



## Clinical trial results:

### A Study of the Safety, Tolerability, and Pharmacokinetics of Intravenous (IV) and Powder for Oral Suspension Formulations of Posaconazole (POS) in Immunocompromised Pediatric Subjects with Neutropenia

#### Summary

|                          |  |
|--------------------------|--|
| EudraCT number           | 2014-002807-10                         |
| Trial protocol           | DE NO SE DK CZ ES BE IT Outside EU/EEA |
| Global end of trial date | 03 September 2018                      |

#### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v2 (current)  |
| This version publication date  | 08 May 2020   |
| First version publication date | 09 March 2019 |
| Version creation reason        |               |

#### Trial information

##### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | 5592-097 |
|-----------------------|----------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02452034 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Merck Sharp & Dohme Corp.  |
| Sponsor organisation address | 2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033                               |
| Public contact               | Clinical Trials Disclosure, Merck Sharp & Dohme Corp.,<br>ClinicalTrialsDisclosure@merck.com |
| Scientific contact           | Clinical Trials Disclosure, Merck Sharp & Dohme Corp.,<br>ClinicalTrialsDisclosure@merck.com |

Notes:

#### Paediatric regulatory details

|  |                     |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-000468-PIP02-12 |
| 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? | Yes                 |

Notes:

## Results analysis stage

|  |                   |
|--|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 03 September 2018 |
| Is this the analysis of the primary completion data? | No                |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 03 September 2018 |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

This study aims to evaluate the pharmacokinetics (PK) of posaconazole (POS) administered intravenously (IV) or orally to immunocompromised pediatric participants.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research

Background therapy: -

Evidence for comparator: -

|   |                   |
|---|-------------------|
| Actual start date of recruitment                          | 07 September 2015 |
| Long term follow-up planned                               | No                |
| Independent data monitoring committee (IDMC) involvement? | Yes               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Belgium: 13        |
| Country: Number of subjects enrolled | Czech Republic: 19 |
| Country: Number of subjects enrolled | Denmark: 3         |
| Country: Number of subjects enrolled | Germany: 27        |
| Country: Number of subjects enrolled | Guatemala: 4       |
| Country: Number of subjects enrolled | Italy: 8           |
| Country: Number of subjects enrolled | Norway: 7          |
| Country: Number of subjects enrolled | Spain: 5           |
| Country: Number of subjects enrolled | Sweden: 4          |
| Country: Number of subjects enrolled | Thailand: 5        |
| Country: Number of subjects enrolled | United States: 23  |
| Worldwide total number of subjects   | 118                |
| EEA total number of subjects         | 86                 |

Notes:

| <b>Subjects enrolled per age group</b>    |    |
|---|----|
| 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)                     | 73 |
| Adolescents (12-17 years)                 | 45 |
| Adults (18-64 years)                      | 0  |
| From 65 to 84 years                       | 0  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Immunocompromised participants aged 2 to 17 years old, with neutropenia expected to last for at least 7 days following start of study treatment, were enrolled in this study.

### Period 1

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

### Arms

|                              |                               |
|------------------------------|-------------------------------|
| Are arms mutually exclusive? | Yes                           |
| <b>Arm title</b>             | 3.5 mg/kg POS (2-7 years old) |

Arm description:

Children 2 to less than 7 years of age received posaconazole (POS) at 3.5 mg/kg by intravenous (IV) solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 3.5 mg/kg POS once daily by powder for oral suspension (PFS) for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

|  |                                 |
|--|---------------------------------|
| Arm type                               | Experimental                    |
| Investigational medicinal product name | Posaconazole                    |
| Investigational medicinal product code |                                 |
| Other name                             | Noxafil                         |
| Pharmaceutical forms                   | Solution for injection/infusion |
| Routes of administration               | Intravenous use                 |

Dosage and administration details:

Posaconazole at 3.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10.

|  |  |
|--|--|
| Investigational medicinal product name | Posaconazole                           |
| Investigational medicinal product code |  |
| Other name                             | Noxafil                                |
| Pharmaceutical forms                   | Powder and solvent for oral suspension |
| Routes of administration               | Oral use                               |

Dosage and administration details:

Posaconazole at 3.5 mg/kg once daily by PFS for a minimum of 10 days

|                  |                                |
|------------------|--------------------------------|
| <b>Arm title</b> | 3.5 mg/kg POS (7-17 years old) |
|------------------|--------------------------------|

Arm description:

Children 7 to 17 years of age received POS at 3.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 3.5 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

|  |                                 |
|--|---------------------------------|
| Arm type                               | Experimental                    |
| Investigational medicinal product name | Posaconazole                    |
| Investigational medicinal product code |                                 |
| Other name                             | Noxafil                         |
| Pharmaceutical forms                   | Solution for injection/infusion |
| Routes of administration               | Intravenous use                 |

Dosage and administration details:

Posaconazole at 3.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10.

|  |  |
|--|--|
| Investigational medicinal product name                               | Posaconazole                           |
| Investigational medicinal product code                               |  |
| Other name   | Noxafil                                |
| Pharmaceutical forms   | Powder and solvent for oral suspension |
| Routes of administration   | Oral use                               |
| Dosage and administration details:                                   |  |
| Posaconazole at 3.5 mg/kg once daily by PFS for a minimum of 10 days |  |
| <b>Arm title</b>   | 4.5 mg/kg POS (2-7 years old)          |

Arm description:

Children 2 to less than 7 years of age received POS at 4.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 4.5 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

|  |                                 |
|--|---------------------------------|
| Arm type                               | Experimental                    |
| Investigational medicinal product name | Posaconazole                    |
| Investigational medicinal product code |                                 |
| Other name                             | Noxafil                         |
| Pharmaceutical forms                   | Solution for injection/infusion |
| Routes of administration               | Intravenous use                 |

Dosage and administration details:

Posaconazole at 4.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10.

|  |  |
|--|--|
| Investigational medicinal product name | Posaconazole                           |
| Investigational medicinal product code |  |
| Other name                             | Noxafil                                |
| Pharmaceutical forms                   | Powder and solvent for oral suspension |
| Routes of administration               | Oral use                               |

Dosage and administration details:

Posaconazole at 4.5 mg/kg once daily by PFS for a minimum of 10 days

|                  |                                |
|------------------|--------------------------------|
| <b>Arm title</b> | 4.5 mg/kg POS (7-17 years old) |
|------------------|--------------------------------|

Arm description:

Children 7 to 17 years of age received POS at 4.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 4.5 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

|  |                                 |
|--|---------------------------------|
| Arm type                               | Experimental                    |
| Investigational medicinal product name | Posaconazole                    |
| Investigational medicinal product code |                                 |
| Other name                             | Noxafil                         |
| Pharmaceutical forms                   | Solution for injection/infusion |
| Routes of administration               | Intravenous use                 |

Dosage and administration details:

Posaconazole at 4.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10.

|  |  |
|--|--|
| Investigational medicinal product name | Posaconazole                           |
| Investigational medicinal product code |  |
| Other name                             | Noxafil                                |
| Pharmaceutical forms                   | Powder and solvent for oral suspension |
| Routes of administration               | Oral use                               |

Dosage and administration details:

Posaconazole at 4.5 mg/kg once daily by PFS for a minimum of 10 days

|                  |                             |
|------------------|-----------------------------|
| <b>Arm title</b> | 6 mg/kg POS (2-7 years old) |
|------------------|-----------------------------|

Arm description:

Children 2 to less than 7 years of age received POS at 6 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 6 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

|  |                                 |
|--|---------------------------------|
| Arm type                               | Experimental                    |
| Investigational medicinal product name | Posaconazole                    |
| Investigational medicinal product code |                                 |
| Other name                             | Noxafil                         |
| Pharmaceutical forms                   | Solution for injection/infusion |
| Routes of administration               | Intravenous use                 |

Dosage and administration details:

Posaconazole at 6 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10.

|  |  |
|--|--|
| Investigational medicinal product name | Posaconazole                           |
| Investigational medicinal product code |  |
| Other name                             | Noxafil                                |
| Pharmaceutical forms                   | Powder and solvent for oral suspension |
| Routes of administration               | Oral use                               |

Dosage and administration details:

Posaconazole at 6 mg/kg once daily by PFS for a minimum of 10 days

|                  |                              |
|------------------|------------------------------|
| <b>Arm title</b> | 6 mg/kg POS (7-17 years old) |
|------------------|------------------------------|

Arm description:

Children 7 to 17 years of age received POS at 6 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 6 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

|  |                                 |
|--|---------------------------------|
| Arm type                               | Experimental                    |
| Investigational medicinal product name | Posaconazole                    |
| Investigational medicinal product code |                                 |
| Other name                             | Noxafil                         |
| Pharmaceutical forms                   | Solution for injection/infusion |
| Routes of administration               | Intravenous use                 |

Dosage and administration details:

Posaconazole at 6 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10.

|  |  |
|--|--|
| Investigational medicinal product name | Posaconazole                           |
| Investigational medicinal product code |  |
| Other name                             | Noxafil                                |
| Pharmaceutical forms                   | Powder and solvent for oral suspension |
| Routes of administration               | Oral use                               |

Dosage and administration details:

Posaconazole at 6 mg/kg once daily by PFS for a minimum of 10 days

| <b>Number of subjects in period 1</b> | 3.5 mg/kg POS (2-7 years old) | 3.5 mg/kg POS (7-17 years old) | 4.5 mg/kg POS (2-7 years old) |
|---------------------------------------|-------------------------------|--------------------------------|-------------------------------|
| Started                               | 16                            | 21                             | 15                            |
| Treated                               | 14                            | 21                             | 15                            |
| Completed                             | 14                            | 20                             | 14                            |
| Not completed                         | 2                             | 1                              | 1                             |
| Physician decision                    | -                             | 1                              | 1                             |
| Screen Failure                        | 1                             | -                              | -                             |
| Adverse event, non-fatal              | -                             | -                              | -                             |
| Death                                 | -                             | -                              | -                             |
| Withdrawn by Parent/Guardian          | 1                             | -                              | -                             |

|                    |   |   |   |
|--------------------|---|---|---|
| Protocol deviation | - | - | - |
|--------------------|---|---|---|

  

| <b>Number of subjects in period 1</b> | <b>4.5 mg/kg POS (7-17 years old)</b> | <b>6 mg/kg POS (2-7 years old)</b> | <b>6 mg/kg POS (7-17 years old)</b> |
|---------------------------------------|---------------------------------------|------------------------------------|-------------------------------------|
| Started                               | 17                                    | 20                                 | 29                                  |
| Treated                               | 16                                    | 20                                 | 29                                  |
| Completed                             | 16                                    | 19                                 | 26                                  |
| Not completed                         | 1                                     | 1                                  | 3                                   |
| Physician decision                    | -                                     | -                                  | -                                   |
| Screen Failure                        | 1                                     | -                                  | -                                   |
| Adverse event, non-fatal              | -                                     | -                                  | 1                                   |
| Death                                 | -                                     | 1                                  | 1                                   |
| Withdrawn by Parent/Guardian          | -                                     | -                                  | -                                   |
| Protocol deviation                    | -                                     | -                                  | 1                                   |

## Baseline characteristics

### Reporting groups

|  |                                |
|--|--------------------------------|
| Reporting group title  | 3.5 mg/kg POS (2-7 years old)  |
| Reporting group description:<br>Children 2 to less than 7 years of age received posaconazole (POS) at 3.5 mg/kg by intravenous (IV) solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 3.5 mg/kg POS once daily by powder for oral suspension (PFS) for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV. |                                |
| Reporting group title  | 3.5 mg/kg POS (7-17 years old) |
| Reporting group description:<br>Children 7 to 17 years of age received POS at 3.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 3.5 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.  |                                |
| Reporting group title  | 4.5 mg/kg POS (2-7 years old)  |
| Reporting group description:<br>Children 2 to less than 7 years of age received POS at 4.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 4.5 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.   |                                |
| Reporting group title  | 4.5 mg/kg POS (7-17 years old) |
| Reporting group description:<br>Children 7 to 17 years of age received POS at 4.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 4.5 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.  |                                |
| Reporting group title  | 6 mg/kg POS (2-7 years old)    |
| Reporting group description:<br>Children 2 to less than 7 years of age received POS at 6 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 6 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.   |                                |
| Reporting group title  | 6 mg/kg POS (7-17 years old)   |
| Reporting group description:<br>Children 7 to 17 years of age received POS at 6 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 6 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.  |                                |

| Reporting group values                             | 3.5 mg/kg POS (2-7 years old) | 3.5 mg/kg POS (7-17 years old) | 4.5 mg/kg POS (2-7 years old) |
|--|-------------------------------|--------------------------------|-------------------------------|
| Number of subjects                                 | 16                            | 21                             | 15                            |
| 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)                              | 16                            | 4                              | 15                            |
| Adolescents (12-17 years)                          | 0                             | 17                             | 0                             |
| Adults (18-64 years)                               | 0                             | 0                              | 0                             |
| From 65-84 years                                   | 0                             | 0                              | 0                             |
| 85 years and over                                  | 0                             | 0                              | 0                             |



|   |              |               |              |
|---|--------------|---------------|--------------|
| Age Continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 3.9<br>± 1.5 | 13.9<br>± 2.1 | 4.1<br>± 1.4 |
| Gender Categorical<br>Units: Subjects                                   |              |               |              |
| Female  | 3            | 11            | 8            |
| Male  | 13           | 10            | 7            |
| Race<br>Units: Subjects   |              |               |              |
| Asian   | 4            | 1             | 2            |
| Black Or African American   | 0            | 0             | 0            |
| Multiple  | 0            | 2             | 0            |
| Native Hawaiian Or Other Pacific Islander                               | 0            | 0             | 1            |
| White   | 12           | 18            | 12           |
| Ethnicity<br>Units: Subjects  |              |               |              |
| Hispanic Or Latino  | 1            | 2             | 2            |
| Not Hispanic Or Latino  | 15           | 19            | 12           |
| Not Reported  | 0            | 0             | 1            |
| Unknown   | 0            | 0             | 0            |

| <b>Reporting group values</b>   | 4.5 mg/kg POS (7-17 years old) | 6 mg/kg POS (2-7 years old) | 6 mg/kg POS (7-17 years old) |
|---|--------------------------------|-----------------------------|------------------------------|
| Number of subjects  | 17                             | 20                          | 29                           |
| 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)   | 5                              | 20                          | 13                           |
| Adolescents (12-17 years)   | 12                             | 0                           | 16                           |
| Adults (18-64 years)  | 0                              | 0                           | 0                            |
| From 65-84 years  | 0                              | 0                           | 0                            |
| 85 years and over   | 0                              | 0                           | 0                            |
| Age Continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 12.5<br>± 2.7                  | 3.9<br>± 1.6                | 12.0<br>± 3.5                |
| Gender Categorical<br>Units: Subjects                                   |                                |                             |                              |
| Female  | 8                              | 10                          | 10                           |
| Male  | 9                              | 10                          | 19                           |
| Race<br>Units: Subjects   |                                |                             |                              |
| Asian   | 2                              | 1                           | 1                            |
| Black Or African American   | 0                              | 1                           | 2                            |
| Multiple  | 2                              | 0                           | 0                            |

|   |    |    |    |
|---|----|----|----|
| Native Hawaiian Or Other Pacific Islander | 0  | 0  | 0  |
| White                                     | 13 | 18 | 26 |
| Ethnicity<br>Units: Subjects              |    |    |    |
| Hispanic Or Latino                        | 4  | 1  | 2  |
| Not Hispanic Or Latino                    | 12 | 18 | 27 |
| Not Reported                              | 1  | 0  | 0  |
| Unknown                                   | 0  | 1  | 0  |

|  |       |  |  |
|--|-------|--|--|
| <b>Reporting group values</b>                      | Total |  |  |
| Number of subjects                                 | 118   |  |  |
| Age Categorical<br>Units: Subjects                 |       |  |  |
| In utero   | 0     |  |  |
| Preterm newborn infants (gestational age < 37 wks) | 0     |  |  |
| Newborns (0-27 days)                               | 0     |  |  |
| Infants and toddlers (28 days-23 months)           | 0     |  |  |
| Children (2-11 years)                              | 73    |  |  |
| Adolescents (12-17 years)                          | 45    |  |  |
| Adults (18-64 years)                               | 0     |  |  |
| From 65-84 years                                   | 0     |  |  |
| 85 years and over                                  | 0     |  |  |
| Age Continuous<br>Units: years                     |       |  |  |
| arithmetic mean                                    |       |  |  |
| standard deviation                                 | -     |  |  |
| Gender Categorical<br>Units: Subjects              |       |  |  |
| Female   | 50    |  |  |
| Male   | 68    |  |  |
| Race<br>Units: Subjects                            |       |  |  |
| Asian  | 11    |  |  |
| Black Or African American                          | 3     |  |  |
| Multiple   | 4     |  |  |
| Native Hawaiian Or Other Pacific Islander          | 1     |  |  |
| White  | 99    |  |  |
| Ethnicity<br>Units: Subjects                       |       |  |  |
| Hispanic Or Latino                                 | 12    |  |  |
| Not Hispanic Or Latino                             | 103   |  |  |
| Not Reported                                       | 2     |  |  |
| Unknown  | 1     |  |  |

## End points

### End points reporting groups

|  |                                |
|--|--------------------------------|
| Reporting group title  | 3.5 mg/kg POS (2-7 years old)  |
| Reporting group description:<br>Children 2 to less than 7 years of age received posaconazole (POS) at 3.5 mg/kg by intravenous (IV) solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 3.5 mg/kg POS once daily by powder for oral suspension (PFS) for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV. |                                |
| Reporting group title  | 3.5 mg/kg POS (7-17 years old) |
| Reporting group description:<br>Children 7 to 17 years of age received POS at 3.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 3.5 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.  |                                |
| Reporting group title  | 4.5 mg/kg POS (2-7 years old)  |
| Reporting group description:<br>Children 2 to less than 7 years of age received POS at 4.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 4.5 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.   |                                |
| Reporting group title  | 4.5 mg/kg POS (7-17 years old) |
| Reporting group description:<br>Children 7 to 17 years of age received POS at 4.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 4.5 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.  |                                |
| Reporting group title  | 6 mg/kg POS (2-7 years old)    |
| Reporting group description:<br>Children 2 to less than 7 years of age received POS at 6 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 6 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.   |                                |
| Reporting group title  | 6 mg/kg POS (7-17 years old)   |
| Reporting group description:<br>Children 7 to 17 years of age received POS at 6 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 6 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.  |                                |

### Primary: Area under the plasma concentration versus time curve (AUC) from time 0 to 24 hours post-dose for POS

|  |  |
|--|--|
| End point title  | Area under the plasma concentration versus time curve (AUC) from time 0 to 24 hours post-dose for POS <sup>[1]</sup> |
| End point description:<br>Blood was collected from pre-dose up to 24 hours post-dose in order to determine the plasma AUC from time 0-24 hours post-dose (AUC <sub>0-24hr</sub> ) of posaconazole. A non-compartmental analysis of posaconazole plasma concentrations was performed. Results are reported for each treatment arm according to the formulation that participants received (IV or PFS). Participants receiving both formulations were counted once for each formulation. The population analyzed was all treated participants who received at least 7 days of POS dosing (IV and PFS), completed the full POS PK sampling, and met pre-specified acceptability criteria. |  |
| End point type   | Primary  |
| End point timeframe:<br>Any day from Day 7 to Day 10 of therapy for each formulation (up to 28 days) at pre-dose, within 15 minutes after end of infusion (up to 2 hours), and 4, 6, 8, 12, 24 hours post-infusion   |  |

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: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

| End point values                                    | 3.5 mg/kg POS<br>(2-7 years old) | 3.5 mg/kg POS<br>(7-17 years old) | 4.5 mg/kg POS<br>(2-7 years old) | 4.5 mg/kg POS<br>(7-17 years old) |
|---|----------------------------------|-----------------------------------|----------------------------------|-----------------------------------|
| Subject group type                                  | Reporting group                  | Reporting group                   | Reporting group                  | Reporting group                   |
| Number of subjects analysed                         | 11 <sup>[2]</sup>                | 19 <sup>[3]</sup>                 | 14 <sup>[4]</sup>                | 15 <sup>[5]</sup>                 |
| Units: hr*ng/mL                                     |                                  |                                   |                                  |                                   |
| geometric mean (geometric coefficient of variation) |                                  |                                   |                                  |                                   |
| IV  | 17800 (± 55.0)                   | 27300 (± 49.7)                    | 25600 (± 30.0)                   | 29800 (± 42.9)                    |
| PFS   | 12200 (± 36.0)                   | 20700 (± 33.8)                    | 21600 (± 64.5)                   | 28700 (± 33.7)                    |

Notes:

[2] - IV n= 11; PFS n= 5

[3] - IV n= 19; PFS n= 10

[4] - IV n= 14; PFS n= 8

[5] - IV n= 15; PFS n= 8

| End point values                                    | 6 mg/kg POS<br>(2-7 years old) | 6 mg/kg POS<br>(7-17 years old) |  |  |
|---|--------------------------------|---------------------------------|--|--|
| Subject group type                                  | Reporting group                | Reporting group                 |  |  |
| Number of subjects analysed                         | 17 <sup>[6]</sup>              | 24 <sup>[7]</sup>               |  |  |
| Units: hr*ng/mL                                     |                                |                                 |  |  |
| geometric mean (geometric coefficient of variation) |                                |                                 |  |  |
| IV  | 31100 (± 48.9)                 | 44200 (± 41.5)                  |  |  |
| PFS   | 23000 (± 47.3)                 | 25000 (± 184.3)                 |  |  |

Notes:

[6] - IV n= 17; PFS n= 7

[7] - IV n= 24; PFS n= 12

## Statistical analyses

No statistical analyses for this end point

## Primary: Maximum plasma concentration (Cmax) for POS

|  |  |
|--|--|
| End point title  | Maximum plasma concentration (Cmax) for POS <sup>[8]</sup> |
| End point description:<br>Blood was collected from pre-dose up to 24 hours post-dose in order to determine the plasma Cmax of posaconazole. A noncompartmental analysis of posaconazole plasma concentrations was performed. Results are reported for each treatment arm according to the formulation that participants received (IV or PFS). Participants receiving both formulations were counted once for each formulation. The population analyzed was all treated participants who received at least 7 days of POS dosing (IV and PFS), completed the full POS PK sampling, and met pre-specified acceptability criteria. |  |
| End point type   | Primary  |
| End point timeframe:<br>Any day from Day 7 to Day 10 of therapy for each formulation (up to 28 days) at pre-dose, within 15 minutes after end of infusion (up to 2 hours), and 4, 6, 8, 12, 24 hours post-infusion   |  |

Notes:

[8] - 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: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

| End point values                                    | 3.5 mg/kg POS<br>(2-7 years old) | 3.5 mg/kg POS<br>(7-17 years old) | 4.5 mg/kg POS<br>(2-7 years old) | 4.5 mg/kg POS<br>(7-17 years old) |
|---|----------------------------------|-----------------------------------|----------------------------------|-----------------------------------|
| Subject group type                                  | Reporting group                  | Reporting group                   | Reporting group                  | Reporting group                   |
| Number of subjects analysed                         | 11 <sup>[9]</sup>                | 19 <sup>[10]</sup>                | 14 <sup>[11]</sup>               | 15 <sup>[12]</sup>                |
| Units: ng/mL  |                                  |                                   |                                  |                                   |
| geometric mean (geometric coefficient of variation) |                                  |                                   |                                  |                                   |
| IV  | 1590 (± 43.1)                    | 2450 (± 72.7)                     | 2320 (± 39.8)                    | 2310 (± 40.3)                     |
| PFS   | 884 (± 44.4)                     | 1340 (± 30.8)                     | 1550 (± 40.8)                    | 1670 (± 28.5)                     |

Notes:

[9] - IV n=11; PFS n=5

[10] - IV n=19; PFS n=10

[11] - IV n=14; PFS n=8

[12] - IV n=15; PFS n=8

| End point values                                    | 6 mg/kg POS<br>(2-7 years old) | 6 mg/kg POS<br>(7-17 years old) |  |  |
|---|--------------------------------|---------------------------------|--|--|
| Subject group type                                  | Reporting group                | Reporting group                 |  |  |
| Number of subjects analysed                         | 17 <sup>[13]</sup>             | 24 <sup>[14]</sup>              |  |  |
| Units: ng/mL  |                                |                                 |  |  |
| geometric mean (geometric coefficient of variation) |                                |                                 |  |  |
| IV  | 3060 (± 54.1)                  | 3340 (± 39.4)                   |  |  |
| PFS   | 1510 (± 43.4)                  | 1370 (± 178.5)                  |  |  |

Notes:

[13] - IV n=17; PFS n=7

[14] - IV n=24; PFS n=12

## Statistical analyses

No statistical analyses for this end point

## Primary: Minimum plasma concentration (Cmin) for POS

|   |   |
|---|---|
| End point title   | Minimum plasma concentration (Cmin) for POS <sup>[15]</sup> |
| End point description:  |   |
| Blood was collected from pre-dose up to 24 hours post-dose in order to determine the plasma Cmin of posaconazole. A non-compartmental analysis of posaconazole plasma concentrations was performed. Results are reported for each treatment arm according to the formulation that participants received (IV or PFS). Participants receiving both formulations were counted once for each formulation. The population analyzed was all treated participants who received at least 7 days of POS dosing (IV and PFS), completed the full POS PK sampling, and met pre-specified acceptability criteria. |   |
| End point type  | Primary   |

End point timeframe:

Any day from Day 7 to Day 10 of therapy for each formulation (up to 28 days) at pre-dose, within 15 minutes after end of infusion (up to 2 hours), and 4, 6, 8, 12, 24 hours post-infusion

Notes:

[15] - 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: Statistical comparisons between treatment groups were neither planned nor performed for

this primary endpoint.

| End point values                                    | 3.5 mg/kg POS<br>(2-7 years old) | 3.5 mg/kg POS<br>(7-17 years old) | 4.5 mg/kg POS<br>(2-7 years old) | 4.5 mg/kg POS<br>(7-17 years old) |
|---|----------------------------------|-----------------------------------|----------------------------------|-----------------------------------|
| Subject group type                                  | Reporting group                  | Reporting group                   | Reporting group                  | Reporting group                   |
| Number of subjects analysed                         | 11 <sup>[16]</sup>               | 19 <sup>[17]</sup>                | 14 <sup>[18]</sup>               | 15 <sup>[19]</sup>                |
| Units: ng/mL  |                                  |                                   |                                  |                                   |
| geometric mean (geometric coefficient of variation) |                                  |                                   |                                  |                                   |
| IV  | 400 (± 81.3)                     | 670 (± 65.1)                      | 501 (± 56.8)                     | 737 (± 66.0)                      |
| PFS   | 254 (± 45.6)                     | 579 (± 44.9)                      | 476 (± 164.6)                    | 790 (± 48.2)                      |

Notes:

[16] - IV n=11; PFS n=5

[17] - IV n=19; PFS n=10

[18] - IV n=14; PFS n=8

[19] - IV n=15; PFS n=8

| End point values                                    | 6 mg/kg POS<br>(2-7 years old) | 6 mg/kg POS<br>(7-17 years old) |  |  |
|---|--------------------------------|---------------------------------|--|--|
| Subject group type                                  | Reporting group                | Reporting group                 |  |  |
| Number of subjects analysed                         | 17 <sup>[20]</sup>             | 24 <sup>[21]</sup>              |  |  |
| Units: ng/mL  |                                |                                 |  |  |
| geometric mean (geometric coefficient of variation) |                                |                                 |  |  |
| IV  | 626 (± 104.8)                  | 1160 (± 60.4)                   |  |  |
| PFS   | 542 (± 68.8)                   | 713 (± 300.6)                   |  |  |

Notes:

[20] - IV n=17; PFS n=7

[21] - IV n=24; PFS n=12

## Statistical analyses

No statistical analyses for this end point

## Primary: Average steady-state plasma concentration (C<sub>avg</sub>) for POS

|                 |   |
|-----------------|---|
| End point title | Average steady-state plasma concentration (C <sub>avg</sub> ) for POS <sup>[22]</sup> |
|-----------------|---|

End point description:

Blood was collected from pre-dose up to 24 hours post-dose in order to determine the plasma C<sub>avg</sub> of posaconazole. A non-compartmental analysis of posaconazole plasma concentrations was performed. Results are reported for each treatment arm according to the formulation that participants received (IV or PFS). Participants receiving both formulations were counted once for each formulation. The population analyzed was all treated participants who received at least 7 days of POS dosing (IV and PFS), completed the full POS PK sampling, and met pre-specified acceptability criteria.

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

End point timeframe:

Any day from Day 7 to Day 10 of therapy for each formulation (up to 28 days) at pre-dose, within 15 minutes after end of infusion (up to 2 hours), and 4, 6, 8, 12, 24 hours post-infusion

Notes:

[22] - 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: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

| End point values                                    | 3.5 mg/kg POS<br>(2-7 years old) | 3.5 mg/kg POS<br>(7-17 years old) | 4.5 mg/kg POS<br>(2-7 years old) | 4.5 mg/kg POS<br>(7-17 years old) |
|---|----------------------------------|-----------------------------------|----------------------------------|-----------------------------------|
| Subject group type                                  | Reporting group                  | Reporting group                   | Reporting group                  | Reporting group                   |
| Number of subjects analysed                         | 11 <sup>[23]</sup>               | 19 <sup>[24]</sup>                | 14 <sup>[25]</sup>               | 15 <sup>[26]</sup>                |
| Units: ng/mL  |                                  |                                   |                                  |                                   |
| geometric mean (geometric coefficient of variation) |                                  |                                   |                                  |                                   |
| IV  | 743 (± 55.0)                     | 1140 (± 49.7)                     | 1070 (± 30.0)                    | 1240 (± 42.9)                     |
| PFS   | 510 (± 36.0)                     | 861 (± 33.8)                      | 901 (± 64.5)                     | 1200 (± 33.7)                     |

Notes:

[23] - IV n=11; PFS n=5

[24] - IV n=19; PFS n=10

[25] - IV n=14; PFS n=8

[26] - IV n=15; PFS n=8

| End point values                                    | 6 mg/kg POS<br>(2-7 years old) | 6 mg/kg POS<br>(7-17 years old) |  |  |
|---|--------------------------------|---------------------------------|--|--|
| Subject group type                                  | Reporting group                | Reporting group                 |  |  |
| Number of subjects analysed                         | 17 <sup>[27]</sup>             | 24 <sup>[28]</sup>              |  |  |
| Units: ng/mL  |                                |                                 |  |  |
| geometric mean (geometric coefficient of variation) |                                |                                 |  |  |
| IV  | 1300 (± 48.9)                  | 1840 (± 41.5)                   |  |  |
| PFS   | 960 (± 47.3)                   | 1040 (± 184.3)                  |  |  |

Notes:

[27] - IV n=17; PFS n=7

[28] - IV n=24; PFS n=12

## Statistical analyses

No statistical analyses for this end point

## Primary: Time of maximum plasma concentration (Tmax) for POS

|                 |   |
|-----------------|---|
| End point title | Time of maximum plasma concentration (Tmax) for POS <sup>[29]</sup> |
|-----------------|---|

End point description:

Blood was collected from pre-dose up to 24 hours post-dose in order to determine the plasma Tmax of posaconazole. A non-compartmental analysis of posaconazole plasma concentrations was performed. Results are reported for each treatment arm according to the formulation that participants received (IV or PFS). Participants receiving both formulations were counted once for each formulation. The population analyzed was all treated participants who received at least 7 days of POS dosing (IV and PFS), completed the full POS PK sampling, and met pre-specified acceptability criteria.

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

End point timeframe:

Any day from Day 7 to Day 10 of therapy for each formulation (up to 28 days) at pre-dose, within 15 minutes after end of infusion (up to 2 hours), and 4, 6, 8, 12, 24 hours post-infusion

Notes:

[29] - 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: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

| End point values              | 3.5 mg/kg POS<br>(2-7 years old) | 3.5 mg/kg POS<br>(7-17 years old) | 4.5 mg/kg POS<br>(2-7 years old) | 4.5 mg/kg POS<br>(7-17 years old) |
|-------------------------------|----------------------------------|-----------------------------------|----------------------------------|-----------------------------------|
| Subject group type            | Reporting group                  | Reporting group                   | Reporting group                  | Reporting group                   |
| Number of subjects analysed   | 11 <sup>[30]</sup>               | 19 <sup>[31]</sup>                | 14 <sup>[32]</sup>               | 15 <sup>[33]</sup>                |
| Units: Hours                  |                                  |                                   |                                  |                                   |
| median (full range (min-max)) |                                  |                                   |                                  |                                   |
| IV                            | 1.78 (1.67 to 5.53)              | 1.77 (0.00 to 3.50)               | 1.78 (1.42 to 5.90)              | 1.75 (1.52 to 1.80)               |
| PFS                           | 3.83 (1.92 to 4.25)              | 2.20 (1.92 to 6.03)               | 3.82 (1.88 to 5.92)              | 6.14 (1.98 to 7.98)               |

Notes:

[30] - IV n=11; PFS n=5

[31] - IV n=19; PFS n=10

[32] - IV n=14; PFS n=8

[33] - IV n=15; PFS n=8

| End point values              | 6 mg/kg POS<br>(2-7 years old) | 6 mg/kg POS<br>(7-17 years old) |  |  |
|-------------------------------|--------------------------------|---------------------------------|--|--|
| Subject group type            | Reporting group                | Reporting group                 |  |  |
| Number of subjects analysed   | 17 <sup>[34]</sup>             | 24 <sup>[35]</sup>              |  |  |
| Units: Hours                  |                                |                                 |  |  |
| median (full range (min-max)) |                                |                                 |  |  |
| IV                            | 1.75 (1.57 to 1.83)            | 1.77 (1.33 to 6.00)             |  |  |
| PFS                           | 4.00 (2.17 to 7.92)            | 2.78 (0.00 to 4.00)             |  |  |

Notes:

[34] - IV n=17; PFS n=7

[35] - IV n=24; PFS n=12

## Statistical analyses

No statistical analyses for this end point

## Primary: Total body clearance (CL) for POS administered by IV

|                 |  |
|-----------------|--|
| End point title | Total body clearance (CL) for POS administered by IV <sup>[36]</sup> |
|-----------------|--|

End point description:

Blood was collected from pre-dose up to 24 hours post-dose in order to determine the plasma CL of posaconazole administered by IV. A non-compartmental analysis of posaconazole plasma concentrations was performed. Results are reported for participants that received IV treatment. The population analyzed was all treated participants who received at least 7 days of POS IV solution therapy, completed the full POS PK sampling while on POS IV solution, and met pre-specified acceptability criteria.

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

End point timeframe:

Any day from Day 7 to Day 10 of therapy at pre-dose, within 15 minutes after end of infusion (up to 2 hours), and 4, 6, 8, 12, 24 hours post-infusion

Notes:

[36] - 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: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.



| End point values                                    | 3.5 mg/kg POS<br>(2-7 years old) | 3.5 mg/kg POS<br>(7-17 years old) | 4.5 mg/kg POS<br>(2-7 years old) | 4.5 mg/kg POS<br>(7-17 years old) |
|---|----------------------------------|-----------------------------------|----------------------------------|-----------------------------------|
| Subject group type                                  | Reporting group                  | Reporting group                   | Reporting group                  | Reporting group                   |
| Number of subjects analysed                         | 11                               | 19                                | 14                               | 15                                |
| Units: L/hr   |                                  |                                   |                                  |                                   |
| geometric mean (geometric coefficient of variation) | 3.39 (± 52.8)                    | 6.64 (± 38.6)                     | 2.97 (± 36.2)                    | 6.69 (± 37.3)                     |

| End point values                                    | 6 mg/kg POS<br>(2-7 years old) | 6 mg/kg POS<br>(7-17 years old) |  |  |
|---|--------------------------------|---------------------------------|--|--|
| Subject group type                                  | Reporting group                | Reporting group                 |  |  |
| Number of subjects analysed                         | 17                             | 24                              |  |  |
| Units: L/hr   |                                |                                 |  |  |
| geometric mean (geometric coefficient of variation) | 3.27 (± 49.3)                  | 4.76 (± 55.7)                   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Apparent total body clearance (CL/F) for POS administered by PFS

|                 |  |
|-----------------|--|
| End point title | Apparent total body clearance (CL/F) for POS administered by PFS <sup>[37]</sup> |
|-----------------|--|

End point description:

Blood was collected from pre-dose up to 24 hours post-dose in order to determine the plasma CL/F of posaconazole administered by PFS. A non-compartmental analysis of posaconazole plasma concentrations was performed. Results are reported for participants that received PFS treatment. The population analyzed was all treated participants who received at least 7 days of POS PFS therapy, completed the full POS PK sampling while on POS PFS, and met pre-specified acceptability criteria.

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

End point timeframe:

Any day from Day 7 to Day 10 of therapy (up to 28 days) at pre-dose, within 15 minutes after end of infusion (up to 2 hours), and 4, 6, 8, 12, 24 hours post-infusion

Notes:

[37] - 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: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

| End point values                                    | 3.5 mg/kg POS<br>(2-7 years old) | 3.5 mg/kg POS<br>(7-17 years old) | 4.5 mg/kg POS<br>(2-7 years old) | 4.5 mg/kg POS<br>(7-17 years old) |
|---|----------------------------------|-----------------------------------|----------------------------------|-----------------------------------|
| Subject group type                                  | Reporting group                  | Reporting group                   | Reporting group                  | Reporting group                   |
| Number of subjects analysed                         | 5                                | 10                                | 8                                | 8                                 |
| Units: L/hr   |                                  |                                   |                                  |                                   |
| geometric mean (geometric coefficient of variation) | 4.97 (± 29.1)                    | 7.67 (± 39.9)                     | 3.49 (± 59.1)                    | 7.84 (± 49.4)                     |

|   |                                |                                 |  |  |
|---|--------------------------------|---------------------------------|--|--|
| <b>End point values</b>                             | 6 mg/kg POS<br>(2-7 years old) | 6 mg/kg POS<br>(7-17 years old) |  |  |
| Subject group type                                  | Reporting group                | Reporting group                 |  |  |
| Number of subjects analysed                         | 7                              | 12                              |  |  |
| Units: L/hr   |                                |                                 |  |  |
| geometric mean (geometric coefficient of variation) | 4.60 ( $\pm$ 35.2)             | 8.39 ( $\pm$ 190.3)             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with an Adverse Event (AE)

|   |   |
|---|---|
| End point title   | Number of participants with an Adverse Event (AE) |
| End point description:  |   |
| An adverse event (AE) is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product or protocol - specified procedure, whether or not considered related to the medicinal product or protocol - specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an AE. The population analyzed was all participants who received at least one dose of study drug. |   |
| End point type  | Secondary   |
| End point timeframe:  |   |
| 14 days after end of treatment (Up to 42 days)  |   |

|                             |                                  |                                   |                                  |                                   |
|-----------------------------|----------------------------------|-----------------------------------|----------------------------------|-----------------------------------|
| <b>End point values</b>     | 3.5 mg/kg POS<br>(2-7 years old) | 3.5 mg/kg POS<br>(7-17 years old) | 4.5 mg/kg POS<br>(2-7 years old) | 4.5 mg/kg POS<br>(7-17 years old) |
| Subject group type          | Reporting group                  | Reporting group                   | Reporting group                  | Reporting group                   |
| Number of subjects analysed | 14                               | 21                                | 15                               | 16                                |
| Units: Participants         | 13                               | 21                                | 15                               | 16                                |

|                             |                                |                                 |  |  |
|-----------------------------|--------------------------------|---------------------------------|--|--|
| <b>End point values</b>     | 6 mg/kg POS<br>(2-7 years old) | 6 mg/kg POS<br>(7-17 years old) |  |  |
| Subject group type          | Reporting group                | Reporting group                 |  |  |
| Number of subjects analysed | 20                             | 29                              |  |  |
| Units: Participants         | 19                             | 29                              |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants who discontinued treatment of study drug due to an Adverse Event (AE)

|                 |  |
|-----------------|--|
| End point title | Number of participants who discontinued treatment of study drug due to an Adverse Event (AE) |
|-----------------|--|

End point description:

An AE is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product or protocol - specified procedure, whether or not considered related to the medicinal product or protocol - specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an AE. The population analyzed was all participants who received at least one dose of study drug.

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

End point timeframe:

Up to 28 days

| End point values            | 3.5 mg/kg POS<br>(2-7 years old) | 3.5 mg/kg POS<br>(7-17 years old) | 4.5 mg/kg POS<br>(2-7 years old) | 4.5 mg/kg POS<br>(7-17 years old) |
|-----------------------------|----------------------------------|-----------------------------------|----------------------------------|-----------------------------------|
| Subject group type          | Reporting group                  | Reporting group                   | Reporting group                  | Reporting group                   |
| Number of subjects analysed | 14                               | 21                                | 15                               | 16                                |
| Units: Participants         | 3                                | 3                                 | 0                                | 2                                 |

| End point values            | 6 mg/kg POS<br>(2-7 years old) | 6 mg/kg POS<br>(7-17 years old) |  |  |
|-----------------------------|--------------------------------|---------------------------------|--|--|
| Subject group type          | Reporting group                | Reporting group                 |  |  |
| Number of subjects analysed | 20                             | 29                              |  |  |
| Units: Participants         | 4                              | 6                               |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

14 days after end of treatment (up to day 42)

Adverse event reporting additional description:

All participants who received at least one dose of study drug. Participants were followed for survival up to 110 days; and deaths that occurred outside of the timeframe for adverse event reporting were recorded in the Disposition

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 21.0 |
|--------------------|------|

### Reporting groups

|                       |   |
|-----------------------|---|
| Reporting group title | 3.5 mg/kg posaconazole (2-<7 years old) |
|-----------------------|---|

Reporting group description:

Children 2 to less than 7 years of age received posaconazole (POS) at 3.5 mg/kg by intravenous (IV) solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 3.5 mg/kg POS once daily by powder for oral suspension (PFS) for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

|                       |   |
|-----------------------|---|
| Reporting group title | 3.5 mg/kg posaconazole (7-17 years old) |
|-----------------------|---|

Reporting group description:

Children 7 to 17 years of age received POS at 3.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 3.5 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

|                       |   |
|-----------------------|---|
| Reporting group title | 4.5 mg/kg posaconazole (2-<7 years old) |
|-----------------------|---|

Reporting group description:

Children 2 to less than 7 years of age received posaconazole (POS) at 4.5 mg/kg by intravenous (IV) solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 4.5 mg/kg POS once daily by powder for oral suspension (PFS) for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

|                       |   |
|-----------------------|---|
| Reporting group title | 4.5 mg/kg posaconazole (7-17 years old) |
|-----------------------|---|

Reporting group description:

Children 7 to 17 years of age received POS at 4.5 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 4.5 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

|                       |   |
|-----------------------|---|
| Reporting group title | 6.0 mg/kg posaconazole (2-<7 years old) |
|-----------------------|---|

Reporting group description:

Children 2 to less than 7 years of age received posaconazole (POS) at 6 mg/kg by intravenous (IV) solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 6 mg/kg POS once daily by powder for oral suspension (PFS) for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

|                       |   |
|-----------------------|---|
| Reporting group title | 6.0 mg/kg posaconazole (7-17 years old) |
|-----------------------|---|

Reporting group description:

Children 7 to 17 years of age received POS at 6 mg/kg by IV solution twice on Day 1, then once daily on Days 2-10. This was followed by treatment with 6 mg/kg POS once daily by PFS for a minimum of 10 days; or, if they were unwilling or unable to tolerate POS PFS, continued treatment with POS IV.

| Serious adverse events                            | 3.5 mg/kg posaconazole (2-<7 years old) | 3.5 mg/kg posaconazole (7-17 years old) | 4.5 mg/kg posaconazole (2-<7 years old) |
|---|---|---|---|
| Total subjects affected by serious adverse events |   |   |   |
| subjects affected / exposed                       | 3 / 14 (21.43%)                         | 8 / 21 (38.10%)                         | 4 / 15 (26.67%)                         |

|   |                |                |                |
|---|----------------|----------------|----------------|
| number of deaths (all causes)                               | 0              | 0              | 0              |
| number of deaths resulting from adverse events              | 0              | 0              | 0              |
| <b>Vascular disorders</b>                                   |                |                |                |
| Capillary leak syndrome                                     |                |                |                |
| subjects affected / exposed                                 | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (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          |
| Hypertension  |                |                |                |
| subjects affected / exposed                                 | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (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          |
| Thrombophlebitis superficial                                |                |                |                |
| subjects affected / exposed                                 | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (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          |
| Venoocclusive disease                                       |                |                |                |
| subjects affected / exposed                                 | 1 / 14 (7.14%) | 0 / 21 (0.00%) | 0 / 15 (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>General disorders and administration site conditions</b> |                |                |                |
| Pyrexia   |                |                |                |
| subjects affected / exposed                                 | 0 / 14 (0.00%) | 2 / 21 (9.52%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all             | 0 / 0          | 0 / 2          | 0 / 0          |
| deaths causally related to treatment / all                  | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Immune system disorders</b>                              |                |                |                |
| Drug hypersensitivity                                       |                |                |                |
| subjects affected / exposed                                 | 1 / 14 (7.14%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all             | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                  | 0 / 0          | 0 / 0          | 0 / 0          |
| Engraftment syndrome  |                |                |                |
| subjects affected / exposed                                 | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all                  | 0 / 0          | 0 / 0          | 0 / 0          |
| Transplant rejection  |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (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 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (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          |
| Hypoxia   |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (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 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |                |                |                |
| Cardiac failure                                 |                |                |                |
| subjects affected / exposed                     | 1 / 14 (7.14%) | 0 / 21 (0.00%) | 0 / 15 (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          |
| Cardiomyopathy                                  |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| 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                        |                |                |                |
| Posterior reversible encephalopathy syndrome    |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (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          |
| Presyncope                                      |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (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            |                |                |                |
| Febrile neutropenia                             |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (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          |
| Gastrointestinal disorders                      |                |                |                |
| Abdominal pain                                  |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (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          |
| Stomatitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (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          |
| Vomiting  |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (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 lesion                                  |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (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          |
| Venoocclusive liver disease                     |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |                |                |                |
| Acute kidney injury                             |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (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 failure                                   |                |                |                |
| subjects affected / exposed                     | 1 / 14 (7.14%) | 0 / 21 (0.00%) | 0 / 15 (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          |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Chest wall haematoma                            |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (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                     |                |                |                |
| Adenovirus infection                            |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (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          |
| Clostridium difficile colitis                   |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (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          |
| Cystitis  |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (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          |
| Device related infection                        |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (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          |
| Enterobacter infection                          |                |                |                |
| subjects affected / exposed                     | 1 / 14 (7.14%) | 0 / 21 (0.00%) | 0 / 15 (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          |



|   |                |                |                |
|---|----------------|----------------|----------------|
| Fungal infection                                |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Herpes zoster                                   |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (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          |
| Parainfluenzae virus infection                  |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (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 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (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 viral                                 |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Streptococcal sepsis                            |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (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          |
| Systemic mycosis                                |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (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          |
| Upper respiratory tract infection               |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary tract infection viral                   |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (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              |                |                |                |
| Hyponatraemia                                   |                |                |                |
| subjects affected / exposed                     | 1 / 14 (7.14%) | 0 / 21 (0.00%) | 0 / 15 (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>Serious adverse events</b>                        | 4.5 mg/kg<br>posaconazole (7-17<br>years old) | 6.0 mg/kg<br>posaconazole (2-<7<br>years old) | 6.0 mg/kg<br>posaconazole (7-17<br>years old) |
|--|---|---|---|
| Total subjects affected by serious adverse events    |   |   |   |
| subjects affected / exposed                          | 5 / 16 (31.25%)                               | 3 / 20 (15.00%)                               | 8 / 29 (27.59%)                               |
| number of deaths (all causes)                        | 0   | 0   | 2   |
| number of deaths resulting from adverse events       | 0   | 0   | 0   |
| Vascular disorders                                   |   |   |   |
| Capillary leak syndrome                              |   |   |   |
| subjects affected / exposed                          | 0 / 16 (0.00%)                                | 0 / 20 (0.00%)                                | 1 / 29 (3.45%)                                |
| occurrences causally related to treatment / all      | 0 / 0   | 0 / 0   | 0 / 1   |
| deaths causally related to treatment / all           | 0 / 0   | 0 / 0   | 0 / 0   |
| Hypertension   |   |   |   |
| subjects affected / exposed                          | 0 / 16 (0.00%)                                | 0 / 20 (0.00%)                                | 1 / 29 (3.45%)                                |
| occurrences causally related to treatment / all      | 0 / 0   | 0 / 0   | 0 / 1   |
| deaths causally related to treatment / all           | 0 / 0   | 0 / 0   | 0 / 0   |
| Thrombophlebitis superficial                         |   |   |   |
| subjects affected / exposed                          | 1 / 16 (6.25%)                                | 0 / 20 (0.00%)                                | 0 / 29 (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   |
| Venoocclusive disease                                |   |   |   |
| subjects affected / exposed                          | 0 / 16 (0.00%)                                | 0 / 20 (0.00%)                                | 1 / 29 (3.45%)                                |
| occurrences causally related to treatment / all      | 0 / 0   | 0 / 0   | 0 / 1   |
| deaths causally related to treatment / all           | 0 / 0   | 0 / 0   | 0 / 1   |
| General disorders and administration site conditions |   |   |   |
| Pyrexia  |   |   |   |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Immune system disorders                         |                |                |                |
| Drug hypersensitivity                           |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (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          |
| Engraftment syndrome                            |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (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          |
| Transplant rejection                            |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| 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 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (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          |
| Hypoxia   |                |                |                |
| subjects affected / exposed                     | 1 / 16 (6.25%) | 0 / 20 (0.00%) | 0 / 29 (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 failure                             |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1          |
| Cardiac disorders                               |                |                |                |
| Cardiac failure                                 |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (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          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Cardiomyopathy                                  |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (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                        |                |                |                |
| Posterior reversible encephalopathy syndrome    |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 1 / 20 (5.00%) | 0 / 29 (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          |
| Presyncope                                      |                |                |                |
| subjects affected / exposed                     | 1 / 16 (6.25%) | 0 / 20 (0.00%) | 0 / 29 (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            |                |                |                |
| Febrile neutropenia                             |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 1 / 20 (5.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                |                |                |
| Abdominal pain                                  |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 1 / 20 (5.00%) | 0 / 29 (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          |
| Stomatitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vomiting  |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 1 / 20 (5.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                         |                |                |                |
| Hepatic lesion                                  |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (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          |
| Venoocclusive liver disease                     |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (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 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal failure                                   |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Chest wall haematoma                            |                |                |                |
| subjects affected / exposed                     | 1 / 16 (6.25%) | 0 / 20 (0.00%) | 0 / 29 (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          |
| Infections and infestations                     |                |                |                |
| Adenovirus infection                            |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Clostridium difficile colitis                   |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (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          |
| Cystitis  |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Device related infection                        |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Enterobacter infection                          |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (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          |
| Fungal infection                                |                |                |                |
| subjects affected / exposed                     | 1 / 16 (6.25%) | 0 / 20 (0.00%) | 0 / 29 (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          |
| Herpes zoster                                   |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (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          |
| Parainfluenzae virus infection                  |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia                                       |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (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 viral                                 |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (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          |
| Streptococcal sepsis                            |                |                |                |
| subjects affected / exposed                     | 1 / 16 (6.25%) | 0 / 20 (0.00%) | 0 / 29 (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          |
| Systemic mycosis                                |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 16 (6.25%) | 0 / 20 (0.00%) | 0 / 29 (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          |
| Upper respiratory tract infection               |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (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          |
| Urinary tract infection viral                   |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders              |                |                |                |
| Hyponatraemia                                   |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (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          |

Frequency threshold for reporting non-serious adverse events: 0 %

| <b>Non-serious adverse events</b>                                   | 3.5 mg/kg<br>posaconazole (2-<7<br>years old) | 3.5 mg/kg<br>posaconazole (7-17<br>years old) | 4.5 mg/kg<br>posaconazole (2-<7<br>years old) |
|---|---|---|---|
| Total subjects affected by non-serious adverse events               |   |   |   |
| subjects affected / exposed   | 13 / 14 (92.86%)                              | 20 / 21 (95.24%)                              | 15 / 15 (100.00%)                             |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |   |   |
| Acute myeloid leukaemia   |   |   |   |
| subjects affected / exposed   | 0 / 14 (0.00%)                                | 0 / 21 (0.00%)                                | 0 / 15 (0.00%)                                |
| occurrences (all)   | 0   | 0   | 0   |
| Vascular disorders  |   |   |   |
| Capillary leak syndrome   |   |   |   |
| subjects affected / exposed   | 0 / 14 (0.00%)                                | 0 / 21 (0.00%)                                | 0 / 15 (0.00%)                                |
| occurrences (all)   | 0   | 0   | 0   |
| Flushing  |   |   |   |
| subjects affected / exposed   | 1 / 14 (7.14%)                                | 1 / 21 (4.76%)                                | 0 / 15 (0.00%)                                |
| occurrences (all)   | 1   | 1   | 0   |
| Haematoma   |   |   |   |

|  |                 |                |                 |
|--|-----------------|----------------|-----------------|
| subjects affected / exposed                          | 0 / 14 (0.00%)  | 1 / 21 (4.76%) | 0 / 15 (0.00%)  |
| occurrences (all)                                    | 0               | 1              | 0               |
| Hyperaemia   |                 |                |                 |
| subjects affected / exposed                          | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0               |
| Hypertension   |                 |                |                 |
| subjects affected / exposed                          | 5 / 14 (35.71%) | 2 / 21 (9.52%) | 2 / 15 (13.33%) |
| occurrences (all)                                    | 5               | 2              | 2               |
| Hypotension  |                 |                |                 |
| subjects affected / exposed                          | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0               |
| Pallor   |                 |                |                 |
| subjects affected / exposed                          | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 1 / 15 (6.67%)  |
| occurrences (all)                                    | 0               | 0              | 2               |
| Phlebitis  |                 |                |                 |
| subjects affected / exposed                          | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0               |
| Venoocclusive disease                                |                 |                |                 |
| subjects affected / exposed                          | 2 / 14 (14.29%) | 0 / 21 (0.00%) | 1 / 15 (6.67%)  |
| occurrences (all)                                    | 2               | 0              | 1               |
| General disorders and administration site conditions |                 |                |                 |
| Axillary pain  |                 |                |                 |
| subjects affected / exposed                          | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 1 / 15 (6.67%)  |
| occurrences (all)                                    | 0               | 0              | 1               |
| Catheter site erythema                               |                 |                |                 |
| subjects affected / exposed                          | 1 / 14 (7.14%)  | 0 / 21 (0.00%) | 1 / 15 (6.67%)  |
| occurrences (all)                                    | 1               | 0              | 1               |
| Catheter site haemorrhage                            |                 |                |                 |
| subjects affected / exposed                          | 0 / 14 (0.00%)  | 1 / 21 (4.76%) | 0 / 15 (0.00%)  |
| occurrences (all)                                    | 0               | 1              | 0               |
| Catheter site oedema                                 |                 |                |                 |
| subjects affected / exposed                          | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0               |
| Catheter site pain                                   |                 |                |                 |



|                                       |                 |                 |                 |
|---------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed           | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                     | 0               | 0               | 1               |
| Catheter site swelling                |                 |                 |                 |
| subjects affected / exposed           | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                     | 0               | 0               | 1               |
| Chills                                |                 |                 |                 |
| subjects affected / exposed           | 0 / 14 (0.00%)  | 1 / 21 (4.76%)  | 0 / 15 (0.00%)  |
| occurrences (all)                     | 0               | 1               | 0               |
| Face oedema                           |                 |                 |                 |
| subjects affected / exposed           | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                     | 0               | 0               | 0               |
| Fatigue                               |                 |                 |                 |
| subjects affected / exposed           | 1 / 14 (7.14%)  | 1 / 21 (4.76%)  | 0 / 15 (0.00%)  |
| occurrences (all)                     | 1               | 1               | 0               |
| General physical health deterioration |                 |                 |                 |
| subjects affected / exposed           | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                     | 0               | 0               | 0               |
| Generalised oedema                    |                 |                 |                 |
| subjects affected / exposed           | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                     | 0               | 0               | 0               |
| Granuloma                             |                 |                 |                 |
| subjects affected / exposed           | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                     | 0               | 0               | 0               |
| Infusion site erythema                |                 |                 |                 |
| subjects affected / exposed           | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                     | 0               | 0               | 1               |
| Malaise                               |                 |                 |                 |
| subjects affected / exposed           | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                     | 0               | 0               | 0               |
| Mucosal inflammation                  |                 |                 |                 |
| subjects affected / exposed           | 3 / 14 (21.43%) | 9 / 21 (42.86%) | 5 / 15 (33.33%) |
| occurrences (all)                     | 3               | 10              | 5               |
| Oedema                                |                 |                 |                 |
| subjects affected / exposed           | 0 / 14 (0.00%)  | 1 / 21 (4.76%)  | 0 / 15 (0.00%)  |
| occurrences (all)                     | 0               | 1               | 0               |
| Oedema peripheral                     |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                         | 0 / 14 (0.00%)  | 1 / 21 (4.76%)  | 0 / 15 (0.00%)  |
| occurrences (all)                                   | 0               | 1               | 0               |
| Pain  |                 |                 |                 |
| subjects affected / exposed                         | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                                   | 0               | 0               | 0               |
| Pyrexia   |                 |                 |                 |
| subjects affected / exposed                         | 8 / 14 (57.14%) | 9 / 21 (42.86%) | 6 / 15 (40.00%) |
| occurrences (all)                                   | 13              | 11              | 9               |
| Systemic inflammatory response syndrome             |                 |                 |                 |
| subjects affected / exposed                         | 0 / 14 (0.00%)  | 1 / 21 (4.76%)  | 0 / 15 (0.00%)  |
| occurrences (all)                                   | 0               | 1               | 0               |
| Immune system disorders                             |                 |                 |                 |
| Drug hypersensitivity                               |                 |                 |                 |
| subjects affected / exposed                         | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                                   | 0               | 0               | 0               |
| Engraftment syndrome                                |                 |                 |                 |
| subjects affected / exposed                         | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                                   | 0               | 0               | 0               |
| Graft versus host disease                           |                 |                 |                 |
| subjects affected / exposed                         | 2 / 14 (14.29%) | 2 / 21 (9.52%)  | 0 / 15 (0.00%)  |
| occurrences (all)                                   | 2               | 2               | 0               |
| Graft versus host disease in gastrointestinal tract |                 |                 |                 |
| subjects affected / exposed                         | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                                   | 0               | 0               | 0               |
| Graft versus host disease in liver                  |                 |                 |                 |
| subjects affected / exposed                         | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                                   | 0               | 0               | 0               |
| Graft versus host disease in skin                   |                 |                 |                 |
| subjects affected / exposed                         | 0 / 14 (0.00%)  | 2 / 21 (9.52%)  | 0 / 15 (0.00%)  |
| occurrences (all)                                   | 0               | 2               | 0               |
| Hypogammaglobulinaemia                              |                 |                 |                 |
| subjects affected / exposed                         | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                                   | 0               | 0               | 0               |
| Immunodeficiency                                    |                 |                 |                 |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Immunodeficiency common variable                |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Serum sickness                                  |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Reproductive system and breast disorders        |                |                |                |
| Menorrhagia                                     |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Metrorrhagia                                    |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Perineal erythema                               |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Perineal pain                                   |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Scrotal oedema                                  |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Testicular oedema                               |                |                |                |
| subjects affected / exposed                     | 1 / 14 (7.14%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0              |
| Vulvovaginal inflammation                       |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0              |
| Vulvovaginal pruritus                           |                |                |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Respiratory, thoracic and mediastinal disorders |                |                |                |

|  |                 |                |                 |
|--|-----------------|----------------|-----------------|
| Cough                                      |                 |                |                 |
| subjects affected / exposed                | 2 / 14 (14.29%) | 0 / 21 (0.00%) | 4 / 15 (26.67%) |
| occurrences (all)                          | 2               | 0              | 4               |
| Dysphonia                                  |                 |                |                 |
| subjects affected / exposed                | 1 / 14 (7.14%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                          | 1               | 0              | 0               |
| Dyspnoea                                   |                 |                |                 |
| subjects affected / exposed                | 0 / 14 (0.00%)  | 2 / 21 (9.52%) | 0 / 15 (0.00%)  |
| occurrences (all)                          | 0               | 2              | 0               |
| Epistaxis                                  |                 |                |                 |
| subjects affected / exposed                | 2 / 14 (14.29%) | 1 / 21 (4.76%) | 1 / 15 (6.67%)  |
| occurrences (all)                          | 4               | 1              | 1               |
| Haemoptysis                                |                 |                |                 |
| subjects affected / exposed                | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                          | 0               | 0              | 0               |
| Hypoxia                                    |                 |                |                 |
| subjects affected / exposed                | 0 / 14 (0.00%)  | 2 / 21 (9.52%) | 0 / 15 (0.00%)  |
| occurrences (all)                          | 0               | 2              | 0               |
| Increased viscosity of bronchial secretion |                 |                |                 |
| subjects affected / exposed                | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                          | 0               | 0              | 0               |
| Lung infiltration                          |                 |                |                 |
| subjects affected / exposed                | 1 / 14 (7.14%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                          | 1               | 0              | 0               |
| Nasal congestion                           |                 |                |                 |
| subjects affected / exposed                | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                          | 0               | 0              | 0               |
| Oropharyngeal pain                         |                 |                |                 |
| subjects affected / exposed                | 0 / 14 (0.00%)  | 1 / 21 (4.76%) | 1 / 15 (6.67%)  |
| occurrences (all)                          | 0               | 1              | 1               |
| Pharyngeal inflammation                    |                 |                |                 |
| subjects affected / exposed                | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)                          | 0               | 0              | 0               |
| Pleural effusion                           |                 |                |                 |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Pleuritic pain              |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Productive cough            |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Pulmonary oedema            |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Rales                       |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)           | 0              | 0              | 1              |
| Rhinitis allergic           |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)           | 0              | 0              | 1              |
| Rhinorrhoea                 |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Tachypnoea                  |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)           | 0              | 0              | 1              |
| Tonsillar exudate           |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)           | 0              | 0              | 1              |
| Psychiatric disorders       |                |                |                |
| Agitation                   |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Anxiety                     |                |                |                |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Depressed mood              |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |

|                                      |                |                |                |
|--------------------------------------|----------------|----------------|----------------|
| Depression                           |                |                |                |
| subjects affected / exposed          | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)                    | 0              | 1              | 0              |
| Insomnia                             |                |                |                |
| subjects affected / exposed          | 1 / 14 (7.14%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                    | 1              | 0              | 0              |
| Irritability                         |                |                |                |
| subjects affected / exposed          | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Investigations                       |                |                |                |
| Alanine aminotransferase increased   |                |                |                |
| subjects affected / exposed          | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 1 / 15 (6.67%) |
| occurrences (all)                    | 0              | 1              | 1              |
| Aspartate aminotransferase increased |                |                |                |
| subjects affected / exposed          | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 1 / 15 (6.67%) |
| occurrences (all)                    | 0              | 1              | 1              |
| BK polyomavirus test positive        |                |                |                |
| subjects affected / exposed          | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Bacterial test positive              |                |                |                |
| subjects affected / exposed          | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Blood albumin decreased              |                |                |                |
| subjects affected / exposed          | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Blood alkaline phosphatase increased |                |                |                |
| subjects affected / exposed          | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)                    | 0              | 0              | 1              |
| Blood bilirubin increased            |                |                |                |
| subjects affected / exposed          | 1 / 14 (7.14%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)                    | 1              | 1              | 0              |
| Blood calcium decreased              |                |                |                |
| subjects affected / exposed          | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)                    | 0              | 1              | 0              |
| Blood creatinine increased           |                |                |                |

|                                       |                |                |                |
|---------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed           | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)                     | 0              | 1              | 0              |
| Blood culture positive                |                |                |                |
| subjects affected / exposed           | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)                     | 0              | 1              | 0              |
| Blood immunoglobulin G decreased      |                |                |                |
| subjects affected / exposed           | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Blood lactate dehydrogenase increased |                |                |                |
| subjects affected / exposed           | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Blood magnesium decreased             |                |                |                |
| subjects affected / exposed           | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Blood phosphorus decreased            |                |                |                |
| subjects affected / exposed           | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 1 / 15 (6.67%) |
| occurrences (all)                     | 0              | 1              | 1              |
| Blood potassium decreased             |                |                |                |
| subjects affected / exposed           | 1 / 14 (7.14%) | 2 / 21 (9.52%) | 0 / 15 (0.00%) |
| occurrences (all)                     | 1              | 2              | 0              |
| Blood potassium increased             |                |                |                |
| subjects affected / exposed           | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Blood urea increased                  |                |                |                |
| subjects affected / exposed           | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Blood uric acid decreased             |                |                |                |
| subjects affected / exposed           | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Blood uric acid increased             |                |                |                |
| subjects affected / exposed           | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Breath sounds abnormal                |                |                |                |
| subjects affected / exposed           | 1 / 14 (7.14%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                     | 1              | 0              | 0              |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| C-reactive protein increased<br>subjects affected / exposed<br>occurrences (all)             | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1 |
| Cytomegalovirus test positive<br>subjects affected / exposed<br>occurrences (all)            | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |
| Drug level increased<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 14 (0.00%)<br>0 | 2 / 21 (9.52%)<br>2 | 0 / 15 (0.00%)<br>0 |
| Electrocardiogram QT prolonged<br>subjects affected / exposed<br>occurrences (all)           | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |
| Fibrin D dimer increased<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |
| Fluid balance positive<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 14 (7.14%)<br>1 | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |
| Neutrophil count decreased<br>subjects affected / exposed<br>occurrences (all)               | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |
| Oxygen saturation decreased<br>subjects affected / exposed<br>occurrences (all)              | 1 / 14 (7.14%)<br>1 | 0 / 21 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1 |
| Platelet count decreased<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 14 (7.14%)<br>2 | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |
| Pulmonary arterial pressure<br>increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |
| Red blood cells urine positive<br>subjects affected / exposed<br>occurrences (all)           | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |
| Transaminases increased  |                     |                     |                     |



|  |                 |                |                |
|--|-----------------|----------------|----------------|
| subjects affected / exposed                    | 2 / 14 (14.29%) | 1 / 21 (4.76%) | 1 / 15 (6.67%) |
| occurrences (all)                              | 2               | 1              | 1              |
| Viral test positive                            |                 |                |                |
| subjects affected / exposed                    | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)                              | 0               | 0              | 1              |
| Vitamin D decreased                            |                 |                |                |
| subjects affected / exposed                    | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                              | 0               | 0              | 0              |
| Weight increased                               |                 |                |                |
| subjects affected / exposed                    | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                              | 0               | 0              | 0              |
| White blood cell count decreased               |                 |                |                |
| subjects affected / exposed                    | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                              | 0               | 0              | 0              |
| Injury, poisoning and procedural complications |                 |                |                |
| Accidental overdose                            |                 |                |                |
| subjects affected / exposed                    | 1 / 14 (7.14%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                              | 1               | 0              | 0              |
| Allergic transfusion reaction                  |                 |                |                |
| subjects affected / exposed                    | 1 / 14 (7.14%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                              | 1               | 0              | 0              |
| Buttock injury                                 |                 |                |                |
| subjects affected / exposed                    | 1 / 14 (7.14%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                              | 1               | 0              | 0              |
| Eye contusion                                  |                 |                |                |
| subjects affected / exposed                    | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)                              | 0               | 0              | 1              |
| Head injury                                    |                 |                |                |
| subjects affected / exposed                    | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)                              | 0               | 0              | 1              |
| Infusion related reaction                      |                 |                |                |
| subjects affected / exposed                    | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                              | 0               | 0              | 0              |
| Procedural pain                                |                 |                |                |

|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 21 (4.76%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 1               | 0              |
| Scratch                     |                |                 |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Transfusion reaction        |                |                 |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 21 (4.76%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 1               | 0              |
| Cardiac disorders           |                |                 |                |
| Bradycardia                 |                |                 |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%)  | 1 / 15 (6.67%) |
| occurrences (all)           | 0              | 0               | 1              |
| Pericardial effusion        |                |                 |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Sinus bradycardia           |                |                 |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Sinus tachycardia           |                |                 |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Tachycardia                 |                |                 |                |
| subjects affected / exposed | 1 / 14 (7.14%) | 2 / 21 (9.52%)  | 1 / 15 (6.67%) |
| occurrences (all)           | 1              | 2               | 1              |
| Nervous system disorders    |                |                 |                |
| Dizziness                   |                |                 |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 21 (4.76%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 1               | 0              |
| Headache                    |                |                 |                |
| subjects affected / exposed | 1 / 14 (7.14%) | 4 / 21 (19.05%) | 0 / 15 (0.00%) |
| occurrences (all)           | 1              | 4               | 0              |
| Hypoaesthesia               |                |                 |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Hypotonia                   |                |                 |                |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed                  | 0 / 14 (0.00%)  | 1 / 21 (4.76%)  | 0 / 15 (0.00%)  |
| occurrences (all)                            | 0               | 1               | 0               |
| Intention tremor                             |                 |                 |                 |
| subjects affected / exposed                  | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                            | 0               | 0               | 0               |
| Myoclonus                                    |                 |                 |                 |
| subjects affected / exposed                  | 0 / 14 (0.00%)  | 1 / 21 (4.76%)  | 0 / 15 (0.00%)  |
| occurrences (all)                            | 0               | 2               | 0               |
| Opisthotonus                                 |                 |                 |                 |
| subjects affected / exposed                  | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                            | 0               | 0               | 0               |
| Paraesthesia                                 |                 |                 |                 |
| subjects affected / exposed                  | 1 / 14 (7.14%)  | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                            | 1               | 0               | 0               |
| Posterior reversible encephalopathy syndrome |                 |                 |                 |
| subjects affected / exposed                  | 1 / 14 (7.14%)  | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                            | 1               | 0               | 0               |
| Somnolence                                   |                 |                 |                 |
| subjects affected / exposed                  | 1 / 14 (7.14%)  | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                            | 1               | 0               | 0               |
| Blood and lymphatic system disorders         |                 |                 |                 |
| Agranulocytosis                              |                 |                 |                 |
| subjects affected / exposed                  | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)                            | 0               | 0               | 1               |
| Anaemia                                      |                 |                 |                 |
| subjects affected / exposed                  | 1 / 14 (7.14%)  | 1 / 21 (4.76%)  | 1 / 15 (6.67%)  |
| occurrences (all)                            | 4               | 1               | 2               |
| Disseminated intravascular coagulation       |                 |                 |                 |
| subjects affected / exposed                  | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)                            | 0               | 0               | 0               |
| Febrile neutropenia                          |                 |                 |                 |
| subjects affected / exposed                  | 2 / 14 (14.29%) | 3 / 21 (14.29%) | 2 / 15 (13.33%) |
| occurrences (all)                            | 2               | 3               | 2               |
| Leukopenia                                   |                 |                 |                 |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1 |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 14 (0.00%)<br>0 | 2 / 21 (9.52%)<br>2 | 0 / 15 (0.00%)<br>0 |
| Pancytopenia<br>subjects affected / exposed<br>occurrences (all)                                   | 1 / 14 (7.14%)<br>1 | 1 / 21 (4.76%)<br>1 | 0 / 15 (0.00%)<br>0 |
| Splenomegaly<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 14 (0.00%)<br>0 | 1 / 21 (4.76%)<br>1 | 0 / 15 (0.00%)<br>0 |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 14 (0.00%)<br>0 | 2 / 21 (9.52%)<br>2 | 0 / 15 (0.00%)<br>0 |
| Ear and labyrinth disorders<br>Ear haemorrhage<br>subjects affected / exposed<br>occurrences (all) | 0 / 14 (0.00%)<br>0 | 1 / 21 (4.76%)<br>1 | 0 / 15 (0.00%)<br>0 |
| Ear pain<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1 |
| Tinnitus<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |
| Vertigo<br>subjects affected / exposed<br>occurrences (all)  | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |
| Eye disorders<br>Conjunctival haemorrhage<br>subjects affected / exposed<br>occurrences (all)      | 1 / 14 (7.14%)<br>1 | 0 / 21 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1 |
| Dry eye<br>subjects affected / exposed<br>occurrences (all)  | 1 / 14 (7.14%)<br>1 | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |
| Eye haemorrhage  |                     |                     |                     |

|                             |                 |                |                 |
|-----------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Eye irritation              |                 |                |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Eye pain                    |                 |                |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Eyelid oedema               |                 |                |                 |
| subjects affected / exposed | 2 / 14 (14.29%) | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 2               | 0              | 0               |
| Ocular hyperaemia           |                 |                |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 1 / 21 (4.76%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 1              | 0               |
| Periorbital oedema          |                 |                |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Photophobia                 |                 |                |                 |
| subjects affected / exposed | 1 / 14 (7.14%)  | 1 / 21 (4.76%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 1               | 1              | 0               |
| Vision blurred              |                 |                |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Visual impairment           |                 |                |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 1 / 21 (4.76%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 1              | 0               |
| Gastrointestinal disorders  |                 |                |                 |
| Abdominal discomfort        |                 |                |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Abdominal distension        |                 |                |                 |
| subjects affected / exposed | 2 / 14 (14.29%) | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 2               | 0              | 0               |
| Abdominal pain              |                 |                |                 |
| subjects affected / exposed | 2 / 14 (14.29%) | 2 / 21 (9.52%) | 2 / 15 (13.33%) |
| occurrences (all)           | 2               | 2              | 2               |

|                             |                 |                |                 |
|-----------------------------|-----------------|----------------|-----------------|
| Abdominal pain upper        |                 |                |                 |
| subjects affected / exposed | 1 / 14 (7.14%)  | 2 / 21 (9.52%) | 2 / 15 (13.33%) |
| occurrences (all)           | 1               | 2              | 2               |
| Anal fissure                |                 |                |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 2 / 21 (9.52%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 2              | 0               |
| Anal inflammation           |                 |                |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Anorectal discomfort        |                 |                |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Anorectal disorder          |                 |                |                 |
| subjects affected / exposed | 1 / 14 (7.14%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0               |
| Aphthous ulcer              |                 |                |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Ascites                     |                 |                |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Colitis                     |                 |                |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Constipation                |                 |                |                 |
| subjects affected / exposed | 3 / 14 (21.43%) | 2 / 21 (9.52%) | 2 / 15 (13.33%) |
| occurrences (all)           | 3               | 2              | 2               |
| Diarrhoea                   |                 |                |                 |
| subjects affected / exposed | 5 / 14 (35.71%) | 2 / 21 (9.52%) | 5 / 15 (33.33%) |
| occurrences (all)           | 5               | 2              | 5               |
| Dyspepsia                   |                 |                |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 1 / 15 (6.67%)  |
| occurrences (all)           | 0               | 0              | 1               |
| Dysphagia                   |                 |                |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 1 / 21 (4.76%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 1              | 0               |

|                                  |                |                |                |
|----------------------------------|----------------|----------------|----------------|
| Faeces hard                      |                |                |                |
| subjects affected / exposed      | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Gastrointestinal haemorrhage     |                |                |                |
| subjects affected / exposed      | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Gastrooesophageal reflux disease |                |                |                |
| subjects affected / exposed      | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0              | 1              | 0              |
| Gingival bleeding                |                |                |                |
| subjects affected / exposed      | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Gingival pain                    |                |                |                |
| subjects affected / exposed      | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0              | 1              | 0              |
| Glossodynia                      |                |                |                |
| subjects affected / exposed      | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0              | 1              | 0              |
| Haematemesis                     |                |                |                |
| subjects affected / exposed      | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0              | 1              | 0              |
| Haematochezia                    |                |                |                |
| subjects affected / exposed      | 1 / 14 (7.14%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                | 1              | 0              | 0              |
| Haemorrhoids                     |                |                |                |
| subjects affected / exposed      | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Lip dry                          |                |                |                |
| subjects affected / exposed      | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0              | 1              | 0              |
| Lip pruritus                     |                |                |                |
| subjects affected / exposed      | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Loose tooth                      |                |                |                |
| subjects affected / exposed      | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |

|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| Mouth ulceration            |                |                 |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Nausea                      |                |                 |                |
| subjects affected / exposed | 1 / 14 (7.14%) | 4 / 21 (19.05%) | 1 / 15 (6.67%) |
| occurrences (all)           | 1              | 5               | 1              |
| Odynophagia                 |                |                 |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 21 (4.76%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 1               | 0              |
| Oesophagitis                |                |                 |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Oral disorder               |                |                 |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%)  | 1 / 15 (6.67%) |
| occurrences (all)           | 0              | 0               | 1              |
| Oral mucosal blistering     |                |                 |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Oral mucosal exfoliation    |                |                 |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%)  | 1 / 15 (6.67%) |
| occurrences (all)           | 0              | 0               | 1              |
| Oral pain                   |                |                 |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Rectal haemorrhage          |                |                 |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 21 (4.76%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 1               | 0              |
| Scalloped tongue            |                |                 |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%)  | 1 / 15 (6.67%) |
| occurrences (all)           | 0              | 0               | 1              |
| Stomatitis                  |                |                 |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 21 (9.52%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 2               | 0              |
| Subileus                    |                |                 |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%)  | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |



|  |                      |                      |                      |
|--|----------------------|----------------------|----------------------|
| Tongue haemorrhage<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 14 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Tooth loss<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 14 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Toothache<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 14 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                                       | 4 / 14 (28.57%)<br>6 | 6 / 21 (28.57%)<br>9 | 2 / 15 (13.33%)<br>3 |
| Hepatobiliary disorders<br>Hepatomegaly<br>subjects affected / exposed<br>occurrences (all)        | 0 / 14 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Hyperbilirubinaemia<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 14 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Jaundice<br>subjects affected / exposed<br>occurrences (all)                                       | 1 / 14 (7.14%)<br>1  | 0 / 21 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Skin and subcutaneous tissue disorders<br>Acne<br>subjects affected / exposed<br>occurrences (all) | 0 / 14 (0.00%)<br>0  | 1 / 21 (4.76%)<br>1  | 0 / 15 (0.00%)<br>0  |
| Alopecia<br>subjects affected / exposed<br>occurrences (all)                                       | 2 / 14 (14.29%)<br>2 | 0 / 21 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Blister<br>subjects affected / exposed<br>occurrences (all)  | 1 / 14 (7.14%)<br>1  | 0 / 21 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Dermatitis<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 14 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Dermatitis atopic  |                      |                      |                      |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| <b>Dermatitis bullous</b>   |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| <b>Dermatitis contact</b>   |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| <b>Dermatitis diaper</b>    |                |                |                |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| <b>Drug eruption</b>        |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| <b>Dry skin</b>             |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| <b>Erythema</b>             |                |                |                |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)           | 1              | 0              | 1              |
| <b>Erythema multiforme</b>  |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| <b>Macule</b>               |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| <b>Night sweats</b>         |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| <b>Palmar erythema</b>      |                |                |                |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| <b>Papule</b>               |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| <b>Petechiae</b>            |                |                |                |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 14 (7.14%)  | 1 / 21 (4.76%)  | 1 / 15 (6.67%)  |
| occurrences (all)           | 1               | 1               | 1               |
| Pruritus                    |                 |                 |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 1 / 21 (4.76%)  | 1 / 15 (6.67%)  |
| occurrences (all)           | 0               | 1               | 1               |
| Pruritus allergic           |                 |                 |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Rash                        |                 |                 |                 |
| subjects affected / exposed | 2 / 14 (14.29%) | 4 / 21 (19.05%) | 3 / 15 (20.00%) |
| occurrences (all)           | 3               | 4               | 4               |
| Rash generalised            |                 |                 |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Rash macular                |                 |                 |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 1 / 21 (4.76%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Rash maculo-papular         |                 |                 |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Rash pruritic               |                 |                 |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Skin burning sensation      |                 |                 |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Skin exfoliation            |                 |                 |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 0 / 21 (0.00%)  | 1 / 15 (6.67%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Skin hyperpigmentation      |                 |                 |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 1 / 21 (4.76%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Skin lesion                 |                 |                 |                 |
| subjects affected / exposed | 1 / 14 (7.14%)  | 1 / 21 (4.76%)  | 0 / 15 (0.00%)  |
| occurrences (all)           | 1               | 1               | 0               |
| Skin mass                   |                 |                 |                 |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Skin ulcer                  |                |                |                |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Swelling face               |                |                |                |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)           | 1              | 1              | 0              |
| Urticaria                   |                |                |                |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)           | 1              | 0              | 1              |
| Renal and urinary disorders |                |                |                |
| Acute kidney injury         |                |                |                |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Cystitis haemorrhagic       |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Dysuria                     |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Glycosuria                  |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Haematuria                  |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)           | 0              | 0              | 1              |
| Micturition urgency         |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Nephropathy toxic           |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Proteinuria                 |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| Tubulointerstitial nephritis<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |
| Urinary retention<br>subjects affected / exposed<br>occurrences (all)   | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |
| Endocrine disorders<br>Cushingoid<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 0 / 14 (0.00%)<br>0 | 1 / 21 (4.76%)<br>1 | 0 / 15 (0.00%)<br>0 |
| Back pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 14 (0.00%)<br>0 | 1 / 21 (4.76%)<br>1 | 0 / 15 (0.00%)<br>0 |
| Bone pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1 |
| Flank pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 14 (0.00%)<br>0 | 1 / 21 (4.76%)<br>1 | 0 / 15 (0.00%)<br>0 |
| Joint range of motion decreased<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |
| Muscle spasms<br>subjects affected / exposed<br>occurrences (all)   | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |
| Muscle tightness<br>subjects affected / exposed<br>occurrences (all)  | 0 / 14 (0.00%)<br>0 | 1 / 21 (4.76%)<br>1 | 0 / 15 (0.00%)<br>0 |
| Musculoskeletal chest pain<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |
| Musculoskeletal pain  |                     |                     |                     |

|                               |                 |                |                |
|-------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed   | 0 / 14 (0.00%)  | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)             | 0               | 1              | 0              |
| Myalgia                       |                 |                |                |
| subjects affected / exposed   | 0 / 14 (0.00%)  | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)             | 0               | 1              | 0              |
| Pain in extremity             |                 |                |                |
| subjects affected / exposed   | 2 / 14 (14.29%) | 1 / 21 (4.76%) | 1 / 15 (6.67%) |
| occurrences (all)             | 2               | 1              | 2              |
| Pain in jaw                   |                 |                |                |
| subjects affected / exposed   | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 0               | 0              | 0              |
| Soft tissue swelling          |                 |                |                |
| subjects affected / exposed   | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)             | 0               | 0              | 1              |
| Infections and infestations   |                 |                |                |
| Adenovirus infection          |                 |                |                |
| subjects affected / exposed   | 1 / 14 (7.14%)  | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)             | 1               | 0              | 1              |
| BK virus infection            |                 |                |                |
| subjects affected / exposed   | 0 / 14 (0.00%)  | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)             | 0               | 1              | 0              |
| Bacteraemia                   |                 |                |                |
| subjects affected / exposed   | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 0               | 0              | 0              |
| Bacterial infection           |                 |                |                |
| subjects affected / exposed   | 1 / 14 (7.14%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 1               | 0              | 0              |
| Bronchitis                    |                 |                |                |
| subjects affected / exposed   | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 0               | 0              | 0              |
| Clostridial infection         |                 |                |                |
| subjects affected / exposed   | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)             | 0               | 0              | 1              |
| Clostridium difficile colitis |                 |                |                |
| subjects affected / exposed   | 1 / 14 (7.14%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)             | 1               | 0              | 0              |

|   |                     |                     |                      |
|---|---------------------|---------------------|----------------------|
| Clostridium difficile infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  |
| Conjunctivitis<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  |
| Corona virus infection<br>subjects affected / exposed<br>occurrences (all)          | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  |
| Cystitis<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 14 (0.00%)<br>0 | 1 / 21 (4.76%)<br>1 | 0 / 15 (0.00%)<br>0  |
| Cytomegalovirus infection<br>subjects affected / exposed<br>occurrences (all)       | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 3 / 15 (20.00%)<br>3 |
| Device related infection<br>subjects affected / exposed<br>occurrences (all)        | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  |
| Ear infection<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 14 (0.00%)<br>0 | 1 / 21 (4.76%)<br>1 | 0 / 15 (0.00%)<br>0  |
| Endocarditis<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  |
| Enterobacter bacteraemia<br>subjects affected / exposed<br>occurrences (all)        | 1 / 14 (7.14%)<br>1 | 0 / 21 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0  |
| Epstein-Barr virus infection<br>subjects affected / exposed<br>occurrences (all)    | 1 / 14 (7.14%)<br>1 | 1 / 21 (4.76%)<br>1 | 1 / 15 (6.67%)<br>1  |
| Escherichia sepsis<br>subjects affected / exposed<br>occurrences (all)              | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  |
| Gingivitis<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 14 (0.00%)<br>0 | 0 / 21 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1  |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Hepatitis E                 |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Human bocavirus infection   |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Infection                   |                |                |                |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Klebsiella bacteraemia      |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Klebsiella infection        |                |                |                |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Localised infection         |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Lung infection              |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Mucosal infection           |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Nasopharyngitis             |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)           | 0              | 0              | 1              |
| Oral herpes                 |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Paronychia                  |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Pneumonia                   |                |                |                |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |



|                                   |                |                |                |
|-----------------------------------|----------------|----------------|----------------|
| Pneumonia parainfluenzae viral    |                |                |                |
| subjects affected / exposed       | 1 / 14 (7.14%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                 | 1              | 0              | 0              |
| Proctitis herpes                  |                |                |                |
| subjects affected / exposed       | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Respiratory tract infection       |                |                |                |
| subjects affected / exposed       | 1 / 14 (7.14%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                 | 1              | 0              | 0              |
| Rhinitis                          |                |                |                |
| subjects affected / exposed       | 1 / 14 (7.14%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                 | 1              | 0              | 0              |
| Rhinovirus infection              |                |                |                |
| subjects affected / exposed       | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Sepsis                            |                |                |                |
| subjects affected / exposed       | 0 / 14 (0.00%) | 1 / 21 (4.76%) | 0 / 15 (0.00%) |
| occurrences (all)                 | 0              | 1              | 0              |
| Staphylococcal bacteraemia        |                |                |                |
| subjects affected / exposed       | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Staphylococcal infection          |                |                |                |
| subjects affected / exposed       | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)                 | 0              | 0              | 1              |
| Staphylococcal sepsis             |                |                |                |
| subjects affected / exposed       | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)                 | 0              | 0              | 1              |
| Upper respiratory tract infection |                |                |                |
| subjects affected / exposed       | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Viraemia                          |                |                |                |
| subjects affected / exposed       | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)                 | 0              | 0              | 1              |
| Viral infection                   |                |                |                |
| subjects affected / exposed       | 0 / 14 (0.00%) | 0 / 21 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all)                 | 0              | 0              | 1              |

|   |                      |                      |                      |
|---|----------------------|----------------------|----------------------|
| Viral upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 14 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Metabolism and nutrition disorders  |                      |                      |                      |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)                      | 2 / 14 (14.29%)<br>2 | 4 / 21 (19.05%)<br>4 | 3 / 15 (20.00%)<br>3 |
| Fluid intake reduced<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 14 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Fluid retention<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 14 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)                          | 2 / 14 (14.29%)<br>2 | 0 / 21 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Hyperkalaemia<br>subjects affected / exposed<br>occurrences (all)                           | 1 / 14 (7.14%)<br>1  | 0 / 21 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Hypernatraemia<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 14 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  |
| Hypertriglyceridaemia<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 14 (7.14%)<br>1  | 0 / 21 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Hypoalbuminaemia<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 14 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Hypocalcaemia<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 14 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Hypochloraemia<br>subjects affected / exposed<br>occurrences (all)                          | 1 / 14 (7.14%)<br>3  | 0 / 21 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |
| Hypoglycaemia   |                      |                      |                      |

|                             |                 |                |                 |
|-----------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 14 (7.14%)  | 0 / 21 (0.00%) | 1 / 15 (6.67%)  |
| occurrences (all)           | 3               | 0              | 1               |
| Hypokalaemia                |                 |                |                 |
| subjects affected / exposed | 2 / 14 (14.29%) | 0 / 21 (0.00%) | 1 / 15 (6.67%)  |
| occurrences (all)           | 2               | 0              | 1               |
| Hypomagnesaemia             |                 |                |                 |
| subjects affected / exposed | 2 / 14 (14.29%) | 1 / 21 (4.76%) | 2 / 15 (13.33%) |
| occurrences (all)           | 2               | 1              | 3               |
| Hyponatraemia               |                 |                |                 |
| subjects affected / exposed | 2 / 14 (14.29%) | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 2               | 0              | 0               |
| Hypophagia                  |                 |                |                 |
| subjects affected / exposed | 1 / 14 (7.14%)  | 0 / 21 (0.00%) | 1 / 15 (6.67%)  |
| occurrences (all)           | 1               | 0              | 1               |
| Hypophosphataemia           |                 |                |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 1 / 15 (6.67%)  |
| occurrences (all)           | 0               | 0              | 1               |
| Magnesium deficiency        |                 |                |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Metabolic acidosis          |                 |                |                 |
| subjects affected / exposed | 0 / 14 (0.00%)  | 1 / 21 (4.76%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 0               | 1              | 0               |
| Vitamin D deficiency        |                 |                |                 |
| subjects affected / exposed | 1 / 14 (7.14%)  | 0 / 21 (0.00%) | 0 / 15 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0               |

| <b>Non-serious adverse events</b>                                      | 4.5 mg/kg<br>posaconazole (7-17<br>years old) | 6.0 mg/kg<br>posaconazole (2-<7<br>years old) | 6.0 mg/kg<br>posaconazole (7-17<br>years old) |
|--|---|---|---|
| Total subjects affected by non-serious<br>adverse events               |   |   |   |
| subjects affected / exposed  | 16 / 16 (100.00%)                             | 19 / 20 (95.00%)                              | 29 / 29 (100.00%)                             |
| Neoplasms benign, malignant and<br>unspecified (incl cysts and polyps) |   |   |   |
| Acute myeloid leukaemia  |   |   |   |
| subjects affected / exposed  | 0 / 16 (0.00%)                                | 0 / 20 (0.00%)                                | 1 / 29 (3.45%)                                |
| occurrences (all)  | 0   | 0   | 1   |
| Vascular disorders   |   |   |   |

|   |                      |                      |                      |
|---|----------------------|----------------------|----------------------|
| Capillary leak syndrome<br>subjects affected / exposed<br>occurrences (all) | 0 / 16 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  | 1 / 29 (3.45%)<br>1  |
| Flushing<br>subjects affected / exposed<br>occurrences (all)                | 0 / 16 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  | 0 / 29 (0.00%)<br>0  |
| Haematoma<br>subjects affected / exposed<br>occurrences (all)               | 0 / 16 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  | 0 / 29 (0.00%)<br>0  |
| Hyperaemia<br>subjects affected / exposed<br>occurrences (all)              | 0 / 16 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1  | 1 / 29 (3.45%)<br>1  |
| Hypertension<br>subjects affected / exposed<br>occurrences (all)            | 1 / 16 (6.25%)<br>1  | 6 / 20 (30.00%)<br>6 | 4 / 29 (13.79%)<br>4 |
| Hypotension<br>subjects affected / exposed<br>occurrences (all)             | 2 / 16 (12.50%)<br>2 | 1 / 20 (5.00%)<br>1  | 2 / 29 (6.90%)<br>2  |
| Pallor<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 16 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  | 0 / 29 (0.00%)<br>0  |
| Phlebitis<br>subjects affected / exposed<br>occurrences (all)               | 1 / 16 (6.25%)<br>1  | 0 / 20 (0.00%)<br>0  | 0 / 29 (0.00%)<br>0  |
| Venoocclusive disease<br>subjects affected / exposed<br>occurrences (all)   | 0 / 16 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  | 1 / 29 (3.45%)<br>2  |
| General disorders and administration<br>site conditions                     |                      |                      |                      |
| Axillary pain<br>subjects affected / exposed<br>occurrences (all)           | 0 / 16 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  | 1 / 29 (3.45%)<br>1  |
| Catheter site erythema<br>subjects affected / exposed<br>occurrences (all)  | 0 / 16 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  | 0 / 29 (0.00%)<br>0  |
| Catheter site haemorrhage   |                      |                      |                      |

|                                       |                |                |                |
|---------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed           | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Catheter site oedema                  |                |                |                |
| subjects affected / exposed           | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                     | 0              | 0              | 2              |
| Catheter site pain                    |                |                |                |
| subjects affected / exposed           | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                     | 0              | 0              | 2              |
| Catheter site swelling                |                |                |                |
| subjects affected / exposed           | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Chills                                |                |                |                |
| subjects affected / exposed           | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Face oedema                           |                |                |                |
| subjects affected / exposed           | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all)                     | 0              | 0              | 2              |
| Fatigue                               |                |                |                |
| subjects affected / exposed           | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                     | 0              | 0              | 1              |
| General physical health deterioration |                |                |                |
| subjects affected / exposed           | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all)                     | 0              | 0              | 3              |
| Generalised oedema                    |                |                |                |
| subjects affected / exposed           | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                     | 0              | 0              | 1              |
| Granuloma                             |                |                |                |
| subjects affected / exposed           | 1 / 16 (6.25%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                     | 1              | 0              | 0              |
| Infusion site erythema                |                |                |                |
| subjects affected / exposed           | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Malaise                               |                |                |                |
| subjects affected / exposed           | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                     | 0              | 0              | 2              |
| Mucosal inflammation                  |                |                |                |

|   |                  |                 |                 |
|---|------------------|-----------------|-----------------|
| subjects affected / exposed                         | 4 / 16 (25.00%)  | 5 / 20 (25.00%) | 6 / 29 (20.69%) |
| occurrences (all)                                   | 4                | 5               | 6               |
| Oedema  |                  |                 |                 |
| subjects affected / exposed                         | 0 / 16 (0.00%)   | 1 / 20 (5.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                                   | 0                | 1               | 0               |
| Oedema peripheral                                   |                  |                 |                 |
| subjects affected / exposed                         | 0 / 16 (0.00%)   | 1 / 20 (5.00%)  | 2 / 29 (6.90%)  |
| occurrences (all)                                   | 0                | 1               | 2               |
| Pain  |                  |                 |                 |
| subjects affected / exposed                         | 1 / 16 (6.25%)   | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                                   | 1                | 0               | 0               |
| Pyrexia   |                  |                 |                 |
| subjects affected / exposed                         | 10 / 16 (62.50%) | 8 / 20 (40.00%) | 8 / 29 (27.59%) |
| occurrences (all)                                   | 13               | 8               | 12              |
| Systemic inflammatory response syndrome             |                  |                 |                 |
| subjects affected / exposed                         | 0 / 16 (0.00%)   | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                                   | 0                | 0               | 0               |
| Immune system disorders                             |                  |                 |                 |
| Drug hypersensitivity                               |                  |                 |                 |
| subjects affected / exposed                         | 0 / 16 (0.00%)   | 2 / 20 (10.00%) | 2 / 29 (6.90%)  |
| occurrences (all)                                   | 0                | 2               | 3               |
| Engraftment syndrome                                |                  |                 |                 |
| subjects affected / exposed                         | 0 / 16 (0.00%)   | 0 / 20 (0.00%)  | 2 / 29 (6.90%)  |
| occurrences (all)                                   | 0                | 0               | 2               |
| Graft versus host disease                           |                  |                 |                 |
| subjects affected / exposed                         | 1 / 16 (6.25%)   | 0 / 20 (0.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)                                   | 1                | 0               | 1               |
| Graft versus host disease in gastrointestinal tract |                  |                 |                 |
| subjects affected / exposed                         | 1 / 16 (6.25%)   | 0 / 20 (0.00%)  | 2 / 29 (6.90%)  |
| occurrences (all)                                   | 1                | 0               | 2               |
| Graft versus host disease in liver                  |                  |                 |                 |
| subjects affected / exposed                         | 0 / 16 (0.00%)   | 1 / 20 (5.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                                   | 0                | 1               | 0               |
| Graft versus host disease in skin                   |                  |                 |                 |

|  |                |                 |                |
|--|----------------|-----------------|----------------|
| subjects affected / exposed              | 1 / 16 (6.25%) | 2 / 20 (10.00%) | 1 / 29 (3.45%) |
| occurrences (all)                        | 1              | 2               | 1              |
| Hypogammaglobulinaemia                   |                |                 |                |
| subjects affected / exposed              | 0 / 16 (0.00%) | 2 / 20 (10.00%) | 0 / 29 (0.00%) |
| occurrences (all)                        | 0              | 2               | 0              |
| Immunodeficiency                         |                |                 |                |
| subjects affected / exposed              | 0 / 16 (0.00%) | 0 / 20 (0.00%)  | 1 / 29 (3.45%) |
| occurrences (all)                        | 0              | 0               | 1              |
| Immunodeficiency common variable         |                |                 |                |
| subjects affected / exposed              | 1 / 16 (6.25%) | 0 / 20 (0.00%)  | 0 / 29 (0.00%) |
| occurrences (all)                        | 1              | 0               | 0              |
| Serum sickness                           |                |                 |                |
| subjects affected / exposed              | 0 / 16 (0.00%) | 0 / 20 (0.00%)  | 0 / 29 (0.00%) |
| occurrences (all)                        | 0              | 0               | 0              |
| Reproductive system and breast disorders |                |                 |                |
| Menorrhagia                              |                |                 |                |
| subjects affected / exposed              | 0 / 16 (0.00%) | 0 / 20 (0.00%)  | 1 / 29 (3.45%) |
| occurrences (all)                        | 0              | 0               | 1              |
| Metrorrhagia                             |                |                 |                |
| subjects affected / exposed              | 1 / 16 (6.25%) | 0 / 20 (0.00%)  | 0 / 29 (0.00%) |
| occurrences (all)                        | 1              | 0               | 0              |
| Perineal erythema                        |                |                 |                |
| subjects affected / exposed              | 0 / 16 (0.00%) | 1 / 20 (5.00%)  | 0 / 29 (0.00%) |
| occurrences (all)                        | 0              | 1               | 0              |
| Perineal pain                            |                |                 |                |
| subjects affected / exposed              | 0 / 16 (0.00%) | 1 / 20 (5.00%)  | 0 / 29 (0.00%) |
| occurrences (all)                        | 0              | 1               | 0              |
| Scrotal oedema                           |                |                 |                |
| subjects affected / exposed              | 0 / 16 (0.00%) | 0 / 20 (0.00%)  | 1 / 29 (3.45%) |
| occurrences (all)                        | 0              | 0               | 1              |
| Testicular oedema                        |                |                 |                |
| subjects affected / exposed              | 0 / 16 (0.00%) | 0 / 20 (0.00%)  | 0 / 29 (0.00%) |
| occurrences (all)                        | 0              | 0               | 0              |
| Vulvovaginal inflammation                |                |                 |                |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0               |
| Vulvovaginal pruritus                           |                 |                |                 |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 1 / 20 (5.00%) | 0 / 29 (0.00%)  |
| occurrences (all)                               | 0               | 1              | 0               |
| Respiratory, thoracic and mediastinal disorders |                 |                |                 |
| Cough   |                 |                |                 |
| subjects affected / exposed                     | 1 / 16 (6.25%)  | 0 / 20 (0.00%) | 3 / 29 (10.34%) |
| occurrences (all)                               | 1               | 0              | 3               |
| Dysphonia                                       |                 |                |                 |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0               |
| Dyspnoea  |                 |                |                 |
| subjects affected / exposed                     | 1 / 16 (6.25%)  | 0 / 20 (0.00%) | 1 / 29 (3.45%)  |
| occurrences (all)                               | 1               | 0              | 1               |
| Epistaxis                                       |                 |                |                 |
| subjects affected / exposed                     | 5 / 16 (31.25%) | 1 / 20 (5.00%) | 3 / 29 (10.34%) |
| occurrences (all)                               | 8               | 1              | 4               |
| Haemoptysis                                     |                 |                |                 |
| subjects affected / exposed                     | 1 / 16 (6.25%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)                               | 1               | 0              | 0               |
| Hypoxia   |                 |                |                 |
| subjects affected / exposed                     | 1 / 16 (6.25%)  | 1 / 20 (5.00%) | 1 / 29 (3.45%)  |
| occurrences (all)                               | 1               | 1              | 1               |
| Increased viscosity of bronchial secretion      |                 |                |                 |
| subjects affected / exposed                     | 1 / 16 (6.25%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)                               | 1               | 0              | 0               |
| Lung infiltration                               |                 |                |                 |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0               |
| Nasal congestion                                |                 |                |                 |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 1 / 29 (3.45%)  |
| occurrences (all)                               | 0               | 0              | 1               |
| Oropharyngeal pain                              |                 |                |                 |



|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 3 / 29 (10.34%) |
| occurrences (all)           | 0              | 0              | 3               |
| Pharyngeal inflammation     |                |                |                 |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%)  |
| occurrences (all)           | 0              | 0              | 1               |
| Pleural effusion            |                |                |                 |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 20 (5.00%) | 0 / 29 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| Pleuritic pain              |                |                |                 |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Productive cough            |                |                |                 |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%)  |
| occurrences (all)           | 0              | 0              | 1               |
| Pulmonary oedema            |                |                |                 |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%)  |
| occurrences (all)           | 0              | 0              | 1               |
| Rales                       |                |                |                 |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Rhinitis allergic           |                |                |                 |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Rhinorrhoea                 |                |                |                 |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%)  |
| occurrences (all)           | 0              | 0              | 1               |
| Tachypnoea                  |                |                |                 |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Tonsillar exudate           |                |                |                 |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Psychiatric disorders       |                |                |                 |
| Agitation                   |                |                |                 |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%)  |
| occurrences (all)           | 0              | 0              | 1               |

|                                      |                |                |                 |
|--------------------------------------|----------------|----------------|-----------------|
| Anxiety                              |                |                |                 |
| subjects affected / exposed          | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 2 / 29 (6.90%)  |
| occurrences (all)                    | 0              | 0              | 2               |
| Depressed mood                       |                |                |                 |
| subjects affected / exposed          | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%)  |
| occurrences (all)                    | 0              | 0              | 1               |
| Depression                           |                |                |                 |
| subjects affected / exposed          | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Insomnia                             |                |                |                 |
| subjects affected / exposed          | 1 / 16 (6.25%) | 0 / 20 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)                    | 1              | 0              | 0               |
| Irritability                         |                |                |                 |
| subjects affected / exposed          | 0 / 16 (0.00%) | 1 / 20 (5.00%) | 0 / 29 (0.00%)  |
| occurrences (all)                    | 0              | 1              | 0               |
| Investigations                       |                |                |                 |
| Alanine aminotransferase increased   |                |                |                 |
| subjects affected / exposed          | 0 / 16 (0.00%) | 1 / 20 (5.00%) | 5 / 29 (17.24%) |
| occurrences (all)                    | 0              | 1              | 5               |
| Aspartate aminotransferase increased |                |                |                 |
| subjects affected / exposed          | 1 / 16 (6.25%) | 0 / 20 (0.00%) | 5 / 29 (17.24%) |
| occurrences (all)                    | 1              | 0              | 6               |
| BK polyomavirus test positive        |                |                |                 |
| subjects affected / exposed          | 0 / 16 (0.00%) | 1 / 20 (5.00%) | 0 / 29 (0.00%)  |
| occurrences (all)                    | 0              | 1              | 0               |
| Bacterial test positive              |                |                |                 |
| subjects affected / exposed          | 1 / 16 (6.25%) | 0 / 20 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)                    | 1              | 0              | 0               |
| Blood albumin decreased              |                |                |                 |
| subjects affected / exposed          | 1 / 16 (6.25%) | 0 / 20 (0.00%) | 1 / 29 (3.45%)  |
| occurrences (all)                    | 1              | 0              | 1               |
| Blood alkaline phosphatase increased |                |                |                 |
| subjects affected / exposed          | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Blood bilirubin increased            |                |                |                 |

|                                       |                 |                |                |
|---------------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed           | 2 / 16 (12.50%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                     | 2               | 0              | 0              |
| Blood calcium decreased               |                 |                |                |
| subjects affected / exposed           | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                     | 0               | 0              | 0              |
| Blood creatinine increased            |                 |                |                |
| subjects affected / exposed           | 1 / 16 (6.25%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                     | 1               | 0              | 0              |
| Blood culture positive                |                 |                |                |
| subjects affected / exposed           | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                     | 0               | 0              | 0              |
| Blood immunoglobulin G decreased      |                 |                |                |
| subjects affected / exposed           | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                     | 0               | 0              | 1              |
| Blood lactate dehydrogenase increased |                 |                |                |
| subjects affected / exposed           | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                     | 0               | 0              | 1              |
| Blood magnesium decreased             |                 |                |                |
| subjects affected / exposed           | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                     | 0               | 0              | 1              |
| Blood phosphorus decreased            |                 |                |                |
| subjects affected / exposed           | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                     | 0               | 0              | 0              |
| Blood potassium decreased             |                 |                |                |
| subjects affected / exposed           | 1 / 16 (6.25%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                     | 1               | 0              | 0              |
| Blood potassium increased             |                 |                |                |
| subjects affected / exposed           | 1 / 16 (6.25%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                     | 2               | 0              | 0              |
| Blood urea increased                  |                 |                |                |
| subjects affected / exposed           | 1 / 16 (6.25%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                     | 1               | 0              | 0              |
| Blood uric acid decreased             |                 |                |                |
| subjects affected / exposed           | 1 / 16 (6.25%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                     | 1               | 0              | 0              |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| Blood uric acid increased<br>subjects affected / exposed<br>occurrences (all)      | 1 / 16 (6.25%)<br>1 | 0 / 20 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0 |
| Breath sounds abnormal<br>subjects affected / exposed<br>occurrences (all)         | 0 / 16 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0 |
| C-reactive protein increased<br>subjects affected / exposed<br>occurrences (all)   | 0 / 16 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0 |
| Cytomegalovirus test positive<br>subjects affected / exposed<br>occurrences (all)  | 1 / 16 (6.25%)<br>1 | 0 / 20 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0 |
| Drug level increased<br>subjects affected / exposed<br>occurrences (all)           | 0 / 16 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0 |
| Electrocardiogram QT prolonged<br>subjects affected / exposed<br>occurrences (all) | 1 / 16 (6.25%)<br>1 | 0 / 20 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1 |
| Fibrin D dimer increased<br>subjects affected / exposed<br>occurrences (all)       | 0 / 16 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1 |
| Fluid balance positive<br>subjects affected / exposed<br>occurrences (all)         | 0 / 16 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0 |
| Neutrophil count decreased<br>subjects affected / exposed<br>occurrences (all)     | 0 / 16 (0.00%)<br>0 | 0 / 20 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1 |
| Oxygen saturation decreased<br>subjects affected / exposed<br>occurrences (all)    | 1 / 16 (6.25%)<br>1 | 0 / 20 (0.00%)<br>0 | 1 / 29 (3.45%)<br>2 |
| Platelet count decreased<br>subjects affected / exposed<br>occurrences (all)       | 1 / 16 (6.25%)<br>2 | 1 / 20 (5.00%)<br>1 | 2 / 29 (6.90%)<br>2 |
| Pulmonary arterial pressure<br>increased   |                     |                     |                     |

|  |                 |                |                |
|--|-----------------|----------------|----------------|
| subjects affected / exposed                    | 1 / 16 (6.25%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                              | 1               | 0              | 0              |
| Red blood cells urine positive                 |                 |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                              | 0               | 0              | 1              |
| Transaminases increased                        |                 |                |                |
| subjects affected / exposed                    | 3 / 16 (18.75%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                              | 3               | 0              | 0              |
| Viral test positive                            |                 |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                              | 0               | 0              | 0              |
| Vitamin D decreased                            |                 |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%)  | 1 / 20 (5.00%) | 0 / 29 (0.00%) |
| occurrences (all)                              | 0               | 1              | 0              |
| Weight increased                               |                 |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all)                              | 0               | 0              | 2              |
| White blood cell count decreased               |                 |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                              | 0               | 0              | 1              |
| Injury, poisoning and procedural complications |                 |                |                |
| Accidental overdose                            |                 |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                              | 0               | 0              | 0              |
| Allergic transfusion reaction                  |                 |                |                |
| subjects affected / exposed                    | 1 / 16 (6.25%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                              | 1               | 0              | 0              |
| Buttock injury                                 |                 |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                              | 0               | 0              | 0              |
| Eye contusion                                  |                 |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                              | 0               | 0              | 0              |
| Head injury                                    |                 |                |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Infusion related reaction   |                |                |                |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 20 (5.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 1              | 1              | 0              |
| Procedural pain             |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 1              |
| Scratch                     |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 1              |
| Transfusion reaction        |                |                |                |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 20 (5.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 1              | 1              | 1              |
| Cardiac disorders           |                |                |                |
| Bradycardia                 |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 1              |
| Pericardial effusion        |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 1              |
| Sinus bradycardia           |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 1              |
| Sinus tachycardia           |                |                |                |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Tachycardia                 |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 20 (5.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 1              | 1              |
| Nervous system disorders    |                |                |                |
| Dizziness                   |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 1              |
| Headache                    |                |                |                |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed                  | 5 / 16 (31.25%) | 1 / 20 (5.00%)  | 5 / 29 (17.24%) |
| occurrences (all)                            | 6               | 1               | 7               |
| Hypoaesthesia                                |                 |                 |                 |
| subjects affected / exposed                  | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)                            | 0               | 0               | 2               |
| Hypotonia                                    |                 |                 |                 |
| subjects affected / exposed                  | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                            | 0               | 0               | 0               |
| Intention tremor                             |                 |                 |                 |
| subjects affected / exposed                  | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)                            | 0               | 0               | 1               |
| Myoclonus                                    |                 |                 |                 |
| subjects affected / exposed                  | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                            | 0               | 0               | 0               |
| Opisthotonus                                 |                 |                 |                 |
| subjects affected / exposed                  | 0 / 16 (0.00%)  | 1 / 20 (5.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                            | 0               | 1               | 0               |
| Paraesthesia                                 |                 |                 |                 |
| subjects affected / exposed                  | 1 / 16 (6.25%)  | 0 / 20 (0.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)                            | 1               | 0               | 1               |
| Posterior reversible encephalopathy syndrome |                 |                 |                 |
| subjects affected / exposed                  | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                            | 0               | 0               | 0               |
| Somnolence                                   |                 |                 |                 |
| subjects affected / exposed                  | 2 / 16 (12.50%) | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                            | 2               | 0               | 0               |
| Blood and lymphatic system disorders         |                 |                 |                 |
| Agranulocytosis                              |                 |                 |                 |
| subjects affected / exposed                  | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                            | 0               | 0               | 0               |
| Anaemia                                      |                 |                 |                 |
| subjects affected / exposed                  | 3 / 16 (18.75%) | 2 / 20 (10.00%) | 2 / 29 (6.90%)  |
| occurrences (all)                            | 4               | 2               | 3               |
| Disseminated intravascular coagulation       |                 |                 |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Febrile neutropenia         |                 |                 |                 |
| subjects affected / exposed | 2 / 16 (12.50%) | 7 / 20 (35.00%) | 7 / 29 (24.14%) |
| occurrences (all)           | 2               | 7               | 8               |
| Leukopenia                  |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Neutropenia                 |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 2 / 29 (6.90%)  |
| occurrences (all)           | 0               | 0               | 2               |
| Pancytopenia                |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Splenomegaly                |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Thrombocytopenia            |                 |                 |                 |
| subjects affected / exposed | 2 / 16 (12.50%) | 1 / 20 (5.00%)  | 2 / 29 (6.90%)  |
| occurrences (all)           | 2               | 3               | 4               |
| Ear and labyrinth disorders |                 |                 |                 |
| Ear haemorrhage             |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Ear pain                    |                 |                 |                 |
| subjects affected / exposed | 1 / 16 (6.25%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0               |
| Tinnitus                    |                 |                 |                 |
| subjects affected / exposed | 1 / 16 (6.25%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0               |
| Vertigo                     |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 1 / 20 (5.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Eye disorders               |                 |                 |                 |
| Conjunctival haemorrhage    |                 |                 |                 |



|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all)           | 0              | 0              | 2              |
| Dry eye                     |                |                |                |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 20 (5.00%) | 2 / 29 (6.90%) |
| occurrences (all)           | 1              | 1              | 2              |
| Eye haemorrhage             |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 1              |
| Eye irritation              |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 1              |
| Eye pain                    |                |                |                |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 1              | 0              | 1              |
| Eyelid oedema               |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all)           | 0              | 0              | 2              |
| Ocular hyperaemia           |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 1              |
| Periorbital oedema          |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 1              |
| Photophobia                 |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Vision blurred              |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 2              |
| Visual impairment           |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Gastrointestinal disorders  |                |                |                |
| Abdominal discomfort        |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 1              |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Abdominal distension        |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Abdominal pain              |                 |                 |                 |
| subjects affected / exposed | 6 / 16 (37.50%) | 2 / 20 (10.00%) | 5 / 29 (17.24%) |
| occurrences (all)           | 8               | 2               | 7               |
| Abdominal pain upper        |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 2 / 20 (10.00%) | 2 / 29 (6.90%)  |
| occurrences (all)           | 0               | 2               | 2               |
| Anal fissure                |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Anal inflammation           |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Anorectal discomfort        |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Anorectal disorder          |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Aphthous ulcer              |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 1 / 20 (5.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Ascites                     |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 1 / 20 (5.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Colitis                     |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 1 / 20 (5.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)           | 0               | 1               | 1               |
| Constipation                |                 |                 |                 |
| subjects affected / exposed | 1 / 16 (6.25%)  | 0 / 20 (0.00%)  | 4 / 29 (13.79%) |
| occurrences (all)           | 1               | 0               | 4               |
| Diarrhoea                   |                 |                 |                 |
| subjects affected / exposed | 4 / 16 (25.00%) | 5 / 20 (25.00%) | 4 / 29 (13.79%) |
| occurrences (all)           | 4               | 6               | 5               |

|                                  |                |                |                |
|----------------------------------|----------------|----------------|----------------|
| Dyspepsia                        |                |                |                |
| subjects affected / exposed      | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                | 0              | 0              | 1              |
| Dysphagia                        |                |                |                |
| subjects affected / exposed      | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Faeces hard                      |                |                |                |
| subjects affected / exposed      | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                | 0              | 0              | 1              |
| Gastrointestinal haemorrhage     |                |                |                |
| subjects affected / exposed      | 1 / 16 (6.25%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                | 1              | 0              | 0              |
| Gastrooesophageal reflux disease |                |                |                |
| subjects affected / exposed      | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Gingival bleeding                |                |                |                |
| subjects affected / exposed      | 0 / 16 (0.00%) | 1 / 20 (5.00%) | 0 / 29 (0.00%) |
| occurrences (all)                | 0              | 1              | 0              |
| Gingival pain                    |                |                |                |
| subjects affected / exposed      | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Glossodynia                      |                |                |                |
| subjects affected / exposed      | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Haematemesis                     |                |                |                |
| subjects affected / exposed      | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Haematochezia                    |                |                |                |
| subjects affected / exposed      | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                | 0              | 0              | 0              |
| Haemorrhoids                     |                |                |                |
| subjects affected / exposed      | 0 / 16 (0.00%) | 1 / 20 (5.00%) | 0 / 29 (0.00%) |
| occurrences (all)                | 0              | 1              | 0              |
| Lip dry                          |                |                |                |
| subjects affected / exposed      | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                | 0              | 0              | 1              |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Lip pruritus                |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Loose tooth                 |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Mouth ulceration            |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Nausea                      |                 |                 |                 |
| subjects affected / exposed | 3 / 16 (18.75%) | 2 / 20 (10.00%) | 7 / 29 (24.14%) |
| occurrences (all)           | 5               | 2               | 9               |
| Odynophagia                 |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Oesophagitis                |                 |                 |                 |
| subjects affected / exposed | 1 / 16 (6.25%)  | 0 / 20 (0.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)           | 1               | 0               | 1               |
| Oral disorder               |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Oral mucosal blistering     |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 2 / 29 (6.90%)  |
| occurrences (all)           | 0               | 0               | 2               |
| Oral mucosal exfoliation    |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Oral pain                   |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Rectal haemorrhage          |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Scalloped tongue            |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| Stomatitis                             |                 |                 |                 |
| subjects affected / exposed            | 1 / 16 (6.25%)  | 3 / 20 (15.00%) | 6 / 29 (20.69%) |
| occurrences (all)                      | 1               | 3               | 6               |
| Subileus                               |                 |                 |                 |
| subjects affected / exposed            | 0 / 16 (0.00%)  | 1 / 20 (5.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                      | 0               | 1               | 0               |
| Tongue haemorrhage                     |                 |                 |                 |
| subjects affected / exposed            | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                      | 0               | 0               | 0               |
| Tooth loss                             |                 |                 |                 |
| subjects affected / exposed            | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)                      | 0               | 0               | 1               |
| Toothache                              |                 |                 |                 |
| subjects affected / exposed            | 0 / 16 (0.00%)  | 1 / 20 (5.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                      | 0               | 1               | 0               |
| Vomiting                               |                 |                 |                 |
| subjects affected / exposed            | 6 / 16 (37.50%) | 6 / 20 (30.00%) | 6 / 29 (20.69%) |
| occurrences (all)                      | 8               | 8               | 13              |
| Hepatobiliary disorders                |                 |                 |                 |
| Hepatomegaly                           |                 |                 |                 |
| subjects affected / exposed            | 1 / 16 (6.25%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                      | 1               | 0               | 0               |
| Hyperbilirubinaemia                    |                 |                 |                 |
| subjects affected / exposed            | 1 / 16 (6.25%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                      | 1               | 0               | 0               |
| Jaundice                               |                 |                 |                 |
| subjects affected / exposed            | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                      | 0               | 0               | 0               |
| Skin and subcutaneous tissue disorders |                 |                 |                 |
| Acne                                   |                 |                 |                 |
| subjects affected / exposed            | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                      | 0               | 0               | 0               |
| Alopecia                               |                 |                 |                 |
| subjects affected / exposed            | 1 / 16 (6.25%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                      | 1               | 0               | 0               |
| Blister                                |                 |                 |                 |

|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%)  | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| <b>Dermatitis</b>           |                |                 |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 20 (5.00%)  | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 1               | 0              |
| <b>Dermatitis atopic</b>    |                |                 |                |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 20 (0.00%)  | 0 / 29 (0.00%) |
| occurrences (all)           | 1              | 0               | 0              |
| <b>Dermatitis bullous</b>   |                |                 |                |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 20 (0.00%)  | 0 / 29 (0.00%) |
| occurrences (all)           | 1              | 0               | 0              |
| <b>Dermatitis contact</b>   |                |                 |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%)  | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| <b>Dermatitis diaper</b>    |                |                 |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%)  | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| <b>Drug eruption</b>        |                |                 |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%)  | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0               | 2              |
| <b>Dry skin</b>             |                |                 |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%)  | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0               | 1              |
| <b>Erythema</b>             |                |                 |                |
| subjects affected / exposed | 1 / 16 (6.25%) | 3 / 20 (15.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 1              | 4               | 1              |
| <b>Erythema multiforme</b>  |                |                 |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 20 (5.00%)  | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 2               | 0              |
| <b>Macule</b>               |                |                 |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 20 (5.00%)  | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 1               | 0              |
| <b>Night sweats</b>         |                |                 |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%)  | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0               | 1              |
| <b>Palmar erythema</b>      |                |                 |                |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Papule                      |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Petechiae                   |                 |                 |                 |
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 20 (0.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)           | 2               | 0               | 1               |
| Pruritus                    |                 |                 |                 |
| subjects affected / exposed | 5 / 16 (31.25%) | 4 / 20 (20.00%) | 7 / 29 (24.14%) |
| occurrences (all)           | 5               | 5               | 7               |
| Pruritus allergic           |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 1 / 20 (5.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Rash                        |                 |                 |                 |
| subjects affected / exposed | 2 / 16 (12.50%) | 4 / 20 (20.00%) | 3 / 29 (10.34%) |
| occurrences (all)           | 2               | 6               | 3               |
| Rash generalised            |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 2 / 20 (10.00%) | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 2               | 0               |
| Rash macular                |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Rash maculo-papular         |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Rash pruritic               |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Skin burning sensation      |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Skin exfoliation            |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Skin hyperpigmentation      |                 |                 |                 |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Skin lesion                 |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Skin mass                   |                |                |                |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Skin ulcer                  |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Swelling face               |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Urticaria                   |                |                |                |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Renal and urinary disorders |                |                |                |
| Acute kidney injury         |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Cystitis haemorrhagic       |                |                |                |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 20 (5.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 1              | 1              | 1              |
| Dysuria                     |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 1              |
| Glycosuria                  |                |                |                |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Haematuria                  |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Micturition urgency         |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 1              |



|   |                      |                     |                      |
|---|----------------------|---------------------|----------------------|
| Nephropathy toxic<br>subjects affected / exposed<br>occurrences (all)   | 0 / 16 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0  |
| Proteinuria<br>subjects affected / exposed<br>occurrences (all)   | 0 / 16 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0  |
| Tubulointerstitial nephritis<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 16 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1 | 0 / 29 (0.00%)<br>0  |
| Urinary retention<br>subjects affected / exposed<br>occurrences (all)   | 0 / 16 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1  |
| Endocrine disorders<br>Cushingoid<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 16 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 0 / 16 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)   | 3 / 16 (18.75%)<br>4 | 1 / 20 (5.00%)<br>1 | 3 / 29 (10.34%)<br>3 |
| Bone pain<br>subjects affected / exposed<br>occurrences (all)   | 1 / 16 (6.25%)<br>1  | 0 / 20 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0  |
| Flank pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 16 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0  |
| Joint range of motion decreased<br>subjects affected / exposed<br>occurrences (all)                               | 1 / 16 (6.25%)<br>1  | 0 / 20 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0  |
| Muscle spasms<br>subjects affected / exposed<br>occurrences (all)   | 0 / 16 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1 | 0 / 29 (0.00%)<br>0  |
| Muscle tightness  |                      |                     |                      |

|                             |                 |                |                 |
|-----------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Musculoskeletal chest pain  |                 |                |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 1 / 29 (3.45%)  |
| occurrences (all)           | 0               | 0              | 1               |
| Musculoskeletal pain        |                 |                |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 1 / 29 (3.45%)  |
| occurrences (all)           | 0               | 0              | 1               |
| Myalgia                     |                 |                |                 |
| subjects affected / exposed | 1 / 16 (6.25%)  | 0 / 20 (0.00%) | 3 / 29 (10.34%) |
| occurrences (all)           | 1               | 0              | 3               |
| Pain in extremity           |                 |                |                 |
| subjects affected / exposed | 3 / 16 (18.75%) | 1 / 20 (5.00%) | 0 / 29 (0.00%)  |
| occurrences (all)           | 5               | 1              | 0               |
| Pain in jaw                 |                 |                |                 |
| subjects affected / exposed | 1 / 16 (6.25%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0               |
| Soft tissue swelling        |                 |                |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Infections and infestations |                 |                |                 |
| Adenovirus infection        |                 |                |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| BK virus infection          |                 |                |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Bacteraemia                 |                 |                |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 2 / 29 (6.90%)  |
| occurrences (all)           | 0               | 0              | 2               |
| Bacterial infection         |                 |                |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Bronchitis                  |                 |                |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 1 / 20 (5.00%) | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 1              | 0               |

|                                 |                |                |                |
|---------------------------------|----------------|----------------|----------------|
| Clostridial infection           |                |                |                |
| subjects affected / exposed     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)               | 0              | 0              | 0              |
| Clostridium difficile colitis   |                |                |                |
| subjects affected / exposed     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)               | 0              | 0              | 0              |
| Clostridium difficile infection |                |                |                |
| subjects affected / exposed     | 1 / 16 (6.25%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)               | 1              | 0              | 0              |
| Conjunctivitis                  |                |                |                |
| subjects affected / exposed     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)               | 0              | 0              | 1              |
| Corona virus infection          |                |                |                |
| subjects affected / exposed     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)               | 0              | 0              | 1              |
| Cystitis                        |                |                |                |
| subjects affected / exposed     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)               | 0              | 0              | 1              |
| Cytomegalovirus infection       |                |                |                |
| subjects affected / exposed     | 1 / 16 (6.25%) | 1 / 20 (5.00%) | 2 / 29 (6.90%) |
| occurrences (all)               | 1              | 1              | 2              |
| Device related infection        |                |                |                |
| subjects affected / exposed     | 0 / 16 (0.00%) | 1 / 20 (5.00%) | 0 / 29 (0.00%) |
| occurrences (all)               | 0              | 1              | 0              |
| Ear infection                   |                |                |                |
| subjects affected / exposed     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)               | 0              | 0              | 0              |
| Endocarditis                    |                |                |                |
| subjects affected / exposed     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)               | 0              | 0              | 1              |
| Enterobacter bacteraemia        |                |                |                |
| subjects affected / exposed     | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)               | 0              | 0              | 0              |
| Epstein-Barr virus infection    |                |                |                |
| subjects affected / exposed     | 0 / 16 (0.00%) | 1 / 20 (5.00%) | 2 / 29 (6.90%) |
| occurrences (all)               | 0              | 1              | 2              |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Escherichia sepsis          |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 1              |
| Gingivitis                  |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Hepatitis E                 |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 1              |
| Human bocavirus infection   |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 1              |
| Infection                   |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 2              |
| Klebsiella bacteraemia      |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 1              |
| Klebsiella infection        |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Localised infection         |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Lung infection              |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 2              |
| Mucosal infection           |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 1              |
| Nasopharyngitis             |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Oral herpes                 |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 1              |

|                                   |                |                |                |
|-----------------------------------|----------------|----------------|----------------|
| Paronychia                        |                |                |                |
| subjects affected / exposed       | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Pneumonia                         |                |                |                |
| subjects affected / exposed       | 1 / 16 (6.25%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                 | 1              | 0              | 1              |
| Pneumonia parainfluenzae viral    |                |                |                |
| subjects affected / exposed       | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Proctitis herpes                  |                |                |                |
| subjects affected / exposed       | 1 / 16 (6.25%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                 | 1              | 0              | 0              |
| Respiratory tract infection       |                |                |                |
| subjects affected / exposed       | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                 | 0              | 0              | 1              |
| Rhinitis                          |                |                |                |
| subjects affected / exposed       | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                 | 0              | 0              | 1              |
| Rhinovirus infection              |                |                |                |
| subjects affected / exposed       | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                 | 0              | 0              | 1              |
| Sepsis                            |                |                |                |
| subjects affected / exposed       | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                 | 0              | 0              | 1              |
| Staphylococcal bacteraemia        |                |                |                |
| subjects affected / exposed       | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                 | 0              | 0              | 1              |
| Staphylococcal infection          |                |                |                |
| subjects affected / exposed       | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all)                 | 0              | 0              | 2              |
| Staphylococcal sepsis             |                |                |                |
| subjects affected / exposed       | 0 / 16 (0.00%) | 0 / 20 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Upper respiratory tract infection |                |                |                |
| subjects affected / exposed       | 0 / 16 (0.00%) | 1 / 20 (5.00%) | 0 / 29 (0.00%) |
| occurrences (all)                 | 0              | 1              | 0              |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| Viraemia                                |                |                 |                 |
| subjects affected / exposed             | 0 / 16 (0.00%) | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                       | 0              | 0               | 0               |
| Viral infection                         |                |                 |                 |
| subjects affected / exposed             | 0 / 16 (0.00%) | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                       | 0              | 0               | 0               |
| Viral upper respiratory tract infection |                |                 |                 |
| subjects affected / exposed             | 0 / 16 (0.00%) | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                       | 0              | 0               | 0               |
| Metabolism and nutrition disorders      |                |                 |                 |
| Decreased appetite                      |                |                 |                 |
| subjects affected / exposed             | 1 / 16 (6.25%) | 3 / 20 (15.00%) | 4 / 29 (13.79%) |
| occurrences (all)                       | 1              | 3               | 4               |
| Fluid intake reduced                    |                |                 |                 |
| subjects affected / exposed             | 0 / 16 (0.00%) | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                       | 0              | 0               | 0               |
| Fluid retention                         |                |                 |                 |
| subjects affected / exposed             | 1 / 16 (6.25%) | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                       | 1              | 0               | 0               |
| Hyperglycaemia                          |                |                 |                 |
| subjects affected / exposed             | 1 / 16 (6.25%) | 1 / 20 (5.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                       | 1              | 1               | 0               |
| Hyperkalaemia                           |                |                 |                 |
| subjects affected / exposed             | 0 / 16 (0.00%) | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                       | 0              | 0               | 0               |
| Hypernatraemia                          |                |                 |                 |
| subjects affected / exposed             | 0 / 16 (0.00%) | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                       | 0              | 0               | 0               |
| Hypertriglyceridaemia                   |                |                 |                 |
| subjects affected / exposed             | 1 / 16 (6.25%) | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)                       | 1              | 0               | 0               |
| Hypoalbuminaemia                        |                |                 |                 |
| subjects affected / exposed             | 0 / 16 (0.00%) | 2 / 20 (10.00%) | 2 / 29 (6.90%)  |
| occurrences (all)                       | 0              | 2               | 2               |
| Hypocalcaemia                           |                |                 |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 16 (0.00%)  | 1 / 20 (5.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)           | 0               | 1               | 1               |
| Hypochloraemia              |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Hypoglycaemia               |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Hypokalaemia                |                 |                 |                 |
| subjects affected / exposed | 3 / 16 (18.75%) | 3 / 20 (15.00%) | 7 / 29 (24.14%) |
| occurrences (all)           | 3               | 3               | 8               |
| Hypomagnesaemia             |                 |                 |                 |
| subjects affected / exposed | 1 / 16 (6.25%)  | 0 / 20 (0.00%)  | 4 / 29 (13.79%) |
| occurrences (all)           | 1               | 0               | 5               |
| Hyponatraemia               |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 1 / 20 (5.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Hypophagia                  |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 1 / 20 (5.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Hypophosphataemia           |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 3 / 20 (15.00%) | 1 / 29 (3.45%)  |
| occurrences (all)           | 0               | 3               | 1               |
| Magnesium deficiency        |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 1 / 20 (5.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Metabolic acidosis          |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Vitamin D deficiency        |                 |                 |                 |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 20 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date        | Amendment   |
|-------------|---|
| 15 May 2015 | Amendment 1: The primary reason for the amendment was to note a change in the suspension vehicle used to prepare the oral formulation of the study medication. In the initial protocol the oral formulation was called oral granules for suspension (OGS) and was to be suspended in water. In amendment 1 the suspension vehicle was changed to Oral-Blend and the name of the oral formulation was changed to powder for oral suspension (PFS). |
| 15 May 2017 | Amendment 2: The primary reason for this amendment was to add a third dose cohort of 6mg/kg. Based on interim analysis of the first 2 dose cohorts, the primary PK targets were not met in both age groups for both formulations (oral and IV). In addition the number of participants enrolled in a dedicated safety cohort was increased.   |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported