



## Clinical trial results:

**A 12-month randomized, multiple dose, open-label, study evaluating safety, tolerability, pharmacokinetics/pharmacodynamics (PK/PD) and efficacy of an anti-CD40 monoclonal antibody, CFZ533, in combination with mycophenolate mofetil (MMF) and corticosteroids (CS), with and without tacrolimus (Tac), in de novo renal transplant recipients**

### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2015-000925-36   |
| Trial protocol           | DE NL ES         |
| Global end of trial date | 29 November 2017 |

### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 12 December 2018 |
| First version publication date | 12 December 2018 |

### Trial information

#### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | CCFZ533X2201 |
|-----------------------|--------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02217410 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Novartis Pharma AG  |
| Sponsor organisation address | CH-4002, Basel, Switzerland,  |
| Public contact               | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com |
| Scientific contact           | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com |

Notes:

### Paediatric regulatory details

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

Notes:

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**Results analysis stage**

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|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 29 November 2017 |
| Is this the analysis of the primary completion data? | No               |

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|                                  |                  |
|----------------------------------|------------------|
| Global end of trial reached?     | Yes              |
| Global end of trial date         | 29 November 2017 |
| Was the trial ended prematurely? | No               |

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Notes:

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**General information about the trial**

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Main objective of the trial:

To assess the safety, tolerability and PK of multiple IV and SC doses of CFZ533 in combination with MMF, CS, and Tac (standard exposure) in de novo renal transplant patients over the treatment and follow-up period.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 05 February 2015 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | Yes              |

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Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

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|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | United States: 19 |
| Country: Number of subjects enrolled | Netherlands: 11   |
| Country: Number of subjects enrolled | Germany: 22       |
| Country: Number of subjects enrolled | Brazil: 7         |
| Worldwide total number of subjects   | 59                |
| EEA total number of subjects         | 33                |

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Notes:

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**Subjects enrolled per age group**

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|   |   |
|---|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days)                      | 0 |
| Infants and toddlers (28 days-23 months)  | 0 |
| Children (2-11 years)                     | 0 |
| Adolescents (12-17 years)                 | 0 |

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|                      |    |
|----------------------|----|
| Adults (18-64 years) | 47 |
| From 65 to 84 years  | 12 |
| 85 years and over    | 0  |

## Subject disposition

### Recruitment

Recruitment details:

In Part 1, patients were enrolled into Arm 1. In Part 2, patients were randomized (2:1) to Arms 2A and 2B.

### Pre-assignment

Screening details:

Study Part 1 focused on measuring the multiple-dose safety, tolerability, PK, and PD of both IV and SC CFZ533 when administered with the SoC treatment regimen. Study Part 2 investigated efficacy, safety, tolerability, PK and PD of CFZ533 in the absence of Tac.

### Period 1

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

### Arms

|                              |                             |
|------------------------------|-----------------------------|
| Are arms mutually exclusive? | Yes                         |
| <b>Arm title</b>             | CFZ533 + TAC + MMF (part 1) |

Arm description:

CFZ533 (3 mg/kg SC) administered with the contemporary standard of care (SoC) consists of concentration-controlled tacrolimus (Tac), combined with mycophenolate mofetil (MMF) and corticosteroids (CS).

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | CFZ533  |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Concentrate for cutaneous solution, Concentrate for solution for injection/infusion |
| Routes of administration               | Intravascular use , Intravenous use   |

Dosage and administration details:

CFZ533 was supplied as 150 mg/mL lyophilized open-label bulk medication requiring reconstitution. 3 mg/kg CFZ533 was administered IV pre-transplant or intra-operatively on Day 1 and subsequently CFZ533 SC was administered for a period of 3 months. MMF (CellCept® or Generics) was taken as 2 tablets of 500 mg or 4 capsules of 250 mg BID (2 g/day) or as per local practice. For patients who remained intubated >24 hours posttransplant and/or whom were otherwise unable to swallow oral medication, IV MMF was substituted until oral conversion was possible. The first dose of MMF was administered within 24 hours after graft reperfusion of the allograft or according to local practice.

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | CFZ533 + MMF (part 2) |
|------------------|-----------------------|

Arm description:

CFZ533 (10mg/kg IV) administered with mycophenolate mofetil (MMF) and corticosteroids (CS) with anti-IL2 induction

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | CFZ533  |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Concentrate for cutaneous solution, Concentrate for solution for injection/infusion |
| Routes of administration               | Intravascular use , Intravenous use   |

Dosage and administration details:

CFZ533 was supplied as 150 mg/mL lyophilized open-label bulk medication requiring reconstitution. CFZ533 150 mg/mL concentrate for solution for infusion/ solution for injection (liquid in vial) was introduced in Part 2. 10 mg/kg CFZ533 was administered IV pre-transplant or intra-operatively on Day 1

and subsequently CFZ533 IV was administered for 12 months. MMF (CellCept® or Generics) was taken as 2 tablets of 500 mg or 4 capsules of 250 mg BID (2 g/day) or as per local practice. For patients who remained intubated >24 hours post-transplant and/or whom were otherwise unable to swallow oral medication, IV MMF was substituted until oral conversion was possible. The first dose of MMF was administered within 24 hours after graft reperfusion of the allograft or according to local practice.

|   |                             |
|---|-----------------------------|
| <b>Arm title</b>  | Tac + MMF (part 2)          |
| Arm description:  |                             |
| Standard of care (SoC) [concentration-controlled tacrolimus (Tac) combined with mycophenolate mofetil (MMF) and corticosteroids (CS) with anti-IL2 induction] |                             |
| Arm type  | Active comparator           |
| Investigational medicinal product name  | Either Prograf® or Generics |
| Investigational medicinal product code  |                             |
| Other name  |                             |
| Pharmaceutical forms  | Capsule                     |
| Routes of administration  | Oral use                    |

**Dosage and administration details:**

Tac was administered as taken by mouth (PO) capsules twice a day (BID) and adjusted to maintain within the target ranges of 4-11 ng/mL. Tac was initiated within 24 hours after reperfusion of the graft. MMF (CellCept® or Generics) was taken as 2 tablets of 500 mg or 4 capsules of 250 mg BID (2 g/day) or as per local practice. For patients who remained intubated >24 hours post-transplant and/or whom were otherwise unable to swallow oral medication, IV MMF was substituted until oral conversion was possible. The first dose of MMF was administered within 24 hours after graft reperfusion of the allograft or according to local practice.

| <b>Number of subjects in period 1</b> | CFZ533 + TAC + MMF (part 1) | CFZ533 + MMF (part 2) | Tac + MMF (part 2) |
|---------------------------------------|-----------------------------|-----------------------|--------------------|
| Started                               | 7                           | 34                    | 18                 |
| Completed                             | 6                           | 30                    | 13                 |
| Not completed                         | 1                           | 4                     | 5                  |
| Physician decision                    | 1                           | 3                     | -                  |
| Graft Loss                            | -                           | -                     | 2                  |
| Consent withdrawn by subject          | -                           | -                     | 2                  |
| Lost to follow-up                     | -                           | -                     | 1                  |
| Lack of efficacy                      | -                           | 1                     | -                  |

## Baseline characteristics

### Reporting groups

|  |                             |
|--|-----------------------------|
| Reporting group title  | CFZ533 + TAC + MMF (part 1) |
| Reporting group description:<br>CFZ533 (3 mg/kg SC) administered with the contemporary standard of care (SoC) consists of concentration-controlled tacrolimus (Tac), combined with mycophenolate mofetil (MMF) and corticosteroids (CS). |                             |
| Reporting group title  | CFZ533 + MMF (part 2)       |
| Reporting group description:<br>CFZ533 (10mg/kg IV) administered with mycophenolate mofetil (MMF) and corticosteroids (CS) with anti-IL2 induction   |                             |
| Reporting group title  | Tac + MMF (part 2)          |
| Reporting group description:<br>Standard of care (SoC) [concentration-controlled tacrolimus (Tac) combined with mycophenolate mofetil (MMF) and corticosteroids (CS) with anti-IL2 induction]  |                             |

| Reporting group values                             | CFZ533 + TAC + MMF (part 1) | CFZ533 + MMF (part 2) | Tac + MMF (part 2) |
|--|-----------------------------|-----------------------|--------------------|
| Number of subjects                                 | 7                           | 34                    | 18                 |
| Age categorical<br>Units: Subjects                 |                             |                       |                    |
| In utero   | 0                           | 0                     | 0                  |
| Preterm newborn infants (gestational age < 37 wks) | 0                           | 0                     | 0                  |
| Newborns (0-27 days)                               | 0                           | 0                     | 0                  |
| Infants and toddlers (28 days-23 months)           | 0                           | 0                     | 0                  |
| Children (2-11 years)                              | 0                           | 0                     | 0                  |
| Adolescents (12-17 years)                          | 0                           | 0                     | 0                  |
| Adults (18-64 years)                               | 6                           | 30                    | 11                 |
| From 65-84 years                                   | 1                           | 4                     | 7                  |
| 85 years and over                                  | 0                           | 0                     | 0                  |
| Age Continuous<br>Units: years                     |                             |                       |                    |
| arithmetic mean                                    | 48.1                        | 49.0                  | 53.4               |
| standard deviation                                 | ± 9.30                      | ± 15.79               | ± 18.01            |
| Sex: Female, Male<br>Units: Subjects               |                             |                       |                    |
| Female   | 3                           | 8                     | 6                  |
| Male   | 4                           | 26                    | 12                 |
| Ethnicity (NIH/OMB)<br>Units: Subjects             |                             |                       |                    |
| Hispanic or Latino                                 | 0                           | 1                     | 0                  |
| Not Hispanic or Latino                             | 2                           | 20                    | 9                  |
| Unknown or Not Reported                            | 5                           | 13                    | 9                  |
| Reporting group values                             | Total                       |                       |                    |
| Number of subjects                                 | 59                          |                       |                    |

|   |    |  |  |
|---|----|--|--|
| Age categorical                                       |    |  |  |
| Units: Subjects                                       |    |  |  |
| In utero  | 0  |  |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0  |  |  |
| Newborns (0-27 days)                                  | 0  |  |  |
| Infants and toddlers (28 days-23<br>months)           | 0  |  |  |
| Children (2-11 years)                                 | 0  |  |  |
| Adolescents (12-17 years)                             | 0  |  |  |
| Adults (18-64 years)                                  | 47 |  |  |
| From 65-84 years                                      | 12 |  |  |
| 85 years and over                                     | 0  |  |  |
| Age Continuous  |    |  |  |
| Units: years  |    |  |  |
| arithmetic mean                                       |    |  |  |
| standard deviation                                    | -  |  |  |
| Sex: Female, Male                                     |    |  |  |
| Units: Subjects                                       |    |  |  |
| Female  | 17 |  |  |
| Male  | 42 |  |  |
| Ethnicity (NIH/OMB)                                   |    |  |  |
| Units: Subjects                                       |    |  |  |
| Hispanic or Latino                                    | 1  |  |  |
| Not Hispanic or Latino                                | 31 |  |  |
| Unknown or Not Reported                               | 27 |  |  |

## End points

### End points reporting groups

|   |                                   |
|---|-----------------------------------|
| Reporting group title   | CFZ533 + TAC + MMF (part 1)       |
| Reporting group description:<br>CFZ533 (3 mg/kg SC) administered with the contemporary standard of care (SoC) consists of concentration-controlled tacrolimus (Tac), combined with mycophenolate mofetil (MMF) and corticosteroids (CS).      |                                   |
| Reporting group title   | CFZ533 + MMF (part 2)             |
| Reporting group description:<br>CFZ533 (10mg/kg IV) administered with mycophenolate mofetil (MMF) and corticosteroids (CS) with anti-IL2 induction  |                                   |
| Reporting group title   | Tac + MMF (part 2)                |
| Reporting group description:<br>Standard of care (SoC) [concentration-controlled tacrolimus (Tac) combined with mycophenolate mofetil (MMF) and corticosteroids (CS) with anti-IL2 induction]   |                                   |
| Subject analysis set title  | sCD40 (part I)                    |
| Subject analysis set type   | Safety analysis                   |
| Subject analysis set description:<br>CFZ533 (3 mg/kg SC) administered with the contemporary standard of care (SoC) consists of concentration-controlled tacrolimus (Tac), combined with mycophenolate mofetil (MMF) and corticosteroids (CS). |                                   |
| Subject analysis set title  | sCD154                            |
| Subject analysis set type   | Safety analysis                   |
| Subject analysis set description:<br>CFZ533 (3 mg/kg SC) administered with the contemporary standard of care (SoC) consists of concentration-controlled tacrolimus (Tac), combined with mycophenolate mofetil (MMF) and corticosteroids (CS). |                                   |
| Subject analysis set title  | Free CD40 on whole blood B ceels  |
| Subject analysis set type   | Sub-group analysis                |
| Subject analysis set description:<br>CFZ533 (10mg/kg IV) administered with mycophenolate mofetil (MMF) and corticosteroids (CS) with anti-IL2 induction   |                                   |
| Subject analysis set title  | Total CD40 on whole blood B cells |
| Subject analysis set type   | Sub-group analysis                |
| Subject analysis set description:<br>CFZ533 (10mg/kg IV) administered with mycophenolate mofetil (MMF) and corticosteroids (CS) with anti-IL2 induction   |                                   |

### Primary: Mean Cmax Pharmacokinetic Parameter- Part I

|   |   |
|---|---|
| End point title   | Mean Cmax Pharmacokinetic Parameter- Part I <sup>[1][2]</sup> |
| End point description:<br>Pharmacokinetics as defined by the systemic concentrations and Cmax of certain immunosuppressant medications used in Part I |   |
| End point type  | Primary   |
| End point timeframe:<br>Day 1   |   |

#### 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: descriptive statistics

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

Justification: descriptive statistics



|                                      |                             |  |  |  |
|--------------------------------------|-----------------------------|--|--|--|
| <b>End point values</b>              | CFZ533 + TAC + MMF (part 1) |  |  |  |
| Subject group type                   | Reporting group             |  |  |  |
| Number of subjects analysed          | 7                           |  |  |  |
| Units: ug/mL                         |                             |  |  |  |
| arithmetic mean (standard deviation) | 66.3 (± 12.3)               |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Mean Tmax Pharmacokinetic Parameter - Part I

|                 |  |
|-----------------|--|
| End point title | Mean Tmax Pharmacokinetic Parameter - Part I <sup>[3]</sup> <sup>[4]</sup> |
|-----------------|--|

End point description:

Quantify pharmacokinetics of CFZ533 in combination with MMF, CS, and tacrolimus in de novo renal transplant patients during the treatment and follow-up periods.

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

End point timeframe:

Day 1

Notes:

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

Justification: descriptive statistics

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

Justification: descriptive statistics

|                               |                             |  |  |  |
|-------------------------------|-----------------------------|--|--|--|
| <b>End point values</b>       | CFZ533 + TAC + MMF (part 1) |  |  |  |
| Subject group type            | Reporting group             |  |  |  |
| Number of subjects analysed   | 7                           |  |  |  |
| Units: day                    |                             |  |  |  |
| median (full range (min-max)) | 0.237 (0 to 1.02)           |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Mean AUClast Pharmacokinetic Parameter - Part I

|                 |   |
|-----------------|---|
| End point title | Mean AUClast Pharmacokinetic Parameter - Part I <sup>[5]</sup> <sup>[6]</sup> |
|-----------------|---|

End point description:

Quantify pharmacokinetics of CFZ533 in combination with MMF, CS, and tacrolimus in de novo renal transplant patients during the treatment and follow-up periods.

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

End point timeframe:

Day 1

Notes:

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

Justification: descriptive statistics

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

Justification: descriptive statistics

| End point values                     | CFZ533 + TAC + MMF (part 1) |  |  |  |
|--------------------------------------|-----------------------------|--|--|--|
| Subject group type                   | Reporting group             |  |  |  |
| Number of subjects analysed          | 7                           |  |  |  |
| Units: day*ug/mL                     |                             |  |  |  |
| arithmetic mean (standard deviation) | 367 (± 52.0)                |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Efficacy as defined by the frequency and severity (Banff classification) of treated biopsy proven acute rejection (tBPAR) adjudicated data - Part II

|                 |   |
|-----------------|---|
| End point title | Efficacy as defined by the frequency and severity (Banff classification) of treated biopsy proven acute rejection (tBPAR) adjudicated data - Part II <sup>[7]</sup> |
|-----------------|---|

End point description:

To assess the activity of the investigational arm as compared to the standard of care control arm in de novo renal transplant patients as measured by the frequency and severity of tBPAR as measured on the Banff classification scale. An adjudication was performed on all on cause renal biopsies by an independent expert committee blinded to therapy.

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

End point timeframe:

3, 6, 9, and 12 months

Notes:

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

Justification: descriptive statistics

| End point values            | CFZ533 + MMF (part 2) | Tac + MMF (part 2) |  |  |
|-----------------------------|-----------------------|--------------------|--|--|
| Subject group type          | Reporting group       | Reporting group    |  |  |
| Number of subjects analysed | 33                    | 18                 |  |  |
| Units: events               |                       |                    |  |  |
| Month 3                     | 6                     | 2                  |  |  |
| Month 6                     | 7                     | 3                  |  |  |
| Month 9                     | 7                     | 3                  |  |  |
| Month 12                    | 7                     | 3                  |  |  |

## Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Frequency and severity of tBPAR-adjudicated data |
| Statistical analysis description:       |  |
| Banff classification                    |  |
| Comparison groups                       | CFZ533 + MMF (part 2) v Tac + MMF (part 2)       |
| Number of subjects included in analysis | 51   |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           |  |
| P-value                                 | = 0.8976   |
| Method                                  | Bayesian posterior probability                   |
| Parameter estimate                      | Mean difference (final values)                   |
| Point estimate                          | 0.095  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -0.067   |
| upper limit                             | 0.263  |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Frequency and severity of tBPAR-adjudicated data |
| Statistical analysis description:       |  |
| Banff classification                    |  |
| Comparison groups                       | CFZ533 + MMF (part 2) v Tac + MMF (part 2)       |
| Number of subjects included in analysis | 51   |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           |  |
| P-value                                 | = 0.8836   |
| Method                                  | Bayesian posterior probability                   |
| Parameter estimate                      | Mean difference (final values)                   |
| Point estimate                          | 0.093  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -0.084   |
| upper limit                             | 0.271  |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Frequency and severity of tBPAR-adjudicated data |
| Statistical analysis description:       |  |
| Banff classification                    |  |
| Comparison groups                       | CFZ533 + MMF (part 2) v Tac + MMF (part 2)       |
| Number of subjects included in analysis | 51   |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           |  |
| P-value                                 | = 0.8822   |
| Method                                  | Bayesian posterior probability                   |
| Parameter estimate                      | Mean difference (final values)                   |
| Point estimate                          | 0.093  |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -0.085  |
| upper limit         | 0.272   |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Frequency and severity of tBPAR-adjudicated data |
| Statistical analysis description:       |  |
| Banff classification                    |  |
| Comparison groups                       | CFZ533 + MMF (part 2) v Tac + MMF (part 2)       |
| Number of subjects included in analysis | 51   |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           |  |
| P-value                                 | = 0.8821   |
| Method                                  | Bayesian posterior probability                   |
| Parameter estimate                      | Mean difference (final values)                   |
| Point estimate                          | 0.093  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -0.087   |
| upper limit                             | 0.273  |

## Secondary: Total soluble CD40 and total soluble CD154 concentrations in plasma - Part 1

|  |  |
|--|--|
| End point title  | Total soluble CD40 and total soluble CD154 concentrations in plasma - Part 1 |
| End point description:   |  |
| To quantify the change from baseline and recovery of peripheral blood total soluble CD40 and total soluble CD154 |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| Baseline to end of study (Day 1, Day 29, Day 337)  |  |

| End point values                     | sCD40 (part I)       | sCD154               |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed          | 7                    | 7                    |  |  |
| Units: ng/ml                         |                      |                      |  |  |
| arithmetic mean (standard deviation) |                      |                      |  |  |
| Baseline                             | 4.03 (± 4.08)        | 0.125 (± 0.007)      |  |  |
| Day 1                                | 8.86 (± 0.0585)      | 0.0585 (± 0.0711)    |  |  |
| Day 2                                | 16.7 (± 4.51)        | 0.139 (± 0.193)      |  |  |

|         |                 |                   |  |  |
|---------|-----------------|-------------------|--|--|
| Day 3   | 24.8 (± 4.47)   | 0.157 (± 0.235)   |  |  |
| Day 4   | 31.3 (± 6.34)   | 0.241 (± 0.418)   |  |  |
| Day 8   | 54.0 (± 11.2)   | 0.399 (± 0.636)   |  |  |
| Day 15  | 84.1 (± 13.8)   | 0.0879 (± 0.139)  |  |  |
| Day 22  | 102 (± 13.9)    | 0.0500 (± 0.132)  |  |  |
| Day 29  | 120 (± 15.7)    | 0.225 (± 0.504)   |  |  |
| Day 36  | 128 (± 19.2)    | 0.116 (± 0.2)     |  |  |
| Day 43  | 145 (± 25.6)    | 0.0193 (± 0.0474) |  |  |
| Day 50  | 156 (± 6.35)    | 0.0478 (± 0.0687) |  |  |
| Day 57  | 161 (± 21.2)    | 0 (± 0)           |  |  |
| Day 64  | 163 (± 24.2)    | 0.0316 (± 0.0492) |  |  |
| Day 71  | 156 (± 19.2)    | 0.0148 (± 0.0363) |  |  |
| Day 85  | 168 (± 21.4)    | 0.0139 (± 0.0340) |  |  |
| Day 99  | 155 (± 23.3)    | 0 (± 0)           |  |  |
| Day 113 | 85.7 (± 47.9)   | 0.0668 (± 0.164)  |  |  |
| Day 127 | 12.2 (± 15.7)   | 0.0488 (± 0.0697) |  |  |
| EoS     | 0.918 (± 0.330) | 0.0184 (± 0.0411) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Free CD40 and total CD40 on B cells - Part II

|   |   |
|---|---|
| End point title   | Free CD40 and total CD40 on B cells - Part II |
| End point description:  |   |
| The magnitude and duration of peripheral blood CD40 occupancy. MESF: molecules of equivalent soluble fluorochrome |   |
| End point type  | Secondary                                     |
| End point timeframe:  |   |
| Baseline to end of study (Day 1/predose)  |   |

| End point values                     | Free CD40 on whole blood B cells | Total CD40 on whole blood B cells |  |  |
|--------------------------------------|----------------------------------|-----------------------------------|--|--|
| Subject group type                   | Subject analysis set             | Subject analysis set              |  |  |
| Number of subjects analysed          | 26                               | 29                                |  |  |
| Units: MESF                          |                                  |                                   |  |  |
| arithmetic mean (standard deviation) |                                  |                                   |  |  |

|                                  |                       |                      |  |  |
|----------------------------------|-----------------------|----------------------|--|--|
| CFZ553 + MMF (Baseline)          | 30836.00 (± 13648.69) | 12778.80 (± 7873.76) |  |  |
| CFZ553 + MMF (D1 - 6h post dose) | 1623.81 (± 1359.85)   | 13806.90 (± 7185.66) |  |  |
| CFZ553 + MMF (D15)               | 799.62 (± 762.38)     | 15160.38 (± 7398.57) |  |  |
| CFZ553 + MMF (D 29)              | 817.63 (± 1540.16)    | 13299.60 (± 6330.89) |  |  |
| CFZ553 + MMF (D 57)              | 597.13 (± 523.55)     | 12234.38 (± 6943.13) |  |  |
| CFZ553 + MMF (D 85)              | 635.47 (± 614.68)     | 9330.86 (± 8484.46)  |  |  |
| CFZ553 + MMF (D 197)             | 3699.0 (± 7298.98)    | 2820.72 (± 2347.11)  |  |  |
| CFZ553 + MMF (253)               | 2667.38 (± 6146.86)   | 1427.14 (± 740.48)   |  |  |
| CFZ553 + MMF (EoS)               | 176.17 (± 266.82)     | 1069.67 (± 809.12)   |  |  |
| Tac + MMF (Baseline)             | 31508.33 (± 12759.49) | 14581.43 (± 9342.79) |  |  |
| Tac + MMF (D1 - 6h post dose)    | 26437.65 (± 11930.50) | 13715.00 (± 8293.33) |  |  |
| Tac + MMF (D15)                  | 24441.67 (± 9125.93)  | 13707.14 (± 6770.14) |  |  |
| Tac + MMF (D29)                  | 27840.00 (± 12106.72) | 12698.75 (± 6002.96) |  |  |
| Tac + MMF (D57)                  | 27994.29 (± 12004.57) | 12583.85 (± 6210.07) |  |  |
| Tac + MMF (D85)                  | 25044.00 (± 10896.65) | 8701.54 (± 4183.00)  |  |  |
| Tac + MMF (D197)                 | 21360.00 (± 3155.67)  | 2067.60 (± 1617.28)  |  |  |
| Tac + MMF (D253)                 | 15752.75 (± 7145.32)  | 1750.50 (± 1005.84)  |  |  |
| Tac + MMF (EoS)                  | 21200.00 (± 4407.95)  | 6276.17 (± 11271.20) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-CFZ533 antibodies - Part I

|                 |  |
|-----------------|--|
| End point title | Anti-CFZ533 antibodies - Part I <sup>[8]</sup> |
|-----------------|--|

End point description:

To evaluate the immunogenicity of CFZ533 via the quantitative analysis of anti-CFZ533 antibodies

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

End point timeframe:

Baseline to end of study

Notes:

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

Justification: descriptive statistics

|                               |                             |  |  |  |
|-------------------------------|-----------------------------|--|--|--|
| <b>End point values</b>       | CFZ533 + TAC + MMF (part 1) |  |  |  |
| Subject group type            | Reporting group             |  |  |  |
| Number of subjects analysed   | 7                           |  |  |  |
| Units: anti-CFZ533 antibodies | 0                           |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-CFZ533 antibodies - Part II

|                 |   |
|-----------------|---|
| End point title | Anti-CFZ533 antibodies - Part II <sup>[9]</sup> |
|-----------------|---|

End point description:

To evaluate the immunogenicity of CFZ533 via the quantitative analysis of anti-CFZ533 antibodies

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

End point timeframe:

Baseline to end of study (screening, baseline, Day 141, Day 225, Day 309, Study Completion)

Notes:

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

Justification: descriptive statistics

|                               |                       |                    |  |  |
|-------------------------------|-----------------------|--------------------|--|--|
| <b>End point values</b>       | CFZ533 + MMF (part 2) | Tac + MMF (part 2) |  |  |
| Subject group type            | Reporting group       | Reporting group    |  |  |
| Number of subjects analysed   | 34                    | 18                 |  |  |
| Units: anti-CFZ533 antibodies |                       |                    |  |  |
| Screening                     | 0                     | 0                  |  |  |
| Baseline                      | 0                     | 0                  |  |  |
| Day 141                       | 0                     | 0                  |  |  |
| Day 225                       | 0                     | 0                  |  |  |
| Day 309                       | 0                     | 0                  |  |  |
| Study Completion              | 0                     | 0                  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: eGFR - Part II

|                 |                                |
|-----------------|--------------------------------|
| End point title | eGFR - Part II <sup>[10]</sup> |
|-----------------|--------------------------------|

End point description:

Renal function as assessed by MDRD (Modification of Diet in Renal Disease) formula. eGFR: Estimated glomerular filtration rate

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

End point timeframe:

Day 1, Day 29, Day 337,

Notes:

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

Justification: descriptive statistics

| End point values                          | CFZ533 + MMF<br>(part 2) | Tac + MMF<br>(part 2) |  |  |
|---|--------------------------|-----------------------|--|--|
| Subject group type                        | Reporting group          | Reporting group       |  |  |
| Number of subjects analysed               | 32                       | 18                    |  |  |
| Units: ml/min                             |                          |                       |  |  |
| arithmetic mean (confidence interval 90%) |                          |                       |  |  |
| Day 1                                     | 9.8 (8.3 to 11.3)        | 9.7 (7.7 to 11.8)     |  |  |
| Day 29                                    | 55.6 (50.4 to 60.7)      | 44.3 (37.2 to 51.4)   |  |  |
| Day 337                                   | 58.2 (52.2 to 64.2)      | 44.2 (36.1 to 52.3)   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: CFZ533 plasma PK concentrations - Part II

|                 |   |
|-----------------|---|
| End point title | CFZ533 plasma PK concentrations - Part II <sup>[11]</sup> |
|-----------------|---|

End point description:

Quantify the systemic concentrations of CFZ533 in combination with MMF, CS, and tacrolimus in de novo renal transplant patients during the treatment and follow-up periods. A full pharmacokinetic analysis can be performed on the concentration-time data to evaluate the impact of renal transplantation on the various medications used in the treatment regimen.

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

End point timeframe:

throughout study period (day 1 to day 336)

Notes:

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

Justification: descriptive statistics

| End point values                     | CFZ533 + MMF<br>(part 2) |  |  |  |
|--------------------------------------|--------------------------|--|--|--|
| Subject group type                   | Reporting group          |  |  |  |
| Number of subjects analysed          | 32                       |  |  |  |
| Units: ug/mL                         |                          |  |  |  |
| arithmetic mean (standard deviation) |                          |  |  |  |
| Day 1                                | 150 (± 42.8)             |  |  |  |
| Day 2                                | 148 (± 77.5)             |  |  |  |
| Day 3                                | 277 (± 91.3)             |  |  |  |
| Day 14                               | 262 (± 59.8)             |  |  |  |
| Day 28                               | 258 (± 52.8)             |  |  |  |
| Day 56                               | 306 (± 61.0)             |  |  |  |
| Day 84                               | 247 (± 58.2)             |  |  |  |



|              |              |  |  |  |
|--------------|--------------|--|--|--|
| Day 112      | 211 (± 51.8) |  |  |  |
| Day 140      | 178 (± 54.9) |  |  |  |
| Day 168      | 157 (± 57.4) |  |  |  |
| Day 196      | 148 (± 53.1) |  |  |  |
| Day 224      | 147 (± 53.8) |  |  |  |
| Day 252      | 151 (± 35.2) |  |  |  |
| Day 280      | 160 (± 87.7) |  |  |  |
| Day 308      | 132 (± 42.5) |  |  |  |
| Day 336      | 156 (± 85.2) |  |  |  |
| End of study | 133 (± 57.8) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Total sCD40 plasma concentrations - Part II

|  |   |
|--|---|
| End point title  | Total sCD40 plasma concentrations - Part II <sup>[12]</sup> |
| End point description:<br>To quantify the change from baseline and recovery of peripheral blood total soluble CD40 |   |
| End point type   | Secondary   |
| End point timeframe:<br>12 months  |   |

Notes:

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

Justification: descriptive statistics

| End point values                     | CFZ533 + MMF<br>(part 2) | Tac + MMF<br>(part 2) |  |  |
|--------------------------------------|--------------------------|-----------------------|--|--|
| Subject group type                   | Reporting group          | Reporting group       |  |  |
| Number of subjects analysed          | 32                       | 17                    |  |  |
| Units: ng/mL                         |                          |                       |  |  |
| arithmetic mean (standard deviation) |                          |                       |  |  |
| Baseline                             | 3.02 (± 2.44)            | 3.67 (± 2.15)         |  |  |
| Day 1                                | 6.95 (± 4.29)            | 1.16 (± 1.15)         |  |  |
| Day 4                                | 24.6 (± 11.0)            | 1.16 (± 1.15)         |  |  |
| Day 15                               | 69.6 (± 21.5)            | 0.869 (± 1.55)        |  |  |
| Day 29                               | 101 (± 18.9)             | 0.362 (± 0.0746)      |  |  |
| Day 57                               | 140 (± 17.4)             | 0.438 (± 0.316)       |  |  |
| Day 85                               | 189 (± 76.4)             | 0.429 (± 0.324)       |  |  |
| Day 113                              | 215 (± 75.5)             | 0.391 (± 0.129)       |  |  |
| Day 141                              | 237 (± 93.1)             | 0.453 (± 0.271)       |  |  |
| Day 169                              | 238 (± 80.3)             | 0.537 (± 0.215)       |  |  |
| Day 197                              | 253 (± 81.3)             | 0.423 (± 0.0908)      |  |  |

|              |              |                  |  |  |
|--------------|--------------|------------------|--|--|
| Day 225      | 258 (± 77.7) | 0.452 (± 0.119)  |  |  |
| Day 253      | 236 (± 36.5) | 0.457 (± 0.0800) |  |  |
| Day 281      | 273 (± 71.3) | 0.455 (± 0.0789) |  |  |
| Day 309      | 286 (± 66.0) | 0.454 (± 0.0957) |  |  |
| Day 337      | 298 (± 57.4) | 0.411 (± 0.0581) |  |  |
| End of Study | 303 (± 59.7) | 0.959 (± 1.88)   |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All AEs reported in this record are from date of First Patient First Treatment until Last Patient Last Visit) up to approximately 3 years.

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 20.1   |

### Reporting groups

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | CFZ533 + TAC + MMF (part 1) |
|-----------------------|-----------------------------|

Reporting group description:

CFZ533 (3 mg/kg SC) administered with the contemporary standard of care (SoC) consists of concentrationcontrolled tacrolimus (Tac), combined with mycophenolate mofetil (MMF) and corticosteroids (CS)

|                       |                       |
|-----------------------|-----------------------|
| Reporting group title | CFZ533 + MMF (part 2) |
|-----------------------|-----------------------|

Reporting group description:

CFZ533 (10mg/kg IV) administered with mycophenolate mofetil (MMF) and corticosteroids (CS) with anti-IL2 induction

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Tac + MMF (part 2) |
|-----------------------|--------------------|

Reporting group description:

Standard of care (SoC) [concentration-controlled tacrolimus (Tac) combined with mycophenolate mofetil (MMF) and corticosteroids (CS) with anti-IL2 induction]

|                       |       |
|-----------------------|-------|
| Reporting group title | Total |
|-----------------------|-------|

Reporting group description:

Total

| Serious adverse events  | CFZ533 + TAC + MMF (part 1) | CFZ533 + MMF (part 2) | Tac + MMF (part 2) |
|---|-----------------------------|-----------------------|--------------------|
| Total subjects affected by serious adverse events                   |                             |                       |                    |
| subjects affected / exposed   | 4 / 7 (57.14%)              | 21 / 34 (61.76%)      | 12 / 18 (66.67%)   |
| number of deaths (all causes)                                       | 0                           | 0                     | 0                  |
| number of deaths resulting from adverse events                      | 0                           | 0                     | 0                  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                             |                       |                    |
| Basosquamous carcinoma  |                             |                       |                    |
| subjects affected / exposed   | 0 / 7 (0.00%)               | 0 / 34 (0.00%)        | 1 / 18 (5.56%)     |
| occurrences causally related to treatment / all                     | 0 / 0                       | 0 / 0                 | 3 / 3              |
| deaths causally related to treatment / all                          | 0 / 0                       | 0 / 0                 | 0 / 0              |
| Squamous cell carcinoma   |                             |                       |                    |
| subjects affected / exposed   | 0 / 7 (0.00%)               | 1 / 34 (2.94%)        | 0 / 18 (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              |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| Vascular disorders                              |                |                 |                |
| Deep vein thrombosis                            |                |                 |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 34 (0.00%)  | 0 / 18 (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          |
| Hypertension                                    |                |                 |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 34 (0.00%)  | 0 / 18 (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          |
| Hypertensive crisis                             |                |                 |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 0 / 18 (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          |
| Lymphocele                                      |                |                 |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Pelvic venous thrombosis                        |                |                 |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Immune system disorders                         |                |                 |                |
| Kidney transplant rejection                     |                |                 |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 5 / 34 (14.71%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 5 / 6           | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Transplant rejection                            |                |                 |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 2 / 34 (5.88%)  | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 2           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                |                 |                |
| Cough   |                |                 |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (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          |
| Pneumothorax                                    |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (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          |
| Pulmonary embolism                              |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 34 (0.00%) | 0 / 18 (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          |
| Psychiatric disorders                           |                |                |                |
| Mental status changes                           |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (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          |
| Investigations                                  |                |                |                |
| Amylase increased                               |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood creatinine increased                      |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| White blood cell count decreased                |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 34 (0.00%) | 0 / 18 (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          |
| Injury, poisoning and procedural complications  |                |                |                |
| Arteriovenous fistula aneurysm                  |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 34 (0.00%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| Complications of transplanted kidney            |                |                |                 |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 1 / 34 (2.94%) | 2 / 18 (11.11%) |
| occurrences causally related to treatment / all | 0 / 1          | 1 / 1          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Delayed graft function                          |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (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           |
| Graft loss                                      |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 34 (0.00%) | 2 / 18 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Incarcerated incisional hernia                  |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 34 (0.00%) | 1 / 18 (5.56%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Incisional hernia                               |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 34 (0.00%) | 1 / 18 (5.56%)  |
| 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 dysfunction                          |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 1 / 18 (5.56%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Transplant failure                              |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Cardiac disorders                               |                |                |                 |
| Atrial fibrillation                             |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 34 (0.00%) | 1 / 18 (5.56%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Tricuspid valve incompetence                    |                |                |                 |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 34 (0.00%) | 1 / 18 (5.56%) |
| 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                        |                |                |                |
| Headache  |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 1 / 34 (2.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |                |                |                |
| Leukopenia                                      |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 34 (0.00%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pancytopenia                                    |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 34 (0.00%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Eye disorders                                   |                |                |                |
| Photophobia                                     |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 34 (0.00%) | 0 / 18 (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          |
| Vision blurred                                  |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 34 (0.00%) | 0 / 18 (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          |
| Gastrointestinal disorders                      |                |                |                |
| Abdominal pain                                  |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 1 / 34 (2.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Diarrhoea                                       |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 7 (14.29%) | 1 / 34 (2.94%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 1          | 1 / 1          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Diarrhoea haemorrhagic                          |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (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 inflammation                   |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Inguinal hernia                                 |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (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          |
| Mouth ulceration                                |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 34 (0.00%) | 0 / 18 (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          |
| Nausea  |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 34 (0.00%) | 0 / 18 (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          |
| Pancreatitis                                    |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 34 (0.00%) | 0 / 18 (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          |
| Retroperitoneal haematoma                       |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 2 / 34 (5.88%) | 0 / 18 (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          |
| Vomiting  |                |                |                |



|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 2 / 7 (28.57%) | 0 / 34 (0.00%) | 1 / 18 (5.56%)  |
| occurrences causally related to treatment / all | 0 / 2          | 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 / 7 (0.00%)  | 1 / 34 (2.94%) | 1 / 18 (5.56%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Renal tubular necrosis                          |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (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           |
| Urinary retention                               |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 34 (0.00%) | 1 / 18 (5.56%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Infections and infestations                     |                |                |                 |
| Bacteraemia                                     |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Cytomegalovirus infection                       |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 3 / 34 (8.82%) | 2 / 18 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0          | 2 / 3          | 1 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Encephalitis                                    |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 34 (0.00%) | 1 / 18 (5.56%)  |
| 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 bacteraemia                        |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Gastroenteritis                                 |                |                |                 |

|   |               |                 |                 |
|---|---------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0           |
| Gastrointestinal infection                      |               |                 |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0           |
| Hepatitis C                                     |               |                 |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 34 (2.94%)  | 0 / 18 (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           |
| Pneumocystis jirovecii pneumonia                |               |                 |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 34 (2.94%)  | 0 / 18 (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           |
| Polyomavirus-associated nephropathy             |               |                 |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 4 / 34 (11.76%) | 1 / 18 (5.56%)  |
| occurrences causally related to treatment / all | 0 / 0         | 2 / 4           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0           |
| Pyelonephritis                                  |               |                 |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 2 / 34 (5.88%)  | 3 / 18 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0         | 1 / 2           | 3 / 4           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0           |
| Renal cyst infection                            |               |                 |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 34 (2.94%)  | 0 / 18 (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           |
| Urosepsis                                       |               |                 |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 34 (0.00%)  | 2 / 18 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0           |
| Metabolism and nutrition disorders              |               |                 |                 |
| Dehydration                                     |               |                 |                 |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (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          |
| Hyperglycaemia                                  |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 34 (0.00%) | 0 / 18 (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          |
| Hyperkalaemia                                   |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 34 (0.00%) | 0 / 18 (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>                                       | Total            |  |  |
|---|------------------|--|--|
| Total subjects affected by serious adverse events                   |                  |  |  |
| subjects affected / exposed   | 37 / 59 (62.71%) |  |  |
| number of deaths (all causes)                                       | 0                |  |  |
| number of deaths resulting from adverse events                      | 0                |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                  |  |  |
| Basosquamous carcinoma  |                  |  |  |
| subjects affected / exposed   | 1 / 59 (1.69%)   |  |  |
| occurrences causally related to treatment / all                     | 3 / 3            |  |  |
| deaths causally related to treatment / all                          | 0 / 0            |  |  |
| Squamous cell carcinoma   |                  |  |  |
| subjects affected / exposed   | 1 / 59 (1.69%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 1            |  |  |
| deaths causally related to treatment / all                          | 0 / 0            |  |  |
| Vascular disorders  |                  |  |  |
| Deep vein thrombosis  |                  |  |  |
| subjects affected / exposed   | 1 / 59 (1.69%)   |  |  |
| occurrences causally related to treatment / all                     | 1 / 1            |  |  |
| deaths causally related to treatment / all                          | 0 / 0            |  |  |
| Hypertension  |                  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 59 (1.69%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hypertensive crisis                             |                 |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Lymphocele                                      |                 |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%)  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pelvic venous thrombosis                        |                 |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%)  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Immune system disorders                         |                 |  |  |
| Kidney transplant rejection                     |                 |  |  |
| subjects affected / exposed                     | 6 / 59 (10.17%) |  |  |
| occurrences causally related to treatment / all | 5 / 7           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Transplant rejection                            |                 |  |  |
| subjects affected / exposed                     | 2 / 59 (3.39%)  |  |  |
| occurrences causally related to treatment / all | 1 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Respiratory, thoracic and mediastinal disorders |                 |  |  |
| Cough   |                 |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pneumothorax                                    |                 |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

|   |                |  |  |
|---|----------------|--|--|
| Pulmonary embolism                              |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Psychiatric disorders                           |                |  |  |
| Mental status changes                           |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Investigations                                  |                |  |  |
| Amylase increased                               |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Blood creatinine increased                      |                |  |  |
| subjects affected / exposed                     | 2 / 59 (3.39%) |  |  |
| occurrences causally related to treatment / all | 1 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| White blood cell count decreased                |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Injury, poisoning and procedural complications  |                |  |  |
| Arteriovenous fistula aneurysm                  |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Complications of transplanted kidney            |                |  |  |
| subjects affected / exposed                     | 4 / 59 (6.78%) |  |  |
| occurrences causally related to treatment / all | 1 / 4          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Delayed graft function                          |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Graft loss                                      |                |  |  |
| subjects affected / exposed                     | 2 / 59 (3.39%) |  |  |
| occurrences causally related to treatment / all | 1 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Incarcerated incisional hernia                  |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Incisional hernia                               |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Transplant dysfunction                          |                |  |  |
| subjects affected / exposed                     | 2 / 59 (3.39%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Transplant failure                              |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cardiac disorders                               |                |  |  |
| Atrial fibrillation                             |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Tricuspid valve incompetence                    |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Nervous system disorders                        |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| Headache  |                |  |  |
| subjects affected / exposed                     | 2 / 59 (3.39%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Blood and lymphatic system disorders            |                |  |  |
| Leukopenia                                      |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pancytopenia                                    |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Eye disorders                                   |                |  |  |
| Photophobia                                     |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Vision blurred                                  |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Gastrointestinal disorders                      |                |  |  |
| Abdominal pain                                  |                |  |  |
| subjects affected / exposed                     | 2 / 59 (3.39%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Diarrhoea                                       |                |  |  |
| subjects affected / exposed                     | 3 / 59 (5.08%) |  |  |
| occurrences causally related to treatment / all | 2 / 3          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Diarrhoea haemorrhagic                          |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Gastrointestinal inflammation                   |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Inguinal hernia                                 |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Mouth ulceration                                |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Nausea  |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pancreatitis                                    |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Retroperitoneal haematoma                       |                |  |  |
| subjects affected / exposed                     | 2 / 59 (3.39%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Vomiting  |                |  |  |
| subjects affected / exposed                     | 3 / 59 (5.08%) |  |  |
| occurrences causally related to treatment / all | 0 / 3          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Renal and urinary disorders                     |                |  |  |
| Acute kidney injury                             |                |  |  |



|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 2 / 59 (3.39%) |  |  |
| occurrences causally related to treatment / all | 0 / 3          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Renal tubular necrosis                          |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Urinary retention                               |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Infections and infestations                     |                |  |  |
| Bacteraemia                                     |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cytomegalovirus infection                       |                |  |  |
| subjects affected / exposed                     | 5 / 59 (8.47%) |  |  |
| occurrences causally related to treatment / all | 3 / 5          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Encephalitis                                    |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Enterobacter bacteraemia                        |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Gastroenteritis                                 |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Gastrointestinal infection                      |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Hepatitis C                                     |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pneumocystis jirovecii pneumonia                |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Polyomavirus-associated nephropathy             |                |  |  |
| subjects affected / exposed                     | 5 / 59 (8.47%) |  |  |
| occurrences causally related to treatment / all | 2 / 5          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pyelonephritis                                  |                |  |  |
| subjects affected / exposed                     | 5 / 59 (8.47%) |  |  |
| occurrences causally related to treatment / all | 4 / 6          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Renal cyst infection                            |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Urosepsis                                       |                |  |  |
| subjects affected / exposed                     | 2 / 59 (3.39%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Metabolism and nutrition disorders              |                |  |  |
| Dehydration                                     |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Hyperglycaemia                                  |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Hyperkalaemia                                   |                |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

Frequency threshold for reporting non-serious adverse events: 2 %

| <b>Non-serious adverse events</b>                                   | CFZ533 + TAC + MMF (part 1) | CFZ533 + MMF (part 2) | Tac + MMF (part 2) |
|---|-----------------------------|-----------------------|--------------------|
| Total subjects affected by non-serious adverse events               |                             |                       |                    |
| subjects affected / exposed   | 7 / 7 (100.00%)             | 33 / 34 (97.06%)      | 18 / 18 (100.00%)  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                             |                       |                    |
| Basal cell carcinoma  |                             |                       |                    |
| subjects affected / exposed   | 0 / 7 (0.00%)               | 1 / 34 (2.94%)        | 0 / 18 (0.00%)     |
| occurrences (all)   | 0                           | 1                     | 0                  |
| Vascular disorders  |                             |                       |                    |
| Deep vein thrombosis  |                             |                       |                    |
| subjects affected / exposed   | 0 / 7 (0.00%)               | 0 / 34 (0.00%)        | 1 / 18 (5.56%)     |
| occurrences (all)   | 0                           | 0                     | 1                  |
| Haematoma   |                             |                       |                    |
| subjects affected / exposed   | 0 / 7 (0.00%)               | 2 / 34 (5.88%)        | 0 / 18 (0.00%)     |
| occurrences (all)   | 0                           | 2                     | 0                  |
| Hot flush   |                             |                       |                    |
| subjects affected / exposed   | 0 / 7 (0.00%)               | 2 / 34 (5.88%)        | 0 / 18 (0.00%)     |
| occurrences (all)   | 0                           | 2                     | 0                  |
| Hypertension  |                             |                       |                    |
| subjects affected / exposed   | 1 / 7 (14.29%)              | 13 / 34 (38.24%)      | 6 / 18 (33.33%)    |
| occurrences (all)   | 1                           | 13                    | 7                  |
| Hypotension   |                             |                       |                    |
| subjects affected / exposed   | 0 / 7 (0.00%)               | 2 / 34 (5.88%)        | 3 / 18 (16.67%)    |
| occurrences (all)   | 0                           | 2                     | 3                  |
| Lymphocele  |                             |                       |                    |

|  |                |                 |                 |
|--|----------------|-----------------|-----------------|
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 1 / 18 (5.56%)  |
| occurrences (all)                                    | 0              | 1               | 1               |
| Orthostatic hypotension                              |                |                 |                 |
| subjects affected / exposed                          | 1 / 7 (14.29%) | 0 / 34 (0.00%)  | 0 / 18 (0.00%)  |
| occurrences (all)                                    | 1              | 0               | 0               |
| Poor venous access                                   |                |                 |                 |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 2 / 34 (5.88%)  | 0 / 18 (0.00%)  |
| occurrences (all)                                    | 0              | 2               | 0               |
| General disorders and administration site conditions |                |                 |                 |
| Asthenia   |                |                 |                 |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                                    | 0              | 0               | 1               |
| Catheter site pain                                   |                |                 |                 |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 2 / 18 (11.11%) |
| occurrences (all)                                    | 0              | 0               | 2               |
| Chills   |                |                 |                 |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 3 / 34 (8.82%)  | 0 / 18 (0.00%)  |
| occurrences (all)                                    | 0              | 3               | 0               |
| Cyst   |                |                 |                 |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences (all)                                    | 0              | 1               | 0               |
| Fatigue  |                |                 |                 |
| subjects affected / exposed                          | 1 / 7 (14.29%) | 5 / 34 (14.71%) | 5 / 18 (27.78%) |
| occurrences (all)                                    | 1              | 5               | 5               |
| Generalised oedema                                   |                |                 |                 |
| subjects affected / exposed                          | 1 / 7 (14.29%) | 0 / 34 (0.00%)  | 0 / 18 (0.00%)  |
| occurrences (all)                                    | 1              | 0               | 0               |
| Impaired healing                                     |                |                 |                 |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 2 / 34 (5.88%)  | 1 / 18 (5.56%)  |
| occurrences (all)                                    | 0              | 2               | 1               |
| Influenza like illness                               |                |                 |                 |
| subjects affected / exposed                          | 1 / 7 (14.29%) | 0 / 34 (0.00%)  | 0 / 18 (0.00%)  |
| occurrences (all)                                    | 1              | 0               | 0               |
| Infusion site swelling                               |                |                 |                 |

|  |                |                 |                 |
|--|----------------|-----------------|-----------------|
| subjects affected / exposed              | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences (all)                        | 0              | 1               | 0               |
| Malaise                                  |                |                 |                 |
| subjects affected / exposed              | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                        | 0              | 0               | 1               |
| Oedema peripheral                        |                |                 |                 |
| subjects affected / exposed              | 2 / 7 (28.57%) | 7 / 34 (20.59%) | 6 / 18 (33.33%) |
| occurrences (all)                        | 3              | 11              | 8               |
| Pain                                     |                |                 |                 |
| subjects affected / exposed              | 1 / 7 (14.29%) | 0 / 34 (0.00%)  | 0 / 18 (0.00%)  |
| occurrences (all)                        | 1              | 0               | 0               |
| Peripheral swelling                      |                |                 |                 |
| subjects affected / exposed              | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                        | 0              | 0               | 1               |
| Pyrexia                                  |                |                 |                 |
| subjects affected / exposed              | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 1 / 18 (5.56%)  |
| occurrences (all)                        | 0              | 1               | 2               |
| Secretion discharge                      |                |                 |                 |
| subjects affected / exposed              | 3 / 7 (42.86%) | 0 / 34 (0.00%)  | 0 / 18 (0.00%)  |
| occurrences (all)                        | 3              | 0               | 0               |
| Swelling                                 |                |                 |                 |
| subjects affected / exposed              | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences (all)                        | 0              | 1               | 0               |
| Immune system disorders                  |                |                 |                 |
| Drug hypersensitivity                    |                |                 |                 |
| subjects affected / exposed              | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                        | 0              | 0               | 1               |
| Kidney transplant rejection              |                |                 |                 |
| subjects affected / exposed              | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                        | 0              | 0               | 1               |
| Reproductive system and breast disorders |                |                 |                 |
| Benign prostatic hyperplasia             |                |                 |                 |
| subjects affected / exposed              | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                        | 0              | 0               | 1               |
| Dysmenorrhoea                            |                |                 |                 |

|   |                |                  |                 |
|---|----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 34 (0.00%)   | 2 / 18 (11.11%) |
| occurrences (all)                               | 0              | 0                | 2               |
| Erectile dysfunction                            |                |                  |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)                               | 0              | 1                | 0               |
| Menorrhagia                                     |                |                  |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)                               | 0              | 1                | 0               |
| Penile oedema                                   |                |                  |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)                               | 0              | 1                | 0               |
| Penile pain                                     |                |                  |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 34 (0.00%)   | 1 / 18 (5.56%)  |
| occurrences (all)                               | 0              | 0                | 1               |
| Prostatomegaly                                  |                |                  |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)                               | 0              | 1                | 0               |
| Scrotal swelling                                |                |                  |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)                               | 0              | 1                | 0               |
| Vulvovaginal pain                               |                |                  |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)                               | 0              | 1                | 0               |
| Respiratory, thoracic and mediastinal disorders |                |                  |                 |
| Cough   |                |                  |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 10 / 34 (29.41%) | 2 / 18 (11.11%) |
| occurrences (all)                               | 0              | 13               | 2               |
| Dyspnoea  |                |                  |                 |
| subjects affected / exposed                     | 3 / 7 (42.86%) | 2 / 34 (5.88%)   | 3 / 18 (16.67%) |
| occurrences (all)                               | 3              | 3                | 3               |
| Dyspnoea exertional                             |                |                  |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)                               | 0              | 1                | 0               |
| Lung infiltration                               |                |                  |                 |

|                             |                |                  |                 |
|-----------------------------|----------------|------------------|-----------------|
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 1                | 0               |
| Nasal congestion            |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 1                | 0               |
| Oropharyngeal pain          |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 3 / 34 (8.82%)   | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 3                | 0               |
| Pleural effusion            |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 1                | 0               |
| Productive cough            |                |                  |                 |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)           | 1              | 1                | 0               |
| Respiratory distress        |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 1                | 0               |
| Rhinorrhoea                 |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 1                | 0               |
| Sleep apnoea syndrome       |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)   | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 0                | 1               |
| Wheezing                    |                |                  |                 |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 34 (0.00%)   | 0 / 18 (0.00%)  |
| occurrences (all)           | 1              | 0                | 0               |
| Psychiatric disorders       |                |                  |                 |
| Anxiety                     |                |                  |                 |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)           | 1              | 1                | 0               |
| Delirium                    |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 1                | 0               |
| Insomnia                    |                |                  |                 |
| subjects affected / exposed | 1 / 7 (14.29%) | 11 / 34 (32.35%) | 5 / 18 (27.78%) |
| occurrences (all)           | 1              | 12               | 5               |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| Mood swings<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 7 (0.00%)<br>0  | 1 / 34 (2.94%)<br>1 | 0 / 18 (0.00%)<br>0 |
| Phonophobia<br>subjects affected / exposed<br>occurrences (all)                            | 1 / 7 (14.29%)<br>1 | 0 / 34 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 |
| Restlessness<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 7 (0.00%)<br>0  | 0 / 34 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 |
| Investigations   |                     |                     |                     |
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)     | 0 / 7 (0.00%)<br>0  | 1 / 34 (2.94%)<br>1 | 0 / 18 (0.00%)<br>0 |
| Amylase increased<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 7 (0.00%)<br>0  | 3 / 34 (8.82%)<br>3 | 1 / 18 (5.56%)<br>1 |
| Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0  | 1 / 34 (2.94%)<br>1 | 0 / 18 (0.00%)<br>0 |
| Blood creatine phosphokinase increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0  | 1 / 34 (2.94%)<br>1 | 1 / 18 (5.56%)<br>1 |
| Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)             | 0 / 7 (0.00%)<br>0  | 3 / 34 (8.82%)<br>3 | 1 / 18 (5.56%)<br>1 |
| Blood glucose increased<br>subjects affected / exposed<br>occurrences (all)                | 0 / 7 (0.00%)<br>0  | 1 / 34 (2.94%)<br>1 | 0 / 18 (0.00%)<br>0 |
| Blood lactate dehydrogenase increased<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0  | 0 / 34 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 |
| Blood phosphorus decreased<br>subjects affected / exposed<br>occurrences (all)             | 1 / 7 (14.29%)<br>1 | 0 / 34 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 |
| Blood phosphorus increased   |                     |                     |                     |



|                                       |                |                |                |
|---------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed           | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (0.00%) |
| occurrences (all)                     | 0              | 1              | 0              |
| C-reactive protein increased          |                |                |                |
| subjects affected / exposed           | 0 / 7 (0.00%)  | 0 / 34 (0.00%) | 1 / 18 (5.56%) |
| occurrences (all)                     | 0              | 0              | 1              |
| Cardiac murmur                        |                |                |                |
| subjects affected / exposed           | 1 / 7 (14.29%) | 0 / 34 (0.00%) | 0 / 18 (0.00%) |
| occurrences (all)                     | 1              | 0              | 0              |
| Cytomegalovirus test positive         |                |                |                |
| subjects affected / exposed           | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (0.00%) |
| occurrences (all)                     | 0              | 1              | 0              |
| Drug level decreased                  |                |                |                |
| subjects affected / exposed           | 0 / 7 (0.00%)  | 0 / 34 (0.00%) | 1 / 18 (5.56%) |
| occurrences (all)                     | 0              | 0              | 1              |
| Electrocardiogram ST segment abnormal |                |                |                |
| subjects affected / exposed           | 1 / 7 (14.29%) | 0 / 34 (0.00%) | 0 / 18 (0.00%) |
| occurrences (all)                     | 1              | 0              | 0              |
| Electrocardiogram T wave abnormal     |                |                |                |
| subjects affected / exposed           | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (0.00%) |
| occurrences (all)                     | 0              | 1              | 0              |
| Gamma-glutamyltransferase increased   |                |                |                |
| subjects affected / exposed           | 0 / 7 (0.00%)  | 2 / 34 (5.88%) | 1 / 18 (5.56%) |
| occurrences (all)                     | 0              | 2              | 1              |
| Haemoglobin decreased                 |                |                |                |
| subjects affected / exposed           | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (0.00%) |
| occurrences (all)                     | 0              | 1              | 0              |
| Heart rate irregular                  |                |                |                |
| subjects affected / exposed           | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (0.00%) |
| occurrences (all)                     | 0              | 1              | 0              |
| Lipase increased                      |                |                |                |
| subjects affected / exposed           | 0 / 7 (0.00%)  | 2 / 34 (5.88%) | 0 / 18 (0.00%) |
| occurrences (all)                     | 0              | 2              | 0              |
| Polyomavirus test positive            |                |                |                |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (0.00%) |
| occurrences (all)                              | 0              | 1              | 0              |
| Vitamin D decreased                            |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 34 (0.00%) | 1 / 18 (5.56%) |
| occurrences (all)                              | 0              | 0              | 1              |
| Weight decreased                               |                |                |                |
| subjects affected / exposed                    | 1 / 7 (14.29%) | 1 / 34 (2.94%) | 0 / 18 (0.00%) |
| occurrences (all)                              | 1              | 1              | 0              |
| Weight increased                               |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 2 / 34 (5.88%) | 1 / 18 (5.56%) |
| occurrences (all)                              | 0              | 2              | 1              |
| White blood cell count decreased               |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (0.00%) |
| occurrences (all)                              | 0              | 1              | 0              |
| White blood cell count increased               |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 3 / 34 (8.82%) | 0 / 18 (0.00%) |
| occurrences (all)                              | 0              | 3              | 0              |
| Injury, poisoning and procedural complications |                |                |                |
| Animal bite                                    |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (0.00%) |
| occurrences (all)                              | 0              | 1              | 0              |
| Arterial injury                                |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (0.00%) |
| occurrences (all)                              | 0              | 1              | 0              |
| Arteriovenous fistula site complication        |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 34 (0.00%) | 1 / 18 (5.56%) |
| occurrences (all)                              | 0              | 0              | 1              |
| Arthropod bite                                 |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (0.00%) |
| occurrences (all)                              | 0              | 1              | 0              |
| Complications of transplant surgery            |                |                |                |
| subjects affected / exposed                    | 1 / 7 (14.29%) | 0 / 34 (0.00%) | 0 / 18 (0.00%) |
| occurrences (all)                              | 1              | 0              | 0              |
| Complications of transplanted kidney           |                |                |                |

|                              |                |                 |                 |
|------------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed  | 0 / 7 (0.00%)  | 3 / 34 (8.82%)  | 2 / 18 (11.11%) |
| occurrences (all)            | 0              | 6               | 2               |
| Delayed graft function       |                |                 |                 |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 3 / 34 (8.82%)  | 3 / 18 (16.67%) |
| occurrences (all)            | 0              | 3               | 3               |
| Fall                         |                |                 |                 |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences (all)            | 0              | 1               | 0               |
| Graft complication           |                |                 |                 |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 1 / 18 (5.56%)  |
| occurrences (all)            | 0              | 1               | 1               |
| Incision site complication   |                |                 |                 |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 1 / 18 (5.56%)  |
| occurrences (all)            | 0              | 1               | 1               |
| Incision site erythema       |                |                 |                 |
| subjects affected / exposed  | 1 / 7 (14.29%) | 0 / 34 (0.00%)  | 0 / 18 (0.00%)  |
| occurrences (all)            | 1              | 0               | 0               |
| Incision site haemorrhage    |                |                 |                 |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)            | 0              | 0               | 1               |
| Incision site pain           |                |                 |                 |
| subjects affected / exposed  | 3 / 7 (42.86%) | 6 / 34 (17.65%) | 2 / 18 (11.11%) |
| occurrences (all)            | 3              | 6               | 2               |
| Incisional hernia            |                |                 |                 |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)            | 0              | 0               | 1               |
| Joint injury                 |                |                 |                 |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences (all)            | 0              | 1               | 0               |
| Ligament sprain              |                |                 |                 |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences (all)            | 0              | 1               | 0               |
| Lip injury                   |                |                 |                 |
| subjects affected / exposed  | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences (all)            | 0              | 2               | 0               |
| Post procedural complication |                |                 |                 |

|  |                |                  |                 |
|--|----------------|------------------|-----------------|
| subjects affected / exposed                | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)                          | 0              | 1                | 0               |
| Post procedural haemorrhage                |                |                  |                 |
| subjects affected / exposed                | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)                          | 0              | 1                | 0               |
| Post procedural swelling                   |                |                  |                 |
| subjects affected / exposed                | 0 / 7 (0.00%)  | 0 / 34 (0.00%)   | 1 / 18 (5.56%)  |
| occurrences (all)                          | 0              | 0                | 1               |
| Postoperative wound complication           |                |                  |                 |
| subjects affected / exposed                | 0 / 7 (0.00%)  | 5 / 34 (14.71%)  | 1 / 18 (5.56%)  |
| occurrences (all)                          | 0              | 6                | 1               |
| Procedural pain                            |                |                  |                 |
| subjects affected / exposed                | 0 / 7 (0.00%)  | 3 / 34 (8.82%)   | 6 / 18 (33.33%) |
| occurrences (all)                          | 0              | 3                | 8               |
| Radius fracture                            |                |                  |                 |
| subjects affected / exposed                | 1 / 7 (14.29%) | 0 / 34 (0.00%)   | 0 / 18 (0.00%)  |
| occurrences (all)                          | 1              | 0                | 0               |
| Seroma                                     |                |                  |                 |
| subjects affected / exposed                | 0 / 7 (0.00%)  | 0 / 34 (0.00%)   | 1 / 18 (5.56%)  |
| occurrences (all)                          | 0              | 0                | 1               |
| Transplant dysfunction                     |                |                  |                 |
| subjects affected / exposed                | 0 / 7 (0.00%)  | 2 / 34 (5.88%)   | 3 / 18 (16.67%) |
| occurrences (all)                          | 0              | 2                | 3               |
| Wound complication                         |                |                  |                 |
| subjects affected / exposed                | 0 / 7 (0.00%)  | 11 / 34 (32.35%) | 8 / 18 (44.44%) |
| occurrences (all)                          | 0              | 11               | 8               |
| Wound dehiscence                           |                |                  |                 |
| subjects affected / exposed                | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)                          | 0              | 1                | 0               |
| Wound haematoma                            |                |                  |                 |
| subjects affected / exposed                | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 1 / 18 (5.56%)  |
| occurrences (all)                          | 0              | 1                | 1               |
| Congenital, familial and genetic disorders |                |                  |                 |
| Hydrocele                                  |                |                  |                 |

|  |                    |                     |                     |
|--|--------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 |
| Cardiac disorders                                |                    |                     |                     |
| Angina pectoris                                  |                    |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)      | 1 / 34 (2.94%)      | 1 / 18 (5.56%)      |
| occurrences (all)                                | 0                  | 1                   | 1                   |
| Arrhythmia                                       |                    |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)      | 2 / 34 (5.88%)      | 1 / 18 (5.56%)      |
| occurrences (all)                                | 0                  | 2                   | 1                   |
| Atrial fibrillation                              |                    |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)      | 2 / 34 (5.88%)      | 1 / 18 (5.56%)      |
| occurrences (all)                                | 0                  | 2                   | 2                   |
| Bradycardia                                      |                    |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)      | 1 / 34 (2.94%)      | 0 / 18 (0.00%)      |
| occurrences (all)                                | 0                  | 1                   | 0                   |
| Extrasystoles                                    |                    |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)      | 1 / 34 (2.94%)      | 0 / 18 (0.00%)      |
| occurrences (all)                                | 0                  | 1                   | 0                   |
| Myocardial infarction                            |                    |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)      | 1 / 34 (2.94%)      | 0 / 18 (0.00%)      |
| occurrences (all)                                | 0                  | 1                   | 0                   |
| Palpitations                                     |                    |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)      | 1 / 34 (2.94%)      | 0 / 18 (0.00%)      |
| occurrences (all)                                | 0                  | 1                   | 0                   |
| Sinus tachycardia                                |                    |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)      | 1 / 34 (2.94%)      | 0 / 18 (0.00%)      |
| occurrences (all)                                | 0                  | 2                   | 0                   |
| Tachycardia                                      |                    |                     |                     |
| subjects affected / exposed                      | 2 / 7 (28.57%)     | 4 / 34 (11.76%)     | 1 / 18 (5.56%)      |
| occurrences (all)                                | 2                  | 4                   | 1                   |
| Tricuspid valve incompetence                     |                    |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)      | 0 / 34 (0.00%)      | 1 / 18 (5.56%)      |
| occurrences (all)                                | 0                  | 0                   | 1                   |
| Nervous system disorders                         |                    |                     |                     |
| Ataxia   |                    |                     |                     |

|                                      |                |                 |                 |
|--------------------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed          | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences (all)                    | 0              | 1               | 0               |
| Burning sensation                    |                |                 |                 |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences (all)                    | 0              | 1               | 0               |
| Dizziness                            |                |                 |                 |
| subjects affected / exposed          | 1 / 7 (14.29%) | 2 / 34 (5.88%)  | 3 / 18 (16.67%) |
| occurrences (all)                    | 1              | 2               | 3               |
| Dizziness postural                   |                |                 |                 |
| subjects affected / exposed          | 1 / 7 (14.29%) | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                    | 1              | 0               | 1               |
| Headache                             |                |                 |                 |
| subjects affected / exposed          | 1 / 7 (14.29%) | 6 / 34 (17.65%) | 4 / 18 (22.22%) |
| occurrences (all)                    | 1              | 7               | 4               |
| Hypoaesthesia                        |                |                 |                 |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                    | 0              | 0               | 1               |
| Migraine                             |                |                 |                 |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences (all)                    | 0              | 1               | 0               |
| Paraesthesia                         |                |                 |                 |
| subjects affected / exposed          | 1 / 7 (14.29%) | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                    | 1              | 0               | 1               |
| Peroneal nerve palsy                 |                |                 |                 |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                    | 0              | 0               | 1               |
| Polyneuropathy                       |                |                 |                 |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences (all)                    | 0              | 1               | 0               |
| Tremor                               |                |                 |                 |
| subjects affected / exposed          | 2 / 7 (28.57%) | 3 / 34 (8.82%)  | 6 / 18 (33.33%) |
| occurrences (all)                    | 2              | 3               | 8               |
| Blood and lymphatic system disorders |                |                 |                 |
| Anaemia                              |                |                 |                 |
| subjects affected / exposed          | 1 / 7 (14.29%) | 3 / 34 (8.82%)  | 4 / 18 (22.22%) |
| occurrences (all)                    | 1              | 3               | 4               |

|                             |                |                  |                 |
|-----------------------------|----------------|------------------|-----------------|
| Iron deficiency anaemia     |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 1                | 1               |
| Leukocytosis                |                |                  |                 |
| subjects affected / exposed | 1 / 7 (14.29%) | 3 / 34 (8.82%)   | 2 / 18 (11.11%) |
| occurrences (all)           | 1              | 4                | 2               |
| Leukopenia                  |                |                  |                 |
| subjects affected / exposed | 1 / 7 (14.29%) | 13 / 34 (38.24%) | 3 / 18 (16.67%) |
| occurrences (all)           | 1              | 18               | 3               |
| Lymphopenia                 |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 2 / 34 (5.88%)   | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 2                | 0               |
| Microcytic anaemia          |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 1                | 0               |
| Nephrogenic anaemia         |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 1                | 0               |
| Neutropenia                 |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 2 / 18 (11.11%) |
| occurrences (all)           | 0              | 1                | 2               |
| Normocytic anaemia          |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)   | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 0                | 1               |
| Pancytopenia                |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)   | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 0                | 1               |
| Polycythaemia               |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)   | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 0                | 1               |
| Thrombocytopenia            |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)   | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 0                | 1               |
| Thrombocytosis              |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 1                | 0               |

|   |   |   |   |
|---|---|---|---|
| Ear and labyrinth disorders<br>Ear discomfort<br>subjects affected / exposed<br>occurrences (all)<br><br>Vertigo<br>subjects affected / exposed<br>occurrences (all)  | <br><br>0 / 7 (0.00%)<br>0<br><br><br><br>0 / 7 (0.00%)<br>0  | <br><br>1 / 34 (2.94%)<br>1<br><br><br><br>1 / 34 (2.94%)<br>1  | <br><br>0 / 18 (0.00%)<br>0<br><br><br><br>0 / 18 (0.00%)<br>0  |
| Eye disorders<br>Chalazion<br>subjects affected / exposed<br>occurrences (all)<br><br>Dry eye<br>subjects affected / exposed<br>occurrences (all)<br><br>Eye movement disorder<br>subjects affected / exposed<br>occurrences (all)<br><br>Ocular hyperaemia<br>subjects affected / exposed<br>occurrences (all)<br><br>Retinal vein occlusion<br>subjects affected / exposed<br>occurrences (all) | <br><br>0 / 7 (0.00%)<br>0<br><br><br><br>0 / 7 (0.00%)<br>0<br><br><br><br>2 / 7 (28.57%)<br>2<br><br><br><br>0 / 7 (0.00%)<br>0<br><br><br><br>0 / 7 (0.00%)<br>0 | <br><br>1 / 34 (2.94%)<br>1<br><br><br><br>1 / 34 (2.94%)<br>1<br><br><br><br>0 / 34 (0.00%)<br>0<br><br><br><br>1 / 34 (2.94%)<br>1<br><br><br><br>1 / 34 (2.94%)<br>1 | <br><br>0 / 18 (0.00%)<br>0<br><br><br><br>0 / 18 (0.00%)<br>0<br><br><br><br>0 / 18 (0.00%)<br>0<br><br><br><br>0 / 18 (0.00%)<br>0<br><br><br><br>0 / 18 (0.00%)<br>0 |
| Gastrointestinal disorders<br>Abdominal discomfort<br>subjects affected / exposed<br>occurrences (all)<br><br>Abdominal distension<br>subjects affected / exposed<br>occurrences (all)<br><br>Abdominal pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Abdominal pain lower<br>subjects affected / exposed<br>occurrences (all)<br><br>Abdominal pain upper                      | <br><br>0 / 7 (0.00%)<br>0<br><br><br><br>1 / 7 (14.29%)<br>1<br><br><br><br>1 / 7 (14.29%)<br>1<br><br><br><br>0 / 7 (0.00%)<br>0<br><br><br><br><br>              | <br><br>1 / 34 (2.94%)<br>1<br><br><br><br>0 / 34 (0.00%)<br>0<br><br><br><br>3 / 34 (8.82%)<br>3<br><br><br><br>1 / 34 (2.94%)<br>1<br><br><br><br><br>                | <br><br>1 / 18 (5.56%)<br>1<br><br><br><br>0 / 18 (0.00%)<br>0<br><br><br><br>3 / 18 (16.67%)<br>3<br><br><br><br>1 / 18 (5.56%)<br>1<br><br><br><br><br>               |



|                             |                |                  |                  |
|-----------------------------|----------------|------------------|------------------|
| subjects affected / exposed | 0 / 7 (0.00%)  | 5 / 34 (14.71%)  | 0 / 18 (0.00%)   |
| occurrences (all)           | 0              | 6                | 0                |
| Anal fissure                |                |                  |                  |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)   | 1 / 18 (5.56%)   |
| occurrences (all)           | 0              | 0                | 1                |
| Aphthous ulcer              |                |                  |                  |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 34 (2.94%)   | 0 / 18 (0.00%)   |
| occurrences (all)           | 1              | 1                | 0                |
| Colitis                     |                |                  |                  |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)   |
| occurrences (all)           | 0              | 1                | 0                |
| Constipation                |                |                  |                  |
| subjects affected / exposed | 1 / 7 (14.29%) | 14 / 34 (41.18%) | 8 / 18 (44.44%)  |
| occurrences (all)           | 1              | 17               | 8                |
| Diarrhoea                   |                |                  |                  |
| subjects affected / exposed | 2 / 7 (28.57%) | 8 / 34 (23.53%)  | 10 / 18 (55.56%) |
| occurrences (all)           | 2              | 9                | 15               |
| Duodenogastric reflux       |                |                  |                  |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)   |
| occurrences (all)           | 0              | 1                | 0                |
| Dyspepsia                   |                |                  |                  |
| subjects affected / exposed | 2 / 7 (28.57%) | 1 / 34 (2.94%)   | 1 / 18 (5.56%)   |
| occurrences (all)           | 3              | 1                | 1                |
| Dysphagia                   |                |                  |                  |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)   | 1 / 18 (5.56%)   |
| occurrences (all)           | 0              | 0                | 1                |
| Flatulence                  |                |                  |                  |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 2 / 18 (11.11%)  |
| occurrences (all)           | 0              | 1                | 2                |
| Gastric polyps              |                |                  |                  |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)   | 1 / 18 (5.56%)   |
| occurrences (all)           | 0              | 0                | 1                |
| Gastritis                   |                |                  |                  |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)   |
| occurrences (all)           | 0              | 1                | 0                |
| Gastritis haemorrhagic      |                |                  |                  |

|                             |                |                  |                 |
|-----------------------------|----------------|------------------|-----------------|
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)   | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 0                | 1               |
| Gingival pain               |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)   | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 0                | 1               |
| Gingival recession          |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)   | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 0                | 1               |
| Gingival swelling           |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)   | 2 / 18 (11.11%) |
| occurrences (all)           | 0              | 0                | 2               |
| Haemorrhoids                |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 2 / 18 (11.11%) |
| occurrences (all)           | 0              | 1                | 2               |
| Ileus                       |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)   | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 0                | 1               |
| Inguinal hernia             |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 2                | 0               |
| Mouth ulceration            |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 2                | 0               |
| Nausea                      |                |                  |                 |
| subjects affected / exposed | 4 / 7 (57.14%) | 10 / 34 (29.41%) | 9 / 18 (50.00%) |
| occurrences (all)           | 4              | 10               | 13              |
| Odynophagia                 |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)   | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 0                | 1               |
| Oesophagitis                |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)   | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 0                | 1               |
| Paraesthesia oral           |                |                  |                 |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)           | 1              | 1                | 0               |
| Stomatitis                  |                |                  |                 |

|  |                     |                      |                      |
|--|---------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0  | 0 / 34 (0.00%)<br>0  | 2 / 18 (11.11%)<br>3 |
| Tongue discomfort<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 7 (0.00%)<br>0  | 0 / 34 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)   | 3 / 7 (42.86%)<br>3 | 8 / 34 (23.53%)<br>8 | 4 / 18 (22.22%)<br>5 |
| Hepatobiliary disorders<br>Hepatic function abnormal<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0  | 0 / 34 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1  |
| Hepatitis<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0  | 1 / 34 (2.94%)<br>1  | 0 / 18 (0.00%)<br>0  |
| Hepatomegaly<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0  | 0 / 34 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1  |
| Skin and subcutaneous tissue disorders<br>Acne<br>subjects affected / exposed<br>occurrences (all)       | 1 / 7 (14.29%)<br>1 | 0 / 34 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  |
| Alopecia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 7 (14.29%)<br>1 | 2 / 34 (5.88%)<br>2  | 2 / 18 (11.11%)<br>2 |
| Decubitus ulcer<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 7 (0.00%)<br>0  | 1 / 34 (2.94%)<br>1  | 0 / 18 (0.00%)<br>0  |
| Dermatitis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0  | 2 / 34 (5.88%)<br>2  | 0 / 18 (0.00%)<br>0  |
| Hyperhidrosis<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0  | 3 / 34 (8.82%)<br>3  | 0 / 18 (0.00%)<br>0  |
| Lipohypertrophy  |                     |                      |                      |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| Night sweats                |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 2 / 34 (5.88%) | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 2              | 1               |
| Pityriasis                  |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%) | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 0              | 1               |
| Pruritus                    |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 2 / 18 (11.11%) |
| occurrences (all)           | 0              | 1              | 2               |
| Rash                        |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%) | 3 / 18 (16.67%) |
| occurrences (all)           | 0              | 0              | 3               |
| Skin lesion                 |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| Urticaria                   |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| Renal and urinary disorders |                |                |                 |
| Bladder pain                |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%) | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 0              | 1               |
| Bladder spasm               |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 3 / 34 (8.82%) | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 3              | 0               |
| Chronic kidney disease      |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%) | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 0              | 1               |
| Dysuria                     |                |                |                 |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 34 (2.94%) | 0 / 18 (0.00%)  |
| occurrences (all)           | 1              | 1              | 0               |
| Haematuria                  |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%) | 2 / 18 (11.11%) |
| occurrences (all)           | 0              | 1              | 2               |

|                             |                |                 |                 |
|-----------------------------|----------------|-----------------|-----------------|
| Leukocyturia                |                |                 |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 1               | 1               |
| Micturition urgency         |                |                 |                 |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 34 (0.00%)  | 0 / 18 (0.00%)  |
| occurrences (all)           | 1              | 0               | 0               |
| Nocturia                    |                |                 |                 |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences (all)           | 1              | 1               | 0               |
| Perinephric collection      |                |                 |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 2 / 34 (5.88%)  | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 2               | 0               |
| Perinephric oedema          |                |                 |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 0               | 1               |
| Polyuria                    |                |                 |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 5 / 34 (14.71%) | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 5               | 0               |
| Proteinuria                 |                |                 |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 2 / 34 (5.88%)  | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 3               | 2               |
| Renal impairment            |                |                 |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 2 / 18 (11.11%) |
| occurrences (all)           | 0              | 0               | 3               |
| Renal tubular acidosis      |                |                 |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 0               | 1               |
| Renal tubular injury        |                |                 |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 0               | 1               |
| Renal tubular necrosis      |                |                 |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 2 / 18 (11.11%) |
| occurrences (all)           | 0              | 0               | 2               |
| Sterile pyuria              |                |                 |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 0               | 1               |

|   |                     |                      |                      |
|---|---------------------|----------------------|----------------------|
| Tubulointerstitial nephritis<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 7 (0.00%)<br>0  | 1 / 34 (2.94%)<br>1  | 0 / 18 (0.00%)<br>0  |
| Urethral pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0  | 1 / 34 (2.94%)<br>1  | 0 / 18 (0.00%)<br>0  |
| Urinary incontinence<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0  | 1 / 34 (2.94%)<br>1  | 2 / 18 (11.11%)<br>2 |
| Urinary retention<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0  | 0 / 34 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1  |
| Urinary tract disorder<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0  | 1 / 34 (2.94%)<br>1  | 0 / 18 (0.00%)<br>0  |
| Urinary tract obstruction<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 7 (0.00%)<br>0  | 0 / 34 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1  |
| Endocrine disorders<br>Hyperparathyroidism<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 7 (0.00%)<br>0  | 1 / 34 (2.94%)<br>1  | 0 / 18 (0.00%)<br>0  |
| Hyperparathyroidism secondary<br>subjects affected / exposed<br>occurrences (all)                                 | 2 / 7 (28.57%)<br>2 | 0 / 34 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0  | 2 / 34 (5.88%)<br>2  | 0 / 18 (0.00%)<br>0  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0  | 5 / 34 (14.71%)<br>5 | 1 / 18 (5.56%)<br>1  |
| Bursitis<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0  | 1 / 34 (2.94%)<br>1  | 0 / 18 (0.00%)<br>0  |
| Flank pain  |                     |                      |                      |

|                             |                |                 |                 |
|-----------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Groin pain                  |                |                 |                 |
| subjects affected / exposed | 1 / 7 (14.29%) | 3 / 34 (8.82%)  | 1 / 18 (5.56%)  |
| occurrences (all)           | 1              | 5               | 2               |
| Hypercreatinaemia           |                |                 |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 0               | 1               |
| Joint effusion              |                |                 |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Muscle spasms               |                |                 |                 |
| subjects affected / exposed | 1 / 7 (14.29%) | 6 / 34 (17.65%) | 1 / 18 (5.56%)  |
| occurrences (all)           | 1              | 8               | 1               |
| Muscle twitching            |                |                 |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 0               | 1               |
| Muscular weakness           |                |                 |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Musculoskeletal discomfort  |                |                 |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Myalgia                     |                |                 |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 4 / 34 (11.76%) | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 4               | 0               |
| Neck pain                   |                |                 |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Osteochondrosis             |                |                 |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Pain in extremity           |                |                 |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 2 / 34 (5.88%)  | 2 / 18 (11.11%) |
| occurrences (all)           | 0              | 3               | 4               |
| Pain in jaw                 |                |                 |                 |

|  |                    |                     |                     |
|--|--------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0 | 1 / 34 (2.94%)<br>1 | 0 / 18 (0.00%)<br>0 |
| Infections and infestations                      |                    |                     |                     |
| Acute sinusitis                                  |                    |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)      | 1 / 34 (2.94%)      | 0 / 18 (0.00%)      |
| occurrences (all)                                | 0                  | 1                   | 0                   |
| BK virus infection                               |                    |                     |                     |
| subjects affected / exposed                      | 3 / 7 (42.86%)     | 10 / 34 (29.41%)    | 6 / 18 (33.33%)     |
| occurrences (all)                                | 3                  | 14                  | 7                   |
| Bronchitis                                       |                    |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)      | 4 / 34 (11.76%)     | 0 / 18 (0.00%)      |
| occurrences (all)                                | 0                  | 4                   | 0                   |
| Conjunctivitis                                   |                    |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)      | 0 / 34 (0.00%)      | 1 / 18 (5.56%)      |
| occurrences (all)                                | 0                  | 0                   | 1                   |
| Cytomegalovirus infection                        |                    |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)      | 6 / 34 (17.65%)     | 2 / 18 (11.11%)     |
| occurrences (all)                                | 0                  | 7                   | 2                   |
| Cytomegalovirus viraemia                         |                    |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)      | 1 / 34 (2.94%)      | 0 / 18 (0.00%)      |
| occurrences (all)                                | 0                  | 1                   | 0                   |
| Diarrhoea infectious                             |                    |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)      | 1 / 34 (2.94%)      | 0 / 18 (0.00%)      |
| occurrences (all)                                | 0                  | 2                   | 0                   |
| Epstein-Barr virus infection                     |                    |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)      | 0 / 34 (0.00%)      | 1 / 18 (5.56%)      |
| occurrences (all)                                | 0                  | 0                   | 1                   |
| Folliculitis                                     |                    |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)      | 1 / 34 (2.94%)      | 0 / 18 (0.00%)      |
| occurrences (all)                                | 0                  | 1                   | 0                   |
| Fungal skin infection                            |                    |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)      | 0 / 34 (0.00%)      | 2 / 18 (11.11%)     |
| occurrences (all)                                | 0                  | 0                   | 2                   |
| Gastroenteritis                                  |                    |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)      | 2 / 34 (5.88%)      | 0 / 18 (0.00%)      |
| occurrences (all)                                | 0                  | 3                   | 0                   |



|  |                    |                     |                     |
|--|--------------------|---------------------|---------------------|
| Gastroenteritis Escherichia coli<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0 | 1 / 34 (2.94%)<br>1 | 0 / 18 (0.00%)<br>0 |
| Gastroenteritis norovirus<br>subjects affected / exposed<br>occurrences (all)        | 0 / 7 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 |
| Gastroenteritis viral<br>subjects affected / exposed<br>occurrences (all)            | 0 / 7 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 |
| Gastrointestinal infection<br>subjects affected / exposed<br>occurrences (all)       | 0 / 7 (0.00%)<br>0 | 1 / 34 (2.94%)<br>1 | 1 / 18 (5.56%)<br>1 |
| Herpes zoster<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 7 (0.00%)<br>0 | 2 / 34 (5.88%)<br>3 | 0 / 18 (0.00%)<br>0 |
| Human polyomavirus infection<br>subjects affected / exposed<br>occurrences (all)     | 0 / 7 (0.00%)<br>0 | 2 / 34 (5.88%)<br>3 | 0 / 18 (0.00%)<br>0 |
| Infection<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 7 (0.00%)<br>0 | 1 / 34 (2.94%)<br>1 | 1 / 18 (5.56%)<br>1 |
| Influenza<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 7 (0.00%)<br>0 | 2 / 34 (5.88%)<br>2 | 1 / 18 (5.56%)<br>1 |
| Laryngitis<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 7 (0.00%)<br>0 | 1 / 34 (2.94%)<br>1 | 0 / 18 (0.00%)<br>0 |
| Latent tuberculosis<br>subjects affected / exposed<br>occurrences (all)              | 0 / 7 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 |
| Lung infection<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 7 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 |
| Mucocutaneous candidiasis<br>subjects affected / exposed<br>occurrences (all)        | 0 / 7 (0.00%)<br>0 | 0 / 34 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 |

|                                     |                |                  |                 |
|-------------------------------------|----------------|------------------|-----------------|
| Nasopharyngitis                     |                |                  |                 |
| subjects affected / exposed         | 1 / 7 (14.29%) | 10 / 34 (29.41%) | 4 / 18 (22.22%) |
| occurrences (all)                   | 1              | 13               | 5               |
| Oral candidiasis                    |                |                  |                 |
| subjects affected / exposed         | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)                   | 0              | 1                | 0               |
| Oral herpes                         |                |                  |                 |
| subjects affected / exposed         | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)                   | 0              | 1                | 0               |
| Oral infection                      |                |                  |                 |
| subjects affected / exposed         | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)                   | 0              | 1                | 0               |
| Otitis media                        |                |                  |                 |
| subjects affected / exposed         | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)                   | 0              | 1                | 0               |
| Pharyngitis streptococcal           |                |                  |                 |
| subjects affected / exposed         | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)                   | 0              | 1                | 0               |
| Pneumocystis jirovecii pneumonia    |                |                  |                 |
| subjects affected / exposed         | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)                   | 0              | 2                | 0               |
| Pneumonia                           |                |                  |                 |
| subjects affected / exposed         | 0 / 7 (0.00%)  | 2 / 34 (5.88%)   | 0 / 18 (0.00%)  |
| occurrences (all)                   | 0              | 2                | 0               |
| Polyomavirus-associated nephropathy |                |                  |                 |
| subjects affected / exposed         | 0 / 7 (0.00%)  | 3 / 34 (8.82%)   | 1 / 18 (5.56%)  |
| occurrences (all)                   | 0              | 3                | 2               |
| Pyelonephritis                      |                |                  |                 |
| subjects affected / exposed         | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 1 / 18 (5.56%)  |
| occurrences (all)                   | 0              | 1                | 1               |
| Pyuria                              |                |                  |                 |
| subjects affected / exposed         | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 1 / 18 (5.56%)  |
| occurrences (all)                   | 0              | 1                | 1               |
| Respiratory tract infection         |                |                  |                 |

|                                   |                |                 |                 |
|-----------------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed       | 0 / 7 (0.00%)  | 2 / 34 (5.88%)  | 0 / 18 (0.00%)  |
| occurrences (all)                 | 0              | 2               | 0               |
| Rhinitis                          |                |                 |                 |
| subjects affected / exposed       | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                 | 0              | 0               | 1               |
| Sinusitis                         |                |                 |                 |
| subjects affected / exposed       | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences (all)                 | 0              | 1               | 0               |
| Skin infection                    |                |                 |                 |
| subjects affected / exposed       | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 1 / 18 (5.56%)  |
| occurrences (all)                 | 0              | 1               | 2               |
| Soft tissue infection             |                |                 |                 |
| subjects affected / exposed       | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences (all)                 | 0              | 1               | 0               |
| Subcutaneous abscess              |                |                 |                 |
| subjects affected / exposed       | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences (all)                 | 0              | 1               | 0               |
| Tinea versicolour                 |                |                 |                 |
| subjects affected / exposed       | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                 | 0              | 0               | 1               |
| Tooth infection                   |                |                 |                 |
| subjects affected / exposed       | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                 | 0              | 0               | 1               |
| Tracheobronchitis                 |                |                 |                 |
| subjects affected / exposed       | 0 / 7 (0.00%)  | 1 / 34 (2.94%)  | 0 / 18 (0.00%)  |
| occurrences (all)                 | 0              | 1               | 0               |
| Upper respiratory tract infection |                |                 |                 |
| subjects affected / exposed       | 0 / 7 (0.00%)  | 2 / 34 (5.88%)  | 0 / 18 (0.00%)  |
| occurrences (all)                 | 0              | 2               | 0               |
| Urinary tract infection           |                |                 |                 |
| subjects affected / exposed       | 1 / 7 (14.29%) | 8 / 34 (23.53%) | 7 / 18 (38.89%) |
| occurrences (all)                 | 1              | 9               | 9               |
| Urinary tract infection viral     |                |                 |                 |
| subjects affected / exposed       | 0 / 7 (0.00%)  | 0 / 34 (0.00%)  | 1 / 18 (5.56%)  |
| occurrences (all)                 | 0              | 0               | 1               |
| Viral infection                   |                |                 |                 |

|   |                     |                       |                      |
|---|---------------------|-----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                              | 0 / 7 (0.00%)<br>0  | 1 / 34 (2.94%)<br>1   | 0 / 18 (0.00%)<br>0  |
| Wound infection bacterial<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0  | 1 / 34 (2.94%)<br>1   | 0 / 18 (0.00%)<br>0  |
| Metabolism and nutrition disorders  |                     |                       |                      |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)        | 0 / 7 (0.00%)<br>0  | 4 / 34 (11.76%)<br>4  | 1 / 18 (5.56%)<br>1  |
| Diabetes mellitus<br>subjects affected / exposed<br>occurrences (all)         | 0 / 7 (0.00%)<br>0  | 3 / 34 (8.82%)<br>3   | 3 / 18 (16.67%)<br>3 |
| Dyslipidaemia<br>subjects affected / exposed<br>occurrences (all)             | 0 / 7 (0.00%)<br>0  | 1 / 34 (2.94%)<br>1   | 0 / 18 (0.00%)<br>0  |
| Fluid overload<br>subjects affected / exposed<br>occurrences (all)            | 0 / 7 (0.00%)<br>0  | 1 / 34 (2.94%)<br>1   | 1 / 18 (5.56%)<br>1  |
| Folate deficiency<br>subjects affected / exposed<br>occurrences (all)         | 0 / 7 (0.00%)<br>0  | 0 / 34 (0.00%)<br>0   | 1 / 18 (5.56%)<br>1  |
| Hypercalcaemia<br>subjects affected / exposed<br>occurrences (all)            | 0 / 7 (0.00%)<br>0  | 2 / 34 (5.88%)<br>2   | 1 / 18 (5.56%)<br>1  |
| Hypercholesterolaemia<br>subjects affected / exposed<br>occurrences (all)     | 0 / 7 (0.00%)<br>0  | 1 / 34 (2.94%)<br>1   | 2 / 18 (11.11%)<br>2 |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)            | 3 / 7 (42.86%)<br>3 | 4 / 34 (11.76%)<br>4  | 4 / 18 (22.22%)<br>4 |
| Hyperkalaemia<br>subjects affected / exposed<br>occurrences (all)             | 1 / 7 (14.29%)<br>1 | 9 / 34 (26.47%)<br>14 | 5 / 18 (27.78%)<br>6 |
| Hyperlipidaemia<br>subjects affected / exposed<br>occurrences (all)           | 1 / 7 (14.29%)<br>1 | 2 / 34 (5.88%)<br>2   | 1 / 18 (5.56%)<br>1  |

|                             |                |                  |                 |
|-----------------------------|----------------|------------------|-----------------|
| Hyperphosphataemia          |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)   | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 0                | 1               |
| Hypertriglyceridaemia       |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 1                | 0               |
| Hyperuricaemia              |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 4 / 34 (11.76%)  | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 4                | 1               |
| Hypervolaemia               |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 34 (0.00%)   | 2 / 18 (11.11%) |
| occurrences (all)           | 0              | 0                | 2               |
| Hypocalcaemia               |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 4 / 34 (11.76%)  | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 4                | 1               |
| Hypokalaemia                |                |                  |                 |
| subjects affected / exposed | 1 / 7 (14.29%) | 6 / 34 (17.65%)  | 5 / 18 (27.78%) |
| occurrences (all)           | 1              | 8                | 5               |
| Hypomagnesaemia             |                |                  |                 |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 34 (0.00%)   | 3 / 18 (16.67%) |
| occurrences (all)           | 2              | 0                | 3               |
| Hyponatraemia               |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 3 / 34 (8.82%)   | 1 / 18 (5.56%)  |
| occurrences (all)           | 0              | 3                | 1               |
| Hypophosphataemia           |                |                  |                 |
| subjects affected / exposed | 5 / 7 (71.43%) | 11 / 34 (32.35%) | 5 / 18 (27.78%) |
| occurrences (all)           | 5              | 12               | 5               |
| Increased appetite          |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 1                | 0               |
| Magnesium deficiency        |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 0 / 18 (0.00%)  |
| occurrences (all)           | 0              | 1                | 0               |
| Metabolic acidosis          |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 34 (2.94%)   | 2 / 18 (11.11%) |
| occurrences (all)           | 0              | 1                | 2               |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| Vitamin D deficiency<br>subjects affected / exposed<br>occurrences (all) | 2 / 7 (28.57%)<br>2 | 2 / 34 (5.88%)<br>2 | 1 / 18 (5.56%)<br>1 |
|--|---------------------|---------------------|---------------------|

| <b>Non-serious adverse events</b>  | Total   |  |  |
|--|---|--|--|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed   | 58 / 59 (98.31%)  |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps)<br>Basal cell carcinoma<br>subjects affected / exposed<br>occurrences (all)  | 1 / 59 (1.69%)<br>1   |  |  |
| Vascular disorders<br>Deep vein thrombosis<br>subjects affected / exposed<br>occurrences (all)<br><br>Haematoma<br>subjects affected / exposed<br>occurrences (all)<br><br>Hot flush<br>subjects affected / exposed<br>occurrences (all)<br><br>Hypertension<br>subjects affected / exposed<br>occurrences (all)<br><br>Hypotension<br>subjects affected / exposed<br>occurrences (all)<br><br>Lymphocele<br>subjects affected / exposed<br>occurrences (all)<br><br>Orthostatic hypotension<br>subjects affected / exposed<br>occurrences (all)<br><br>Poor venous access<br>subjects affected / exposed<br>occurrences (all) | 1 / 59 (1.69%)<br>1<br><br>2 / 59 (3.39%)<br>2<br><br>2 / 59 (3.39%)<br>2<br><br>20 / 59 (33.90%)<br>21<br><br>5 / 59 (8.47%)<br>5<br><br>2 / 59 (3.39%)<br>2<br><br>1 / 59 (1.69%)<br>1<br><br>2 / 59 (3.39%)<br>2 |  |  |
| General disorders and administration   |   |  |  |

|                             |                  |  |  |
|-----------------------------|------------------|--|--|
| site conditions             |                  |  |  |
| Asthenia                    |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Catheter site pain          |                  |  |  |
| subjects affected / exposed | 2 / 59 (3.39%)   |  |  |
| occurrences (all)           | 2                |  |  |
| Chills                      |                  |  |  |
| subjects affected / exposed | 3 / 59 (5.08%)   |  |  |
| occurrences (all)           | 3                |  |  |
| Cyst                        |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Fatigue                     |                  |  |  |
| subjects affected / exposed | 11 / 59 (18.64%) |  |  |
| occurrences (all)           | 11               |  |  |
| Generalised oedema          |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Impaired healing            |                  |  |  |
| subjects affected / exposed | 3 / 59 (5.08%)   |  |  |
| occurrences (all)           | 3                |  |  |
| Influenza like illness      |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Infusion site swelling      |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Malaise                     |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Oedema peripheral           |                  |  |  |
| subjects affected / exposed | 15 / 59 (25.42%) |  |  |
| occurrences (all)           | 22               |  |  |
| Pain                        |                  |  |  |

|  |                |  |  |
|--|----------------|--|--|
| subjects affected / exposed              | 1 / 59 (1.69%) |  |  |
| occurrences (all)                        | 1              |  |  |
| Peripheral swelling                      |                |  |  |
| subjects affected / exposed              | 1 / 59 (1.69%) |  |  |
| occurrences (all)                        | 1              |  |  |
| Pyrexia                                  |                |  |  |
| subjects affected / exposed              | 2 / 59 (3.39%) |  |  |
| occurrences (all)                        | 3              |  |  |
| Secretion discharge                      |                |  |  |
| subjects affected / exposed              | 3 / 59 (5.08%) |  |  |
| occurrences (all)                        | 3              |  |  |
| Swelling                                 |                |  |  |
| subjects affected / exposed              | 1 / 59 (1.69%) |  |  |
| occurrences (all)                        | 1              |  |  |
| Immune system disorders                  |                |  |  |
| Drug hypersensitivity                    |                |  |  |
| subjects affected / exposed              | 1 / 59 (1.69%) |  |  |
| occurrences (all)                        | 1              |  |  |
| Kidney transplant rejection              |                |  |  |
| subjects affected / exposed              | 1 / 59 (1.69%) |  |  |
| occurrences (all)                        | 1              |  |  |
| Reproductive system and breast disorders |                |  |  |
| Benign prostatic hyperplasia             |                |  |  |
| subjects affected / exposed              | 1 / 59 (1.69%) |  |  |
| occurrences (all)                        | 1              |  |  |
| Dysmenorrhoea                            |                |  |  |
| subjects affected / exposed              | 2 / 59 (3.39%) |  |  |
| occurrences (all)                        | 2              |  |  |
| Erectile dysfunction                     |                |  |  |
| subjects affected / exposed              | 1 / 59 (1.69%) |  |  |
| occurrences (all)                        | 1              |  |  |
| Menorrhagia                              |                |  |  |
| subjects affected / exposed              | 1 / 59 (1.69%) |  |  |
| occurrences (all)                        | 1              |  |  |
| Penile oedema                            |                |  |  |



|   |                  |  |  |
|---|------------------|--|--|
| subjects affected / exposed                     | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                               | 1                |  |  |
| Penile pain                                     |                  |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                               | 1                |  |  |
| Prostatomegaly                                  |                  |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                               | 1                |  |  |
| Scrotal swelling                                |                  |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                               | 1                |  |  |
| Vulvovaginal pain                               |                  |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                               | 1                |  |  |
| Respiratory, thoracic and mediastinal disorders |                  |  |  |
| Cough   |                  |  |  |
| subjects affected / exposed                     | 12 / 59 (20.34%) |  |  |
| occurrences (all)                               | 15               |  |  |
| Dyspnoea  |                  |  |  |
| subjects affected / exposed                     | 8 / 59 (13.56%)  |  |  |
| occurrences (all)                               | 9                |  |  |
| Dyspnoea exertional                             |                  |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                               | 1                |  |  |
| Lung infiltration                               |                  |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                               | 1                |  |  |
| Nasal congestion                                |                  |  |  |
| subjects affected / exposed                     | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                               | 1                |  |  |
| Oropharyngeal pain                              |                  |  |  |
| subjects affected / exposed                     | 3 / 59 (5.08%)   |  |  |
| occurrences (all)                               | 3                |  |  |
| Pleural effusion                                |                  |  |  |

|                             |                  |  |  |
|-----------------------------|------------------|--|--|
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Productive cough            |                  |  |  |
| subjects affected / exposed | 2 / 59 (3.39%)   |  |  |
| occurrences (all)           | 2                |  |  |
| Respiratory distress        |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Rhinorrhoea                 |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Sleep apnoea syndrome       |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Wheezing                    |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Psychiatric disorders       |                  |  |  |
| Anxiety                     |                  |  |  |
| subjects affected / exposed | 2 / 59 (3.39%)   |  |  |
| occurrences (all)           | 2                |  |  |
| Delirium                    |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Insomnia                    |                  |  |  |
| subjects affected / exposed | 17 / 59 (28.81%) |  |  |
| occurrences (all)           | 18               |  |  |
| Mood swings                 |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Phonophobia                 |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Restlessness                |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |

|  |                |  |  |
|--|----------------|--|--|
| Investigations                         |                |  |  |
| Alanine aminotransferase increased     |                |  |  |
| subjects affected / exposed            | 1 / 59 (1.69%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Amylase increased                      |                |  |  |
| subjects affected / exposed            | 4 / 59 (6.78%) |  |  |
| occurrences (all)                      | 4              |  |  |
| Aspartate aminotransferase increased   |                |  |  |
| subjects affected / exposed            | 1 / 59 (1.69%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Blood creatine phosphokinase increased |                |  |  |
| subjects affected / exposed            | 2 / 59 (3.39%) |  |  |
| occurrences (all)                      | 2              |  |  |
| Blood creatinine increased             |                |  |  |
| subjects affected / exposed            | 4 / 59 (6.78%) |  |  |
| occurrences (all)                      | 4              |  |  |
| Blood glucose increased                |                |  |  |
| subjects affected / exposed            | 1 / 59 (1.69%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Blood lactate dehydrogenase increased  |                |  |  |
| subjects affected / exposed            | 1 / 59 (1.69%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Blood phosphorus decreased             |                |  |  |
| subjects affected / exposed            | 1 / 59 (1.69%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Blood phosphorus increased             |                |  |  |
| subjects affected / exposed            | 1 / 59 (1.69%) |  |  |
| occurrences (all)                      | 1              |  |  |
| C-reactive protein increased           |                |  |  |
| subjects affected / exposed            | 1 / 59 (1.69%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Cardiac murmur                         |                |  |  |
| subjects affected / exposed            | 1 / 59 (1.69%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Cytomegalovirus test positive          |                |  |  |

|                                       |                |  |  |
|---------------------------------------|----------------|--|--|
| subjects affected / exposed           | 1 / 59 (1.69%) |  |  |
| occurrences (all)                     | 1              |  |  |
| Drug level decreased                  |                |  |  |
| subjects affected / exposed           | 1 / 59 (1.69%) |  |  |
| occurrences (all)                     | 1              |  |  |
| Electrocardiogram ST segment abnormal |                |  |  |
| subjects affected / exposed           | 1 / 59 (1.69%) |  |  |
| occurrences (all)                     | 1              |  |  |
| Electrocardiogram T wave abnormal     |                |  |  |
| subjects affected / exposed           | 1 / 59 (1.69%) |  |  |
| occurrences (all)                     | 1              |  |  |
| Gamma-glutamyltransferase increased   |                |  |  |
| subjects affected / exposed           | 3 / 59 (5.08%) |  |  |
| occurrences (all)                     | 3              |  |  |
| Haemoglobin decreased                 |                |  |  |
| subjects affected / exposed           | 1 / 59 (1.69%) |  |  |
| occurrences (all)                     | 1              |  |  |
| Heart rate irregular                  |                |  |  |
| subjects affected / exposed           | 1 / 59 (1.69%) |  |  |
| occurrences (all)                     | 1              |  |  |
| Lipase increased                      |                |  |  |
| subjects affected / exposed           | 2 / 59 (3.39%) |  |  |
| occurrences (all)                     | 2              |  |  |
| Polyomavirus test positive            |                |  |  |
| subjects affected / exposed           | 1 / 59 (1.69%) |  |  |
| occurrences (all)                     | 1              |  |  |
| Vitamin D decreased                   |                |  |  |
| subjects affected / exposed           | 1 / 59 (1.69%) |  |  |
| occurrences (all)                     | 1              |  |  |
| Weight decreased                      |                |  |  |
| subjects affected / exposed           | 2 / 59 (3.39%) |  |  |
| occurrences (all)                     | 2              |  |  |
| Weight increased                      |                |  |  |

|  |                 |  |  |
|--|-----------------|--|--|
| subjects affected / exposed                    | 3 / 59 (5.08%)  |  |  |
| occurrences (all)                              | 3               |  |  |
| White blood cell count decreased               |                 |  |  |
| subjects affected / exposed                    | 1 / 59 (1.69%)  |  |  |
| occurrences (all)                              | 1               |  |  |
| White blood cell count increased               |                 |  |  |
| subjects affected / exposed                    | 3 / 59 (5.08%)  |  |  |
| occurrences (all)                              | 3               |  |  |
| Injury, poisoning and procedural complications |                 |  |  |
| Animal bite                                    |                 |  |  |
| subjects affected / exposed                    | 1 / 59 (1.69%)  |  |  |
| occurrences (all)                              | 1               |  |  |
| Arterial injury                                |                 |  |  |
| subjects affected / exposed                    | 1 / 59 (1.69%)  |  |  |
| occurrences (all)                              | 1               |  |  |
| Arteriovenous fistula site complication        |                 |  |  |
| subjects affected / exposed                    | 1 / 59 (1.69%)  |  |  |
| occurrences (all)                              | 1               |  |  |
| Arthropod bite                                 |                 |  |  |
| subjects affected / exposed                    | 1 / 59 (1.69%)  |  |  |
| occurrences (all)                              | 1               |  |  |
| Complications of transplant surgery            |                 |  |  |
| subjects affected / exposed                    | 1 / 59 (1.69%)  |  |  |
| occurrences (all)                              | 1               |  |  |
| Complications of transplanted kidney           |                 |  |  |
| subjects affected / exposed                    | 5 / 59 (8.47%)  |  |  |
| occurrences (all)                              | 8               |  |  |
| Delayed graft function                         |                 |  |  |
| subjects affected / exposed                    | 6 / 59 (10.17%) |  |  |
| occurrences (all)                              | 6               |  |  |
| Fall   |                 |  |  |
| subjects affected / exposed                    | 1 / 59 (1.69%)  |  |  |
| occurrences (all)                              | 1               |  |  |
| Graft complication                             |                 |  |  |

|                                  |                  |  |  |
|----------------------------------|------------------|--|--|
| subjects affected / exposed      | 2 / 59 (3.39%)   |  |  |
| occurrences (all)                | 2                |  |  |
| Incision site complication       |                  |  |  |
| subjects affected / exposed      | 2 / 59 (3.39%)   |  |  |
| occurrences (all)                | 2                |  |  |
| Incision site erythema           |                  |  |  |
| subjects affected / exposed      | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                | 1                |  |  |
| Incision site haemorrhage        |                  |  |  |
| subjects affected / exposed      | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                | 1                |  |  |
| Incision site pain               |                  |  |  |
| subjects affected / exposed      | 11 / 59 (18.64%) |  |  |
| occurrences (all)                | 11               |  |  |
| Incisional hernia                |                  |  |  |
| subjects affected / exposed      | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                | 1                |  |  |
| Joint injury                     |                  |  |  |
| subjects affected / exposed      | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                | 1                |  |  |
| Ligament sprain                  |                  |  |  |
| subjects affected / exposed      | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                | 1                |  |  |
| Lip injury                       |                  |  |  |
| subjects affected / exposed      | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                | 2                |  |  |
| Post procedural complication     |                  |  |  |
| subjects affected / exposed      | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                | 1                |  |  |
| Post procedural haemorrhage      |                  |  |  |
| subjects affected / exposed      | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                | 1                |  |  |
| Post procedural swelling         |                  |  |  |
| subjects affected / exposed      | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                | 1                |  |  |
| Postoperative wound complication |                  |  |  |

|  |                  |  |  |
|--|------------------|--|--|
| subjects affected / exposed                | 6 / 59 (10.17%)  |  |  |
| occurrences (all)                          | 7                |  |  |
| Procedural pain                            |                  |  |  |
| subjects affected / exposed                | 9 / 59 (15.25%)  |  |  |
| occurrences (all)                          | 11               |  |  |
| Radius fracture                            |                  |  |  |
| subjects affected / exposed                | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                          | 1                |  |  |
| Seroma                                     |                  |  |  |
| subjects affected / exposed                | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                          | 1                |  |  |
| Transplant dysfunction                     |                  |  |  |
| subjects affected / exposed                | 5 / 59 (8.47%)   |  |  |
| occurrences (all)                          | 5                |  |  |
| Wound complication                         |                  |  |  |
| subjects affected / exposed                | 19 / 59 (32.20%) |  |  |
| occurrences (all)                          | 19               |  |  |
| Wound dehiscence                           |                  |  |  |
| subjects affected / exposed                | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                          | 1                |  |  |
| Wound haematoma                            |                  |  |  |
| subjects affected / exposed                | 2 / 59 (3.39%)   |  |  |
| occurrences (all)                          | 2                |  |  |
| Congenital, familial and genetic disorders |                  |  |  |
| Hydrocele                                  |                  |  |  |
| subjects affected / exposed                | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                          | 1                |  |  |
| Cardiac disorders                          |                  |  |  |
| Angina pectoris                            |                  |  |  |
| subjects affected / exposed                | 2 / 59 (3.39%)   |  |  |
| occurrences (all)                          | 2                |  |  |
| Arrhythmia                                 |                  |  |  |
| subjects affected / exposed                | 3 / 59 (5.08%)   |  |  |
| occurrences (all)                          | 3                |  |  |
| Atrial fibrillation                        |                  |  |  |

|                              |                 |  |  |
|------------------------------|-----------------|--|--|
| subjects affected / exposed  | 3 / 59 (5.08%)  |  |  |
| occurrences (all)            | 4               |  |  |
| Bradycardia                  |                 |  |  |
| subjects affected / exposed  | 1 / 59 (1.69%)  |  |  |
| occurrences (all)            | 1               |  |  |
| Extrasystoles                |                 |  |  |
| subjects affected / exposed  | 1 / 59 (1.69%)  |  |  |
| occurrences (all)            | 1               |  |  |
| Myocardial infarction        |                 |  |  |
| subjects affected / exposed  | 1 / 59 (1.69%)  |  |  |
| occurrences (all)            | 1               |  |  |
| Palpitations                 |                 |  |  |
| subjects affected / exposed  | 1 / 59 (1.69%)  |  |  |
| occurrences (all)            | 1               |  |  |
| Sinus tachycardia            |                 |  |  |
| subjects affected / exposed  | 1 / 59 (1.69%)  |  |  |
| occurrences (all)            | 2               |  |  |
| Tachycardia                  |                 |  |  |
| subjects affected / exposed  | 7 / 59 (11.86%) |  |  |
| occurrences (all)            | 7               |  |  |
| Tricuspid valve incompetence |                 |  |  |
| subjects affected / exposed  | 1 / 59 (1.69%)  |  |  |
| occurrences (all)            | 1               |  |  |
| Nervous system disorders     |                 |  |  |
| Ataxia                       |                 |  |  |
| subjects affected / exposed  | 1 / 59 (1.69%)  |  |  |
| occurrences (all)            | 1               |  |  |
| Burning sensation            |                 |  |  |
| subjects affected / exposed  | 1 / 59 (1.69%)  |  |  |
| occurrences (all)            | 1               |  |  |
| Dizziness                    |                 |  |  |
| subjects affected / exposed  | 6 / 59 (10.17%) |  |  |
| occurrences (all)            | 6               |  |  |
| Dizziness postural           |                 |  |  |
| subjects affected / exposed  | 2 / 59 (3.39%)  |  |  |
| occurrences (all)            | 2               |  |  |



|                                      |                  |  |  |
|--------------------------------------|------------------|--|--|
| Headache                             |                  |  |  |
| subjects affected / exposed          | 11 / 59 (18.64%) |  |  |
| occurrences (all)                    | 12               |  |  |
| Hypoaesthesia                        |                  |  |  |
| subjects affected / exposed          | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                    | 1                |  |  |
| Migraine                             |                  |  |  |
| subjects affected / exposed          | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                    | 1                |  |  |
| Paraesthesia                         |                  |  |  |
| subjects affected / exposed          | 2 / 59 (3.39%)   |  |  |
| occurrences (all)                    | 2                |  |  |
| Peroneal nerve palsy                 |                  |  |  |
| subjects affected / exposed          | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                    | 1                |  |  |
| Polyneuropathy                       |                  |  |  |
| subjects affected / exposed          | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                    | 1                |  |  |
| Tremor                               |                  |  |  |
| subjects affected / exposed          | 11 / 59 (18.64%) |  |  |
| occurrences (all)                    | 13               |  |  |
| Blood and lymphatic system disorders |                  |  |  |
| Anaemia                              |                  |  |  |
| subjects affected / exposed          | 8 / 59 (13.56%)  |  |  |
| occurrences (all)                    | 8                |  |  |
| Iron deficiency anaemia              |                  |  |  |
| subjects affected / exposed          | 2 / 59 (3.39%)   |  |  |
| occurrences (all)                    | 2                |  |  |
| Leukocytosis                         |                  |  |  |
| subjects affected / exposed          | 6 / 59 (10.17%)  |  |  |
| occurrences (all)                    | 7                |  |  |
| Leukopenia                           |                  |  |  |
| subjects affected / exposed          | 17 / 59 (28.81%) |  |  |
| occurrences (all)                    | 22               |  |  |
| Lymphopenia                          |                  |  |  |

|                             |                |  |  |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 2 / 59 (3.39%) |  |  |
| occurrences (all)           | 2              |  |  |
| Microcytic anaemia          |                |  |  |
| subjects affected / exposed | 1 / 59 (1.69%) |  |  |
| occurrences (all)           | 1              |  |  |
| Nephrogenic anaemia         |                |  |  |
| subjects affected / exposed | 1 / 59 (1.69%) |  |  |
| occurrences (all)           | 1              |  |  |
| Neutropenia                 |                |  |  |
| subjects affected / exposed | 3 / 59 (5.08%) |  |  |
| occurrences (all)           | 3              |  |  |
| Normocytic anaemia          |                |  |  |
| subjects affected / exposed | 1 / 59 (1.69%) |  |  |
| occurrences (all)           | 1              |  |  |
| Pancytopenia                |                |  |  |
| subjects affected / exposed | 1 / 59 (1.69%) |  |  |
| occurrences (all)           | 1              |  |  |
| Polycythaemia               |                |  |  |
| subjects affected / exposed | 1 / 59 (1.69%) |  |  |
| occurrences (all)           | 1              |  |  |
| Thrombocytopenia            |                |  |  |
| subjects affected / exposed | 1 / 59 (1.69%) |  |  |
| occurrences (all)           | 1              |  |  |
| Thrombocytosis              |                |  |  |
| subjects affected / exposed | 1 / 59 (1.69%) |  |  |
| occurrences (all)           | 1              |  |  |
| Ear and labyrinth disorders |                |  |  |
| Ear discomfort              |                |  |  |
| subjects affected / exposed | 1 / 59 (1.69%) |  |  |
| occurrences (all)           | 1              |  |  |
| Vertigo                     |                |  |  |
| subjects affected / exposed | 1 / 59 (1.69%) |  |  |
| occurrences (all)           | 1              |  |  |
| Eye disorders               |                |  |  |
| Chalazion                   |                |  |  |

|                             |                 |  |  |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 59 (1.69%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Dry eye                     |                 |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Eye movement disorder       |                 |  |  |
| subjects affected / exposed | 2 / 59 (3.39%)  |  |  |
| occurrences (all)           | 2               |  |  |
| Ocular hyperaemia           |                 |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Retinal vein occlusion      |                 |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Gastrointestinal disorders  |                 |  |  |
| Abdominal discomfort        |                 |  |  |
| subjects affected / exposed | 2 / 59 (3.39%)  |  |  |
| occurrences (all)           | 2               |  |  |
| Abdominal distension        |                 |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Abdominal pain              |                 |  |  |
| subjects affected / exposed | 7 / 59 (11.86%) |  |  |
| occurrences (all)           | 7               |  |  |
| Abdominal pain lower        |                 |  |  |
| subjects affected / exposed | 2 / 59 (3.39%)  |  |  |
| occurrences (all)           | 2               |  |  |
| Abdominal pain upper        |                 |  |  |
| subjects affected / exposed | 5 / 59 (8.47%)  |  |  |
| occurrences (all)           | 6               |  |  |
| Anal fissure                |                 |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Aphthous ulcer              |                 |  |  |
| subjects affected / exposed | 2 / 59 (3.39%)  |  |  |
| occurrences (all)           | 2               |  |  |

|                             |                  |  |  |
|-----------------------------|------------------|--|--|
| Colitis                     |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Constipation                |                  |  |  |
| subjects affected / exposed | 23 / 59 (38.98%) |  |  |
| occurrences (all)           | 26               |  |  |
| Diarrhoea                   |                  |  |  |
| subjects affected / exposed | 20 / 59 (33.90%) |  |  |
| occurrences (all)           | 26               |  |  |
| Duodenogastric reflux       |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Dyspepsia                   |                  |  |  |
| subjects affected / exposed | 4 / 59 (6.78%)   |  |  |
| occurrences (all)           | 5                |  |  |
| Dysphagia                   |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Flatulence                  |                  |  |  |
| subjects affected / exposed | 3 / 59 (5.08%)   |  |  |
| occurrences (all)           | 3                |  |  |
| Gastric polyps              |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Gastritis                   |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Gastritis haemorrhagic      |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Gingival pain               |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Gingival recession          |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |

|                             |                  |  |  |
|-----------------------------|------------------|--|--|
| Gingival swelling           |                  |  |  |
| subjects affected / exposed | 2 / 59 (3.39%)   |  |  |
| occurrences (all)           | 2                |  |  |
| Haemorrhoids                |                  |  |  |
| subjects affected / exposed | 3 / 59 (5.08%)   |  |  |
| occurrences (all)           | 3                |  |  |
| Ileus                       |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Inguinal hernia             |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 2                |  |  |
| Mouth ulceration            |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 2                |  |  |
| Nausea                      |                  |  |  |
| subjects affected / exposed | 23 / 59 (38.98%) |  |  |
| occurrences (all)           | 27               |  |  |
| Odynophagia                 |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Oesophagitis                |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Paraesthesia oral           |                  |  |  |
| subjects affected / exposed | 2 / 59 (3.39%)   |  |  |
| occurrences (all)           | 2                |  |  |
| Stomatitis                  |                  |  |  |
| subjects affected / exposed | 2 / 59 (3.39%)   |  |  |
| occurrences (all)           | 3                |  |  |
| Tongue discomfort           |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Vomiting                    |                  |  |  |
| subjects affected / exposed | 15 / 59 (25.42%) |  |  |
| occurrences (all)           | 16               |  |  |

|  |                             |                |  |  |
|--|-----------------------------|----------------|--|--|
| Hepatobiliary disorders                | Hepatic function abnormal   |                |  |  |
|  | subjects affected / exposed | 1 / 59 (1.69%) |  |  |
|  | occurrences (all)           | 1              |  |  |
|  | Hepatitis                   |                |  |  |
|  | subjects affected / exposed | 1 / 59 (1.69%) |  |  |
|  | occurrences (all)           | 1              |  |  |
|  | Hepatomegaly                |                |  |  |
|  | subjects affected / exposed | 1 / 59 (1.69%) |  |  |
|  | occurrences (all)           | 1              |  |  |
| Skin and subcutaneous tissue disorders | Acne                        |                |  |  |
|  | subjects affected / exposed | 1 / 59 (1.69%) |  |  |
|  | occurrences (all)           | 1              |  |  |
|  | Alopecia                    |                |  |  |
|  | subjects affected / exposed | 5 / 59 (8.47%) |  |  |
|  | occurrences (all)           | 5              |  |  |
|  | Decubitus ulcer             |                |  |  |
|  | subjects affected / exposed | 1 / 59 (1.69%) |  |  |
|  | occurrences (all)           | 1              |  |  |
|  | Dermatitis                  |                |  |  |
|  | subjects affected / exposed | 2 / 59 (3.39%) |  |  |
|  | occurrences (all)           | 2              |  |  |
|  | Hyperhidrosis               |                |  |  |
|  | subjects affected / exposed | 3 / 59 (5.08%) |  |  |
|  | occurrences (all)           | 3              |  |  |
|  | Lipohypertrophy             |                |  |  |
|  | subjects affected / exposed | 1 / 59 (1.69%) |  |  |
|  | occurrences (all)           | 1              |  |  |
|  | Night sweats                |                |  |  |
|  | subjects affected / exposed | 3 / 59 (5.08%) |  |  |
|  | occurrences (all)           | 3              |  |  |
|  | Pityriasis                  |                |  |  |
|  | subjects affected / exposed | 1 / 59 (1.69%) |  |  |
|  | occurrences (all)           | 1              |  |  |
|  | Pruritus                    |                |  |  |

|                             |                |  |  |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 3 / 59 (5.08%) |  |  |
| occurrences (all)           | 3              |  |  |
| Rash                        |                |  |  |
| subjects affected / exposed | 3 / 59 (5.08%) |  |  |
| occurrences (all)           | 3              |  |  |
| Skin lesion                 |                |  |  |
| subjects affected / exposed | 1 / 59 (1.69%) |  |  |
| occurrences (all)           | 1              |  |  |
| Urticaria                   |                |  |  |
| subjects affected / exposed | 1 / 59 (1.69%) |  |  |
| occurrences (all)           | 1              |  |  |
| Renal and urinary disorders |                |  |  |
| Bladder pain                |                |  |  |
| subjects affected / exposed | 1 / 59 (1.69%) |  |  |
| occurrences (all)           | 1              |  |  |
| Bladder spasm               |                |  |  |
| subjects affected / exposed | 3 / 59 (5.08%) |  |  |
| occurrences (all)           | 3              |  |  |
| Chronic kidney disease      |                |  |  |
| subjects affected / exposed | 1 / 59 (1.69%) |  |  |
| occurrences (all)           | 1              |  |  |
| Dysuria                     |                |  |  |
| subjects affected / exposed | 2 / 59 (3.39%) |  |  |
| occurrences (all)           | 2              |  |  |
| Haematuria                  |                |  |  |
| subjects affected / exposed | 3 / 59 (5.08%) |  |  |
| occurrences (all)           | 3              |  |  |
| Leukocyturia                |                |  |  |
| subjects affected / exposed | 2 / 59 (3.39%) |  |  |
| occurrences (all)           | 2              |  |  |
| Micturition urgency         |                |  |  |
| subjects affected / exposed | 1 / 59 (1.69%) |  |  |
| occurrences (all)           | 1              |  |  |
| Nocturia                    |                |  |  |
| subjects affected / exposed | 2 / 59 (3.39%) |  |  |
| occurrences (all)           | 2              |  |  |

|                              |                |  |  |
|------------------------------|----------------|--|--|
| Perinephric collection       |                |  |  |
| subjects affected / exposed  | 2 / 59 (3.39%) |  |  |
| occurrences (all)            | 2              |  |  |
| Perinephric oedema           |                |  |  |
| subjects affected / exposed  | 1 / 59 (1.69%) |  |  |
| occurrences (all)            | 1              |  |  |
| Polyuria                     |                |  |  |
| subjects affected / exposed  | 5 / 59 (8.47%) |  |  |
| occurrences (all)            | 5              |  |  |
| Proteinuria                  |                |  |  |
| subjects affected / exposed  | 3 / 59 (5.08%) |  |  |
| occurrences (all)            | 5              |  |  |
| Renal impairment             |                |  |  |
| subjects affected / exposed  | 2 / 59 (3.39%) |  |  |
| occurrences (all)            | 3              |  |  |
| Renal tubular acidosis       |                |  |  |
| subjects affected / exposed  | 1 / 59 (1.69%) |  |  |
| occurrences (all)            | 1              |  |  |
| Renal tubular injury         |                |  |  |
| subjects affected / exposed  | 1 / 59 (1.69%) |  |  |
| occurrences (all)            | 1              |  |  |
| Renal tubular necrosis       |                |  |  |
| subjects affected / exposed  | 2 / 59 (3.39%) |  |  |
| occurrences (all)            | 2              |  |  |
| Sterile pyuria               |                |  |  |
| subjects affected / exposed  | 1 / 59 (1.69%) |  |  |
| occurrences (all)            | 1              |  |  |
| Tubulointerstitial nephritis |                |  |  |
| subjects affected / exposed  | 1 / 59 (1.69%) |  |  |
| occurrences (all)            | 1              |  |  |
| Urethral pain                |                |  |  |
| subjects affected / exposed  | 1 / 59 (1.69%) |  |  |
| occurrences (all)            | 1              |  |  |
| Urinary incontinence         |                |  |  |
| subjects affected / exposed  | 3 / 59 (5.08%) |  |  |
| occurrences (all)            | 3              |  |  |



|   |                      |  |  |
|---|----------------------|--|--|
| Urinary retention<br>subjects affected / exposed<br>occurrences (all)   | 1 / 59 (1.69%)<br>1  |  |  |
| Urinary tract disorder<br>subjects affected / exposed<br>occurrences (all)  | 1 / 59 (1.69%)<br>1  |  |  |
| Urinary tract obstruction<br>subjects affected / exposed<br>occurrences (all)                                     | 1 / 59 (1.69%)<br>1  |  |  |
| Endocrine disorders<br>Hyperparathyroidism<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 59 (1.69%)<br>1  |  |  |
| Hyperparathyroidism secondary<br>subjects affected / exposed<br>occurrences (all)                                 | 3 / 59 (5.08%)<br>3  |  |  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 2 / 59 (3.39%)<br>2  |  |  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)   | 6 / 59 (10.17%)<br>6 |  |  |
| Bursitis<br>subjects affected / exposed<br>occurrences (all)  | 1 / 59 (1.69%)<br>1  |  |  |
| Flank pain<br>subjects affected / exposed<br>occurrences (all)  | 1 / 59 (1.69%)<br>1  |  |  |
| Groin pain<br>subjects affected / exposed<br>occurrences (all)  | 5 / 59 (8.47%)<br>8  |  |  |
| Hypercreatinaemia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 59 (1.69%)<br>1  |  |  |
| Joint effusion  |                      |  |  |

|                             |                  |  |  |
|-----------------------------|------------------|--|--|
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Muscle spasms               |                  |  |  |
| subjects affected / exposed | 8 / 59 (13.56%)  |  |  |
| occurrences (all)           | 10               |  |  |
| Muscle twitching            |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Muscular weakness           |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Musculoskeletal discomfort  |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Myalgia                     |                  |  |  |
| subjects affected / exposed | 4 / 59 (6.78%)   |  |  |
| occurrences (all)           | 4                |  |  |
| Neck pain                   |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Osteochondrosis             |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Pain in extremity           |                  |  |  |
| subjects affected / exposed | 4 / 59 (6.78%)   |  |  |
| occurrences (all)           | 7                |  |  |
| Pain in jaw                 |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Infections and infestations |                  |  |  |
| Acute sinusitis             |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| BK virus infection          |                  |  |  |
| subjects affected / exposed | 19 / 59 (32.20%) |  |  |
| occurrences (all)           | 24               |  |  |

|                                  |                 |  |  |
|----------------------------------|-----------------|--|--|
| Bronchitis                       |                 |  |  |
| subjects affected / exposed      | 4 / 59 (6.78%)  |  |  |
| occurrences (all)                | 4               |  |  |
| Conjunctivitis                   |                 |  |  |
| subjects affected / exposed      | 1 / 59 (1.69%)  |  |  |
| occurrences (all)                | 1               |  |  |
| Cytomegalovirus infection        |                 |  |  |
| subjects affected / exposed      | 8 / 59 (13.56%) |  |  |
| occurrences (all)                | 9               |  |  |
| Cytomegalovirus viraemia         |                 |  |  |
| subjects affected / exposed      | 1 / 59 (1.69%)  |  |  |
| occurrences (all)                | 1               |  |  |
| Diarrhoea infectious             |                 |  |  |
| subjects affected / exposed      | 1 / 59 (1.69%)  |  |  |
| occurrences (all)                | 2               |  |  |
| Epstein-Barr virus infection     |                 |  |  |
| subjects affected / exposed      | 1 / 59 (1.69%)  |  |  |
| occurrences (all)                | 1               |  |  |
| Folliculitis                     |                 |  |  |
| subjects affected / exposed      | 1 / 59 (1.69%)  |  |  |
| occurrences (all)                | 1               |  |  |
| Fungal skin infection            |                 |  |  |
| subjects affected / exposed      | 2 / 59 (3.39%)  |  |  |
| occurrences (all)                | 2               |  |  |
| Gastroenteritis                  |                 |  |  |
| subjects affected / exposed      | 2 / 59 (3.39%)  |  |  |
| occurrences (all)                | 3               |  |  |
| Gastroenteritis Escherichia coli |                 |  |  |
| subjects affected / exposed      | 1 / 59 (1.69%)  |  |  |
| occurrences (all)                | 1               |  |  |
| Gastroenteritis norovirus        |                 |  |  |
| subjects affected / exposed      | 1 / 59 (1.69%)  |  |  |
| occurrences (all)                | 1               |  |  |
| Gastroenteritis viral            |                 |  |  |
| subjects affected / exposed      | 1 / 59 (1.69%)  |  |  |
| occurrences (all)                | 1               |  |  |

|                              |                  |  |  |
|------------------------------|------------------|--|--|
| Gastrointestinal infection   |                  |  |  |
| subjects affected / exposed  | 2 / 59 (3.39%)   |  |  |
| occurrences (all)            | 2                |  |  |
| Herpes zoster                |                  |  |  |
| subjects affected / exposed  | 2 / 59 (3.39%)   |  |  |
| occurrences (all)            | 3                |  |  |
| Human polyomavirus infection |                  |  |  |
| subjects affected / exposed  | 2 / 59 (3.39%)   |  |  |
| occurrences (all)            | 3                |  |  |
| Infection                    |                  |  |  |
| subjects affected / exposed  | 2 / 59 (3.39%)   |  |  |
| occurrences (all)            | 2                |  |  |
| Influenza                    |                  |  |  |
| subjects affected / exposed  | 3 / 59 (5.08%)   |  |  |
| occurrences (all)            | 3                |  |  |
| Laryngitis                   |                  |  |  |
| subjects affected / exposed  | 1 / 59 (1.69%)   |  |  |
| occurrences (all)            | 1                |  |  |
| Latent tuberculosis          |                  |  |  |
| subjects affected / exposed  | 1 / 59 (1.69%)   |  |  |
| occurrences (all)            | 1                |  |  |
| Lung infection               |                  |  |  |
| subjects affected / exposed  | 1 / 59 (1.69%)   |  |  |
| occurrences (all)            | 1                |  |  |
| Mucocutaneous candidiasis    |                  |  |  |
| subjects affected / exposed  | 1 / 59 (1.69%)   |  |  |
| occurrences (all)            | 1                |  |  |
| Nasopharyngitis              |                  |  |  |
| subjects affected / exposed  | 15 / 59 (25.42%) |  |  |
| occurrences (all)            | 19               |  |  |
| Oral candidiasis             |                  |  |  |
| subjects affected / exposed  | 1 / 59 (1.69%)   |  |  |
| occurrences (all)            | 1                |  |  |
| Oral herpes                  |                  |  |  |
| subjects affected / exposed  | 1 / 59 (1.69%)   |  |  |
| occurrences (all)            | 1                |  |  |

|                                     |                |  |  |
|-------------------------------------|----------------|--|--|
| Oral infection                      |                |  |  |
| subjects affected / exposed         | 1 / 59 (1.69%) |  |  |
| occurrences (all)                   | 1              |  |  |
| Otitis media                        |                |  |  |
| subjects affected / exposed         | 1 / 59 (1.69%) |  |  |
| occurrences (all)                   | 1              |  |  |
| Pharyngitis streptococcal           |                |  |  |
| subjects affected / exposed         | 1 / 59 (1.69%) |  |  |
| occurrences (all)                   | 1              |  |  |
| Pneumocystis jirovecii pneumonia    |                |  |  |
| subjects affected / exposed         | 1 / 59 (1.69%) |  |  |
| occurrences (all)                   | 2              |  |  |
| Pneumonia                           |                |  |  |
| subjects affected / exposed         | 2 / 59 (3.39%) |  |  |
| occurrences (all)                   | 2              |  |  |
| Polyomavirus-associated nephropathy |                |  |  |
| subjects affected / exposed         | 4 / 59 (6.78%) |  |  |
| occurrences (all)                   | 5              |  |  |
| Pyelonephritis                      |                |  |  |
| subjects affected / exposed         | 2 / 59 (3.39%) |  |  |
| occurrences (all)                   | 2              |  |  |
| Pyuria                              |                |  |  |
| subjects affected / exposed         | 2 / 59 (3.39%) |  |  |
| occurrences (all)                   | 2              |  |  |
| Respiratory tract infection         |                |  |  |
| subjects affected / exposed         | 2 / 59 (3.39%) |  |  |
| occurrences (all)                   | 2              |  |  |
| Rhinitis                            |                |  |  |
| subjects affected / exposed         | 1 / 59 (1.69%) |  |  |
| occurrences (all)                   | 1              |  |  |
| Sinusitis                           |                |  |  |
| subjects affected / exposed         | 1 / 59 (1.69%) |  |  |
| occurrences (all)                   | 1              |  |  |
| Skin infection                      |                |  |  |

|                                    |                  |  |  |
|------------------------------------|------------------|--|--|
| subjects affected / exposed        | 2 / 59 (3.39%)   |  |  |
| occurrences (all)                  | 3                |  |  |
| Soft tissue infection              |                  |  |  |
| subjects affected / exposed        | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                  | 1                |  |  |
| Subcutaneous abscess               |                  |  |  |
| subjects affected / exposed        | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                  | 1                |  |  |
| Tinea versicolour                  |                  |  |  |
| subjects affected / exposed        | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                  | 1                |  |  |
| Tooth infection                    |                  |  |  |
| subjects affected / exposed        | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                  | 1                |  |  |
| Tracheobronchitis                  |                  |  |  |
| subjects affected / exposed        | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                  | 1                |  |  |
| Upper respiratory tract infection  |                  |  |  |
| subjects affected / exposed        | 2 / 59 (3.39%)   |  |  |
| occurrences (all)                  | 2                |  |  |
| Urinary tract infection            |                  |  |  |
| subjects affected / exposed        | 16 / 59 (27.12%) |  |  |
| occurrences (all)                  | 19               |  |  |
| Urinary tract infection viral      |                  |  |  |
| subjects affected / exposed        | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                  | 1                |  |  |
| Viral infection                    |                  |  |  |
| subjects affected / exposed        | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                  | 1                |  |  |
| Wound infection bacterial          |                  |  |  |
| subjects affected / exposed        | 1 / 59 (1.69%)   |  |  |
| occurrences (all)                  | 1                |  |  |
| Metabolism and nutrition disorders |                  |  |  |
| Decreased appetite                 |                  |  |  |
| subjects affected / exposed        | 5 / 59 (8.47%)   |  |  |
| occurrences (all)                  | 5                |  |  |

|                             |                  |  |  |
|-----------------------------|------------------|--|--|
| Diabetes mellitus           |                  |  |  |
| subjects affected / exposed | 6 / 59 (10.17%)  |  |  |
| occurrences (all)           | 6                |  |  |
| Dyslipidaemia               |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Fluid overload              |                  |  |  |
| subjects affected / exposed | 2 / 59 (3.39%)   |  |  |
| occurrences (all)           | 2                |  |  |
| Folate deficiency           |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Hypercalcaemia              |                  |  |  |
| subjects affected / exposed | 3 / 59 (5.08%)   |  |  |
| occurrences (all)           | 3                |  |  |
| Hypercholesterolaemia       |                  |  |  |
| subjects affected / exposed | 3 / 59 (5.08%)   |  |  |
| occurrences (all)           | 3                |  |  |
| Hyperglycaemia              |                  |  |  |
| subjects affected / exposed | 11 / 59 (18.64%) |  |  |
| occurrences (all)           | 11               |  |  |
| Hyperkalaemia               |                  |  |  |
| subjects affected / exposed | 15 / 59 (25.42%) |  |  |
| occurrences (all)           | 21               |  |  |
| Hyperlipidaemia             |                  |  |  |
| subjects affected / exposed | 4 / 59 (6.78%)   |  |  |
| occurrences (all)           | 4                |  |  |
| Hyperphosphataemia          |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Hypertriglyceridaemia       |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Hyperuricaemia              |                  |  |  |
| subjects affected / exposed | 5 / 59 (8.47%)   |  |  |
| occurrences (all)           | 5                |  |  |

|                             |                  |  |  |
|-----------------------------|------------------|--|--|
| Hypervolaemia               |                  |  |  |
| subjects affected / exposed | 2 / 59 (3.39%)   |  |  |
| occurrences (all)           | 2                |  |  |
| Hypocalcaemia               |                  |  |  |
| subjects affected / exposed | 5 / 59 (8.47%)   |  |  |
| occurrences (all)           | 5                |  |  |
| Hypokalaemia                |                  |  |  |
| subjects affected / exposed | 12 / 59 (20.34%) |  |  |
| occurrences (all)           | 14               |  |  |
| Hypomagnesaemia             |                  |  |  |
| subjects affected / exposed | 5 / 59 (8.47%)   |  |  |
| occurrences (all)           | 5                |  |  |
| Hyponatraemia               |                  |  |  |
| subjects affected / exposed | 4 / 59 (6.78%)   |  |  |
| occurrences (all)           | 4                |  |  |
| Hypophosphataemia           |                  |  |  |
| subjects affected / exposed | 21 / 59 (35.59%) |  |  |
| occurrences (all)           | 22               |  |  |
| Increased appetite          |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Magnesium deficiency        |                  |  |  |
| subjects affected / exposed | 1 / 59 (1.69%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Metabolic acidosis          |                  |  |  |
| subjects affected / exposed | 3 / 59 (5.08%)   |  |  |
| occurrences (all)           | 3                |  |  |
| Vitamin D deficiency        |                  |  |  |
| subjects affected / exposed | 5 / 59 (8.47%)   |  |  |
| occurrences (all)           | 5                |  |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment  |
|-------------------|--|
| 07 July 2015      | Removal of the 3 mg/kg CFZ533 SC arm (former treatment arm 2A) and introduction of a more frequent dosing regimen during the first 2 months in the 10 mg/kg CFZ533 intravenous (IV) arm in Part 2  |
| 11 April 2016     | Introduction of a new CFZ533 presentation, a concentrate for solution for infusion/solution for injection (also referred to as liquid in vial in the protocol). Initially, CFZ533 was developed as a lyophilized powder for solution for infusion/injection requiring reconstitution with water for injection prior to infusion or injection.  |
| 20 September 2017 | Introduced by the open-label design in Part 2, to centrally evaluate all biopsies taken for suspected rejection reactions and other kidney disease related events in an unbiased, standardized and blinded manner. The decision was taken not to pursue CFZ533 exposure-response profiling (Part 3) in the scope of the present study, but to open a separate study. Therefore, Part 3 is being removed from this study protocol and the protocol is adapted accordingly including adaptation of the statistical analysis section. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported