 2, 4, 6, 8 hours of C1D8

| End point values                                    | Part 1 and 2 :<br>8mg QD<br>INCB057643 | Part 1 and 2 :<br>12 mg QD<br>INCB057643 | Part 1 and 2 :<br>16 mg QD<br>INCB057643 |  |
|---|--|--|--|--|
| Subject group type                                  | Subject analysis set                   | Subject analysis set                     | Subject analysis set                     |  |
| Number of subjects analysed                         | 10                                     | 89                                       | 7  |  |
| Units: Liters/Hour                                  |  |  |  |  |
| geometric mean (geometric coefficient of variation) | 9.92 (± 45.1)                          | 10.5 (± 43.2)                            | 10.7 (± 71.9)                            |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Objective Response Rate (ORR) With INCB057643 in Lymphoma

|                 |   |
|-----------------|---|
| End point title | Objective Response Rate (ORR) With INCB057643 in Lymphoma <sup>[12]</sup> |
|-----------------|---|

End point description:

Objective response rate is defined as the proportion of subjects who have an objective response using the applicable disease assessment criteria.

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

End point timeframe:

Efficacy measures from screening through end of treatment and follow-up (every 9 weeks), up to approximately 24 months

Notes:

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

Justification: ORR is summarized by tumor type.

| End point values            | Part1/Treatment Group A :<br>8mg QD<br>INCB057643 | Part1/Treatment Group A :<br>12mg QD<br>INCB057643 | Part1/Treatment Group A :<br>16mg QD<br>INCB057643 | Part2/Treatment Group A :<br>12 mg<br>INCB057643<br>Expansion<br>Cohort |
|-----------------------------|---|--|--|---|
| Subject group type          | Reporting group                                   | Reporting group                                    | Reporting group                                    | Reporting group   |
| Number of subjects analysed | 1 <sup>[13]</sup>                                 | 1 <sup>[14]</sup>                                  | 2 <sup>[15]</sup>                                  | 16 <sup>[16]</sup>  |
| Units: Subjects             | 1   | 0  | 1  | 2   |

Notes:

[13] - Efficacy Evaluable Population

[14] - Efficacy Evaluable Population

[15] - Efficacy Evaluable Population

[16] - Efficacy Evaluable Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Objective Response Rate (ORR) With INCB057643 in Acute Myeloid

## Leukemia

|                 |   |
|-----------------|---|
| End point title | Objective Response Rate (ORR) With INCB057643 in Acute Myeloid Leukemia <sup>[17]</sup> |
|-----------------|---|

### End point description:

Objective response rate is defined as the proportion of subjects who have an objective response using the applicable disease assessment criteria.

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

### End point timeframe:

Efficacy measures from screening through end of treatment and follow-up (every 9 weeks), up to approximately 24 months

### Notes:

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

Justification: ORR is summarized by tumor type.

| End point values            | Part1/Treatment Group B : 8mg QD INCB057643 | Part1/Treatment Group B : 12mg QD INCB057643 | Part2/Treatment Group B : 12 mg INCB057643 Expansion Cohort | Part3/Treatment Group F : 8 mg INCB057643 + Azacitidine 75mg |
|-----------------------------|---|--|---|--|
| Subject group type          | Reporting group                             | Reporting group                              | Reporting group   | Reporting group  |
| Number of subjects analysed | 5 <sup>[18]</sup>                           | 2 <sup>[19]</sup>                            | 3 <sup>[20]</sup>   | 2 <sup>[21]</sup>  |
| Units: Subjects             | 0   | 0  | 1   | 0  |

### Notes:

[18] - Efficacy Evaluable Subjects

[19] - Efficacy Evaluable Subjects

[20] - Efficacy Evaluable Subjects

[21] - Efficacy Evaluable Subjects

## Statistical analyses

No statistical analyses for this end point

## Secondary: Objective Response Rate (ORR) With INCB057643 in Glioblastoma

|                 |   |
|-----------------|---|
| End point title | Objective Response Rate (ORR) With INCB057643 in Glioblastoma <sup>[22]</sup> |
|-----------------|---|

### End point description:

Objective response rate is defined as the proportion of subjects who have an objective response using the applicable disease assessment criteria.

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

### End point timeframe:

Efficacy measures from screening through end of treatment and follow-up (every 9 weeks), up to approximately 24 months

### Notes:

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

Justification: ORR is summarized by tumor type.

|                             |   |  |  |  |
|-----------------------------|---|--|--|--|
| <b>End point values</b>     | Part2/Treatment Group A :<br>12 mg<br>INCB057643<br>Expansion<br>Cohort |  |  |  |
| Subject group type          | Reporting group   |  |  |  |
| Number of subjects analysed | 7 <sup>[23]</sup>   |  |  |  |
| Units: Subjects             | 0   |  |  |  |

Notes:

[23] - Efficacy Evaluable Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Objective Response Rate (ORR) With INCB057643 in Myelodysplastic Syndrome

|                 |   |
|-----------------|---|
| End point title | Objective Response Rate (ORR) With INCB057643 in Myelodysplastic Syndrome <sup>[24]</sup> |
|-----------------|---|

End point description:

Objective response rate is defined as the proportion of subjects who have an objective response using the applicable disease assessment criteria.

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

End point timeframe:

Efficacy measures from screening through end of treatment and follow-up (every 9 weeks), up to approximately 24 months

Notes:

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

Justification: ORR is summarized by tumor type.

|                             |   |  |   |  |
|-----------------------------|---|--|---|--|
| <b>End point values</b>     | Part1/Treatment Group B :<br>8mg QD<br>INCB057643 | Part1/Treatment Group B :<br>12mg QD<br>INCB057643 | Part2/Treatment Group B :<br>12 mg<br>INCB057643<br>Expansion<br>Cohort |  |
| Subject group type          | Reporting group                                   | Reporting group                                    | Reporting group   |  |
| Number of subjects analysed | 1 <sup>[25]</sup>                                 | 3 <sup>[26]</sup>                                  | 1 <sup>[27]</sup>   |  |
| Units: Subjects             | 0   | 0  | 0   |  |

Notes:

[25] - Efficacy Evaluable Subjects

[26] - Efficacy Evaluable Subjects

[27] - Efficacy Evaluable Subjects

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From screening through at least 30 days after end of treatment, up to approximately 24 months

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

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 19 |
|--------------------|----|

### Reporting groups

|                       |                |
|-----------------------|----------------|
| Reporting group title | PART1A 8 MG QD |
|-----------------------|----------------|

Reporting group description:

PART1A 8 MG QD

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | PART1A 12 MG QD |
|-----------------------|-----------------|

Reporting group description:

PART1A 12 MG QD

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | PART1A 16 MG QD |
|-----------------------|-----------------|

Reporting group description:

PART1A 16 MG QD

|                       |                |
|-----------------------|----------------|
| Reporting group title | PART1B 8 MG QD |
|-----------------------|----------------|

Reporting group description:

PART1B 8 MG QD

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | PART1B 12 MG QD |
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Reporting group description:

PART1B 12 MG QD

|                       |                |
|-----------------------|----------------|
| Reporting group title | PART1C 8 MG QD |
|-----------------------|----------------|

Reporting group description:

PART1C 8 MG QD

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | PART2A 12 MG QD |
|-----------------------|-----------------|

Reporting group description:

PART2A 12 MG QD

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | PART2B 12 MG QD |
|-----------------------|-----------------|

Reporting group description:

PART2B 12 MG QD

|                       |   |
|-----------------------|---|
| Reporting group title | PART3A 8 MG QD + Gemcitabine 1000 MG/M2 |
|-----------------------|---|

Reporting group description:

PART3A 8 MG QD + Gemcitabine 1000 MG/M2

|                       |                                |
|-----------------------|--------------------------------|
| Reporting group title | PART3B 8 MG QD + Paci 80 MG/M2 |
|-----------------------|--------------------------------|

Reporting group description:

PART3B 8 MG QD + Paci 80 MG/M2

|                       |                               |
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| Reporting group title | PART3C 8 MG QD + Rucap 600 MG |
|-----------------------|-------------------------------|

Reporting group description:

PART3C 8 MG QD + Rucap 600 MG

|                       |  |
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| Reporting group title | PART3D 8 MG QD + Arbir 1000 MG + Predni 5 MG |
|-----------------------|--|

Reporting group description:

PART3D 8 MG QD + Arbir 1000 MG + Predni 5 MG

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | PART3E 8 MG QD + Rux 20 MG |
|-----------------------|----------------------------|

Reporting group description:

PART3E 8 MG QD + Rux 20 MG

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | PART3F 8 MG QD + Azacitadine 75 MG/M2 |
|-----------------------|---------------------------------------|

| <b>Serious adverse events</b>                                       | <b>PART1A 8 MG QD</b> | <b>PART1A 12 MG QD</b> | <b>PART1A 16 MG QD</b> |
|---|-----------------------|------------------------|------------------------|
| Total subjects affected by serious adverse events                   |                       |                        |                        |
| subjects affected / exposed   | 2 / 4 (50.00%)        | 1 / 5 (20.00%)         | 5 / 8 (62.50%)         |
| number of deaths (all causes)                                       | 2                     | 4                      | 5                      |
| number of deaths resulting from adverse events                      | 0                     | 1                      | 1                      |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                       |                        |                        |
| Tumour pain   |                       |                        |                        |
| subjects affected / exposed   | 1 / 4 (25.00%)        | 0 / 5 (0.00%)          | 0 / 8 (0.00%)          |
| occurrences causally related to treatment / all                     | 0 / 2                 | 0 / 0                  | 0 / 0                  |
| deaths causally related to treatment / all                          | 0 / 0                 | 0 / 0                  | 0 / 0                  |
| General disorders and administration site conditions                |                       |                        |                        |
| Performance status decreased  |                       |                        |                        |
| subjects affected / exposed   | 1 / 4 (25.00%)        | 0 / 5 (0.00%)          | 0 / 8 (0.00%)          |
| occurrences causally related to treatment / all                     | 0 / 1                 | 0 / 0                  | 0 / 0                  |
| deaths causally related to treatment / all                          | 0 / 0                 | 0 / 0                  | 0 / 0                  |
| Respiratory, thoracic and mediastinal disorders                     |                       |                        |                        |
| Acute respiratory distress syndrome                                 |                       |                        |                        |
| subjects affected / exposed   | 0 / 4 (0.00%)         | 0 / 5 (0.00%)          | 0 / 8 (0.00%)          |
| occurrences causally related to treatment / all                     | 0 / 0                 | 0 / 0                  | 0 / 0                  |
| deaths causally related to treatment / all                          | 0 / 0                 | 0 / 0                  | 0 / 0                  |
| Dyspnoea  |                       |                        |                        |
| subjects affected / exposed   | 0 / 4 (0.00%)         | 0 / 5 (0.00%)          | 0 / 8 (0.00%)          |
| occurrences causally related to treatment / all                     | 0 / 0                 | 0 / 0                  | 0 / 0                  |
| deaths causally related to treatment / all                          | 0 / 0                 | 0 / 0                  | 0 / 0                  |
| Lung infiltration   |                       |                        |                        |
| subjects affected / exposed   | 0 / 4 (0.00%)         | 0 / 5 (0.00%)          | 0 / 8 (0.00%)          |
| occurrences causally related to treatment / all                     | 0 / 0                 | 0 / 0                  | 0 / 0                  |
| deaths causally related to treatment / all                          | 0 / 0                 | 0 / 0                  | 0 / 0                  |
| Pleural effusion  |                       |                        |                        |



|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 8 (12.50%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Pneumothorax spontaneous                        |               |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Pulmonary embolism                              |               |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Pulmonary oedema                                |               |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Respiratory failure                             |               |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Psychiatric disorders                           |               |               |                |
| Confusional state                               |               |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 8 (12.50%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Delirium  |               |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Investigations                                  |               |               |                |
| International normalised ratio increased        |               |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 8 (12.50%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |

|   |               |               |                |
|---|---------------|---------------|----------------|
| Cardiac disorders                               |               |               |                |
| Atrial fibrillation                             |               |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Tachycardia                                     |               |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Nervous system disorders                        |               |               |                |
| Syncope   |               |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 8 (12.50%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Blood and lymphatic system disorders            |               |               |                |
| Anaemia   |               |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Febrile neutropenia                             |               |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Thrombocytopenia                                |               |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Gastrointestinal disorders                      |               |               |                |
| Abdominal pain upper                            |               |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 8 (12.50%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Periodontal disease                             |               |               |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Small intestinal obstruction                    |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                         |               |                |                |
| Hepatic failure                                 |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 1          | 0 / 0          |
| Renal and urinary disorders                     |               |                |                |
| Acute kidney injury                             |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| End stage renal disease                         |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Nephrolithiasis                                 |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Infections and infestations                     |               |                |                |
| Herpes zoster                                   |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Lung infection                                  |               |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |

|   |                |               |                |
|---|----------------|---------------|----------------|
| Pneumonia                                       |                |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 1 / 8 (12.50%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 1          |
| Pneumonia bacterial                             |                |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Pneumonia respiratory syncytial viral           |                |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Sepsis  |                |               |                |
| subjects affected / exposed                     | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Metabolism and nutrition disorders              |                |               |                |
| Dehydration                                     |                |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Hyperglycaemia                                  |                |               |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |

| <b>Serious adverse events</b>                                       | PART1B 8 MG QD | PART1B 12 MG QD | PART1C 8 MG QD  |
|---|----------------|-----------------|-----------------|
| Total subjects affected by serious adverse events                   |                |                 |                 |
| subjects affected / exposed   | 5 / 7 (71.43%) | 4 / 5 (80.00%)  | 1 / 1 (100.00%) |
| number of deaths (all causes)                                       | 6              | 4               | 1               |
| number of deaths resulting from adverse events                      | 3              | 0               | 1               |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |                 |                 |
| Tumour pain   |                |                 |                 |

|  |                |               |               |
|--|----------------|---------------|---------------|
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 5 (0.00%) | 0 / 1 (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         |
| General disorders and administration site conditions |                |               |               |
| Performance status decreased                         |                |               |               |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 5 (0.00%) | 0 / 1 (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      |                |               |               |
| Acute respiratory distress syndrome                  |                |               |               |
| subjects affected / exposed                          | 1 / 7 (14.29%) | 0 / 5 (0.00%) | 0 / 1 (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         |
| Dyspnoea   |                |               |               |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 5 (0.00%) | 0 / 1 (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         |
| Lung infiltration                                    |                |               |               |
| subjects affected / exposed                          | 1 / 7 (14.29%) | 0 / 5 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0         |
| Pleural effusion                                     |                |               |               |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 5 (0.00%) | 0 / 1 (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         |
| Pneumothorax spontaneous                             |                |               |               |
| subjects affected / exposed                          | 1 / 7 (14.29%) | 0 / 5 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0         |
| Pulmonary embolism                                   |                |               |               |
| subjects affected / exposed                          | 1 / 7 (14.29%) | 0 / 5 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0         |

|   |                |                |               |
|---|----------------|----------------|---------------|
| Pulmonary oedema                                |                |                |               |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (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         |
| Respiratory failure                             |                |                |               |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Psychiatric disorders                           |                |                |               |
| Confusional state                               |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (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         |
| Delirium  |                |                |               |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (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         |
| Investigations                                  |                |                |               |
| International normalised ratio increased        |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Cardiac disorders                               |                |                |               |
| Atrial fibrillation                             |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Tachycardia                                     |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (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                        |                |                |               |
| Syncope   |                |                |               |

|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (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>Blood and lymphatic system disorders</b>     |                |                |               |
| Anaemia   |                |                |               |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 1 / 1          | 0 / 0          | 0 / 0         |
| Febrile neutropenia                             |                |                |               |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 2 / 5 (40.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 2          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Thrombocytopenia                                |                |                |               |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 1 / 1          | 0 / 0          | 0 / 0         |
| <b>Gastrointestinal disorders</b>               |                |                |               |
| Abdominal pain upper                            |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (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         |
| Periodontal disease                             |                |                |               |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Small intestinal obstruction                    |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (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>Hepatobiliary disorders</b>                  |                |                |               |
| Hepatic failure                                 |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (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                     | 2 / 7 (28.57%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0         |
| End stage renal disease                         |                |                |               |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Nephrolithiasis                                 |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (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                     |                |                |               |
| Herpes zoster                                   |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (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         |
| Lung infection                                  |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Pneumonia                                       |                |                |               |
| subjects affected / exposed                     | 2 / 7 (28.57%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Pneumonia bacterial                             |                |                |               |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (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         |
| Pneumonia respiratory syncytial viral           |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (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                     | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (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         |
| Metabolism and nutrition disorders              |                |                |               |
| Dehydration                                     |                |                |               |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Hyperglycaemia                                  |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |

| <b>Serious adverse events</b>                                       | PART2A 12 MG QD  | PART2B 12 MG QD | PART3A 8 MG QD +<br>Gemcitabine 1000<br>MG/M2 |
|---|------------------|-----------------|---|
| Total subjects affected by serious adverse events                   |                  |                 |   |
| subjects affected / exposed   | 32 / 86 (37.21%) | 4 / 5 (80.00%)  | 0 / 1 (0.00%)                                 |
| number of deaths (all causes)                                       | 68               | 3               | 0   |
| number of deaths resulting from adverse events                      | 12               | 1               | 0   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                  |                 |   |
| Tumour pain   |                  |                 |   |
| subjects affected / exposed   | 0 / 86 (0.00%)   | 0 / 5 (0.00%)   | 0 / 1 (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   |
| General disorders and administration site conditions                |                  |                 |   |
| Performance status decreased  |                  |                 |   |
| subjects affected / exposed   | 0 / 86 (0.00%)   | 0 / 5 (0.00%)   | 0 / 1 (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                     |                  |                 |   |
| Acute respiratory distress syndrome                                 |                  |                 |   |
| subjects affected / exposed   | 0 / 86 (0.00%)   | 0 / 5 (0.00%)   | 0 / 1 (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   |

|   |                |                |               |
|---|----------------|----------------|---------------|
| Dyspnoea  |                |                |               |
| subjects affected / exposed                     | 2 / 86 (2.33%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Lung infiltration                               |                |                |               |
| subjects affected / exposed                     | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (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         |
| Pleural effusion                                |                |                |               |
| subjects affected / exposed                     | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (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         |
| Pneumothorax spontaneous                        |                |                |               |
| subjects affected / exposed                     | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Pulmonary embolism                              |                |                |               |
| subjects affected / exposed                     | 2 / 86 (2.33%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Pulmonary oedema                                |                |                |               |
| subjects affected / exposed                     | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Respiratory failure                             |                |                |               |
| subjects affected / exposed                     | 4 / 86 (4.65%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 4          | 0 / 1          | 0 / 0         |
| Psychiatric disorders                           |                |                |               |
| Confusional state                               |                |                |               |
| subjects affected / exposed                     | 1 / 86 (1.16%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Delirium  |                |                |               |

|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (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                                  |                |                |               |
| International normalised ratio increased        |                |                |               |
| subjects affected / exposed                     | 1 / 86 (1.16%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Cardiac disorders                               |                |                |               |
| Atrial fibrillation                             |                |                |               |
| subjects affected / exposed                     | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (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         |
| Tachycardia                                     |                |                |               |
| subjects affected / exposed                     | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (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                        |                |                |               |
| Syncope   |                |                |               |
| subjects affected / exposed                     | 1 / 86 (1.16%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Blood and lymphatic system disorders            |                |                |               |
| Anaemia   |                |                |               |
| subjects affected / exposed                     | 2 / 86 (2.33%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0         |
| Febrile neutropenia                             |                |                |               |
| subjects affected / exposed                     | 0 / 86 (0.00%) | 2 / 5 (40.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 4          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Thrombocytopenia                                |                |                |               |

|   |                |               |               |
|---|----------------|---------------|---------------|
| subjects affected / exposed                     | 1 / 86 (1.16%) | 0 / 5 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| <b>Gastrointestinal disorders</b>               |                |               |               |
| Abdominal pain upper                            |                |               |               |
| subjects affected / exposed                     | 1 / 86 (1.16%) | 0 / 5 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Periodontal disease                             |                |               |               |
| subjects affected / exposed                     | 0 / 86 (0.00%) | 0 / 5 (0.00%) | 0 / 1 (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                     | 1 / 86 (1.16%) | 0 / 5 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| <b>Hepatobiliary disorders</b>                  |                |               |               |
| Hepatic failure                                 |                |               |               |
| subjects affected / exposed                     | 2 / 86 (2.33%) | 0 / 5 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0         | 0 / 0         |
| <b>Renal and urinary disorders</b>              |                |               |               |
| Acute kidney injury                             |                |               |               |
| subjects affected / exposed                     | 1 / 86 (1.16%) | 0 / 5 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| End stage renal disease                         |                |               |               |
| subjects affected / exposed                     | 0 / 86 (0.00%) | 0 / 5 (0.00%) | 0 / 1 (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         |
| Nephrolithiasis                                 |                |               |               |
| subjects affected / exposed                     | 0 / 86 (0.00%) | 0 / 5 (0.00%) | 0 / 1 (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<br>Herpes zoster<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all      | 0 / 86 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 5 (0.00%)<br>0 / 0<br>0 / 0  | 0 / 1 (0.00%)<br>0 / 0<br>0 / 0 |
| Lung infection<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                                    | 0 / 86 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 5 (0.00%)<br>0 / 0<br>0 / 0  | 0 / 1 (0.00%)<br>0 / 0<br>0 / 0 |
| Pneumonia<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all   | 1 / 86 (1.16%)<br>0 / 1<br>0 / 0 | 1 / 5 (20.00%)<br>0 / 1<br>0 / 0 | 0 / 1 (0.00%)<br>0 / 0<br>0 / 0 |
| Pneumonia bacterial<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                               | 0 / 86 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 5 (0.00%)<br>0 / 0<br>0 / 0  | 0 / 1 (0.00%)<br>0 / 0<br>0 / 0 |
| Pneumonia respiratory syncytial viral<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all             | 0 / 86 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 5 (20.00%)<br>0 / 1<br>0 / 0 | 0 / 1 (0.00%)<br>0 / 0<br>0 / 0 |
| Sepsis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all  | 4 / 86 (4.65%)<br>0 / 4<br>0 / 3 | 1 / 5 (20.00%)<br>0 / 1<br>0 / 0 | 0 / 1 (0.00%)<br>0 / 0<br>0 / 0 |
| Metabolism and nutrition disorders<br>Dehydration<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all | 2 / 86 (2.33%)<br>0 / 2<br>0 / 0 | 0 / 5 (0.00%)<br>0 / 0<br>0 / 0  | 0 / 1 (0.00%)<br>0 / 0<br>0 / 0 |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                                    | 0 / 86 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 5 (0.00%)<br>0 / 0<br>0 / 0  | 0 / 1 (0.00%)<br>0 / 0<br>0 / 0 |

| <b>Serious adverse events</b>                                       | <b>PART3B 8 MG QD +<br/>Paci 80 MG/M2</b> | <b>PART3C 8 MG QD +<br/>Rucap 600 MG</b> | <b>PART3D 8 MG QD +<br/>Arbir 1000 MG +<br/>Predni 5 MG</b> |
|---|---|--|---|
| Total subjects affected by serious adverse events                   |   |  |   |
| subjects affected / exposed   | 0 / 2 (0.00%)                             | 0 / 4 (0.00%)                            | 1 / 3 (33.33%)  |
| number of deaths (all causes)                                       | 1   | 1  | 1   |
| number of deaths resulting from adverse events                      | 0   | 0  | 0   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |  |   |
| Tumour pain   |   |  |   |
| subjects affected / exposed   | 0 / 2 (0.00%)                             | 0 / 4 (0.00%)                            | 0 / 3 (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   |
| General disorders and administration site conditions                |   |  |   |
| Performance status decreased  |   |  |   |
| subjects affected / exposed   | 0 / 2 (0.00%)                             | 0 / 4 (0.00%)                            | 0 / 3 (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                     |   |  |   |
| Acute respiratory distress syndrome                                 |   |  |   |
| subjects affected / exposed   | 0 / 2 (0.00%)                             | 0 / 4 (0.00%)                            | 0 / 3 (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   |
| Dyspnoea  |   |  |   |
| subjects affected / exposed   | 0 / 2 (0.00%)                             | 0 / 4 (0.00%)                            | 1 / 3 (33.33%)  |
| occurrences causally related to treatment / all                     | 0 / 0                                     | 0 / 0                                    | 0 / 1   |
| deaths causally related to treatment / all                          | 0 / 0                                     | 0 / 0                                    | 0 / 0   |
| Lung infiltration   |   |  |   |
| subjects affected / exposed   | 0 / 2 (0.00%)                             | 0 / 4 (0.00%)                            | 0 / 3 (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   |
| Pleural effusion  |   |  |   |
| subjects affected / exposed   | 0 / 2 (0.00%)                             | 0 / 4 (0.00%)                            | 1 / 3 (33.33%)  |
| occurrences causally related to treatment / all                     | 0 / 0                                     | 0 / 0                                    | 0 / 1   |
| deaths causally related to treatment / all                          | 0 / 0                                     | 0 / 0                                    | 0 / 0   |
| Pneumothorax spontaneous  |   |  |   |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pulmonary embolism                              |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pulmonary oedema                                |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Respiratory failure                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (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 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (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         |
| Delirium  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (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                                  |               |               |               |
| International normalised ratio increased        |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cardiac disorders                               |               |               |               |
| Atrial fibrillation                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (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         |

|   |               |               |                |
|---|---------------|---------------|----------------|
| Tachycardia                                     |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Nervous system disorders                        |               |               |                |
| Syncope   |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (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 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Febrile neutropenia                             |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (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 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (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 upper                            |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (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          |
| Periodontal disease                             |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (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 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Hepatobiliary disorders                         |               |               |                |
| Hepatic failure                                 |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (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 / 2 (0.00%) | 0 / 4 (0.00%) | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| End stage renal disease                         |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (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          |
| Nephrolithiasis                                 |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (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                     |               |               |                |
| Herpes zoster                                   |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (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          |
| Lung infection                                  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (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 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (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                     | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (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 respiratory syncytial viral           |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (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 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Metabolism and nutrition disorders              |               |               |               |
| Dehydration                                     |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (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         |
| Hyperglycaemia                                  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (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>                                       | PART3E 8 MG QD +<br>Rux 20 MG | PART3F 8 MG QD +<br>Azacitadine 75<br>MG/M2 |  |
|---|-------------------------------|---|--|
| Total subjects affected by serious adverse events                   |                               |   |  |
| subjects affected / exposed   | 1 / 1 (100.00%)               | 0 / 2 (0.00%)                               |  |
| number of deaths (all causes)                                       | 0                             | 0   |  |
| number of deaths resulting from adverse events                      | 0                             | 0   |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                               |   |  |
| Tumour pain   |                               |   |  |
| subjects affected / exposed   | 0 / 1 (0.00%)                 | 0 / 2 (0.00%)                               |  |
| occurrences causally related to treatment / all                     | 0 / 0                         | 0 / 0                                       |  |
| deaths causally related to treatment / all                          | 0 / 0                         | 0 / 0                                       |  |
| General disorders and administration site conditions                |                               |   |  |
| Performance status decreased  |                               |   |  |

|   |               |               |  |
|---|---------------|---------------|--|
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Respiratory, thoracic and mediastinal disorders |               |               |  |
| Acute respiratory distress syndrome             |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Dyspnoea  |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Lung infiltration                               |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Pleural effusion                                |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Pneumothorax spontaneous                        |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Pulmonary embolism                              |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Pulmonary oedema                                |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Respiratory failure                             |               |               |  |

|   |               |               |  |
|---|---------------|---------------|--|
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Psychiatric disorders                           |               |               |  |
| Confusional state                               |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Delirium  |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Investigations                                  |               |               |  |
| International normalised ratio increased        |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Cardiac disorders                               |               |               |  |
| Atrial fibrillation                             |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Tachycardia                                     |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Nervous system disorders                        |               |               |  |
| Syncope   |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Blood and lymphatic system disorders            |               |               |  |
| Anaemia   |               |               |  |

|   |               |               |  |
|---|---------------|---------------|--|
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Febrile neutropenia                             |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Thrombocytopenia                                |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Gastrointestinal disorders                      |               |               |  |
| Abdominal pain upper                            |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Periodontal disease                             |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Small intestinal obstruction                    |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (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                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Renal and urinary disorders                     |               |               |  |
| Acute kidney injury                             |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |

|   |                 |               |  |
|---|-----------------|---------------|--|
| End stage renal disease                         |                 |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Nephrolithiasis                                 |                 |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Infections and infestations                     |                 |               |  |
| Herpes zoster                                   |                 |               |  |
| subjects affected / exposed                     | 1 / 1 (100.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Lung infection                                  |                 |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Pneumonia                                       |                 |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Pneumonia bacterial                             |                 |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Pneumonia respiratory syncytial viral           |                 |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Sepsis  |                 |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Metabolism and nutrition disorders              |                 |               |  |

|   |               |               |  |
|---|---------------|---------------|--|
| Dehydration                                     |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Hyperglycaemia                                  |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| 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>                                   | PART1A 8 MG QD  | PART1A 12 MG QD | PART1A 16 MG QD |
|---|-----------------|-----------------|-----------------|
| Total subjects affected by non-serious adverse events               |                 |                 |                 |
| subjects affected / exposed   | 4 / 4 (100.00%) | 5 / 5 (100.00%) | 7 / 8 (87.50%)  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |                 |                 |
| Basal cell carcinoma  |                 |                 |                 |
| subjects affected / exposed   | 0 / 4 (0.00%)   | 0 / 5 (0.00%)   | 0 / 8 (0.00%)   |
| occurrences (all)   | 0               | 0               | 0               |
| Benign neoplasm   |                 |                 |                 |
| subjects affected / exposed   | 0 / 4 (0.00%)   | 0 / 5 (0.00%)   | 0 / 8 (0.00%)   |
| occurrences (all)   | 0               | 0               | 0               |
| Squamous cell carcinoma of skin                                     |                 |                 |                 |
| subjects affected / exposed   | 0 / 4 (0.00%)   | 0 / 5 (0.00%)   | 0 / 8 (0.00%)   |
| occurrences (all)   | 0               | 0               | 0               |
| Vascular disorders  |                 |                 |                 |
| Haematoma   |                 |                 |                 |
| subjects affected / exposed   | 0 / 4 (0.00%)   | 0 / 5 (0.00%)   | 1 / 8 (12.50%)  |
| occurrences (all)   | 0               | 0               | 1               |
| Hot flush   |                 |                 |                 |
| subjects affected / exposed   | 0 / 4 (0.00%)   | 0 / 5 (0.00%)   | 1 / 8 (12.50%)  |
| occurrences (all)   | 0               | 0               | 1               |
| Hypertension  |                 |                 |                 |
| subjects affected / exposed   | 0 / 4 (0.00%)   | 1 / 5 (20.00%)  | 2 / 8 (25.00%)  |
| occurrences (all)   | 0               | 1               | 2               |
| Hypotension   |                 |                 |                 |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0              |
| General disorders and administration site conditions |                |                |                |
| Asthenia   |                |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                                    | 0              | 0              | 1              |
| Catheter site erythema                               |                |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                                    | 0              | 0              | 1              |
| Catheter site haemorrhage                            |                |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0              |
| Catheter site pain                                   |                |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0              |
| Chills   |                |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                                    | 0              | 0              | 1              |
| Drug withdrawal syndrome                             |                |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 1 / 5 (20.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                                    | 0              | 1              | 0              |
| Fatigue  |                |                |                |
| subjects affected / exposed                          | 2 / 4 (50.00%) | 4 / 5 (80.00%) | 4 / 8 (50.00%) |
| occurrences (all)                                    | 2              | 4              | 4              |
| Influenza like illness                               |                |                |                |
| subjects affected / exposed                          | 1 / 4 (25.00%) | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                                    | 1              | 0              | 1              |
| Localised oedema                                     |                |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0              |
| Mucosal dryness                                      |                |                |                |
| subjects affected / exposed                          | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                                    | 0              | 0              | 0              |
| Mucosal haemorrhage                                  |                |                |                |



|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Non-cardiac chest pain                          |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Oedema peripheral                               |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Performance status decreased                    |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Pyrexia   |                |                |                |
| subjects affected / exposed                     | 1 / 4 (25.00%) | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 2              | 0              | 0              |
| Reproductive system and breast disorders        |                |                |                |
| Penile oedema                                   |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Vulvovaginal erythema                           |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Chronic obstructive pulmonary disease           |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Cough   |                |                |                |
| subjects affected / exposed                     | 1 / 4 (25.00%) | 1 / 5 (20.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                               | 1              | 1              | 0              |
| Dyspnoea  |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 1 / 5 (20.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0              |
| Dyspnoea exertional                             |                |                |                |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Epistaxis                                       |                |                |                |

|                             |                |               |                |
|-----------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Haemoptysis                 |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Hypoxia                     |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all)           | 0              | 0             | 1              |
| Nasal congestion            |                |               |                |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 1              | 0             | 0              |
| Oropharyngeal pain          |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Pleural effusion            |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Pneumonitis                 |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Productive cough            |                |               |                |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 1              | 0             | 0              |
| Pulmonary oedema            |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Respiratory failure         |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Sneezing                    |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all)           | 0              | 0             | 1              |
| Upper-airway cough syndrome |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all)           | 0              | 0             | 1              |
| Wheezing                    |                |               |                |

|  |                    |                    |                    |
|--|--------------------|--------------------|--------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0 |
| Psychiatric disorders                            |                    |                    |                    |
| Agitation  |                    |                    |                    |
| subjects affected / exposed                      | 0 / 4 (0.00%)      | 0 / 5 (0.00%)      | 0 / 8 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Anxiety  |                    |                    |                    |
| subjects affected / exposed                      | 1 / 4 (25.00%)     | 0 / 5 (0.00%)      | 0 / 8 (0.00%)      |
| occurrences (all)                                | 1                  | 0                  | 0                  |
| Depression                                       |                    |                    |                    |
| subjects affected / exposed                      | 2 / 4 (50.00%)     | 0 / 5 (0.00%)      | 0 / 8 (0.00%)      |
| occurrences (all)                                | 2                  | 0                  | 0                  |
| Insomnia   |                    |                    |                    |
| subjects affected / exposed                      | 0 / 4 (0.00%)      | 0 / 5 (0.00%)      | 0 / 8 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Investigations                                   |                    |                    |                    |
| Activated partial thromboplastin time prolonged  |                    |                    |                    |
| subjects affected / exposed                      | 0 / 4 (0.00%)      | 0 / 5 (0.00%)      | 0 / 8 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Alanine aminotransferase increased               |                    |                    |                    |
| subjects affected / exposed                      | 0 / 4 (0.00%)      | 0 / 5 (0.00%)      | 1 / 8 (12.50%)     |
| occurrences (all)                                | 0                  | 0                  | 1                  |
| Aspartate aminotransferase increased             |                    |                    |                    |
| subjects affected / exposed                      | 0 / 4 (0.00%)      | 0 / 5 (0.00%)      | 1 / 8 (12.50%)     |
| occurrences (all)                                | 0                  | 0                  | 1                  |
| Bilirubin conjugated increased                   |                    |                    |                    |
| subjects affected / exposed                      | 0 / 4 (0.00%)      | 0 / 5 (0.00%)      | 1 / 8 (12.50%)     |
| occurrences (all)                                | 0                  | 0                  | 1                  |
| Blood alkaline phosphatase increased             |                    |                    |                    |
| subjects affected / exposed                      | 0 / 4 (0.00%)      | 0 / 5 (0.00%)      | 0 / 8 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Blood bilirubin increased                        |                    |                    |                    |
| subjects affected / exposed                      | 0 / 4 (0.00%)      | 0 / 5 (0.00%)      | 1 / 8 (12.50%)     |
| occurrences (all)                                | 0                  | 0                  | 3                  |
| Blood creatinine increased                       |                    |                    |                    |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                    | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Blood pressure increased                       |                |                |                |
| subjects affected / exposed                    | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| International normalised ratio increased       |                |                |                |
| subjects affected / exposed                    | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                              | 0              | 0              | 1              |
| Neutrophil count decreased                     |                |                |                |
| subjects affected / exposed                    | 0 / 4 (0.00%)  | 1 / 5 (20.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                              | 0              | 2              | 0              |
| Platelet count decreased                       |                |                |                |
| subjects affected / exposed                    | 1 / 4 (25.00%) | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                              | 1              | 0              | 0              |
| Prothrombin time prolonged                     |                |                |                |
| subjects affected / exposed                    | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Troponin I increased                           |                |                |                |
| subjects affected / exposed                    | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Troponin increased                             |                |                |                |
| subjects affected / exposed                    | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Weight decreased                               |                |                |                |
| subjects affected / exposed                    | 2 / 4 (50.00%) | 1 / 5 (20.00%) | 1 / 8 (12.50%) |
| occurrences (all)                              | 2              | 1              | 3              |
| Weight increased                               |                |                |                |
| subjects affected / exposed                    | 1 / 4 (25.00%) | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                              | 1              | 0              | 0              |
| White blood cell count decreased               |                |                |                |
| subjects affected / exposed                    | 0 / 4 (0.00%)  | 1 / 5 (20.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                              | 0              | 3              | 0              |
| Injury, poisoning and procedural complications |                |                |                |

|                                      |                |               |                |
|--------------------------------------|----------------|---------------|----------------|
| Arthropod bite                       |                |               |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Contusion                            |                |               |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all)                    | 0              | 0             | 1              |
| Eye contusion                        |                |               |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Fall                                 |                |               |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all)                    | 0              | 0             | 1              |
| Fractured sacrum                     |                |               |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Infusion related reaction            |                |               |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Laceration                           |                |               |                |
| subjects affected / exposed          | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                    | 1              | 0             | 0              |
| Transfusion reaction                 |                |               |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Cardiac disorders                    |                |               |                |
| Atrial fibrillation                  |                |               |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Atrioventricular block second degree |                |               |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Sinus bradycardia                    |                |               |                |
| subjects affected / exposed          | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Sinus tachycardia                    |                |               |                |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Tachycardia<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 4 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Ventricular arrhythmia<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 4 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 | 0 / 8 (0.00%)<br>0  |
| Nervous system disorders<br>Brain oedema<br>subjects affected / exposed<br>occurrences (all)        | 0 / 4 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)                                       | 1 / 4 (25.00%)<br>1 | 1 / 5 (20.00%)<br>1 | 1 / 8 (12.50%)<br>1 |
| Dysgeusia<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 4 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 | 2 / 8 (25.00%)<br>2 |
| Headache<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 1 / 8 (12.50%)<br>3 |
| Neuropathy peripheral<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 4 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Post herpetic neuralgia<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 4 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Syncope<br>subjects affected / exposed<br>occurrences (all)   | 0 / 4 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0  | 1 / 5 (20.00%)<br>2 | 3 / 8 (37.50%)<br>3 |
| Febrile neutropenia   |                     |                     |                     |

|                              |               |               |                |
|------------------------------|---------------|---------------|----------------|
| subjects affected / exposed  | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)            | 0             | 0             | 0              |
| Increased tendency to bruise |               |               |                |
| subjects affected / exposed  | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)            | 0             | 0             | 0              |
| Iron deficiency anaemia      |               |               |                |
| subjects affected / exposed  | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all)            | 0             | 0             | 1              |
| Leukocytosis                 |               |               |                |
| subjects affected / exposed  | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)            | 0             | 0             | 0              |
| Leukopenia                   |               |               |                |
| subjects affected / exposed  | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)            | 0             | 0             | 0              |
| Lymph node pain              |               |               |                |
| subjects affected / exposed  | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)            | 0             | 0             | 0              |
| Lymphopenia                  |               |               |                |
| subjects affected / exposed  | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)            | 0             | 0             | 0              |
| Neutropenia                  |               |               |                |
| subjects affected / exposed  | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)            | 0             | 0             | 0              |
| Splenic infarction           |               |               |                |
| subjects affected / exposed  | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)            | 0             | 0             | 0              |
| Splenomegaly                 |               |               |                |
| subjects affected / exposed  | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)            | 0             | 0             | 0              |
| Thrombocytopenia             |               |               |                |
| subjects affected / exposed  | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 3 / 8 (37.50%) |
| occurrences (all)            | 0             | 0             | 6              |
| Ear and labyrinth disorders  |               |               |                |
| Vertigo                      |               |               |                |
| subjects affected / exposed  | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)            | 0             | 0             | 0              |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Eye disorders               |                |                |                |
| Cataract                    |                |                |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)           | 0              | 0              | 1              |
| Eye pain                    |                |                |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)           | 0              | 0              | 1              |
| Eyelid oedema               |                |                |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Retinal haemorrhage         |                |                |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Vitreous floaters           |                |                |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Gastrointestinal disorders  |                |                |                |
| Abdominal distension        |                |                |                |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Abdominal pain              |                |                |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 2 / 5 (40.00%) | 2 / 8 (25.00%) |
| occurrences (all)           | 0              | 2              | 2              |
| Abdominal pain upper        |                |                |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Anal fissure                |                |                |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Constipation                |                |                |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 2 / 5 (40.00%) | 1 / 8 (12.50%) |
| occurrences (all)           | 0              | 2              | 1              |
| Diarrhoea                   |                |                |                |
| subjects affected / exposed | 1 / 4 (25.00%) | 2 / 5 (40.00%) | 3 / 8 (37.50%) |
| occurrences (all)           | 1              | 2              | 3              |
| Dry mouth                   |                |                |                |



|                                  |                |                |                |
|----------------------------------|----------------|----------------|----------------|
| subjects affected / exposed      | 1 / 4 (25.00%) | 1 / 5 (20.00%) | 1 / 8 (12.50%) |
| occurrences (all)                | 1              | 1              | 1              |
| Dyspepsia                        |                |                |                |
| subjects affected / exposed      | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                | 0              | 0              | 1              |
| Flatulence                       |                |                |                |
| subjects affected / exposed      | 1 / 4 (25.00%) | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                | 1              | 0              | 0              |
| Gastrooesophageal reflux disease |                |                |                |
| subjects affected / exposed      | 1 / 4 (25.00%) | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                | 1              | 0              | 0              |
| Haemorrhoids                     |                |                |                |
| subjects affected / exposed      | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0              |
| Lip haemorrhage                  |                |                |                |
| subjects affected / exposed      | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0              |
| Nausea                           |                |                |                |
| subjects affected / exposed      | 3 / 4 (75.00%) | 4 / 5 (80.00%) | 4 / 8 (50.00%) |
| occurrences (all)                | 5              | 4              | 6              |
| Oesophageal haemorrhage          |                |                |                |
| subjects affected / exposed      | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0              |
| Oral pain                        |                |                |                |
| subjects affected / exposed      | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0              |
| Stomatitis                       |                |                |                |
| subjects affected / exposed      | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                | 0              | 0              | 1              |
| Vomiting                         |                |                |                |
| subjects affected / exposed      | 2 / 4 (50.00%) | 2 / 5 (40.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                | 2              | 2              | 0              |
| Hepatobiliary disorders          |                |                |                |
| Hyperbilirubinaemia              |                |                |                |
| subjects affected / exposed      | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0              |

|  |                |                |                |
|--|----------------|----------------|----------------|
| Skin and subcutaneous tissue disorders |                |                |                |
| Acne                                   |                |                |                |
| subjects affected / exposed            | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Alopecia                               |                |                |                |
| subjects affected / exposed            | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Angioedema                             |                |                |                |
| subjects affected / exposed            | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Dry skin                               |                |                |                |
| subjects affected / exposed            | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Erythema                               |                |                |                |
| subjects affected / exposed            | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Pain of skin                           |                |                |                |
| subjects affected / exposed            | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Petechiae                              |                |                |                |
| subjects affected / exposed            | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Pruritus                               |                |                |                |
| subjects affected / exposed            | 1 / 4 (25.00%) | 1 / 5 (20.00%) | 1 / 8 (12.50%) |
| occurrences (all)                      | 1              | 1              | 1              |
| Purpura                                |                |                |                |
| subjects affected / exposed            | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Rash                                   |                |                |                |
| subjects affected / exposed            | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Scab                                   |                |                |                |
| subjects affected / exposed            | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Skin ulcer                             |                |                |                |

|  |                     |                    |                    |
|--|---------------------|--------------------|--------------------|
| subjects affected / exposed<br>occurrences (all) | 1 / 4 (25.00%)<br>1 | 0 / 5 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0 |
| Renal and urinary disorders                      |                     |                    |                    |
| Acute kidney injury                              |                     |                    |                    |
| subjects affected / exposed                      | 0 / 4 (0.00%)       | 0 / 5 (0.00%)      | 1 / 8 (12.50%)     |
| occurrences (all)                                | 0                   | 0                  | 1                  |
| Dysuria  |                     |                    |                    |
| subjects affected / exposed                      | 0 / 4 (0.00%)       | 0 / 5 (0.00%)      | 0 / 8 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                  |
| Haematuria                                       |                     |                    |                    |
| subjects affected / exposed                      | 0 / 4 (0.00%)       | 0 / 5 (0.00%)      | 0 / 8 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                  |
| Urinary retention                                |                     |                    |                    |
| subjects affected / exposed                      | 0 / 4 (0.00%)       | 0 / 5 (0.00%)      | 0 / 8 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                  |
| Musculoskeletal and connective tissue disorders  |                     |                    |                    |
| Arthralgia                                       |                     |                    |                    |
| subjects affected / exposed                      | 0 / 4 (0.00%)       | 0 / 5 (0.00%)      | 0 / 8 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                  |
| Back pain  |                     |                    |                    |
| subjects affected / exposed                      | 1 / 4 (25.00%)      | 1 / 5 (20.00%)     | 1 / 8 (12.50%)     |
| occurrences (all)                                | 1                   | 1                  | 1                  |
| Flank pain                                       |                     |                    |                    |
| subjects affected / exposed                      | 0 / 4 (0.00%)       | 0 / 5 (0.00%)      | 0 / 8 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                  |
| Muscle spasms                                    |                     |                    |                    |
| subjects affected / exposed                      | 1 / 4 (25.00%)      | 0 / 5 (0.00%)      | 1 / 8 (12.50%)     |
| occurrences (all)                                | 2                   | 0                  | 1                  |
| Muscular weakness                                |                     |                    |                    |
| subjects affected / exposed                      | 0 / 4 (0.00%)       | 0 / 5 (0.00%)      | 0 / 8 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                  |
| Musculoskeletal pain                             |                     |                    |                    |
| subjects affected / exposed                      | 0 / 4 (0.00%)       | 0 / 5 (0.00%)      | 0 / 8 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                  |
| Neck pain  |                     |                    |                    |

|                             |                |               |                |
|-----------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Pain in jaw                 |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Rotator cuff syndrome       |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Infections and infestations |                |               |                |
| Acute sinusitis             |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Bronchitis                  |                |               |                |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 2              | 0             | 0              |
| Chancroid                   |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Conjunctivitis              |                |               |                |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 1              | 0             | 0              |
| Fungal infection            |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Gingivitis                  |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Groin infection             |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all)           | 0              | 0             | 1              |
| Herpes simplex              |                |               |                |
| subjects affected / exposed | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Herpes zoster               |                |               |                |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all)           | 1              | 0             | 1              |

|   |                |               |               |
|---|----------------|---------------|---------------|
| Lower respiratory tract infection bacterial |                |               |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)                           | 0              | 0             | 0             |
| Lung infection                              |                |               |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)                           | 0              | 0             | 0             |
| Lymph gland infection                       |                |               |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)                           | 0              | 0             | 0             |
| Oral candidiasis                            |                |               |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)                           | 0              | 0             | 0             |
| Pneumonia                                   |                |               |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)                           | 0              | 0             | 0             |
| Sinusitis                                   |                |               |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)                           | 0              | 0             | 0             |
| Skin infection                              |                |               |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)                           | 0              | 0             | 0             |
| Staphylococcal infection                    |                |               |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)                           | 0              | 0             | 0             |
| Systemic candida                            |                |               |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)                           | 0              | 0             | 0             |
| Tooth infection                             |                |               |               |
| subjects affected / exposed                 | 0 / 4 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)                           | 0              | 0             | 0             |
| Upper respiratory tract infection           |                |               |               |
| subjects affected / exposed                 | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all)                           | 2              | 0             | 0             |
| Urinary tract infection                     |                |               |               |

|                                    |                |                |                |
|------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed        | 3 / 4 (75.00%) | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                  | 3              | 0              | 1              |
| Viral infection                    |                |                |                |
| subjects affected / exposed        | 1 / 4 (25.00%) | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                  | 1              | 0              | 0              |
| Metabolism and nutrition disorders |                |                |                |
| Decreased appetite                 |                |                |                |
| subjects affected / exposed        | 2 / 4 (50.00%) | 2 / 5 (40.00%) | 3 / 8 (37.50%) |
| occurrences (all)                  | 2              | 2              | 3              |
| Dehydration                        |                |                |                |
| subjects affected / exposed        | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Hyperglycaemia                     |                |                |                |
| subjects affected / exposed        | 2 / 4 (50.00%) | 0 / 5 (0.00%)  | 3 / 8 (37.50%) |
| occurrences (all)                  | 2              | 0              | 6              |
| Hypertriglyceridaemia              |                |                |                |
| subjects affected / exposed        | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Hypoalbuminaemia                   |                |                |                |
| subjects affected / exposed        | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Hypocalcaemia                      |                |                |                |
| subjects affected / exposed        | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Hypokalaemia                       |                |                |                |
| subjects affected / exposed        | 0 / 4 (0.00%)  | 1 / 5 (20.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                  | 0              | 1              | 0              |
| Hypomagnesaemia                    |                |                |                |
| subjects affected / exposed        | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Hyponatraemia                      |                |                |                |
| subjects affected / exposed        | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                  | 0              | 0              | 1              |
| Hypophosphataemia                  |                |                |                |
| subjects affected / exposed        | 0 / 4 (0.00%)  | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                  | 0              | 0              | 1              |

|  |                     |                    |                    |
|--|---------------------|--------------------|--------------------|
| Metabolic acidosis<br>subjects affected / exposed<br>occurrences (all)     | 0 / 4 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0 |
| Vitamin B12 deficiency<br>subjects affected / exposed<br>occurrences (all) | 1 / 4 (25.00%)<br>1 | 0 / 5 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0 |

| <b>Non-serious adverse events</b>   | PART1B 8 MG QD      | PART1B 12 MG QD     | PART1C 8 MG QD     |
|---|---------------------|---------------------|--------------------|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed  | 7 / 7 (100.00%)     | 5 / 5 (100.00%)     | 0 / 1 (0.00%)      |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps)<br>Basal cell carcinoma<br>subjects affected / exposed<br>occurrences (all) | 1 / 7 (14.29%)<br>1 | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Benign neoplasm<br>subjects affected / exposed<br>occurrences (all)   | 1 / 7 (14.29%)<br>1 | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Squamous cell carcinoma of skin<br>subjects affected / exposed<br>occurrences (all)   | 1 / 7 (14.29%)<br>1 | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Vascular disorders<br>Haematoma<br>subjects affected / exposed<br>occurrences (all)   | 1 / 7 (14.29%)<br>1 | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Hot flush<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Hypertension<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 | 0 / 1 (0.00%)<br>0 |
| Hypotension<br>subjects affected / exposed<br>occurrences (all)   | 1 / 7 (14.29%)<br>1 | 1 / 5 (20.00%)<br>2 | 0 / 1 (0.00%)<br>0 |
| General disorders and administration site conditions<br>Asthenia  |                     |                     |                    |

|                             |                |                |               |
|-----------------------------|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Catheter site erythema      |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Catheter site haemorrhage   |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Catheter site pain          |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Chills                      |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Drug withdrawal syndrome    |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Fatigue                     |                |                |               |
| subjects affected / exposed | 3 / 7 (42.86%) | 2 / 5 (40.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 3              | 2              | 0             |
| Influenza like illness      |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Localised oedema            |                |                |               |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Mucosal dryness             |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Mucosal haemorrhage         |                |                |               |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 2              | 0              | 0             |
| Non-cardiac chest pain      |                |                |               |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 2              | 1              | 0             |
| Oedema peripheral           |                |                |               |



|  |                     |                     |                    |
|--|---------------------|---------------------|--------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Performance status decreased<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)  | 2 / 7 (28.57%)<br>2 | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Reproductive system and breast disorders<br>Penile oedema<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 7 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Vulvovaginal erythema<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal disorders<br>Chronic obstructive pulmonary disease<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Cough<br>subjects affected / exposed<br>occurrences (all)  | 1 / 7 (14.29%)<br>1 | 2 / 5 (40.00%)<br>2 | 0 / 1 (0.00%)<br>0 |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)   | 2 / 7 (28.57%)<br>2 | 2 / 5 (40.00%)<br>2 | 0 / 1 (0.00%)<br>0 |
| Dyspnoea exertional<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)  | 2 / 7 (28.57%)<br>2 | 4 / 5 (80.00%)<br>9 | 0 / 1 (0.00%)<br>0 |
| Haemoptysis<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 | 0 / 1 (0.00%)<br>0 |
| Hypoxia  |                     |                     |                    |

|                             |                |                |               |
|-----------------------------|----------------|----------------|---------------|
| subjects affected / exposed | 2 / 7 (28.57%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 2              | 1              | 0             |
| Nasal congestion            |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Oropharyngeal pain          |                |                |               |
| subjects affected / exposed | 2 / 7 (28.57%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 2              | 2              | 0             |
| Pleural effusion            |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Pneumonitis                 |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Productive cough            |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Pulmonary oedema            |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Respiratory failure         |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Sneezing                    |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Upper-airway cough syndrome |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Wheezing                    |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Psychiatric disorders       |                |                |               |
| Agitation                   |                |                |               |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |

|   |                |                |               |
|---|----------------|----------------|---------------|
| Anxiety   |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0             |
| Depression                                      |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0             |
| Insomnia  |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Investigations                                  |                |                |               |
| Activated partial thromboplastin time prolonged |                |                |               |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 1              | 1              | 0             |
| Alanine aminotransferase increased              |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Aspartate aminotransferase increased            |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Bilirubin conjugated increased                  |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Blood alkaline phosphatase increased            |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Blood bilirubin increased                       |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 2              | 0             |
| Blood creatinine increased                      |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Blood pressure increased                        |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0             |
| International normalised ratio increased        |                |                |               |

|  |                |                |               |
|--|----------------|----------------|---------------|
| subjects affected / exposed                    | 1 / 7 (14.29%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                              | 1              | 1              | 0             |
| Neutrophil count decreased                     |                |                |               |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 2              | 0             |
| Platelet count decreased                       |                |                |               |
| subjects affected / exposed                    | 1 / 7 (14.29%) | 2 / 5 (40.00%) | 0 / 1 (0.00%) |
| occurrences (all)                              | 1              | 2              | 0             |
| Prothrombin time prolonged                     |                |                |               |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Troponin I increased                           |                |                |               |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Troponin increased                             |                |                |               |
| subjects affected / exposed                    | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 1              | 0              | 0             |
| Weight decreased                               |                |                |               |
| subjects affected / exposed                    | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 2              | 0              | 0             |
| Weight increased                               |                |                |               |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| White blood cell count decreased               |                |                |               |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 2 / 5 (40.00%) | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 2              | 0             |
| Injury, poisoning and procedural complications |                |                |               |
| Arthropod bite                                 |                |                |               |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Contusion                                      |                |                |               |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Eye contusion                                  |                |                |               |

|                                      |                |                |               |
|--------------------------------------|----------------|----------------|---------------|
| subjects affected / exposed          | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 1              | 0             |
| Fall                                 |                |                |               |
| subjects affected / exposed          | 2 / 7 (28.57%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 2              | 1              | 0             |
| Fractured sacrum                     |                |                |               |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0             |
| Infusion related reaction            |                |                |               |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0             |
| Laceration                           |                |                |               |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0             |
| Transfusion reaction                 |                |                |               |
| subjects affected / exposed          | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 1              | 0              | 0             |
| Cardiac disorders                    |                |                |               |
| Atrial fibrillation                  |                |                |               |
| subjects affected / exposed          | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 1              | 0              | 0             |
| Atrioventricular block second degree |                |                |               |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0             |
| Sinus bradycardia                    |                |                |               |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0             |
| Sinus tachycardia                    |                |                |               |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 2 / 5 (40.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 2              | 0             |
| Tachycardia                          |                |                |               |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0             |
| Ventricular arrhythmia               |                |                |               |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0             |

|                                      |                |                |               |
|--------------------------------------|----------------|----------------|---------------|
| Nervous system disorders             |                |                |               |
| Brain oedema                         |                |                |               |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0             |
| Dizziness                            |                |                |               |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0             |
| Dysgeusia                            |                |                |               |
| subjects affected / exposed          | 3 / 7 (42.86%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 3              | 1              | 0             |
| Headache                             |                |                |               |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 1              | 0             |
| Neuropathy peripheral                |                |                |               |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0             |
| Post herpetic neuralgia              |                |                |               |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0             |
| Syncope                              |                |                |               |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0             |
| Blood and lymphatic system disorders |                |                |               |
| Anaemia                              |                |                |               |
| subjects affected / exposed          | 4 / 7 (57.14%) | 3 / 5 (60.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 4              | 9              | 0             |
| Febrile neutropenia                  |                |                |               |
| subjects affected / exposed          | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 1              | 0              | 0             |
| Increased tendency to bruise         |                |                |               |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 1              | 0             |
| Iron deficiency anaemia              |                |                |               |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0             |
| Leukocytosis                         |                |                |               |

|                             |                |                |               |
|-----------------------------|----------------|----------------|---------------|
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Leukopenia                  |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Lymph node pain             |                |                |               |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Lymphopenia                 |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Neutropenia                 |                |                |               |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 1              | 0             |
| Splenic infarction          |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Splenomegaly                |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Thrombocytopenia            |                |                |               |
| subjects affected / exposed | 5 / 7 (71.43%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 6              | 1              | 0             |
| Ear and labyrinth disorders |                |                |               |
| Vertigo                     |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Eye disorders               |                |                |               |
| Cataract                    |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Eye pain                    |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Eyelid oedema               |                |                |               |

|                             |                |                |               |
|-----------------------------|----------------|----------------|---------------|
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Retinal haemorrhage         |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Vitreous floaters           |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Gastrointestinal disorders  |                |                |               |
| Abdominal distension        |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Abdominal pain              |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Abdominal pain upper        |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Anal fissure                |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 2              | 0             |
| Constipation                |                |                |               |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Diarrhoea                   |                |                |               |
| subjects affected / exposed | 4 / 7 (57.14%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 5              | 1              | 0             |
| Dry mouth                   |                |                |               |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 2              | 0              | 0             |
| Dyspepsia                   |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Flatulence                  |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |



|  |                     |                     |                    |
|--|---------------------|---------------------|--------------------|
| Gastrooesophageal reflux disease<br>subjects affected / exposed<br>occurrences (all)               | 0 / 7 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Haemorrhoids<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 7 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 | 0 / 1 (0.00%)<br>0 |
| Lip haemorrhage<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 7 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 | 0 / 1 (0.00%)<br>0 |
| Nausea<br>subjects affected / exposed<br>occurrences (all)   | 3 / 7 (42.86%)<br>3 | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Oesophageal haemorrhage<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 7 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 | 0 / 1 (0.00%)<br>0 |
| Oral pain<br>subjects affected / exposed<br>occurrences (all)                                      | 3 / 7 (42.86%)<br>3 | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Stomatitis<br>subjects affected / exposed<br>occurrences (all)                                     | 2 / 7 (28.57%)<br>2 | 1 / 5 (20.00%)<br>3 | 0 / 1 (0.00%)<br>0 |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                                       | 3 / 7 (42.86%)<br>5 | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Hepatobiliary disorders<br>Hyperbilirubinaemia<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Skin and subcutaneous tissue disorders<br>Acne<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Alopecia<br>subjects affected / exposed<br>occurrences (all)                                       | 1 / 7 (14.29%)<br>1 | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Angioedema   |                     |                     |                    |

|                             |                |                |               |
|-----------------------------|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Dry skin                    |                |                |               |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 2              | 0              | 0             |
| Erythema                    |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Pain of skin                |                |                |               |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Petechiae                   |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 2              | 0             |
| Pruritus                    |                |                |               |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Purpura                     |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 3              | 0             |
| Rash                        |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Scab                        |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Skin ulcer                  |                |                |               |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Renal and urinary disorders |                |                |               |
| Acute kidney injury         |                |                |               |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 2              | 0              | 0             |
| Dysuria                     |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |

|   |                |                |               |
|---|----------------|----------------|---------------|
| Haematuria                                      |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Urinary retention                               |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0             |
| Musculoskeletal and connective tissue disorders |                |                |               |
| Arthralgia                                      |                |                |               |
| subjects affected / exposed                     | 2 / 7 (28.57%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 2              | 0              | 0             |
| Back pain                                       |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Flank pain                                      |                |                |               |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0             |
| Muscle spasms                                   |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0             |
| Muscular weakness                               |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0             |
| Musculoskeletal pain                            |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Neck pain                                       |                |                |               |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0             |
| Pain in jaw                                     |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0             |
| Rotator cuff syndrome                           |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Infections and infestations                     |                |                |               |

|  |                |                |               |
|--|----------------|----------------|---------------|
| Acute sinusitis                                |                |                |               |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Bronchitis                                     |                |                |               |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Chancroid                                      |                |                |               |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Conjunctivitis                                 |                |                |               |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Fungal infection                               |                |                |               |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Gingivitis                                     |                |                |               |
| subjects affected / exposed                    | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 1              | 0              | 0             |
| Groin infection                                |                |                |               |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Herpes simplex                                 |                |                |               |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Herpes zoster                                  |                |                |               |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Lower respiratory tract infection<br>bacterial |                |                |               |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 2              | 0             |
| Lung infection                                 |                |                |               |
| subjects affected / exposed                    | 2 / 7 (28.57%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                              | 2              | 1              | 0             |
| Lymph gland infection                          |                |                |               |

|                                    |                |                |               |
|------------------------------------|----------------|----------------|---------------|
| subjects affected / exposed        | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                  | 1              | 0              | 0             |
| Oral candidiasis                   |                |                |               |
| subjects affected / exposed        | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                  | 1              | 0              | 0             |
| Pneumonia                          |                |                |               |
| subjects affected / exposed        | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                  | 0              | 1              | 0             |
| Sinusitis                          |                |                |               |
| subjects affected / exposed        | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0             |
| Skin infection                     |                |                |               |
| subjects affected / exposed        | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0             |
| Staphylococcal infection           |                |                |               |
| subjects affected / exposed        | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                  | 0              | 1              | 0             |
| Systemic candida                   |                |                |               |
| subjects affected / exposed        | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                  | 1              | 0              | 0             |
| Tooth infection                    |                |                |               |
| subjects affected / exposed        | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                  | 1              | 0              | 0             |
| Upper respiratory tract infection  |                |                |               |
| subjects affected / exposed        | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0             |
| Urinary tract infection            |                |                |               |
| subjects affected / exposed        | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0             |
| Viral infection                    |                |                |               |
| subjects affected / exposed        | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0             |
| Metabolism and nutrition disorders |                |                |               |
| Decreased appetite                 |                |                |               |
| subjects affected / exposed        | 3 / 7 (42.86%) | 2 / 5 (40.00%) | 0 / 1 (0.00%) |
| occurrences (all)                  | 3              | 2              | 0             |

|                             |                |                |               |
|-----------------------------|----------------|----------------|---------------|
| Dehydration                 |                |                |               |
| subjects affected / exposed | 1 / 7 (14.29%) | 2 / 5 (40.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 2              | 2              | 0             |
| Hyperglycaemia              |                |                |               |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Hypertriglyceridaemia       |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Hypoalbuminaemia            |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Hypocalcaemia               |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Hypokalaemia                |                |                |               |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Hypomagnesaemia             |                |                |               |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Hyponatraemia               |                |                |               |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 1              | 0             |
| Hypophosphataemia           |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Metabolic acidosis          |                |                |               |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Vitamin B12 deficiency      |                |                |               |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |

| Non-serious adverse events             | PART2A 12 MG QD | PART2B 12 MG QD | PART3A 8 MG QD +<br>Gemcitabine 1000<br>MG/M2 |
|--|-----------------|-----------------|---|
| Total subjects affected by non-serious |                 |                 |   |

|   |                  |                 |                 |
|---|------------------|-----------------|-----------------|
| adverse events  |                  |                 |                 |
| subjects affected / exposed   | 82 / 86 (95.35%) | 5 / 5 (100.00%) | 1 / 1 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                  |                 |                 |
| Basal cell carcinoma  |                  |                 |                 |
| subjects affected / exposed   | 0 / 86 (0.00%)   | 0 / 5 (0.00%)   | 0 / 1 (0.00%)   |
| occurrences (all)   | 0                | 0               | 0               |
| Benign neoplasm   |                  |                 |                 |
| subjects affected / exposed   | 0 / 86 (0.00%)   | 0 / 5 (0.00%)   | 0 / 1 (0.00%)   |
| occurrences (all)   | 0                | 0               | 0               |
| Squamous cell carcinoma of skin                                     |                  |                 |                 |
| subjects affected / exposed   | 0 / 86 (0.00%)   | 0 / 5 (0.00%)   | 0 / 1 (0.00%)   |
| occurrences (all)   | 0                | 0               | 0               |
| Vascular disorders  |                  |                 |                 |
| Haematoma   |                  |                 |                 |
| subjects affected / exposed   | 1 / 86 (1.16%)   | 0 / 5 (0.00%)   | 0 / 1 (0.00%)   |
| occurrences (all)   | 1                | 0               | 0               |
| Hot flush   |                  |                 |                 |
| subjects affected / exposed   | 2 / 86 (2.33%)   | 0 / 5 (0.00%)   | 0 / 1 (0.00%)   |
| occurrences (all)   | 2                | 0               | 0               |
| Hypertension  |                  |                 |                 |
| subjects affected / exposed   | 3 / 86 (3.49%)   | 1 / 5 (20.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)   | 3                | 1               | 0               |
| Hypotension   |                  |                 |                 |
| subjects affected / exposed   | 3 / 86 (3.49%)   | 1 / 5 (20.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)   | 3                | 2               | 0               |
| General disorders and administration site conditions                |                  |                 |                 |
| Asthenia  |                  |                 |                 |
| subjects affected / exposed   | 3 / 86 (3.49%)   | 0 / 5 (0.00%)   | 0 / 1 (0.00%)   |
| occurrences (all)   | 4                | 0               | 0               |
| Catheter site erythema  |                  |                 |                 |
| subjects affected / exposed   | 0 / 86 (0.00%)   | 0 / 5 (0.00%)   | 0 / 1 (0.00%)   |
| occurrences (all)   | 0                | 0               | 0               |
| Catheter site haemorrhage   |                  |                 |                 |
| subjects affected / exposed   | 0 / 86 (0.00%)   | 0 / 5 (0.00%)   | 0 / 1 (0.00%)   |
| occurrences (all)   | 0                | 0               | 0               |
| Catheter site pain  |                  |                 |                 |

|                                |                  |                |               |
|--------------------------------|------------------|----------------|---------------|
| subjects affected / exposed    | 0 / 86 (0.00%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)              | 0                | 1              | 0             |
| Chills                         |                  |                |               |
| subjects affected / exposed    | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)              | 0                | 0              | 0             |
| Drug withdrawal syndrome       |                  |                |               |
| subjects affected / exposed    | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)              | 0                | 0              | 0             |
| Fatigue                        |                  |                |               |
| subjects affected / exposed    | 36 / 86 (41.86%) | 3 / 5 (60.00%) | 0 / 1 (0.00%) |
| occurrences (all)              | 41               | 3              | 0             |
| Influenza like illness         |                  |                |               |
| subjects affected / exposed    | 1 / 86 (1.16%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)              | 1                | 0              | 0             |
| Localised oedema               |                  |                |               |
| subjects affected / exposed    | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)              | 0                | 0              | 0             |
| Mucosal dryness                |                  |                |               |
| subjects affected / exposed    | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)              | 0                | 0              | 0             |
| Mucosal haemorrhage            |                  |                |               |
| subjects affected / exposed    | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)              | 0                | 0              | 0             |
| Non-cardiac chest pain         |                  |                |               |
| subjects affected / exposed    | 2 / 86 (2.33%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)              | 2                | 0              | 0             |
| Oedema peripheral              |                  |                |               |
| subjects affected / exposed    | 2 / 86 (2.33%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)              | 2                | 1              | 0             |
| Performance status decreased   |                  |                |               |
| subjects affected / exposed    | 1 / 86 (1.16%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)              | 1                | 0              | 0             |
| Pyrexia                        |                  |                |               |
| subjects affected / exposed    | 10 / 86 (11.63%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)              | 11               | 0              | 0             |
| Reproductive system and breast |                  |                |               |



|   |                  |                |               |
|---|------------------|----------------|---------------|
| disorders                                       |                  |                |               |
| Penile oedema                                   |                  |                |               |
| subjects affected / exposed                     | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 0                | 0              | 0             |
| Vulvovaginal erythema                           |                  |                |               |
| subjects affected / exposed                     | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 0                | 0              | 0             |
| Respiratory, thoracic and mediastinal disorders |                  |                |               |
| Chronic obstructive pulmonary disease           |                  |                |               |
| subjects affected / exposed                     | 0 / 86 (0.00%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0                | 1              | 0             |
| Cough   |                  |                |               |
| subjects affected / exposed                     | 10 / 86 (11.63%) | 2 / 5 (40.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 12               | 2              | 0             |
| Dyspnoea  |                  |                |               |
| subjects affected / exposed                     | 9 / 86 (10.47%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 9                | 1              | 0             |
| Dyspnoea exertional                             |                  |                |               |
| subjects affected / exposed                     | 1 / 86 (1.16%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 1                | 1              | 0             |
| Epistaxis                                       |                  |                |               |
| subjects affected / exposed                     | 5 / 86 (5.81%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 5                | 1              | 0             |
| Haemoptysis                                     |                  |                |               |
| subjects affected / exposed                     | 3 / 86 (3.49%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 3                | 0              | 0             |
| Hypoxia   |                  |                |               |
| subjects affected / exposed                     | 1 / 86 (1.16%)   | 3 / 5 (60.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 1                | 3              | 0             |
| Nasal congestion                                |                  |                |               |
| subjects affected / exposed                     | 3 / 86 (3.49%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 3                | 1              | 0             |
| Oropharyngeal pain                              |                  |                |               |
| subjects affected / exposed                     | 4 / 86 (4.65%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 4                | 0              | 0             |
| Pleural effusion                                |                  |                |               |

|                             |                |                |               |
|-----------------------------|----------------|----------------|---------------|
| subjects affected / exposed | 6 / 86 (6.98%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 6              | 1              | 0             |
| Pneumonitis                 |                |                |               |
| subjects affected / exposed | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Productive cough            |                |                |               |
| subjects affected / exposed | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Pulmonary oedema            |                |                |               |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Respiratory failure         |                |                |               |
| subjects affected / exposed | 2 / 86 (2.33%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 2              | 1              | 0             |
| Sneezing                    |                |                |               |
| subjects affected / exposed | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Upper-airway cough syndrome |                |                |               |
| subjects affected / exposed | 1 / 86 (1.16%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 1              | 0             |
| Wheezing                    |                |                |               |
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 2              | 0              | 0             |
| Psychiatric disorders       |                |                |               |
| Agitation                   |                |                |               |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Anxiety                     |                |                |               |
| subjects affected / exposed | 3 / 86 (3.49%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 3              | 1              | 0             |
| Depression                  |                |                |               |
| subjects affected / exposed | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Insomnia                    |                |                |               |
| subjects affected / exposed | 2 / 86 (2.33%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 2              | 1              | 0             |

|   |                  |                |               |
|---|------------------|----------------|---------------|
| Investigations                                  |                  |                |               |
| Activated partial thromboplastin time prolonged |                  |                |               |
| subjects affected / exposed                     | 4 / 86 (4.65%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 5                | 0              | 0             |
| Alanine aminotransferase increased              |                  |                |               |
| subjects affected / exposed                     | 7 / 86 (8.14%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 7                | 0              | 0             |
| Aspartate aminotransferase increased            |                  |                |               |
| subjects affected / exposed                     | 7 / 86 (8.14%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 7                | 0              | 0             |
| Bilirubin conjugated increased                  |                  |                |               |
| subjects affected / exposed                     | 1 / 86 (1.16%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 1                | 0              | 0             |
| Blood alkaline phosphatase increased            |                  |                |               |
| subjects affected / exposed                     | 5 / 86 (5.81%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 5                | 0              | 0             |
| Blood bilirubin increased                       |                  |                |               |
| subjects affected / exposed                     | 10 / 86 (11.63%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 10               | 0              | 0             |
| Blood creatinine increased                      |                  |                |               |
| subjects affected / exposed                     | 5 / 86 (5.81%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 8                | 0              | 0             |
| Blood pressure increased                        |                  |                |               |
| subjects affected / exposed                     | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 0                | 0              | 0             |
| International normalised ratio increased        |                  |                |               |
| subjects affected / exposed                     | 6 / 86 (6.98%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 8                | 1              | 0             |
| Neutrophil count decreased                      |                  |                |               |
| subjects affected / exposed                     | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 0                | 0              | 0             |
| Platelet count decreased                        |                  |                |               |
| subjects affected / exposed                     | 8 / 86 (9.30%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 8                | 0              | 0             |
| Prothrombin time prolonged                      |                  |                |               |

|  |                |                |               |
|--|----------------|----------------|---------------|
| subjects affected / exposed                    | 6 / 86 (6.98%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 7              | 0              | 0             |
| Troponin I increased                           |                |                |               |
| subjects affected / exposed                    | 0 / 86 (0.00%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 1              | 0             |
| Troponin increased                             |                |                |               |
| subjects affected / exposed                    | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Weight decreased                               |                |                |               |
| subjects affected / exposed                    | 6 / 86 (6.98%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                              | 6              | 1              | 0             |
| Weight increased                               |                |                |               |
| subjects affected / exposed                    | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| White blood cell count decreased               |                |                |               |
| subjects affected / exposed                    | 5 / 86 (5.81%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 6              | 0              | 0             |
| Injury, poisoning and procedural complications |                |                |               |
| Arthropod bite                                 |                |                |               |
| subjects affected / exposed                    | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Contusion                                      |                |                |               |
| subjects affected / exposed                    | 6 / 86 (6.98%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 6              | 0              | 0             |
| Eye contusion                                  |                |                |               |
| subjects affected / exposed                    | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Fall   |                |                |               |
| subjects affected / exposed                    | 4 / 86 (4.65%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 5              | 0              | 0             |
| Fractured sacrum                               |                |                |               |
| subjects affected / exposed                    | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Infusion related reaction                      |                |                |               |

|                                      |                  |                |               |
|--------------------------------------|------------------|----------------|---------------|
| subjects affected / exposed          | 1 / 86 (1.16%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 1                | 1              | 0             |
| Laceration                           |                  |                |               |
| subjects affected / exposed          | 1 / 86 (1.16%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 1                | 0              | 0             |
| Transfusion reaction                 |                  |                |               |
| subjects affected / exposed          | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 0                | 0              | 0             |
| Cardiac disorders                    |                  |                |               |
| Atrial fibrillation                  |                  |                |               |
| subjects affected / exposed          | 1 / 86 (1.16%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 1                | 0              | 0             |
| Atrioventricular block second degree |                  |                |               |
| subjects affected / exposed          | 0 / 86 (0.00%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 0                | 1              | 0             |
| Sinus bradycardia                    |                  |                |               |
| subjects affected / exposed          | 0 / 86 (0.00%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 0                | 1              | 0             |
| Sinus tachycardia                    |                  |                |               |
| subjects affected / exposed          | 1 / 86 (1.16%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 1                | 0              | 0             |
| Tachycardia                          |                  |                |               |
| subjects affected / exposed          | 4 / 86 (4.65%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 4                | 1              | 0             |
| Ventricular arrhythmia               |                  |                |               |
| subjects affected / exposed          | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 0                | 0              | 0             |
| Nervous system disorders             |                  |                |               |
| Brain oedema                         |                  |                |               |
| subjects affected / exposed          | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 0                | 0              | 0             |
| Dizziness                            |                  |                |               |
| subjects affected / exposed          | 10 / 86 (11.63%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 12               | 2              | 0             |
| Dysgeusia                            |                  |                |               |

|                                      |                  |                |               |
|--------------------------------------|------------------|----------------|---------------|
| subjects affected / exposed          | 16 / 86 (18.60%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 16               | 1              | 0             |
| Headache                             |                  |                |               |
| subjects affected / exposed          | 5 / 86 (5.81%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 5                | 0              | 0             |
| Neuropathy peripheral                |                  |                |               |
| subjects affected / exposed          | 1 / 86 (1.16%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 1                | 0              | 0             |
| Post herpetic neuralgia              |                  |                |               |
| subjects affected / exposed          | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 0                | 0              | 0             |
| Syncope                              |                  |                |               |
| subjects affected / exposed          | 1 / 86 (1.16%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 1                | 1              | 0             |
| Blood and lymphatic system disorders |                  |                |               |
| Anaemia                              |                  |                |               |
| subjects affected / exposed          | 15 / 86 (17.44%) | 4 / 5 (80.00%) | 0 / 1 (0.00%) |
| occurrences (all)                    | 17               | 11             | 0             |
| Febrile neutropenia                  |                  |                |               |
| subjects affected / exposed          | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 0                | 0              | 0             |
| Increased tendency to bruise         |                  |                |               |
| subjects affected / exposed          | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 0                | 0              | 0             |
| Iron deficiency anaemia              |                  |                |               |
| subjects affected / exposed          | 1 / 86 (1.16%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 1                | 0              | 0             |
| Leukocytosis                         |                  |                |               |
| subjects affected / exposed          | 1 / 86 (1.16%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 1                | 0              | 0             |
| Leukopenia                           |                  |                |               |
| subjects affected / exposed          | 1 / 86 (1.16%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 1                | 0              | 0             |
| Lymph node pain                      |                  |                |               |
| subjects affected / exposed          | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                    | 0                | 0              | 0             |

|                             |                  |                |               |
|-----------------------------|------------------|----------------|---------------|
| Lymphopenia                 |                  |                |               |
| subjects affected / exposed | 1 / 86 (1.16%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1                | 0              | 0             |
| Neutropenia                 |                  |                |               |
| subjects affected / exposed | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0                | 0              | 0             |
| Splenic infarction          |                  |                |               |
| subjects affected / exposed | 0 / 86 (0.00%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0                | 1              | 0             |
| Splenomegaly                |                  |                |               |
| subjects affected / exposed | 0 / 86 (0.00%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0                | 1              | 0             |
| Thrombocytopenia            |                  |                |               |
| subjects affected / exposed | 19 / 86 (22.09%) | 3 / 5 (60.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 26               | 3              | 0             |
| Ear and labyrinth disorders |                  |                |               |
| Vertigo                     |                  |                |               |
| subjects affected / exposed | 1 / 86 (1.16%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1                | 1              | 0             |
| Eye disorders               |                  |                |               |
| Cataract                    |                  |                |               |
| subjects affected / exposed | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0                | 0              | 0             |
| Eye pain                    |                  |                |               |
| subjects affected / exposed | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0                | 0              | 0             |
| Eyelid oedema               |                  |                |               |
| subjects affected / exposed | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0                | 0              | 0             |
| Retinal haemorrhage         |                  |                |               |
| subjects affected / exposed | 0 / 86 (0.00%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0                | 1              | 0             |
| Vitreous floaters           |                  |                |               |
| subjects affected / exposed | 0 / 86 (0.00%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0                | 1              | 0             |
| Gastrointestinal disorders  |                  |                |               |

|                                  |                  |                |               |
|----------------------------------|------------------|----------------|---------------|
| Abdominal distension             |                  |                |               |
| subjects affected / exposed      | 1 / 86 (1.16%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                | 1                | 0              | 0             |
| Abdominal pain                   |                  |                |               |
| subjects affected / exposed      | 3 / 86 (3.49%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                | 3                | 2              | 0             |
| Abdominal pain upper             |                  |                |               |
| subjects affected / exposed      | 2 / 86 (2.33%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                | 2                | 0              | 0             |
| Anal fissure                     |                  |                |               |
| subjects affected / exposed      | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                | 0                | 0              | 0             |
| Constipation                     |                  |                |               |
| subjects affected / exposed      | 19 / 86 (22.09%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                | 19               | 1              | 0             |
| Diarrhoea                        |                  |                |               |
| subjects affected / exposed      | 21 / 86 (24.42%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                | 25               | 1              | 0             |
| Dry mouth                        |                  |                |               |
| subjects affected / exposed      | 8 / 86 (9.30%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                | 8                | 0              | 0             |
| Dyspepsia                        |                  |                |               |
| subjects affected / exposed      | 3 / 86 (3.49%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                | 4                | 0              | 0             |
| Flatulence                       |                  |                |               |
| subjects affected / exposed      | 1 / 86 (1.16%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                | 1                | 1              | 0             |
| Gastrooesophageal reflux disease |                  |                |               |
| subjects affected / exposed      | 1 / 86 (1.16%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                | 1                | 0              | 0             |
| Haemorrhoids                     |                  |                |               |
| subjects affected / exposed      | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                | 0                | 0              | 0             |
| Lip haemorrhage                  |                  |                |               |
| subjects affected / exposed      | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                | 0                | 0              | 0             |



|  |                  |                |               |
|--|------------------|----------------|---------------|
| Nausea                                 |                  |                |               |
| subjects affected / exposed            | 43 / 86 (50.00%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 47               | 1              | 0             |
| Oesophageal haemorrhage                |                  |                |               |
| subjects affected / exposed            | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                      | 0                | 0              | 0             |
| Oral pain                              |                  |                |               |
| subjects affected / exposed            | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                      | 0                | 0              | 0             |
| Stomatitis                             |                  |                |               |
| subjects affected / exposed            | 1 / 86 (1.16%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 1                | 2              | 0             |
| Vomiting                               |                  |                |               |
| subjects affected / exposed            | 26 / 86 (30.23%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 35               | 1              | 0             |
| Hepatobiliary disorders                |                  |                |               |
| Hyperbilirubinaemia                    |                  |                |               |
| subjects affected / exposed            | 2 / 86 (2.33%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                      | 2                | 0              | 0             |
| Skin and subcutaneous tissue disorders |                  |                |               |
| Acne                                   |                  |                |               |
| subjects affected / exposed            | 1 / 86 (1.16%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                      | 1                | 1              | 0             |
| Alopecia                               |                  |                |               |
| subjects affected / exposed            | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                      | 0                | 0              | 0             |
| Angioedema                             |                  |                |               |
| subjects affected / exposed            | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                      | 0                | 0              | 0             |
| Dry skin                               |                  |                |               |
| subjects affected / exposed            | 1 / 86 (1.16%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                      | 1                | 0              | 0             |
| Erythema                               |                  |                |               |
| subjects affected / exposed            | 2 / 86 (2.33%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                      | 2                | 0              | 0             |
| Pain of skin                           |                  |                |               |

|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Petechiae                                       |                |                |               |
| subjects affected / exposed                     | 0 / 86 (0.00%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0             |
| Pruritus  |                |                |               |
| subjects affected / exposed                     | 4 / 86 (4.65%) | 2 / 5 (40.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 4              | 2              | 0             |
| Purpura   |                |                |               |
| subjects affected / exposed                     | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Rash  |                |                |               |
| subjects affected / exposed                     | 2 / 86 (2.33%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 2              | 0              | 0             |
| Scab  |                |                |               |
| subjects affected / exposed                     | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Skin ulcer                                      |                |                |               |
| subjects affected / exposed                     | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Renal and urinary disorders                     |                |                |               |
| Acute kidney injury                             |                |                |               |
| subjects affected / exposed                     | 7 / 86 (8.14%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 8              | 1              | 0             |
| Dysuria   |                |                |               |
| subjects affected / exposed                     | 1 / 86 (1.16%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0             |
| Haematuria                                      |                |                |               |
| subjects affected / exposed                     | 2 / 86 (2.33%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                               | 2              | 0              | 0             |
| Urinary retention                               |                |                |               |
| subjects affected / exposed                     | 1 / 86 (1.16%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 1              | 1              | 0             |
| Musculoskeletal and connective tissue disorders |                |                |               |

|                             |                |               |               |
|-----------------------------|----------------|---------------|---------------|
| Arthralgia                  |                |               |               |
| subjects affected / exposed | 4 / 86 (4.65%) | 0 / 5 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 4              | 0             | 0             |
| Back pain                   |                |               |               |
| subjects affected / exposed | 6 / 86 (6.98%) | 0 / 5 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 6              | 0             | 0             |
| Flank pain                  |                |               |               |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 5 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 0             | 0             |
| Muscle spasms               |                |               |               |
| subjects affected / exposed | 4 / 86 (4.65%) | 0 / 5 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 4              | 0             | 0             |
| Muscular weakness           |                |               |               |
| subjects affected / exposed | 4 / 86 (4.65%) | 0 / 5 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 4              | 0             | 0             |
| Musculoskeletal pain        |                |               |               |
| subjects affected / exposed | 3 / 86 (3.49%) | 0 / 5 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 3              | 0             | 0             |
| Neck pain                   |                |               |               |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 5 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 0             | 0             |
| Pain in jaw                 |                |               |               |
| subjects affected / exposed | 0 / 86 (0.00%) | 0 / 5 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Rotator cuff syndrome       |                |               |               |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 5 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 0             | 0             |
| Infections and infestations |                |               |               |
| Acute sinusitis             |                |               |               |
| subjects affected / exposed | 0 / 86 (0.00%) | 0 / 5 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Bronchitis                  |                |               |               |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 5 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1              | 0             | 0             |
| Chancroid                   |                |               |               |

|  |                |                |               |
|--|----------------|----------------|---------------|
| subjects affected / exposed                    | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Conjunctivitis                                 |                |                |               |
| subjects affected / exposed                    | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Fungal infection                               |                |                |               |
| subjects affected / exposed                    | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Gingivitis                                     |                |                |               |
| subjects affected / exposed                    | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Groin infection                                |                |                |               |
| subjects affected / exposed                    | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Herpes simplex                                 |                |                |               |
| subjects affected / exposed                    | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Herpes zoster                                  |                |                |               |
| subjects affected / exposed                    | 5 / 86 (5.81%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 6              | 0              | 0             |
| Lower respiratory tract infection<br>bacterial |                |                |               |
| subjects affected / exposed                    | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Lung infection                                 |                |                |               |
| subjects affected / exposed                    | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Lymph gland infection                          |                |                |               |
| subjects affected / exposed                    | 0 / 86 (0.00%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0             |
| Oral candidiasis                               |                |                |               |
| subjects affected / exposed                    | 1 / 86 (1.16%) | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)                              | 1              | 1              | 0             |
| Pneumonia                                      |                |                |               |
| subjects affected / exposed                    | 3 / 86 (3.49%) | 2 / 5 (40.00%) | 0 / 1 (0.00%) |
| occurrences (all)                              | 3              | 2              | 0             |

|                                    |                  |                |                 |
|------------------------------------|------------------|----------------|-----------------|
| Sinusitis                          |                  |                |                 |
| subjects affected / exposed        | 2 / 86 (2.33%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                  | 2                | 1              | 0               |
| Skin infection                     |                  |                |                 |
| subjects affected / exposed        | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 1 / 1 (100.00%) |
| occurrences (all)                  | 0                | 0              | 1               |
| Staphylococcal infection           |                  |                |                 |
| subjects affected / exposed        | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                  | 0                | 0              | 0               |
| Systemic candida                   |                  |                |                 |
| subjects affected / exposed        | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                  | 0                | 0              | 0               |
| Tooth infection                    |                  |                |                 |
| subjects affected / exposed        | 0 / 86 (0.00%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                  | 0                | 0              | 0               |
| Upper respiratory tract infection  |                  |                |                 |
| subjects affected / exposed        | 1 / 86 (1.16%)   | 1 / 5 (20.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                  | 1                | 1              | 0               |
| Urinary tract infection            |                  |                |                 |
| subjects affected / exposed        | 5 / 86 (5.81%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                  | 5                | 0              | 0               |
| Viral infection                    |                  |                |                 |
| subjects affected / exposed        | 1 / 86 (1.16%)   | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                  | 1                | 0              | 0               |
| Metabolism and nutrition disorders |                  |                |                 |
| Decreased appetite                 |                  |                |                 |
| subjects affected / exposed        | 27 / 86 (31.40%) | 3 / 5 (60.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                  | 28               | 3              | 0               |
| Dehydration                        |                  |                |                 |
| subjects affected / exposed        | 11 / 86 (12.79%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                  | 15               | 0              | 0               |
| Hyperglycaemia                     |                  |                |                 |
| subjects affected / exposed        | 13 / 86 (15.12%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                  | 15               | 0              | 0               |
| Hypertriglyceridaemia              |                  |                |                 |

|                             |                 |                |               |
|-----------------------------|-----------------|----------------|---------------|
| subjects affected / exposed | 2 / 86 (2.33%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 2               | 0              | 0             |
| Hypoalbuminaemia            |                 |                |               |
| subjects affected / exposed | 3 / 86 (3.49%)  | 1 / 5 (20.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 3               | 1              | 0             |
| Hypocalcaemia               |                 |                |               |
| subjects affected / exposed | 4 / 86 (4.65%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 4               | 0              | 0             |
| Hypokalaemia                |                 |                |               |
| subjects affected / exposed | 5 / 86 (5.81%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 6               | 0              | 0             |
| Hypomagnesaemia             |                 |                |               |
| subjects affected / exposed | 4 / 86 (4.65%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 6               | 0              | 0             |
| Hyponatraemia               |                 |                |               |
| subjects affected / exposed | 6 / 86 (6.98%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 8               | 0              | 0             |
| Hypophosphataemia           |                 |                |               |
| subjects affected / exposed | 9 / 86 (10.47%) | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 9               | 0              | 0             |
| Metabolic acidosis          |                 |                |               |
| subjects affected / exposed | 0 / 86 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |
| Vitamin B12 deficiency      |                 |                |               |
| subjects affected / exposed | 0 / 86 (0.00%)  | 0 / 5 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |

| <b>Non-serious adverse events</b>                                   | <b>PART3B 8 MG QD +<br/>Paci 80 MG/M2</b> | <b>PART3C 8 MG QD +<br/>Rucap 600 MG</b> | <b>PART3D 8 MG QD +<br/>Arbir 1000 MG +<br/>Predni 5 MG</b> |
|---|---|--|---|
| Total subjects affected by non-serious adverse events               |   |  |   |
| subjects affected / exposed   | 2 / 2 (100.00%)                           | 4 / 4 (100.00%)                          | 3 / 3 (100.00%)   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |  |   |
| Basal cell carcinoma  |   |  |   |
| subjects affected / exposed   | 0 / 2 (0.00%)                             | 0 / 4 (0.00%)                            | 0 / 3 (0.00%)   |
| occurrences (all)   | 0   | 0  | 0   |
| Benign neoplasm   |   |  |   |

|  |               |               |               |
|--|---------------|---------------|---------------|
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                                    | 0             | 0             | 0             |
| Squamous cell carcinoma of skin                      |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                                    | 0             | 0             | 0             |
| Vascular disorders                                   |               |               |               |
| Haematoma  |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                                    | 0             | 0             | 0             |
| Hot flush  |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                                    | 0             | 0             | 0             |
| Hypertension   |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                                    | 0             | 0             | 0             |
| Hypotension  |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                                    | 0             | 0             | 0             |
| General disorders and administration site conditions |               |               |               |
| Asthenia   |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                                    | 0             | 0             | 0             |
| Catheter site erythema                               |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                                    | 0             | 0             | 0             |
| Catheter site haemorrhage                            |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                                    | 0             | 0             | 0             |
| Catheter site pain                                   |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                                    | 0             | 0             | 0             |
| Chills   |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                                    | 0             | 0             | 0             |
| Drug withdrawal syndrome                             |               |               |               |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                        | 0              | 0              | 0              |
| Fatigue                                  |                |                |                |
| subjects affected / exposed              | 1 / 2 (50.00%) | 3 / 4 (75.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                        | 1              | 5              | 0              |
| Influenza like illness                   |                |                |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                        | 0              | 0              | 0              |
| Localised oedema                         |                |                |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                        | 0              | 0              | 0              |
| Mucosal dryness                          |                |                |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                        | 0              | 0              | 0              |
| Mucosal haemorrhage                      |                |                |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                        | 0              | 0              | 0              |
| Non-cardiac chest pain                   |                |                |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                        | 0              | 0              | 0              |
| Oedema peripheral                        |                |                |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                        | 0              | 0              | 2              |
| Performance status decreased             |                |                |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                        | 0              | 0              | 0              |
| Pyrexia                                  |                |                |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                        | 0              | 0              | 0              |
| Reproductive system and breast disorders |                |                |                |
| Penile oedema                            |                |                |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                        | 0              | 0              | 1              |
| Vulvovaginal erythema                    |                |                |                |



|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Respiratory, thoracic and mediastinal disorders |                |                |               |
| Chronic obstructive pulmonary disease           |                |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Cough   |                |                |               |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0             |
| Dyspnoea  |                |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 4 (25.00%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0             |
| Dyspnoea exertional                             |                |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 4 (25.00%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0             |
| Epistaxis                                       |                |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Haemoptysis                                     |                |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Hypoxia   |                |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Nasal congestion                                |                |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Oropharyngeal pain                              |                |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Pleural effusion                                |                |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 4 (25.00%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0             |
| Pneumonitis                                     |                |                |               |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Productive cough                                |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 2 / 4 (50.00%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 2              | 0             |
| Pulmonary oedema                                |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Respiratory failure                             |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Sneezing  |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Upper-airway cough syndrome                     |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Wheezing  |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 1 / 4 (25.00%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 1              | 0             |
| Psychiatric disorders                           |               |                |               |
| Agitation                                       |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Anxiety   |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 1 / 4 (25.00%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 1              | 0             |
| Depression                                      |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Insomnia  |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Investigations                                  |               |                |               |
| Activated partial thromboplastin time prolonged |               |                |               |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                        | 0              | 0              | 0              |
| Alanine aminotransferase increased       |                |                |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                        | 0              | 0              | 0              |
| Aspartate aminotransferase increased     |                |                |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                        | 0              | 0              | 0              |
| Bilirubin conjugated increased           |                |                |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                        | 0              | 0              | 0              |
| Blood alkaline phosphatase increased     |                |                |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                        | 0              | 0              | 0              |
| Blood bilirubin increased                |                |                |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                        | 0              | 0              | 1              |
| Blood creatinine increased               |                |                |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                        | 0              | 0              | 0              |
| Blood pressure increased                 |                |                |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                        | 0              | 0              | 0              |
| International normalised ratio increased |                |                |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                        | 0              | 0              | 0              |
| Neutrophil count decreased               |                |                |                |
| subjects affected / exposed              | 1 / 2 (50.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                        | 1              | 0              | 0              |
| Platelet count decreased                 |                |                |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 1 / 4 (25.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                        | 0              | 1              | 0              |
| Prothrombin time prolonged               |                |                |                |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Troponin I increased                           |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Troponin increased                             |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Weight decreased                               |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Weight increased                               |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| White blood cell count decreased               |                |                |                |
| subjects affected / exposed                    | 1 / 2 (50.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 1              | 0              | 0              |
| Injury, poisoning and procedural complications |                |                |                |
| Arthropod bite                                 |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                              | 0              | 0              | 1              |
| Contusion                                      |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Eye contusion                                  |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Fall   |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Fractured sacrum                               |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 1 / 4 (25.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0              | 1              | 0              |
| Infusion related reaction                      |                |                |                |

|                                      |                |               |               |
|--------------------------------------|----------------|---------------|---------------|
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Laceration                           |                |               |               |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Transfusion reaction                 |                |               |               |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Cardiac disorders                    |                |               |               |
| Atrial fibrillation                  |                |               |               |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Atrioventricular block second degree |                |               |               |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Sinus bradycardia                    |                |               |               |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Sinus tachycardia                    |                |               |               |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Tachycardia                          |                |               |               |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Ventricular arrhythmia               |                |               |               |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Nervous system disorders             |                |               |               |
| Brain oedema                         |                |               |               |
| subjects affected / exposed          | 1 / 2 (50.00%) | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                    | 1              | 0             | 0             |
| Dizziness                            |                |               |               |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 4 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 0             | 0             |
| Dysgeusia                            |                |               |               |

|                                      |                |                |               |
|--------------------------------------|----------------|----------------|---------------|
| subjects affected / exposed          | 1 / 2 (50.00%) | 2 / 4 (50.00%) | 0 / 3 (0.00%) |
| occurrences (all)                    | 1              | 2              | 0             |
| Headache                             |                |                |               |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0             |
| Neuropathy peripheral                |                |                |               |
| subjects affected / exposed          | 1 / 2 (50.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                    | 1              | 0              | 0             |
| Post herpetic neuralgia              |                |                |               |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0             |
| Syncope                              |                |                |               |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0             |
| Blood and lymphatic system disorders |                |                |               |
| Anaemia                              |                |                |               |
| subjects affected / exposed          | 1 / 2 (50.00%) | 2 / 4 (50.00%) | 0 / 3 (0.00%) |
| occurrences (all)                    | 3              | 2              | 0             |
| Febrile neutropenia                  |                |                |               |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0             |
| Increased tendency to bruise         |                |                |               |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0             |
| Iron deficiency anaemia              |                |                |               |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0             |
| Leukocytosis                         |                |                |               |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0             |
| Leukopenia                           |                |                |               |
| subjects affected / exposed          | 1 / 2 (50.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                    | 1              | 0              | 0             |
| Lymph node pain                      |                |                |               |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0             |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Lymphopenia                 |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Neutropenia                 |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Splenic infarction          |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Splenomegaly                |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Thrombocytopenia            |                |                |                |
| subjects affected / exposed | 1 / 2 (50.00%) | 2 / 4 (50.00%) | 1 / 3 (33.33%) |
| occurrences (all)           | 1              | 5              | 1              |
| Ear and labyrinth disorders |                |                |                |
| Vertigo                     |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Eye disorders               |                |                |                |
| Cataract                    |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Eye pain                    |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Eyelid oedema               |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Retinal haemorrhage         |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Vitreous floaters           |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Gastrointestinal disorders  |                |                |                |

|                                  |               |                |                |
|----------------------------------|---------------|----------------|----------------|
| Abdominal distension             |               |                |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0             | 0              | 0              |
| Abdominal pain                   |               |                |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 1 / 4 (25.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                | 0             | 1              | 0              |
| Abdominal pain upper             |               |                |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0             | 0              | 0              |
| Anal fissure                     |               |                |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0             | 0              | 0              |
| Constipation                     |               |                |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0             | 0              | 0              |
| Diarrhoea                        |               |                |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 2 / 4 (50.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                | 0             | 3              | 0              |
| Dry mouth                        |               |                |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                | 0             | 0              | 1              |
| Dyspepsia                        |               |                |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0             | 0              | 0              |
| Flatulence                       |               |                |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0             | 0              | 0              |
| Gastrooesophageal reflux disease |               |                |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 1 / 4 (25.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                | 0             | 1              | 0              |
| Haemorrhoids                     |               |                |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0             | 0              | 0              |
| Lip haemorrhage                  |               |                |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0             | 0              | 0              |



|  |                |                |                |
|--|----------------|----------------|----------------|
| Nausea                                 |                |                |                |
| subjects affected / exposed            | 1 / 2 (50.00%) | 3 / 4 (75.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                      | 2              | 3              | 0              |
| Oesophageal haemorrhage                |                |                |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Oral pain                              |                |                |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Stomatitis                             |                |                |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 1 / 4 (25.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                      | 0              | 1              | 0              |
| Vomiting                               |                |                |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 3 / 4 (75.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                      | 0              | 5              | 0              |
| Hepatobiliary disorders                |                |                |                |
| Hyperbilirubinaemia                    |                |                |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Skin and subcutaneous tissue disorders |                |                |                |
| Acne                                   |                |                |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Alopecia                               |                |                |                |
| subjects affected / exposed            | 1 / 2 (50.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                      | 1              | 0              | 0              |
| Angioedema                             |                |                |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Dry skin                               |                |                |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Erythema                               |                |                |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Pain of skin                           |                |                |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Petechiae                                       |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Pruritus  |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Purpura   |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Rash  |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                               | 0             | 0              | 1              |
| Scab  |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Skin ulcer                                      |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Renal and urinary disorders                     |               |                |                |
| Acute kidney injury                             |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Dysuria   |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Haematuria                                      |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 1 / 4 (25.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 1              | 0              |
| Urinary retention                               |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Musculoskeletal and connective tissue disorders |               |                |                |

|                             |               |                |                |
|-----------------------------|---------------|----------------|----------------|
| Arthralgia                  |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Back pain                   |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Flank pain                  |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Muscle spasms               |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Muscular weakness           |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Musculoskeletal pain        |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)           | 0             | 0              | 1              |
| Neck pain                   |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Pain in jaw                 |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Rotator cuff syndrome       |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Infections and infestations |               |                |                |
| Acute sinusitis             |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 4 (25.00%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0              |
| Bronchitis                  |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 4 (25.00%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0              |
| Chancroid                   |               |                |                |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                              | 0              | 0              | 1              |
| Conjunctivitis                                 |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Fungal infection                               |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 1 / 4 (25.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0              | 1              | 0              |
| Gingivitis                                     |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Groin infection                                |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Herpes simplex                                 |                |                |                |
| subjects affected / exposed                    | 1 / 2 (50.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 1              | 0              | 0              |
| Herpes zoster                                  |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Lower respiratory tract infection<br>bacterial |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Lung infection                                 |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Lymph gland infection                          |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Oral candidiasis                               |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Pneumonia                                      |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |

|                                    |               |                |                |
|------------------------------------|---------------|----------------|----------------|
| Sinusitis                          |               |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0             | 0              | 0              |
| Skin infection                     |               |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0             | 0              | 0              |
| Staphylococcal infection           |               |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0             | 0              | 0              |
| Systemic candida                   |               |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0             | 0              | 0              |
| Tooth infection                    |               |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%) | 1 / 4 (25.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0             | 1              | 0              |
| Upper respiratory tract infection  |               |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0             | 0              | 0              |
| Urinary tract infection            |               |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%) | 1 / 4 (25.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0             | 1              | 0              |
| Viral infection                    |               |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0             | 0              | 0              |
| Metabolism and nutrition disorders |               |                |                |
| Decreased appetite                 |               |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%) | 3 / 4 (75.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0             | 3              | 0              |
| Dehydration                        |               |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%) | 2 / 4 (50.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0             | 2              | 0              |
| Hyperglycaemia                     |               |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                  | 0             | 0              | 1              |
| Hypertriglyceridaemia              |               |                |                |

|                             |               |                |               |
|-----------------------------|---------------|----------------|---------------|
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hypoalbuminaemia            |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hypocalcaemia               |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 4 (25.00%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0             | 2              | 0             |
| Hypokalaemia                |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hypomagnesaemia             |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hyponatraemia               |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hypophosphataemia           |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 4 (25.00%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0             | 1              | 0             |
| Metabolic acidosis          |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Vitamin B12 deficiency      |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 4 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |

| <b>Non-serious adverse events</b>                                      | PART3E 8 MG QD +<br>Rux 20 MG | PART3F 8 MG QD +<br>Azacitadine 75<br>MG/M2 |  |
|--|-------------------------------|---|--|
| Total subjects affected by non-serious<br>adverse events               |                               |   |  |
| subjects affected / exposed  | 1 / 1 (100.00%)               | 2 / 2 (100.00%)                             |  |
| Neoplasms benign, malignant and<br>unspecified (incl cysts and polyps) |                               |   |  |
| Basal cell carcinoma   |                               |   |  |
| subjects affected / exposed  | 0 / 1 (0.00%)                 | 0 / 2 (0.00%)                               |  |
| occurrences (all)  | 0                             | 0   |  |
| Benign neoplasm  |                               |   |  |

|  |               |               |  |
|--|---------------|---------------|--|
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                                    | 0             | 0             |  |
| Squamous cell carcinoma of skin                      |               |               |  |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                                    | 0             | 0             |  |
| Vascular disorders                                   |               |               |  |
| Haematoma  |               |               |  |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                                    | 0             | 0             |  |
| Hot flush  |               |               |  |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                                    | 0             | 0             |  |
| Hypertension   |               |               |  |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                                    | 0             | 0             |  |
| Hypotension  |               |               |  |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                                    | 0             | 0             |  |
| General disorders and administration site conditions |               |               |  |
| Asthenia   |               |               |  |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                                    | 0             | 0             |  |
| Catheter site erythema                               |               |               |  |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                                    | 0             | 0             |  |
| Catheter site haemorrhage                            |               |               |  |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                                    | 0             | 0             |  |
| Catheter site pain                                   |               |               |  |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                                    | 0             | 0             |  |
| Chills   |               |               |  |
| subjects affected / exposed                          | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                                    | 0             | 0             |  |
| Drug withdrawal syndrome                             |               |               |  |

|  |                 |                |  |
|--|-----------------|----------------|--|
| subjects affected / exposed              | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                        | 0               | 0              |  |
| Fatigue                                  |                 |                |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   | 1 / 2 (50.00%) |  |
| occurrences (all)                        | 0               | 1              |  |
| Influenza like illness                   |                 |                |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                        | 0               | 0              |  |
| Localised oedema                         |                 |                |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                        | 0               | 0              |  |
| Mucosal dryness                          |                 |                |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                        | 0               | 0              |  |
| Mucosal haemorrhage                      |                 |                |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                        | 0               | 0              |  |
| Non-cardiac chest pain                   |                 |                |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                        | 0               | 0              |  |
| Oedema peripheral                        |                 |                |  |
| subjects affected / exposed              | 1 / 1 (100.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                        | 1               | 0              |  |
| Performance status decreased             |                 |                |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                        | 0               | 0              |  |
| Pyrexia                                  |                 |                |  |
| subjects affected / exposed              | 1 / 1 (100.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                        | 1               | 0              |  |
| Reproductive system and breast disorders |                 |                |  |
| Penile oedema                            |                 |                |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                        | 0               | 0              |  |
| Vulvovaginal erythema                    |                 |                |  |



|   |               |                |  |
|---|---------------|----------------|--|
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                               | 0             | 0              |  |
| Respiratory, thoracic and mediastinal disorders |               |                |  |
| Chronic obstructive pulmonary disease           |               |                |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                               | 0             | 0              |  |
| Cough   |               |                |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                               | 0             | 0              |  |
| Dyspnoea  |               |                |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                               | 0             | 0              |  |
| Dyspnoea exertional                             |               |                |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                               | 0             | 0              |  |
| Epistaxis                                       |               |                |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                               | 0             | 0              |  |
| Haemoptysis                                     |               |                |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                               | 0             | 0              |  |
| Hypoxia   |               |                |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                               | 0             | 0              |  |
| Nasal congestion                                |               |                |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                               | 0             | 0              |  |
| Oropharyngeal pain                              |               |                |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 1 / 2 (50.00%) |  |
| occurrences (all)                               | 0             | 1              |  |
| Pleural effusion                                |               |                |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                               | 0             | 0              |  |
| Pneumonitis                                     |               |                |  |

|   |               |               |  |
|---|---------------|---------------|--|
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                               | 0             | 0             |  |
| Productive cough                                |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                               | 0             | 0             |  |
| Pulmonary oedema                                |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                               | 0             | 0             |  |
| Respiratory failure                             |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                               | 0             | 0             |  |
| Sneezing  |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                               | 0             | 0             |  |
| Upper-airway cough syndrome                     |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                               | 0             | 0             |  |
| Wheezing  |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                               | 0             | 0             |  |
| Psychiatric disorders                           |               |               |  |
| Agitation                                       |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                               | 0             | 0             |  |
| Anxiety   |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                               | 0             | 0             |  |
| Depression                                      |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                               | 0             | 0             |  |
| Insomnia  |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                               | 0             | 0             |  |
| Investigations                                  |               |               |  |
| Activated partial thromboplastin time prolonged |               |               |  |

|  |                 |                |  |
|--|-----------------|----------------|--|
| subjects affected / exposed              | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                        | 0               | 0              |  |
| Alanine aminotransferase increased       |                 |                |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   | 1 / 2 (50.00%) |  |
| occurrences (all)                        | 0               | 1              |  |
| Aspartate aminotransferase increased     |                 |                |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                        | 0               | 0              |  |
| Bilirubin conjugated increased           |                 |                |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                        | 0               | 0              |  |
| Blood alkaline phosphatase increased     |                 |                |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                        | 0               | 0              |  |
| Blood bilirubin increased                |                 |                |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                        | 0               | 0              |  |
| Blood creatinine increased               |                 |                |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                        | 0               | 0              |  |
| Blood pressure increased                 |                 |                |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                        | 0               | 0              |  |
| International normalised ratio increased |                 |                |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                        | 0               | 0              |  |
| Neutrophil count decreased               |                 |                |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                        | 0               | 0              |  |
| Platelet count decreased                 |                 |                |  |
| subjects affected / exposed              | 1 / 1 (100.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                        | 1               | 0              |  |
| Prothrombin time prolonged               |                 |                |  |

|  |                 |                |  |
|--|-----------------|----------------|--|
| subjects affected / exposed                    | 0 / 1 (0.00%)   | 1 / 2 (50.00%) |  |
| occurrences (all)                              | 0               | 1              |  |
| Troponin I increased                           |                 |                |  |
| subjects affected / exposed                    | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                              | 0               | 0              |  |
| Troponin increased                             |                 |                |  |
| subjects affected / exposed                    | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                              | 0               | 0              |  |
| Weight decreased                               |                 |                |  |
| subjects affected / exposed                    | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                              | 0               | 0              |  |
| Weight increased                               |                 |                |  |
| subjects affected / exposed                    | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                              | 0               | 0              |  |
| White blood cell count decreased               |                 |                |  |
| subjects affected / exposed                    | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                              | 0               | 0              |  |
| Injury, poisoning and procedural complications |                 |                |  |
| Arthropod bite                                 |                 |                |  |
| subjects affected / exposed                    | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                              | 0               | 0              |  |
| Contusion                                      |                 |                |  |
| subjects affected / exposed                    | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                              | 0               | 0              |  |
| Eye contusion                                  |                 |                |  |
| subjects affected / exposed                    | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                              | 0               | 0              |  |
| Fall   |                 |                |  |
| subjects affected / exposed                    | 1 / 1 (100.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                              | 1               | 0              |  |
| Fractured sacrum                               |                 |                |  |
| subjects affected / exposed                    | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                              | 0               | 0              |  |
| Infusion related reaction                      |                 |                |  |

|                                      |                 |               |  |
|--------------------------------------|-----------------|---------------|--|
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                    | 0               | 0             |  |
| Laceration                           |                 |               |  |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                    | 0               | 0             |  |
| Transfusion reaction                 |                 |               |  |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                    | 0               | 0             |  |
| Cardiac disorders                    |                 |               |  |
| Atrial fibrillation                  |                 |               |  |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                    | 0               | 0             |  |
| Atrioventricular block second degree |                 |               |  |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                    | 0               | 0             |  |
| Sinus bradycardia                    |                 |               |  |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                    | 0               | 0             |  |
| Sinus tachycardia                    |                 |               |  |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                    | 0               | 0             |  |
| Tachycardia                          |                 |               |  |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                    | 0               | 0             |  |
| Ventricular arrhythmia               |                 |               |  |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                    | 0               | 0             |  |
| Nervous system disorders             |                 |               |  |
| Brain oedema                         |                 |               |  |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                    | 0               | 0             |  |
| Dizziness                            |                 |               |  |
| subjects affected / exposed          | 1 / 1 (100.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                    | 1               | 0             |  |
| Dysgeusia                            |                 |               |  |

|                                      |                 |                |  |
|--------------------------------------|-----------------|----------------|--|
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                    | 0               | 0              |  |
| Headache                             |                 |                |  |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                    | 0               | 0              |  |
| Neuropathy peripheral                |                 |                |  |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                    | 0               | 0              |  |
| Post herpetic neuralgia              |                 |                |  |
| subjects affected / exposed          | 1 / 1 (100.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                    | 1               | 0              |  |
| Syncope                              |                 |                |  |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                    | 0               | 0              |  |
| Blood and lymphatic system disorders |                 |                |  |
| Anaemia                              |                 |                |  |
| subjects affected / exposed          | 1 / 1 (100.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                    | 1               | 0              |  |
| Febrile neutropenia                  |                 |                |  |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                    | 0               | 0              |  |
| Increased tendency to bruise         |                 |                |  |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                    | 0               | 0              |  |
| Iron deficiency anaemia              |                 |                |  |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                    | 0               | 0              |  |
| Leukocytosis                         |                 |                |  |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                    | 0               | 0              |  |
| Leukopenia                           |                 |                |  |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 1 / 2 (50.00%) |  |
| occurrences (all)                    | 0               | 1              |  |
| Lymph node pain                      |                 |                |  |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)                    | 0               | 0              |  |

|                             |               |                |  |
|-----------------------------|---------------|----------------|--|
| Lymphopenia                 |               |                |  |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 2 (50.00%) |  |
| occurrences (all)           | 0             | 1              |  |
| Neutropenia                 |               |                |  |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 2 (50.00%) |  |
| occurrences (all)           | 0             | 2              |  |
| Splenic infarction          |               |                |  |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0             | 0              |  |
| Splenomegaly                |               |                |  |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0             | 0              |  |
| Thrombocytopenia            |               |                |  |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0             | 0              |  |
| Ear and labyrinth disorders |               |                |  |
| Vertigo                     |               |                |  |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0             | 0              |  |
| Eye disorders               |               |                |  |
| Cataract                    |               |                |  |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0             | 0              |  |
| Eye pain                    |               |                |  |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0             | 0              |  |
| Eyelid oedema               |               |                |  |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0             | 0              |  |
| Retinal haemorrhage         |               |                |  |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0             | 0              |  |
| Vitreous floaters           |               |                |  |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0             | 0              |  |
| Gastrointestinal disorders  |               |                |  |

|                                  |                 |                |
|----------------------------------|-----------------|----------------|
| Abdominal distension             |                 |                |
| subjects affected / exposed      | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |
| occurrences (all)                | 0               | 0              |
| Abdominal pain                   |                 |                |
| subjects affected / exposed      | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |
| occurrences (all)                | 0               | 0              |
| Abdominal pain upper             |                 |                |
| subjects affected / exposed      | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |
| occurrences (all)                | 0               | 0              |
| Anal fissure                     |                 |                |
| subjects affected / exposed      | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |
| occurrences (all)                | 0               | 0              |
| Constipation                     |                 |                |
| subjects affected / exposed      | 0 / 1 (0.00%)   | 1 / 2 (50.00%) |
| occurrences (all)                | 0               | 1              |
| Diarrhoea                        |                 |                |
| subjects affected / exposed      | 1 / 1 (100.00%) | 1 / 2 (50.00%) |
| occurrences (all)                | 1               | 2              |
| Dry mouth                        |                 |                |
| subjects affected / exposed      | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |
| occurrences (all)                | 0               | 0              |
| Dyspepsia                        |                 |                |
| subjects affected / exposed      | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |
| occurrences (all)                | 0               | 0              |
| Flatulence                       |                 |                |
| subjects affected / exposed      | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |
| occurrences (all)                | 0               | 0              |
| Gastrooesophageal reflux disease |                 |                |
| subjects affected / exposed      | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |
| occurrences (all)                | 0               | 0              |
| Haemorrhoids                     |                 |                |
| subjects affected / exposed      | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |
| occurrences (all)                | 0               | 0              |
| Lip haemorrhage                  |                 |                |
| subjects affected / exposed      | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |
| occurrences (all)                | 0               | 0              |



|  |               |                |  |
|--|---------------|----------------|--|
| Nausea                                 |               |                |  |
| subjects affected / exposed            | 0 / 1 (0.00%) | 1 / 2 (50.00%) |  |
| occurrences (all)                      | 0             | 1              |  |
| Oesophageal haemorrhage                |               |                |  |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                      | 0             | 0              |  |
| Oral pain                              |               |                |  |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                      | 0             | 0              |  |
| Stomatitis                             |               |                |  |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                      | 0             | 0              |  |
| Vomiting                               |               |                |  |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                      | 0             | 0              |  |
| Hepatobiliary disorders                |               |                |  |
| Hyperbilirubinaemia                    |               |                |  |
| subjects affected / exposed            | 0 / 1 (0.00%) | 1 / 2 (50.00%) |  |
| occurrences (all)                      | 0             | 1              |  |
| Skin and subcutaneous tissue disorders |               |                |  |
| Acne                                   |               |                |  |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                      | 0             | 0              |  |
| Alopecia                               |               |                |  |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                      | 0             | 0              |  |
| Angioedema                             |               |                |  |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                      | 0             | 0              |  |
| Dry skin                               |               |                |  |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                      | 0             | 0              |  |
| Erythema                               |               |                |  |
| subjects affected / exposed            | 0 / 1 (0.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)                      | 0             | 0              |  |
| Pain of skin                           |               |                |  |

|   |               |               |  |
|---|---------------|---------------|--|
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                               | 0             | 0             |  |
| Petechiae                                       |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                               | 0             | 0             |  |
| Pruritus  |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                               | 0             | 0             |  |
| Purpura   |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                               | 0             | 0             |  |
| Rash  |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                               | 0             | 0             |  |
| Scab  |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                               | 0             | 0             |  |
| Skin ulcer                                      |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                               | 0             | 0             |  |
| Renal and urinary disorders                     |               |               |  |
| Acute kidney injury                             |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                               | 0             | 0             |  |
| Dysuria   |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                               | 0             | 0             |  |
| Haematuria                                      |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                               | 0             | 0             |  |
| Urinary retention                               |               |               |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                               | 0             | 0             |  |
| Musculoskeletal and connective tissue disorders |               |               |  |

|                             |                 |                |  |
|-----------------------------|-----------------|----------------|--|
| Arthralgia                  |                 |                |  |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0               | 0              |  |
| Back pain                   |                 |                |  |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0               | 0              |  |
| Flank pain                  |                 |                |  |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0               | 0              |  |
| Muscle spasms               |                 |                |  |
| subjects affected / exposed | 0 / 1 (0.00%)   | 1 / 2 (50.00%) |  |
| occurrences (all)           | 0               | 1              |  |
| Muscular weakness           |                 |                |  |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0               | 0              |  |
| Musculoskeletal pain        |                 |                |  |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0               | 0              |  |
| Neck pain                   |                 |                |  |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0               | 0              |  |
| Pain in jaw                 |                 |                |  |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0               | 0              |  |
| Rotator cuff syndrome       |                 |                |  |
| subjects affected / exposed | 1 / 1 (100.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 1               | 0              |  |
| Infections and infestations |                 |                |  |
| Acute sinusitis             |                 |                |  |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0               | 0              |  |
| Bronchitis                  |                 |                |  |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0               | 0              |  |
| Chancroid                   |                 |                |  |

|  |                 |               |  |
|--|-----------------|---------------|--|
| subjects affected / exposed                    | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 0               | 0             |  |
| Conjunctivitis                                 |                 |               |  |
| subjects affected / exposed                    | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 0               | 0             |  |
| Fungal infection                               |                 |               |  |
| subjects affected / exposed                    | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 0               | 0             |  |
| Gingivitis                                     |                 |               |  |
| subjects affected / exposed                    | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 0               | 0             |  |
| Groin infection                                |                 |               |  |
| subjects affected / exposed                    | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 0               | 0             |  |
| Herpes simplex                                 |                 |               |  |
| subjects affected / exposed                    | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 0               | 0             |  |
| Herpes zoster                                  |                 |               |  |
| subjects affected / exposed                    | 1 / 1 (100.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 1               | 0             |  |
| Lower respiratory tract infection<br>bacterial |                 |               |  |
| subjects affected / exposed                    | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 0               | 0             |  |
| Lung infection                                 |                 |               |  |
| subjects affected / exposed                    | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 0               | 0             |  |
| Lymph gland infection                          |                 |               |  |
| subjects affected / exposed                    | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 0               | 0             |  |
| Oral candidiasis                               |                 |               |  |
| subjects affected / exposed                    | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 0               | 0             |  |
| Pneumonia                                      |                 |               |  |
| subjects affected / exposed                    | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                              | 0               | 0             |  |

|                                    |                 |               |  |
|------------------------------------|-----------------|---------------|--|
| Sinusitis                          |                 |               |  |
| subjects affected / exposed        | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                  | 0               | 0             |  |
| Skin infection                     |                 |               |  |
| subjects affected / exposed        | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                  | 0               | 0             |  |
| Staphylococcal infection           |                 |               |  |
| subjects affected / exposed        | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                  | 0               | 0             |  |
| Systemic candida                   |                 |               |  |
| subjects affected / exposed        | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                  | 0               | 0             |  |
| Tooth infection                    |                 |               |  |
| subjects affected / exposed        | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                  | 0               | 0             |  |
| Upper respiratory tract infection  |                 |               |  |
| subjects affected / exposed        | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                  | 0               | 0             |  |
| Urinary tract infection            |                 |               |  |
| subjects affected / exposed        | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                  | 0               | 0             |  |
| Viral infection                    |                 |               |  |
| subjects affected / exposed        | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                  | 0               | 0             |  |
| Metabolism and nutrition disorders |                 |               |  |
| Decreased appetite                 |                 |               |  |
| subjects affected / exposed        | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                  | 0               | 0             |  |
| Dehydration                        |                 |               |  |
| subjects affected / exposed        | 0 / 1 (0.00%)   | 0 / 2 (0.00%) |  |
| occurrences (all)                  | 0               | 0             |  |
| Hyperglycaemia                     |                 |               |  |
| subjects affected / exposed        | 1 / 1 (100.00%) | 0 / 2 (0.00%) |  |
| occurrences (all)                  | 1               | 0             |  |
| Hypertriglyceridaemia              |                 |               |  |

|                             |                 |                |  |
|-----------------------------|-----------------|----------------|--|
| subjects affected / exposed | 1 / 1 (100.00%) | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 1               | 0              |  |
| Hypoalbuminaemia            |                 |                |  |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0               | 0              |  |
| Hypocalcaemia               |                 |                |  |
| subjects affected / exposed | 0 / 1 (0.00%)   | 1 / 2 (50.00%) |  |
| occurrences (all)           | 0               | 1              |  |
| Hypokalaemia                |                 |                |  |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0               | 0              |  |
| Hypomagnesaemia             |                 |                |  |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0               | 0              |  |
| Hyponatraemia               |                 |                |  |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0               | 0              |  |
| Hypophosphataemia           |                 |                |  |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0               | 0              |  |
| Metabolic acidosis          |                 |                |  |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0               | 0              |  |
| Vitamin B12 deficiency      |                 |                |  |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 2 (0.00%)  |  |
| occurrences (all)           | 0               | 0              |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported