



## Clinical trial results:

**A 24 month, multicenter, randomized, open-label safety and efficacy study of concentration-controlled everolimus with reduced calcineurin inhibitor vs mycophenolate with standard calcineurin inhibitor in de novo renal transplantation Advancing renal TRANSplant eFFicacy and safety Outcomes with an eveRolimus-based regiMen (TRANSFORM)**

### Summary

|                          |  |
|--------------------------|--|
| EudraCT number           | 2013-000322-66                                     |
| Trial protocol           | DE IT SK ES PT AT NL BE GR CZ SI BG PL HR NO SE FR |
| Global end of trial date | 17 January 2018                                    |

### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 19 October 2018 |
| First version publication date | 19 October 2018 |

### Trial information

#### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | CRAD001A2433 |
|-----------------------|--------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01950819 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

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

## Results analysis stage

|  |                 |
|--|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 17 January 2018 |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 17 January 2018 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective for this trial was to evaluate the effect of everolimus with reduced exposure CNI versus MPA with standard exposure CNI on the binary composite of treated biopsy-proven acute rejection (tBPAR) or eGFR <50 mL/min/1.73m<sup>2</sup> (estimated glomerular filtration rate by MDRD4 formula) at Month 12 post-transplantation.

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                          | 03 December 2013 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Argentina: 77      |
| Country: Number of subjects enrolled | Australia: 98      |
| Country: Number of subjects enrolled | Austria: 34        |
| Country: Number of subjects enrolled | Belgium: 56        |
| Country: Number of subjects enrolled | Brazil: 86         |
| Country: Number of subjects enrolled | Bulgaria: 12       |
| Country: Number of subjects enrolled | Chile: 8           |
| Country: Number of subjects enrolled | Colombia: 22       |
| Country: Number of subjects enrolled | Croatia: 35        |
| Country: Number of subjects enrolled | Czech Republic: 30 |
| Country: Number of subjects enrolled | Egypt: 25          |
| Country: Number of subjects enrolled | France: 85         |
| Country: Number of subjects enrolled | Germany: 168       |
| Country: Number of subjects enrolled | Greece: 24         |
| Country: Number of subjects enrolled | India: 38          |
| Country: Number of subjects enrolled | Israel: 20         |
| Country: Number of subjects enrolled | Italy: 94          |
| Country: Number of subjects enrolled | Japan: 34          |

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Korea, Republic of: 53 |
| Country: Number of subjects enrolled | Kuwait: 6              |
| Country: Number of subjects enrolled | Lebanon: 17            |
| Country: Number of subjects enrolled | Malaysia: 5            |
| Country: Number of subjects enrolled | Mexico: 2              |
| Country: Number of subjects enrolled | Netherlands: 143       |
| Country: Number of subjects enrolled | Norway: 15             |
| Country: Number of subjects enrolled | Philippines: 29        |
| Country: Number of subjects enrolled | Poland: 25             |
| Country: Number of subjects enrolled | Portugal: 19           |
| Country: Number of subjects enrolled | Russian Federation: 47 |
| Country: Number of subjects enrolled | Saudi Arabia: 21       |
| Country: Number of subjects enrolled | Serbia: 14             |
| Country: Number of subjects enrolled | Singapore: 5           |
| Country: Number of subjects enrolled | Slovakia: 35           |
| Country: Number of subjects enrolled | Slovenia: 9            |
| Country: Number of subjects enrolled | South Africa: 1        |
| Country: Number of subjects enrolled | Spain: 159             |
| Country: Number of subjects enrolled | Sweden: 38             |
| Country: Number of subjects enrolled | Switzerland: 22        |
| Country: Number of subjects enrolled | Taiwan: 23             |
| Country: Number of subjects enrolled | Thailand: 27           |
| Country: Number of subjects enrolled | Turkey: 24             |
| Country: Number of subjects enrolled | United States: 352     |
| Worldwide total number of subjects   | 2037                   |
| EEA total number of subjects         | 981                    |

Notes:

### Subjects enrolled per age group

|   |      |
|---|------|
| In utero                                  | 0    |
| Preterm newborn - gestational age < 37 wk | 0    |
| Newborns (0-27 days)                      | 0    |
| Infants and toddlers (28 days-23 months)  | 0    |
| Children (2-11 years)                     | 0    |
| Adolescents (12-17 years)                 | 0    |
| Adults (18-64 years)                      | 1731 |
| From 65 to 84 years                       | 306  |
| 85 years and over                         | 0    |

## Subject disposition

### Recruitment

Recruitment details:

The full analysis set consisted of all randomized and transplanted patients. The safety set consisted of all patients who received at least one dose of study drug

### Pre-assignment

Screening details:

2226 patients screened; 2037 patients transplanted and randomized to treatment.

### 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>             | EVR+rCNI |

Arm description:

Everolimus with reduced calcineurin inhibitor- everolimus (target trough level of 3-8 ng/mL) in combination with reduced exposure to CNI (cyclosporine or tacrolimus)

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

Dosage and administration details:

Everolimus was provided as 0.25, 0.5 and 0.75 and 1.0 mg tablets depending on locally approved dosage forms.

|                  |          |
|------------------|----------|
| <b>Arm title</b> | MPA+sCNI |
|------------------|----------|

Arm description:

Mycophenolate (mycophenolic acid sodium or mycophenolate mofetil) in combination with standard exposure to calcineurin inhibitor (cyclosporine or tacrolimus).

|  |                   |
|--|-------------------|
| Arm type                               | Active comparator |
| Investigational medicinal product name | mycophenolate     |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Capsule           |
| Routes of administration               | Oral use          |

Dosage and administration details:

MPA as either mycophenolic acid (sodium) 180 or 360mg enteric-coated tablets or mycophenolate mofetil 250 or 500 mg film coated tablets or 250mg capsules, depending on locally approved dosage forms.

| <b>Number of subjects in period 1</b> | <b>EVR+rCNI</b> | <b>MPA+sCNI</b> |
|---------------------------------------|-----------------|-----------------|
| Started                               | 1022            | 1015            |
| Completed                             | 893             | 881             |
| Not completed                         | 129             | 134             |
| Adverse event, serious fatal          | 29              | 34              |
| technical problems                    | 2               | -               |
| Graft Loss                            | 35              | 30              |
| Pregnancy                             | -               | 2               |
| Subject / Gardian decision            | 54              | 51              |
| Lost to follow-up                     | 9               | 17              |

## Baseline characteristics

### Reporting groups

|   |          |
|---|----------|
| Reporting group title   | EVR+rCNI |
| Reporting group description:  |          |
| Everolimus with reduced calcineurin inhibitor- everolimus (target trough level of 3-8 ng/mL) in combination with reduced exposure to CNI (cyclosporine or tacrolimus) |          |
| Reporting group title   | MPA+sCNI |
| Reporting group description:  |          |
| Mycophenolate (mycophenolic acid sodium or mycophenolate mofetil) in combination with standard exposure to calcineurin inhibitor (cyclosporine or tacrolimus).        |          |

| Reporting group values                             | EVR+rCNI | MPA+sCNI | Total |
|--|----------|----------|-------|
| Number of subjects                                 | 1022     | 1015     | 2037  |
| Age categorical                                    |          |          |       |
| Units: Subjects                                    |          |          |       |
| In utero   | 0        | 0        | 0     |
| Preterm newborn infants (gestational age < 37 wks) | 0        | 0        | 0     |
| Newborns (0-27 days)                               | 0        | 0        | 0     |
| Infants and toddlers (28 days-23 months)           | 0        | 0        | 0     |
| Children (2-11 years)                              | 0        | 0        | 0     |
| Adolescents (12-17 years)                          | 0        | 0        | 0     |
| Adults (18-64 years)                               | 873      | 858      | 1731  |
| From 65-84 years                                   | 149      | 157      | 306   |
| 85 years and over                                  | 0        | 0        | 0     |
| Age Continuous                                     |          |          |       |
| Units: years                                       |          |          |       |
| arithmetic mean                                    | 48.79    | 48.75    |       |
| standard deviation                                 | ± 14.123 | ± 14.515 | -     |
| Sex: Female, Male                                  |          |          |       |
| Units: Subjects                                    |          |          |       |
| Female   | 312      | 308      | 620   |
| Male   | 710      | 707      | 1417  |
| Race/Ethnicity, Customized                         |          |          |       |
| Ethnicity  |          |          |       |
| Units: Subjects                                    |          |          |       |
| Hispany or Latino                                  | 157      | 132      | 289   |
| not Hispanic or Latino                             | 646      | 661      | 1307  |
| Unknown or not reported                            | 102      | 105      | 207   |
| Other  | 117      | 117      | 234   |
| Race/Ethnicity, Customized                         |          |          |       |
| Race   |          |          |       |
| Units: Subjects                                    |          |          |       |
| Caucasian  | 743      | 735      | 1478  |
| Asian  | 136      | 157      | 293   |
| Black  | 43       | 35       | 78    |
| Other  | 100      | 88       | 188   |



## End points

### End points reporting groups

|   |          |
|---|----------|
| Reporting group title   | EVR+rCNI |
| Reporting group description:<br>Everolimus with reduced calcineurin inhibitor- everolimus (target trough level of 3-8 ng/mL) in combination with reduced exposure to CNI (cyclosporine or tacrolimus) |          |
| Reporting group title   | MPA+sCNI |
| Reporting group description:<br>Mycophenolate (mycophenolic acid sodium or mycophenolate mofetil) in combination with standard exposure to calcineurin inhibitor (cyclosporine or tacrolimus).        |          |

### Primary: Incidence of failure on the composite of treated biopsy-proven acute rejection (tBPAR) or estimated glomerular filtration rate (eGFR) < 50 mL/min/1.73m<sup>2</sup>.

|  |  |
|--|--|
| End point title  | Incidence of failure on the composite of treated biopsy-proven acute rejection (tBPAR) or estimated glomerular filtration rate (eGFR) < 50 mL/min/1.73m <sup>2</sup> . |
| End point description:<br>Incidence of failure on the composite of treated biopsy-proven acute rejection (tBPAR) or estimated glomerular filtration rate (eGFR) < 50 mL/min/1.73m <sup>2</sup> . |  |
| End point type   | Primary  |
| End point timeframe:<br>Month 12 is Primary, Month 24 secondary  |  |

| End point values            | EVR+rCNI        | MPA+sCNI        |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1022            | 1015            |  |  |
| Units: participants         |                 |                 |  |  |
| month 12                    | 489             | 456             |  |  |
| month 24                    | 489             | 443             |  |  |

### Statistical analyses

|   |                               |
|---|-------------------------------|
| Statistical analysis title                                  | Difference between treatments |
| Statistical analysis description:<br>calculated at month 12 |                               |
| Comparison groups   | EVR+rCNI v MPA+sCNI           |
| Number of subjects included in analysis                     | 2037                          |
| Analysis specification                                      | Pre-specified                 |
| Analysis type   |                               |
| P-value   | = 0.001                       |
| Method  | Logistic Regression Model     |
| Parameter estimate  | Odds ratio (OR)               |
| Point estimate  | 3                             |



|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -1.4    |
| upper limit         | 7.3     |

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**Secondary: Incidence of failure on the composite of (treated biopsy proven acute rejection (tBPAR), graft loss or death**

|  |  |
|--|--|
| End point title  | Incidence of failure on the composite of (treated biopsy proven acute rejection (tBPAR), graft loss or death |
| End point description:<br>Incidence of failure on the composite of (treated biopsy proven acute rejection (tBPAR), graft loss or death |  |
| End point type   | Secondary  |
| End point timeframe:<br>Month 12 and 24  |  |

| End point values            | EVR+rCNI        | MPA+sCNI        |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1022            | 1015            |  |  |
| Units: participants         |                 |                 |  |  |
| month 12                    | 146             | 131             |  |  |
| month 24                    | 169             | 147             |  |  |

**Statistical analyses**

No statistical analyses for this end point

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**Secondary: Incidence of failure on the composite endpoint of tBPAR, graft loss, death or eGFR < 50 mL/min/1.73m<sup>2</sup>**

|   |   |
|---|---|
| End point title   | Incidence of failure on the composite endpoint of tBPAR, graft loss, death or eGFR < 50 mL/min/1.73m <sup>2</sup> |
| End point description:<br>Incidence of failure on the composite endpoint of tBPAR, graft loss, death or eGFR < 50 mL/min/1.73m <sup>2</sup> |   |
| End point type  | Secondary   |
| End point timeframe:<br>Month 12 and 24   |   |

| End point values            | EVR+rCNI        | MPA+sCNI        |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1022            | 1015            |  |  |
| Units: participants         |                 |                 |  |  |
| month 12                    | 497             | 466             |  |  |
| month 24                    | 497             | 457             |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Incidence of failure on the composite endpoint of graft loss or death.

|                        |  |
|------------------------|--|
| End point title        | Incidence of failure on the composite endpoint of graft loss or death. |
| End point description: | Incidence of failure on the composite endpoint of graft loss or death. |
| End point type         | Secondary  |
| End point timeframe:   | Month 12 and 24  |

| End point values            | EVR+rCNI        | MPA+sCNI        |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1022            | 1015            |  |  |
| Units: participants         |                 |                 |  |  |
| month 12                    | 51              | 54              |  |  |
| month 24                    | 67              | 65              |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Incidence of death, graft loss, tBPAR, BPAR, tAR, AR and humoral rejection

|                        |  |
|------------------------|--|
| End point title        | Incidence of death, graft loss, tBPAR, BPAR, tAR, AR and humoral rejection   |
| End point description: | Incidence of death, graft loss, tBPAR (treated biopsy proven acute rejection), BPAR (biopsy proven acute rejection), tAR (treated acute rejection), AR (acute rejection) and humoral rejection (aAMR : active antibody mediated rejection and cAMR: chronic antibody mediated rejection) |
| End point type         | Secondary  |
| End point timeframe:   | Month 12 and 24  |

| <b>End point values</b>     | EVR+rCNI        | MPA+sCNI        |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1022            | 1015            |  |  |
| Units: participants         |                 |                 |  |  |
| deaths month 12             | 20              | 28              |  |  |
| deaths month 24             | 32              | 36              |  |  |
| graft loss month 12         | 33              | 28              |  |  |
| graft loss month 24         | 37              | 32              |  |  |
| tBPAR month 12              | 107             | 91              |  |  |
| tBPAR month 24              | 118             | 98              |  |  |
| BPAR month 12               | 114             | 95              |  |  |
| BPAR month 24               | 127             | 104             |  |  |
| tAR month 12                | 129             | 117             |  |  |
| tAR month 24                | 145             | 126             |  |  |
| AR month 12                 | 147             | 133             |  |  |
| AR month 24                 | 167             | 144             |  |  |
| aAMR month 12               | 73              | 61              |  |  |
| aAMR month 24               | 84              | 69              |  |  |
| cAMR month 12               | 9               | 14              |  |  |
| cAMR month 24               | 13              | 18              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Incidence of eGFR < 50 mL/min/1.73m<sup>2</sup>

|                        |  |
|------------------------|--|
| End point title        | Incidence of eGFR < 50 mL/min/1.73m <sup>2</sup> |
| End point description: | Incidence of eGFR < 50 mL/min/1.73m <sup>2</sup> |
| End point type         | Secondary  |
| End point timeframe:   | Month 12 and 24                                  |

| <b>End point values</b>     | EVR+rCNI        | MPA+sCNI        |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1022            | 1015            |  |  |
| Units: participants         |                 |                 |  |  |
| month 12                    | 456             | 424             |  |  |
| month 24                    | 474             | 423             |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Renal allograft function (mean estimated glomerular filtration rate, eGFR)

|                 |  |
|-----------------|--|
| End point title | Renal allograft function (mean estimated glomerular filtration rate, eGFR) |
|-----------------|--|

End point description:

Renal allograft function (mean estimated glomerular filtration rate, eGFR)

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

End point timeframe:

Month 12 and 24

| End point values                 | EVR+rCNI        | MPA+sCNI        |  |  |
|----------------------------------|-----------------|-----------------|--|--|
| Subject group type               | Reporting group | Reporting group |  |  |
| Number of subjects analysed      | 1022            | 1015            |  |  |
| Units: mL/min/1.73m <sup>2</sup> |                 |                 |  |  |
| arithmetic mean (standard error) |                 |                 |  |  |
| baseline (week 4)                | 53.13 (± 0.765) | 52.25 (± 0.684) |  |  |
| month 12                         | 53.29 (± 0.698) | 54.49 (± 0.667) |  |  |
| month 24                         | 52.63 (± 0.744) | 54.91 (± 0.719) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Evolution of renal function, as eGFR, over time by slope analysis.

|                 |  |
|-----------------|--|
| End point title | Evolution of renal function, as eGFR, over time by slope analysis. |
|-----------------|--|

End point description:

Rate of change of renal function, as eGFR, over time by slope analysis.

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

End point timeframe:

Month 12 and 24

| End point values                 | EVR+rCNI          | MPA+sCNI          |  |  |
|----------------------------------|-------------------|-------------------|--|--|
| Subject group type               | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed      | 1022              | 1015              |  |  |
| Units: mL/min/1.73m <sup>2</sup> |                   |                   |  |  |
| arithmetic mean (standard error) |                   |                   |  |  |
| slope of eGFR                    | 0.0001 (± 0.0008) | 0.0047 (± 0.0008) |  |  |
| eGFR at month 12                 | 55.32 (± 0.68)    | 57.44 (± 0.67)    |  |  |
| eGFR at month 24                 | 55.43 (± 0.60)    | 57.28 (± 0.60)    |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Renal function by Cystatin C-based and other alternate formulae (e.g. CKD-EPI).

|   |   |
|---|---|
| End point title   | Renal function by Cystatin C-based and other alternate formulae (e.g. CKD-EPI). |
| End point description:  |   |
| Mean Renal function by eGFR or creatinine clearance Cystatin C-based and other alternate formulae (e.g. CKD-EPI). Analysis is done without considering missing values for analysis. |   |
| End point type  | Secondary   |
| End point timeframe:  |   |
| Month 12 and 24   |   |

| End point values                                   | EVR+rCNI         | MPA+sCNI         |  |  |
|--|------------------|------------------|--|--|
| Subject group type                                 | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed                        | 1022             | 1015             |  |  |
| Units: micromol/L; mL/min/1.73m <sup>2</sup>       |                  |                  |  |  |
| arithmetic mean (standard deviation)               |                  |                  |  |  |
| screening baseline (creatinine, micromol/L)        | 590.1 (± 262.78) | 601.8 (± 265.08) |  |  |
| month 12 (creatinine, micromol/L)                  | 129.8 (± 49.12)  | 128.6 (± 50.80)  |  |  |
| month 24 (creatinine, micromol/L)                  | 130.1 (± 53.54)  | 127.6 (± 52.50)  |  |  |
| eGFR (Hoek) baseline (mL/min/1.73m <sup>2</sup> )  | 21.38 (± 14.296) | 20.10 (± 12.408) |  |  |
| eGFR (Hoek) month 12 (mL/min/1.73m <sup>2</sup> )  | 50.08 (± 14.430) | 52.00 (± 14.533) |  |  |
| eGFR (Hoek) month 24 (mL/min/1.73m <sup>2</sup> )  | 49.86 (± 14.604) | 52.75 (± 15.406) |  |  |
| eGFR (MDRD4) baseline (mL/min/1.73m <sup>2</sup> ) | 11.79 (± 8.697)  | 11.56 (± 8.853)  |  |  |
| eGFR (MDRD4) month 12 (mL/min/1.73m <sup>2</sup> ) | 57.59 (± 19.685) | 57.58 (± 18.768) |  |  |

|  |                     |                     |  |  |
|--|---------------------|---------------------|--|--|
| eGFR (MDRD4) month 24<br>(mL/min/1.73m2) | 58.07 (±<br>20.168) | 58.68 (±<br>19.541) |  |  |
| eGFR-CKDEPI baseline<br>(mL/min/1.73m2)  | 11.29 (±<br>9.094)  | 11.05 (±<br>9.195)  |  |  |
| eGFR-CKDEPI month<br>12(mL/min/1.73m2)   | 58.83 (±<br>20.686) | 58.75 (±<br>19.757) |  |  |
| eGFR-CKDEPI month 24<br>(mL/min/1.73m2)  | 59.39 (±<br>21.077) | 59.95 (±<br>20.652) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Incidence of adverse events, serious adverse events and adverse events leading to study regimen discontinuation.

|                        |  |
|------------------------|--|
| End point title        | Incidence of adverse events, serious adverse events and adverse events leading to study regimen discontinuation. |
| End point description: | Incidence of adverse events, serious adverse events and adverse events leading to study regimen discontinuation. |
| End point type         | Secondary  |
| End point timeframe:   | Month 24   |

| End point values            | EVR+rCNI        | MPA+sCNI        |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1014            | 1012            |  |  |
| Units: participants         | 276             | 152             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Incidence of cytomegalovirus and BK virus, new onset diabetes mellitus, chronic kidney disease with associated proteinuria and calcineurin inhibitor associated adverse events.

|                        |   |
|------------------------|---|
| End point title        | Incidence of cytomegalovirus and BK virus, new onset diabetes mellitus, chronic kidney disease with associated proteinuria and calcineurin inhibitor associated adverse events. |
| End point description: | Incidence of cytomegalovirus and BK virus, new onset diabetes mellitus, chronic kidney disease with associated proteinuria and calcineurin inhibitor associated adverse events. |
| End point type         | Secondary   |
| End point timeframe:   | Month 24  |

| End point values                | EVR+rCNI        | MPA+sCNI        |  |  |
|---------------------------------|-----------------|-----------------|--|--|
| Subject group type              | Reporting group | Reporting group |  |  |
| Number of subjects analysed     | 1014            | 1012            |  |  |
| Units: participants             |                 |                 |  |  |
| clinical signs of CMV infection | 53              | 132             |  |  |
| any BKV infection               | 103             | 154             |  |  |
| new onset of diabetes mellitus  | 144             | 138             |  |  |
| at least one event of interest  | 871             | 764             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Urinary protein and albumin excretion by treatment estimated by urinary protein/creatinine and urinary albumin/creatinine ratios.

|                 |   |
|-----------------|---|
| End point title | Urinary protein and albumin excretion by treatment estimated by urinary protein/creatinine and urinary albumin/creatinine ratios. |
|-----------------|---|

End point description:

Mean urinary protein and albumin excretion by treatment estimated by mean urinary protein/creatinine and urinary albumin/creatinine ratios.

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

End point timeframe:

Month 12 and 24

| End point values                     | EVR+rCNI            | MPA+sCNI            |  |  |
|--------------------------------------|---------------------|---------------------|--|--|
| Subject group type                   | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed          | 1014                | 1012                |  |  |
| Units: mg/g                          |                     |                     |  |  |
| arithmetic mean (standard deviation) |                     |                     |  |  |
| albumine /creatinine ratio baseline  | 1019.75 (± 2737.96) | 646.111 (± 799.234) |  |  |
| albumine /creatinine ratio month 12  | 150.061 (± 482.394) | 111.322 (± 444.631) |  |  |
| albumine /creatinine ratio month 24  | 149.049 (± 464.470) | 116.618 (± 433.392) |  |  |
| protein /creatinine ratio baseline   | 1648.10 (± 3768.22) | 1142.59 (± 1003.69) |  |  |
| protein /creatinine ratio month 12   | 298.557 (± 642.103) | 234.698 (± 583.632) |  |  |
| protein /creatinine ratio month 24   | 290.242 (± 588.119) | 233.009 (± 524.383) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Incidence of major cardiovascular events.

|                 |   |
|-----------------|---|
| End point title | Incidence of major cardiovascular events. |
|-----------------|---|

End point description:

Incidence of major cardiovascular events by Preferred Term

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

End point timeframe:

Month 24

| End point values            | EVR+rCNI        | MPA+sCNI        |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1014            | 1012            |  |  |
| Units: participants         | 66              | 86              |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Incidence of malignancies.

|                 |                            |
|-----------------|----------------------------|
| End point title | Incidence of malignancies. |
|-----------------|----------------------------|

End point description:

Incidence of malignancies.

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

End point timeframe:

Month 24

| End point values            | EVR+rCNI        | MPA+sCNI        |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1014            | 1012            |  |  |
| Units: participants         | 41              | 39              |  |  |



## Statistical analyses

No statistical analyses for this end point

### Secondary: Incidence of failure on the composite of treated biopsy-proven acute rejection (tBPAR) or estimated glomerular filtration rate (eGFR) < 50 mL/min/1.73m<sup>2</sup> among compliant subjects.

|                 |  |
|-----------------|--|
| End point title | Incidence of failure on the composite of treated biopsy-proven acute rejection (tBPAR) or estimated glomerular filtration rate (eGFR) < 50 mL/min/1.73m <sup>2</sup> among compliant subjects. |
|-----------------|--|

End point description:

Incidence of failure on the composite of treated biopsy-proven acute rejection (tBPAR) or estimated glomerular filtration rate (eGFR) < 50 mL/min/1.73m<sup>2</sup> among compliant subjects.

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

End point timeframe:

Month 12 and 24

| End point values            | EVR+rCNI        | MPA+sCNI        |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 187             | 277             |  |  |
| Units: participants         |                 |                 |  |  |
| month 12                    | 60              | 106             |  |  |
| month 24                    | 62              | 102             |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Incidence tBPAR by severity and time to event

|                 |   |
|-----------------|---|
| End point title | Incidence tBPAR by severity and time to event |
|-----------------|---|

End point description:

Incidence tBPAR by severity and time to event

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

End point timeframe:

Month 12 and 24

| End point values                  | EVR+rCNI        | MPA+sCNI        |  |  |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type                | Reporting group | Reporting group |  |  |
| Number of subjects analysed       | 1022            | 1015            |  |  |
| Units: participants               |                 |                 |  |  |
| no grade (missing)                | 25              | 18              |  |  |
| Patient's maximum tBPAR grade IA  | 34              | 36              |  |  |
| Patient's maximum tBPAR grade IB  | 23              | 17              |  |  |
| Patient's maximum tBPAR grade IIA | 21              | 24              |  |  |

|  |     |     |  |  |
|--|-----|-----|--|--|
| Patient's maximum tBPAR grade IIB                | 9   | 3   |  |  |
| Patient's maximum tBPAR grade III                | 6   | 0   |  |  |
| overall number of tBPAR regardless of grade      | 146 | 116 |  |  |
| number of tBPAR regardless of grade days 1-90    | 72  | 63  |  |  |
| number of tBPAR regardless of grade days 91-180  | 24  | 14  |  |  |
| number of tBPAR regardless of grade days 181-360 | 25  | 20  |  |  |
| number of tBPAR regardless of grade days 361-540 | 12  | 15  |  |  |
| number of tBPAR regardless of grade days 541-720 | 11  | 2   |  |  |
| number of tBPAR regardless of grade days 721-810 | 2   | 2   |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Incidence of tBPAR excluding grade IA rejections

|                        |  |
|------------------------|--|
| End point title        | Incidence of tBPAR excluding grade IA rejections |
| End point description: | Incidence of tBPAR excluding grade IA rejections |
| End point type         | Secondary  |
| End point timeframe:   | Month 12 and 24                                  |

| End point values            | EVR+rCNI        | MPA+sCNI        |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1022            | 1015            |  |  |
| Units: participants         |                 |                 |  |  |
| month 12                    | 66              | 53              |  |  |
| month 24                    | 74              | 55              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Incidence of composite of tBPAR or eGFR<50 mL/min/1.73m2 by subgroup

|                        |  |
|------------------------|--|
| End point title        | Incidence of composite of tBPAR or eGFR<50 mL/min/1.73m2 by subgroup |
| End point description: | Incidence of composite of tBPAR or eGFR<50 mL/min/1.73m2 by subgroup |

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Month 12 and 24      |           |

| End point values            | EVR+rCNI        | MPA+sCNI        |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1022            | 1015            |  |  |
| Units: participants         |                 |                 |  |  |
| month 12                    | 489             | 456             |  |  |
| month 24                    | 489             | 443             |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Incidence of tBPAR (excluding grade IA rejections) or GFR<50 mL/min/1.73m2

|  |  |
|--|--|
| End point title  | Incidence of tBPAR (excluding grade IA rejections) or GFR<50 mL/min/1.73m2 |
| End point description:   |  |
| Incidence of tBPAR (excluding grade IA rejections) or GFR<50 mL/min/1.73m2 |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| Month 12 and 24  |  |

| End point values            | EVR+rCNI        | MPA+sCNI        |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1022            | 1015            |  |  |
| Units: participants         |                 |                 |  |  |
| month 12                    | 475             | 441             |  |  |
| month 24                    | 475             | 426             |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Incidence of failure on the composite of (treated biopsy proven acute rejection (tBPAR), graft loss or death or loss to follow-up

|                 |   |
|-----------------|---|
| End point title | Incidence of failure on the composite of (treated biopsy proven acute rejection (tBPAR), graft loss or death or loss to follow-up |
|-----------------|---|

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End point description:

Incidence of failure on the composite of (treated biopsy proven acute rejection (tBPAR), graft loss or death or loss to follow-up

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

---

End point timeframe:

Month 12 and 24

---

| End point values            | EVR+rCNI        | MPA+sCNI        |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1022            | 1015            |  |  |
| Units: participants         |                 |                 |  |  |
| month 12                    | 181             | 170             |  |  |
| month 24                    | 218             | 201             |  |  |

### Statistical analyses

---

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Timeframe for AE

Adverse event reporting additional description:

AE additional description

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

### Reporting groups

|                       |                       |
|-----------------------|-----------------------|
| Reporting group title | MPA plus standard@CNI |
|-----------------------|-----------------------|

Reporting group description:

MPA plus standard@CNI

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | Everolimus plus@reduced CNI |
|-----------------------|-----------------------------|

Reporting group description:

Everolimus plus@reduced CNI

| Serious adverse events  | MPA plus<br>standard@CNI | Everolimus<br>plus@reduced CNI |  |
|---|--------------------------|--------------------------------|--|
| Total subjects affected by serious adverse events                   |                          |                                |  |
| subjects affected / exposed   | 613 / 1012<br>(60.57%)   | 593 / 1014<br>(58.48%)         |  |
| number of deaths (all causes)                                       | 29                       | 20                             |  |
| number of deaths resulting from adverse events                      | 0                        | 0                              |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                          |                                |  |
| Adenocarcinoma gastric  |                          |                                |  |
| subjects affected / exposed   | 0 / 1012 (0.00%)         | 1 / 1014 (0.10%)               |  |
| occurrences causally related to treatment / all                     | 0 / 0                    | 0 / 1                          |  |
| deaths causally related to treatment / all                          | 0 / 0                    | 0 / 1                          |  |
| Adenocarcinoma pancreas   |                          |                                |  |
| subjects affected / exposed   | 1 / 1012 (0.10%)         | 0 / 1014 (0.00%)               |  |
| occurrences causally related to treatment / all                     | 0 / 1                    | 0 / 0                          |  |
| deaths causally related to treatment / all                          | 0 / 0                    | 0 / 0                          |  |
| Basal cell carcinoma  |                          |                                |  |
| subjects affected / exposed   | 4 / 1012 (0.40%)         | 10 / 1014 (0.99%)              |  |
| occurrences causally related to treatment / all                     | 4 / 5                    | 8 / 11                         |  |
| deaths causally related to treatment / all                          | 0 / 0                    | 0 / 0                          |  |
| Benign gastrointestinal neoplasm                                    |                          |                                |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Benign neoplasm of thyroid gland                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Benign pancreatic neoplasm                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder cancer                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 2 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bowen's disease                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Brain neoplasm                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Breast cancer                                   |                  |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bronchioloalveolar carcinoma                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Cerebral haemangioma                            |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Clear cell renal cell carcinoma                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Epstein-Barr virus associated lymphoma          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Gastric cancer                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Leydig cell tumour of the testis                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lipoma  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lung adenocarcinoma                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lymphoproliferative disorder                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Malignant melanoma                              |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 4 / 1014 (0.39%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 4 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Malignant neoplasm of pleura metastatic         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Metastases to bone                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metastases to lymph nodes                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metastases to peritoneum                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Metastases to spine                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metastatic squamous cell carcinoma              |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Monoclonal gammopathy                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neoplasm malignant                              |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Non-small cell lung cancer                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oesophageal adenocarcinoma                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Papillary tumour of renal pelvis                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Plasmacytoma                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Polycythaemia vera                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post transplant lymphoproliferative disorder    |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 2 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| Prostate cancer                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 3 / 1014 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal cancer                                    |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Renal cell carcinoma                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Salivary gland cancer                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Skin cancer                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Squamous cell carcinoma                         |                  |                  |  |
| subjects affected / exposed                     | 4 / 1012 (0.40%) | 8 / 1014 (0.79%) |  |
| occurrences causally related to treatment / all | 5 / 5            | 5 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Squamous cell carcinoma of skin                 |                  |                  |  |
| subjects affected / exposed                     | 5 / 1012 (0.49%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 4 / 5            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Testicular neoplasm                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tumour of ampulla of Vater                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Uterine leiomyoma                               |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular disorders                              |                  |                  |  |
| Accelerated hypertension                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aortic aneurysm                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aortic perforation                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arterial stenosis                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arterial thrombosis                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arteriovenous fistula                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Artery dissection                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Deep vein thrombosis                            |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 12 / 1012 (1.19%) | 20 / 1014 (1.97%) |  |
| occurrences causally related to treatment / all | 2 / 14            | 9 / 21            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Embolism venous                                 |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Haematoma                                       |                   |                   |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hypertension                                    |                   |                   |  |
| subjects affected / exposed                     | 6 / 1012 (0.59%)  | 2 / 1014 (0.20%)  |  |
| occurrences causally related to treatment / all | 0 / 6             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hypertensive crisis                             |                   |                   |  |
| subjects affected / exposed                     | 5 / 1012 (0.49%)  | 3 / 1014 (0.30%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hypertensive emergency                          |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hypotension                                     |                   |                   |  |
| subjects affected / exposed                     | 8 / 1012 (0.79%)  | 3 / 1014 (0.30%)  |  |
| occurrences causally related to treatment / all | 1 / 8             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Intermittent claudication                       |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Lymphocele                                      |                   |                   |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 21 / 1012 (2.08%) | 34 / 1014 (3.35%) |  |
| occurrences causally related to treatment / all | 4 / 22            | 18 / 36           |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Lymphorrhoea                                    |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 3 / 1014 (0.30%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 2 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Malignant hypertension                          |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Orthostatic hypotension                         |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pelvic venous thrombosis                        |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Peripheral arterial occlusive disease           |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Peripheral artery stenosis                      |                   |                   |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Peripheral artery thrombosis                    |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 2 / 1014 (0.20%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Peripheral ischaemia                            |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Phlebitis                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Shock haemorrhagic                              |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thrombophlebitis superficial                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thrombosis                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Varicose ulceration                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Venous stenosis                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Venous thrombosis                               |                  |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Venous thrombosis limb                          |                  |                  |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| subjects affected / exposed                          | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Surgical and medical procedures                      |                  |                  |  |
| Arteriovenous fistula operation                      |                  |                  |  |
| subjects affected / exposed                          | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Orchidectomy   |                  |                  |  |
| subjects affected / exposed                          | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Pregnancy, puerperium and perinatal conditions       |                  |                  |  |
| Cephalhaematoma                                      |                  |                  |  |
| subjects affected / exposed                          | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| General disorders and administration site conditions |                  |                  |  |
| Asthenia   |                  |                  |  |
| subjects affected / exposed                          | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Catheter site haemorrhage                            |                  |                  |  |
| subjects affected / exposed                          | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Chest discomfort                                     |                  |                  |  |
| subjects affected / exposed                          | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Chest pain   |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chills  |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Death   |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| Fatigue   |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gait inability                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| General physical health deterioration           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Generalised oedema                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyperthermia                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypothermia                                     |                  |                  |  |



|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Ill-defined disorder                            |                  |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Impaired healing                                |                  |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 10 / 1014 (0.99%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 10 / 11           |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Malaise   |                  |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Medical device site discomfort                  |                  |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Medical device site inflammation                |                  |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Microlithiasis                                  |                  |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Multiple organ dysfunction syndrome             |                  |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Non-cardiac chest pain                          |                  |                   |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 2 / 1012 (0.20%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 1 / 3             | 1 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Oedema peripheral                               |                   |                   |  |
| subjects affected / exposed                     | 4 / 1012 (0.40%)  | 7 / 1014 (0.69%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 5 / 8             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pain  |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Peripheral swelling                             |                   |                   |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pyrexia   |                   |                   |  |
| subjects affected / exposed                     | 36 / 1012 (3.56%) | 35 / 1014 (3.45%) |  |
| occurrences causally related to treatment / all | 13 / 40           | 16 / 45           |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Sudden death                                    |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Suprapubic pain                                 |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Swelling  |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Systemic inflammatory response syndrome         |                   |                   |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 2 / 1012 (0.20%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 1 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Immune system disorders                         |                   |                   |  |
| Anaphylactic reaction                           |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Chronic allograft nephropathy                   |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hypersensitivity                                |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Immunosuppression                               |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Kidney transplant rejection                     |                   |                   |  |
| subjects affected / exposed                     | 17 / 1012 (1.68%) | 18 / 1014 (1.78%) |  |
| occurrences causally related to treatment / all | 9 / 19            | 8 / 20            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Renal transplant failure                        |                   |                   |  |
| subjects affected / exposed                     | 5 / 1012 (0.49%)  | 4 / 1014 (0.39%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 1 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Transplant rejection                            |                   |                   |  |
| subjects affected / exposed                     | 25 / 1012 (2.47%) | 45 / 1014 (4.44%) |  |
| occurrences causally related to treatment / all | 7 / 27            | 16 / 49           |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Social circumstances                            |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| Loss of personal independence in daily activities |                  |                  |  |
| subjects affected / exposed                       | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all   | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0            |  |
| Walking disability                                |                  |                  |  |
| subjects affected / exposed                       | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all   | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0            |  |
| Reproductive system and breast disorders          |                  |                  |  |
| Acquired hydrocele                                |                  |                  |  |
| subjects affected / exposed                       | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0            |  |
| Benign prostatic hyperplasia                      |                  |                  |  |
| subjects affected / exposed                       | 3 / 1012 (0.30%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all   | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0            |  |
| Cervical dysplasia                                |                  |                  |  |
| subjects affected / exposed                       | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all   | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0            |  |
| Endometriosis                                     |                  |                  |  |
| subjects affected / exposed                       | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all   | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0            |  |
| Erectile dysfunction                              |                  |                  |  |
| subjects affected / exposed                       | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all   | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0            |  |
| Menorrhagia                                       |                  |                  |  |
| subjects affected / exposed                       | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all   | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0            |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| Ovarian cyst ruptured                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Prostatitis                                     |                  |                  |  |
| subjects affected / exposed                     | 4 / 1012 (0.40%) | 3 / 1014 (0.30%) |  |
| occurrences causally related to treatment / all | 3 / 4            | 1 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Scrotal oedema                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Testicular oedema                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Respiratory, thoracic and mediastinal disorders |                  |                  |  |
| Acute pulmonary oedema                          |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Acute respiratory failure                       |                  |                  |  |
| subjects affected / exposed                     | 4 / 1012 (0.40%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 1 / 5            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Asthma  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Asthmatic crisis                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| Bronchospasm                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cough   |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 2 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dyspnoea  |                  |                  |  |
| subjects affected / exposed                     | 7 / 1012 (0.69%) | 8 / 1014 (0.79%) |  |
| occurrences causally related to treatment / all | 1 / 8            | 3 / 10           |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dyspnoea exertional                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Epistaxis                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemoptysis                                     |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyperventilation                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoxia   |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Interstitial lung disease                       |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lung disorder                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lung infiltration                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pleural effusion                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pleurisy  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pleuritic pain                                  |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia aspiration                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonitis                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 4 / 1014 (0.39%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 3 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Productive cough                                |                  |                  |  |

|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pulmonary artery thrombosis                     |                  |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pulmonary congestion                            |                  |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pulmonary embolism                              |                  |                   |  |
| subjects affected / exposed                     | 6 / 1012 (0.59%) | 17 / 1014 (1.68%) |  |
| occurrences causally related to treatment / all | 1 / 6            | 6 / 17            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1             |  |
| Pulmonary hypertension                          |                  |                   |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pulmonary mass                                  |                  |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pulmonary oedema                                |                  |                   |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 3 / 1014 (0.30%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 1 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Respiratory failure                             |                  |                   |  |
| subjects affected / exposed                     | 4 / 1012 (0.40%) | 3 / 1014 (0.30%)  |  |
| occurrences causally related to treatment / all | 0 / 4            | 2 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Psychiatric disorders                           |                  |                   |  |
| Acute psychosis                                 |                  |                   |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aggression                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anxiety   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Depression                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hallucination, visual                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mental disorder                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mental status changes                           |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post-traumatic stress disorder                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Psychotic disorder                              |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Suicide attempt                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Product issues                                  |                  |                  |  |
| Device dislocation                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Device leakage                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Device malfunction                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatobiliary disorders                         |                  |                  |  |
| Bile duct stone                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Biliary colic                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Biliary dilatation                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cholangitis                                     |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cholecystitis                                   |                  |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cholecystitis acute                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cholelithiasis                                  |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cholestasis                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatocellular injury                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Perforation bile duct                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Investigations                                  |                  |                  |  |
| Alanine aminotransferase increased              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anticoagulation drug level above therapeutic    |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Aspartate aminotransferase increased            |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Biopsy kidney                                   |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood creatine increased                        |                   |                   |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%)  | 2 / 1014 (0.20%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 1 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood creatinine abnormal                       |                   |                   |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 1 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood creatinine increased                      |                   |                   |  |
| subjects affected / exposed                     | 36 / 1012 (3.56%) | 50 / 1014 (4.93%) |  |
| occurrences causally related to treatment / all | 6 / 44            | 18 / 63           |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood glucose increased                         |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood phosphorus decreased                      |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood urea increased                            |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| C-reactive protein increased                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Catheterisation cardiac                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ejection fraction abnormal                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Electrocardiogram T wave inversion              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemoglobin decreased                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haptoglobin decreased                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Immunosuppressant drug level increased          |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Inflammatory marker increased                   |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Liver function test increased                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Norovirus test positive                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Occult blood positive                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Polyomavirus test positive                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Transaminases increased                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Troponin increased                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urine output decreased                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 3 / 1014 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Weight decreased                                |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Injury, poisoning and procedural complications  |                  |                  |  |
| Accidental overdose                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anaemia postoperative                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anaesthetic complication                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anastomotic haemorrhage                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ankle fracture                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aponeurosis contusion                           |                  |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arterial injury                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arteriovenous fistula aneurysm                  |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 3 / 1012 (0.30%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Arteriovenous fistula site complication         |                   |                   |  |
| subjects affected / exposed                     | 4 / 1012 (0.40%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Arteriovenous fistula thrombosis                |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 2 / 1014 (0.20%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Avulsion fracture                               |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Complications of transplant surgery             |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Complications of transplanted kidney            |                   |                   |  |
| subjects affected / exposed                     | 28 / 1012 (2.77%) | 34 / 1014 (3.35%) |  |
| occurrences causally related to treatment / all | 3 / 32            | 9 / 41            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Contusion                                       |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Coronary bypass stenosis                        |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Delayed graft function                          |                   |                   |  |



|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 2 / 1012 (0.20%)  | 7 / 1014 (0.69%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 1 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Fall  |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Femoral neck fracture                           |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 2 / 1014 (0.20%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Femur fracture                                  |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 2 / 1014 (0.20%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Forearm fracture                                |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Graft complication                              |                   |                   |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%)  | 2 / 1014 (0.20%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Graft haemorrhage                               |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Graft loss                                      |                   |                   |  |
| subjects affected / exposed                     | 12 / 1012 (1.19%) | 16 / 1014 (1.58%) |  |
| occurrences causally related to treatment / all | 2 / 12            | 3 / 16            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Graft thrombosis                                |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Humerus fracture                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Incision site complication                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Incisional hernia                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 8 / 1014 (0.79%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 2 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Injury  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Joint dislocation                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Laceration                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Limb injury                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lower limb fracture                             |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lumbar vertebral fracture                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Muscle strain                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Musculoskeletal injury                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Overdose  |                  |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pelvic fracture                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peripheral arterial reocclusion                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Perirenal haematoma                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post procedural complication                    |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 3 / 1014 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post procedural discharge                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post procedural haematoma                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 3 / 1014 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 2 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post procedural haematuria                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post procedural haemorrhage                     |                  |                  |  |
| subjects affected / exposed                     | 4 / 1012 (0.40%) | 4 / 1014 (0.39%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post procedural persistent drain fluid          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post procedural urine leak                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Postoperative fever                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Postoperative hernia                            |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Procedural haemorrhage                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Radius fracture                                 |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal lymphocele                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 3 / 1014 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal transplant torsion                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rib fracture                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Scar  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Scrotal haematoma                               |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Seroma  |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 5 / 1014 (0.49%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 2 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Shunt aneurysm                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Shunt stenosis                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal fracture                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Stress fracture                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Subarachnoid haemorrhage                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Subcutaneous haematoma                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tendon rupture                                  |                  |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tibia fracture                                  |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Toxicity to various agents                      |                  |                  |  |
| subjects affected / exposed                     | 4 / 1012 (0.40%) | 5 / 1014 (0.49%) |  |
| occurrences causally related to treatment / all | 3 / 4            | 2 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Transplant dysfunction                          |                  |                  |  |
| subjects affected / exposed                     | 7 / 1012 (0.69%) | 7 / 1014 (0.69%) |  |
| occurrences causally related to treatment / all | 2 / 8            | 2 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Transplant failure                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Transplantation complication                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 5 / 1014 (0.49%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Traumatic fracture                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ulna fracture                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Upper limb fracture                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ureteric anastomosis complication               |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urinary anastomotic leak                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vaccination complication                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular graft complication                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular graft stenosis                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular graft thrombosis                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular pseudoaneurysm                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Wound decomposition                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Wound dehiscence                                |                  |                  |  |



|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 10 / 1014 (0.99%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 7 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Wound secretion                                 |                  |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Wrist fracture                                  |                  |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Congenital, familial and genetic disorders      |                  |                   |  |
| Arteriovenous malformation                      |                  |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Congenital cystic kidney disease                |                  |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Congenital megaureter                           |                  |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Hydrocele                                       |                  |                   |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Tracheo-oesophageal fistula                     |                  |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Cardiac disorders                               |                  |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| Acute coronary syndrome                         |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 4 / 1014 (0.39%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Acute myocardial infarction                     |                  |                  |  |
| subjects affected / exposed                     | 6 / 1012 (0.59%) | 6 / 1014 (0.59%) |  |
| occurrences causally related to treatment / all | 1 / 6            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Angina pectoris                                 |                  |                  |  |
| subjects affected / exposed                     | 5 / 1012 (0.49%) | 6 / 1014 (0.59%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Angina unstable                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aortic valve stenosis                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arrhythmia                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arrhythmia supraventricular                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arteriosclerosis coronary artery                |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Atrial fibrillation                             |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 12 / 1012 (1.19%) | 12 / 1014 (1.18%) |  |
| occurrences causally related to treatment / all | 2 / 15            | 0 / 15            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Atrial flutter                                  |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 4 / 1014 (0.39%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Bradycardia                                     |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 3 / 1014 (0.30%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cardiac arrest                                  |                   |                   |  |
| subjects affected / exposed                     | 4 / 1012 (0.40%)  | 4 / 1014 (0.39%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 1 / 4             |  |
| deaths causally related to treatment / all      | 0 / 3             | 0 / 3             |  |
| Cardiac asthma                                  |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cardiac dysfunction                             |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cardiac failure                                 |                   |                   |  |
| subjects affected / exposed                     | 7 / 1012 (0.69%)  | 9 / 1014 (0.89%)  |  |
| occurrences causally related to treatment / all | 0 / 11            | 1 / 14            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Cardiac failure acute                           |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 2 / 1014 (0.20%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Cardiac failure chronic                         |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Cardiac failure congestive                      |                  |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 6 / 1014 (0.59%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 1 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cardio-respiratory arrest                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Cardiorenal syndrome                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Coronary artery disease                         |                  |                  |  |
| subjects affected / exposed                     | 6 / 1012 (0.59%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 9            | 1 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Coronary artery insufficiency                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Coronary artery stenosis                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypertensive heart disease                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ischaemic cardiomyopathy                        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Left ventricular failure                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Left ventricular hypertrophy                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Myocardial infarction                           |                  |                  |  |
| subjects affected / exposed                     | 6 / 1012 (0.59%) | 5 / 1014 (0.49%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 2            |  |
| Myocardial ischaemia                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pericarditis                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pericarditis constrictive                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pulseless electrical activity                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tachycardia                                     |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ventricular extrasystoles                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ventricular tachyarrhythmia                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Ventricular tachycardia                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nervous system disorders                        |                  |                  |  |
| Ataxia  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Autoimmune encephalopathy                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Brain injury                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Brain stem infarction                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Central nervous system lesion                   |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cerebellar stroke                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cerebral haemorrhage                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cerebral infarction                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cerebral ischaemia                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cerebrovascular accident                        |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Coma  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dizziness                                       |                  |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Encephalopathy                                  |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Headache  |                  |                  |  |
| subjects affected / exposed                     | 7 / 1012 (0.69%) | 3 / 1014 (0.30%) |  |
| occurrences causally related to treatment / all | 3 / 7            | 2 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyponatraemic seizure                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypotonia                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoxic-ischaemic encephalopathy                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ischaemic stroke                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metabolic encephalopathy                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Migraine  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Myelitis transverse                             |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neuropathy peripheral                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neurotoxicity                                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Presyncope                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sciatica  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Seizure   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal cord compression                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Syncope   |                  |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Transient ischaemic attack                      |                  |                  |  |

|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Transverse sinus thrombosis                     |                  |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Tremor  |                  |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Visual field defect                             |                  |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Blood and lymphatic system disorders            |                  |                   |  |
| Agranulocytosis                                 |                  |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 2 / 1014 (0.20%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 2 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Anaemia   |                  |                   |  |
| subjects affected / exposed                     | 6 / 1012 (0.59%) | 14 / 1014 (1.38%) |  |
| occurrences causally related to treatment / all | 2 / 9            | 6 / 14            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Atypical haemolytic uraemic syndrome            |                  |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Bone marrow failure                             |                  |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Febrile neutropenia                             |                  |                   |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 5 / 1012 (0.49%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 3 / 5             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Granulocytopenia                                |                   |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Haemolysis                                      |                   |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Haemolytic uraemic syndrome                     |                   |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%)  | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 1 / 2             | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Iron deficiency anaemia                         |                   |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Leukocytosis                                    |                   |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Leukopenia                                      |                   |                  |  |
| subjects affected / exposed                     | 12 / 1012 (1.19%) | 4 / 1014 (0.39%) |  |
| occurrences causally related to treatment / all | 10 / 14           | 5 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Lymphadenopathy                                 |                   |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Lymphatic obstruction                           |                   |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lymphopenia                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nephrogenic anaemia                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neutropenia                                     |                  |                  |  |
| subjects affected / exposed                     | 6 / 1012 (0.59%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 4 / 6            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pancytopenia                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 2 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Polycythaemia                                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sickle cell anaemia with crisis                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Splenomegaly                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thrombocytopenia                                |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 3 / 1014 (0.30%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 3 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thrombotic microangiopathy                      |                  |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 8 / 1014 (0.79%) |  |
| occurrences causally related to treatment / all | 2 / 3            | 6 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ear and labyrinth disorders                     |                  |                  |  |
| Mastoid effusion                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sudden hearing loss                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tinnitus  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vertigo   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Eye disorders                                   |                  |                  |  |
| Cataract  |                  |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Glaucoma  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Optic ischaemic neuropathy                      |                  |                  |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Retinal detachment                              |                   |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Vision blurred                                  |                   |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Visual acuity reduced                           |                   |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Gastrointestinal disorders                      |                   |                  |  |
| Abdominal hernia                                |                   |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%)  | 4 / 1014 (0.39%) |  |
| occurrences causally related to treatment / all | 0 / 2             | 1 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Abdominal pain                                  |                   |                  |  |
| subjects affected / exposed                     | 14 / 1012 (1.38%) | 9 / 1014 (0.89%) |  |
| occurrences causally related to treatment / all | 5 / 18            | 1 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Abdominal pain lower                            |                   |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Abdominal pain upper                            |                   |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%)  | 4 / 1014 (0.39%) |  |
| occurrences causally related to treatment / all | 3 / 3             | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Abdominal wall haematoma                        |                   |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Acute abdomen                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anal polyp                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anogenital dysplasia                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Barrett's oesophagus                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chronic gastritis                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colitis   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colitis ischaemic                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Colitis ulcerative                              |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Constipation                                    |                   |                   |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 2 / 3             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Crohn's disease                                 |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 1 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Diabetic gastroparesis                          |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Diarrhoea                                       |                   |                   |  |
| subjects affected / exposed                     | 55 / 1012 (5.43%) | 27 / 1014 (2.66%) |  |
| occurrences causally related to treatment / all | 32 / 60           | 9 / 31            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Diverticulum                                    |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Diverticulum intestinal                         |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Diverticulum intestinal haemorrhagic            |                   |                   |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Duodenal perforation                            |                   |                   |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 2 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Duodenal ulcer                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Encapsulating peritoneal sclerosis              |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Enteritis                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Enterocolitis                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Food poisoning                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastric haemorrhage                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastric ulcer                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastritis                                       |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastritis erosive                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastritis haemorrhagic                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal fistula                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal haemorrhage                    |                  |                  |  |
| subjects affected / exposed                     | 4 / 1012 (0.40%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 1 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Gastrooesophageal reflux disease                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haematochezia                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemorrhoidal haemorrhage                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemorrhoids                                    |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hernial eventration                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hiatus hernia                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ileus   |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 5 / 1014 (0.49%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Impaired gastric emptying                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Inguinal hernia                                 |                  |                  |  |
| subjects affected / exposed                     | 5 / 1012 (0.49%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intestinal obstruction                          |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intestinal perforation                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Intra-abdominal fluid collection                |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 5 / 1014 (0.49%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 3 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intra-abdominal haematoma                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intra-abdominal haemorrhage                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Large intestine perforation                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Large intestine polyp                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lumbar hernia                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mallory-Weiss syndrome                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Melaena   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mouth ulceration                                |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nausea  |                  |                  |  |
| subjects affected / exposed                     | 9 / 1012 (0.89%) | 3 / 1014 (0.30%) |  |
| occurrences causally related to treatment / all | 3 / 11           | 1 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oesophageal achalasia                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oesophageal spasm                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oesophagitis                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pancreatitis                                    |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pancreatitis acute                              |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pancreatitis chronic                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rectal haemorrhage                              |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Retching  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Retroperitoneal haematoma                       |                  |                  |  |
| subjects affected / exposed                     | 5 / 1012 (0.49%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Retroperitoneal haemorrhage                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Salivary gland enlargement                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Small intestinal obstruction                    |                  |                  |  |
| subjects affected / exposed                     | 4 / 1012 (0.40%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 1 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Stomatitis                                      |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 2 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Umbilical hernia                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 3 / 1014 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Volvulus  |                  |                  |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Volvulus of small bowel                         |                   |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Vomiting  |                   |                  |  |
| subjects affected / exposed                     | 13 / 1012 (1.28%) | 6 / 1014 (0.59%) |  |
| occurrences causally related to treatment / all | 5 / 18            | 3 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Skin and subcutaneous tissue disorders          |                   |                  |  |
| Blister   |                   |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Capillaritis                                    |                   |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Dermatitis allergic                             |                   |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Diabetic foot                                   |                   |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Erythema  |                   |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Hyperhidrosis                                   |                   |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Neuropathic ulcer                               |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Peau d'orange                                   |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 1 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Skin necrosis                                   |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Skin oedema                                     |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 1 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Skin ulcer                                      |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 1 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urticaria                                       |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Renal and urinary disorders                     |                   |                   |  |
| Acute kidney injury                             |                   |                   |  |
| subjects affected / exposed                     | 37 / 1012 (3.66%) | 46 / 1014 (4.54%) |  |
| occurrences causally related to treatment / all | 12 / 47           | 10 / 50           |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Anuria  |                   |                   |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder neck obstruction                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder obstruction                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder perforation                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Calculus urinary                                |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chronic kidney disease                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cystitis haemorrhagic                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetic nephropathy                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Dysuria   |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 5 / 1012 (0.49%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 1 / 5            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| End stage renal disease                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Focal segmental glomerulosclerosis              |                  |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 1 / 4            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Glomerulonephritis                              |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Glomerulonephritis chronic                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Glomerulonephritis membranoproliferative        |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Glomerulonephritis membranous                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Glycosuria                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haematuria                                      |                  |                  |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 14 / 1012 (1.38%) | 9 / 1014 (0.89%) |  |
| occurrences causally related to treatment / all | 0 / 15            | 0 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Haemorrhage urinary tract                       |                   |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Hydronephrosis                                  |                   |                  |  |
| subjects affected / exposed                     | 6 / 1012 (0.59%)  | 9 / 1014 (0.89%) |  |
| occurrences causally related to treatment / all | 0 / 6             | 1 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Hydroureter                                     |                   |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Hypertonic bladder                              |                   |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| IgM nephropathy                                 |                   |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Ischaemic nephropathy                           |                   |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Leukocyturia                                    |                   |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Mesangioproliferative glomerulonephritis        |                   |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nephritis                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nephrolithiasis                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nephropathy                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nephropathy toxic                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nephrotic syndrome                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Obstructive nephropathy                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oliguria  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pelvi-ureteric obstruction                      |                  |                  |  |

|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Perinephric collection                          |                  |                   |  |
| subjects affected / exposed                     | 5 / 1012 (0.49%) | 2 / 1014 (0.20%)  |  |
| occurrences causally related to treatment / all | 0 / 5            | 1 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pollakiuria                                     |                  |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 2 / 1014 (0.20%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Prerenal failure                                |                  |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Proteinuria                                     |                  |                   |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 15 / 1014 (1.48%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 10 / 15           |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pyelocaliectasis                                |                  |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Renal artery dissection                         |                  |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Renal artery occlusion                          |                  |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Renal artery stenosis                           |                  |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 7 / 1012 (0.69%) | 4 / 1014 (0.39%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 1 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal artery thrombosis                         |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal cortical necrosis                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal cyst                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal cyst haemorrhage                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal cyst ruptured                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal failure                                   |                  |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal haematoma                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal impairment                                |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 25 / 1012 (2.47%) | 23 / 1014 (2.27%) |  |
| occurrences causally related to treatment / all | 7 / 26            | 11 / 30           |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Renal ischaemia                                 |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Renal necrosis                                  |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Renal tubular atrophy                           |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Renal tubular necrosis                          |                   |                   |  |
| subjects affected / exposed                     | 5 / 1012 (0.49%)  | 3 / 1014 (0.30%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 2 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Renal vein thrombosis                           |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 2 / 1014 (0.20%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 1 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Tubulointerstitial nephritis                    |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Ureteric dilatation                             |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Ureteric obstruction                            |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 3 / 1014 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ureteric stenosis                               |                  |                  |  |
| subjects affected / exposed                     | 6 / 1012 (0.59%) | 3 / 1014 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urethral obstruction                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urethral stenosis                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urge incontinence                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urinary bladder haemorrhage                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urinary bladder polyp                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urinary fistula                                 |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 3 / 1014 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 1 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urinary incontinence                            |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 9 / 1014 (0.89%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 3 / 10           |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urinary retention                               |                  |                  |  |
| subjects affected / exposed                     | 8 / 1012 (0.79%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 11           | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urinary tract obstruction                       |                  |                  |  |
| subjects affected / exposed                     | 4 / 1012 (0.40%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urinoma   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vesicoureteric reflux                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Endocrine disorders                             |                  |                  |  |
| Goitre  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyperparathyroidism                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyperparathyroidism tertiary                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Musculoskeletal and connective tissue disorders |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| Arthralgia                                      |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Back pain                                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 3 / 1014 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Flank pain                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gouty arthritis                                 |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Groin pain                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intervertebral disc protrusion                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intervertebral disc space narrowing             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lumbar spinal stenosis                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Muscular weakness                               |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Musculoskeletal pain                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Myalgia intercostal                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Osteitis  |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Osteoarthritis                                  |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 4 / 1014 (0.39%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Osteonecrosis                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 9 / 1014 (0.89%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 1 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pain in extremity                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pubic pain                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sacroiliitis                                    |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal column stenosis                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal osteoarthritis                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Synovial cyst                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tendonitis                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Infections and infestations                     |                  |                  |  |
| Abdominal abscess                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abdominal infection                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 2 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Actinomycosis                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Adenoviral haemorrhagic cystitis                |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Adenovirus infection                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 2 / 2            | 2 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anal abscess                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Appendicitis                                    |                  |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arteriovenous fistula site infection            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arthritis bacterial                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arthritis infective                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Asymptomatic bacteriuria                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Atypical pneumonia                              |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 2 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| BK virus infection                              |                  |                  |  |
| subjects affected / exposed                     | 5 / 1012 (0.49%) | 3 / 1014 (0.30%) |  |
| occurrences causally related to treatment / all | 3 / 5            | 3 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bacteraemia                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 3 / 1014 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 2 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bacterial diarrhoea                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bacterial infection                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bacterial prostatitis                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bacterial pyelonephritis                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 1 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bacterial sepsis                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bacteriuria                                     |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Blister infected                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bronchitis                                      |                  |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 1 / 3            | 1 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bronchopulmonary aspergillosis                  |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 2 / 2            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Campylobacter gastroenteritis                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Candida infection                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Candiduria                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cellulitis                                      |                  |                  |  |
| subjects affected / exposed                     | 6 / 1012 (0.59%) | 5 / 1014 (0.49%) |  |
| occurrences causally related to treatment / all | 1 / 6            | 1 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chest wall abscess                              |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chronic sinusitis                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chronic tonsillitis                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Clostridium difficile colitis                   |                  |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 4 / 1014 (0.39%) |  |
| occurrences causally related to treatment / all | 1 / 3            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Clostridium difficile infection                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Corona virus infection                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cryptococcosis                                  |                  |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 3 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cystitis viral                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cytomegalovirus colitis                         |                  |                  |  |



|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 9 / 1012 (0.89%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 5 / 9             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Cytomegalovirus enteritis                       |                   |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Cytomegalovirus gastroenteritis                 |                   |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 3             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Cytomegalovirus gastrointestinal infection      |                   |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Cytomegalovirus hepatitis                       |                   |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 2             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Cytomegalovirus infection                       |                   |                  |  |
| subjects affected / exposed                     | 48 / 1012 (4.74%) | 6 / 1014 (0.59%) |  |
| occurrences causally related to treatment / all | 40 / 55           | 6 / 8            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0            |  |
| Dengue fever                                    |                   |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Dermatophytosis                                 |                   |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Device related infection                        |                   |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 1 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Device related sepsis                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetic foot infection                         |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diarrhoea infectious                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Disseminated tuberculosis                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diverticulitis                                  |                  |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 3 / 1014 (0.30%) |  |
| occurrences causally related to treatment / all | 1 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ear infection                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Encephalitis                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Endocarditis                                    |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Enteritis infectious                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Enterococcal infection                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Enterococcal sepsis                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Enterocolitis viral                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Epididymitis                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Erysipelas                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 3 / 1014 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 2 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Escherichia bacteraemia                         |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Escherichia infection                           |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Escherichia pyelonephritis                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Escherichia sepsis                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 5 / 1014 (0.49%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 2 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Escherichia urinary tract infection             |                  |                  |  |
| subjects affected / exposed                     | 7 / 1012 (0.69%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 4 / 9            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Febrile infection                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Fungal infection                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Fungal sepsis                                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 2 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Gangrene  |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastroenteritis                                 |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 23 / 1012 (2.27%) | 18 / 1014 (1.78%) |  |
| occurrences causally related to treatment / all | 8 / 25            | 0 / 19            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastroenteritis clostridial                     |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastroenteritis cryptosporidial                 |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastroenteritis norovirus                       |                   |                   |  |
| subjects affected / exposed                     | 6 / 1012 (0.59%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 2 / 6             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastroenteritis viral                           |                   |                   |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 1 / 3             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastrointestinal infection                      |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 2 / 1014 (0.20%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 1 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Groin abscess                                   |                   |                   |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%)  | 3 / 1014 (0.30%)  |  |
| occurrences causally related to treatment / all | 1 / 2             | 1 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| HIV infection                                   |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Haematoma infection                             |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 2 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatic cyst infection                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 2 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatitis C                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatitis E                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatitis viral                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Herpes simplex                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Herpes simplex pneumonia                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Herpes zoster                                   |                  |                  |  |
| subjects affected / exposed                     | 4 / 1012 (0.40%) | 5 / 1014 (0.49%) |  |
| occurrences causally related to treatment / all | 1 / 4            | 3 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Herpes zoster disseminated                      |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ileal gangrene                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Infected lymphocele                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 4 / 1014 (0.39%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 5 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Infected seroma                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Infected skin ulcer                             |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 3 / 1014 (0.30%) |  |
| occurrences causally related to treatment / all | 2 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Infection                                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 1 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Infectious colitis                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Infectious pleural effusion                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Influenza                                       |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 5 / 1012 (0.49%) | 6 / 1014 (0.59%) |  |
| occurrences causally related to treatment / all | 1 / 5            | 1 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intervertebral discitis                         |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intestinal sepsis                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Kidney infection                                |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Klebsiella bacteraemia                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Klebsiella sepsis                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lower respiratory tract infection               |                  |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 2 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lung infection                                  |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Medical device site cellulitis                  |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Medical device site infection                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Meningitis bacterial                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Meningitis cryptococcal                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nasopharyngitis                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neutropenic sepsis                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nocardiosis                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oral candidiasis                                |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oral herpes                                     |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Orchitis  |                  |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 5 / 6            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Osteomyelitis                                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%) | 5 / 1014 (0.49%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 4 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Osteomyelitis chronic                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 3 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Parvovirus B19 infection                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Perinephric abscess                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peritonitis                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peritonsillar abscess                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pharyngotonsillitis                             |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pneumococcal sepsis                             |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 1 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pneumocystis jirovecii pneumonia                |                   |                   |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%)  | 6 / 1014 (0.59%)  |  |
| occurrences causally related to treatment / all | 2 / 3             | 6 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Pneumonia                                       |                   |                   |  |
| subjects affected / exposed                     | 36 / 1012 (3.56%) | 55 / 1014 (5.42%) |  |
| occurrences causally related to treatment / all | 18 / 41           | 31 / 63           |  |
| deaths causally related to treatment / all      | 0 / 2             | 0 / 0             |  |
| Pneumonia bacterial                             |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 1 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pneumonia cryptococcal                          |                   |                   |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 2 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pneumonia cytomegaloviral                       |                   |                   |  |
| subjects affected / exposed                     | 4 / 1012 (0.40%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 1             |  |
| Pneumonia fungal                                |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pneumonia haemophilus                           |                   |                   |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Pneumonia influenzal                            |                   |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Pneumonia legionella                            |                   |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 1 / 1             | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Polyomavirus-associated nephropathy             |                   |                  |  |
| subjects affected / exposed                     | 10 / 1012 (0.99%) | 4 / 1014 (0.39%) |  |
| occurrences causally related to treatment / all | 10 / 10           | 4 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Postoperative abscess                           |                   |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Postoperative wound infection                   |                   |                  |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%)  | 3 / 1014 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 3             | 2 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Pseudomembranous colitis                        |                   |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0            |  |
| Pseudomonal bacteraemia                         |                   |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Pseudomonal sepsis                              |                   |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pulmonary tuberculosis                          |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 2 / 1014 (0.20%)  |  |
| occurrences causally related to treatment / all | 1 / 1             | 1 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pyelonephritis                                  |                   |                   |  |
| subjects affected / exposed                     | 33 / 1012 (3.26%) | 24 / 1014 (2.37%) |  |
| occurrences causally related to treatment / all | 15 / 40           | 15 / 30           |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pyelonephritis acute                            |                   |                   |  |
| subjects affected / exposed                     | 13 / 1012 (1.28%) | 6 / 1014 (0.59%)  |  |
| occurrences causally related to treatment / all | 8 / 19            | 1 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pyelonephritis chronic                          |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pyuria  |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 2 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Renal cyst infection                            |                   |                   |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 1 / 3             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Renal graft infection                           |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 2 / 1014 (0.20%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Respiratory tract infection                     |                   |                   |  |

|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 5 / 1012 (0.49%) | 5 / 1014 (0.49%)  |  |
| occurrences causally related to treatment / all | 2 / 5            | 2 / 5             |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0             |  |
| Respiratory tract infection fungal              |                  |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0             |  |
| Respiratory tract infection viral               |                  |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Rhinitis  |                  |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Rhinovirus infection                            |                  |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Salmonellosis                                   |                  |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Sepsis  |                  |                   |  |
| subjects affected / exposed                     | 7 / 1012 (0.69%) | 20 / 1014 (1.97%) |  |
| occurrences causally related to treatment / all | 4 / 7            | 9 / 23            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 3             |  |
| Septic shock                                    |                  |                   |  |
| subjects affected / exposed                     | 8 / 1012 (0.79%) | 6 / 1014 (0.59%)  |  |
| occurrences causally related to treatment / all | 3 / 9            | 2 / 6             |  |
| deaths causally related to treatment / all      | 0 / 4            | 0 / 1             |  |
| Sinusitis                                       |                  |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sinusitis fungal                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Staphylococcal bacteraemia                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Streptococcal sepsis                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Subcutaneous abscess                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Systemic candida                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tonsillitis bacterial                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 3 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tooth abscess                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tracheobronchitis                               |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Transplant abscess                              |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Tuberculosis                                    |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Tuberculosis gastrointestinal                   |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Upper respiratory tract infection               |                   |                   |  |
| subjects affected / exposed                     | 4 / 1012 (0.40%)  | 5 / 1014 (0.49%)  |  |
| occurrences causally related to treatment / all | 3 / 5             | 3 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urinary tract infection                         |                   |                   |  |
| subjects affected / exposed                     | 93 / 1012 (9.19%) | 78 / 1014 (7.69%) |  |
| occurrences causally related to treatment / all | 49 / 124          | 37 / 110          |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urinary tract infection bacterial               |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 4 / 1014 (0.39%)  |  |
| occurrences causally related to treatment / all | 1 / 1             | 3 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urinary tract infection enterococcal            |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 1 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urinary tract infection fungal                  |                   |                   |  |



|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urosepsis                                       |                   |                   |  |
| subjects affected / exposed                     | 23 / 1012 (2.27%) | 23 / 1014 (2.27%) |  |
| occurrences causally related to treatment / all | 14 / 28           | 9 / 28            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Varicella                                       |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Viral diarrhoea                                 |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 1 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Viral infection                                 |                   |                   |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%)  | 2 / 1014 (0.20%)  |  |
| occurrences causally related to treatment / all | 1 / 2             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Viral myocarditis                               |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Viral upper respiratory tract infection         |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Vulvovaginal mycotic infection                  |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Wound abscess                                   |                   |                   |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Wound infection                                 |                   |                  |  |
| subjects affected / exposed                     | 4 / 1012 (0.40%)  | 5 / 1014 (0.49%) |  |
| occurrences causally related to treatment / all | 1 / 4             | 3 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Metabolism and nutrition disorders              |                   |                  |  |
| Cachexia  |                   |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%)  | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Calciophylaxis                                  |                   |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Decreased appetite                              |                   |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%)  | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 1 / 2             | 1 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Dehydration                                     |                   |                  |  |
| subjects affected / exposed                     | 11 / 1012 (1.09%) | 6 / 1014 (0.59%) |  |
| occurrences causally related to treatment / all | 2 / 11            | 1 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Diabetes mellitus                               |                   |                  |  |
| subjects affected / exposed                     | 10 / 1012 (0.99%) | 9 / 1014 (0.89%) |  |
| occurrences causally related to treatment / all | 5 / 10            | 6 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Diabetes mellitus inadequate control            |                   |                  |  |
| subjects affected / exposed                     | 2 / 1012 (0.20%)  | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Diabetic ketoacidosis                           |                   |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 2 / 1012 (0.20%)  | 3 / 1014 (0.30%)  |  |
| occurrences causally related to treatment / all | 1 / 2             | 1 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Electrolyte imbalance                           |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Fluid overload                                  |                   |                   |  |
| subjects affected / exposed                     | 3 / 1012 (0.30%)  | 5 / 1014 (0.49%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 3 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Fluid retention                                 |                   |                   |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gout  |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 1 / 1014 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hypercalcaemia                                  |                   |                   |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%)  | 0 / 1014 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hyperglycaemia                                  |                   |                   |  |
| subjects affected / exposed                     | 6 / 1012 (0.59%)  | 5 / 1014 (0.49%)  |  |
| occurrences causally related to treatment / all | 4 / 6             | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hyperkalaemia                                   |                   |                   |  |
| subjects affected / exposed                     | 10 / 1012 (0.99%) | 11 / 1014 (1.08%) |  |
| occurrences causally related to treatment / all | 2 / 11            | 2 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hyperlipidaemia                                 |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypertriglyceridaemia                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypervolaemia                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypocalcaemia                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 2 / 1014 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoglycaemia                                   |                  |                  |  |
| subjects affected / exposed                     | 5 / 1012 (0.49%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypokalaemia                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 1012 (0.00%) | 3 / 1014 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypomagnesaemia                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyponatraemia                                   |                  |                  |  |
| subjects affected / exposed                     | 5 / 1012 (0.49%) | 1 / 1014 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypophosphataemia                               |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypovolaemia                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Iron deficiency                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Malnutrition                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metabolic acidosis                              |                  |                  |  |
| subjects affected / exposed                     | 4 / 1012 (0.40%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 5            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Type 1 diabetes mellitus                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 1012 (0.10%) | 0 / 1014 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

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

| <b>Non-serious adverse events</b>                     | <b>MPA plus<br/>standard@CNI</b> | <b>Everolimus<br/>plus@reduced CNI</b> |  |
|---|----------------------------------|--|--|
| Total subjects affected by non-serious adverse events |                                  |  |  |
| subjects affected / exposed                           | 942 / 1012<br>(93.08%)           | 951 / 1014<br>(93.79%)                 |  |
| Vascular disorders                                    |                                  |  |  |
| Hypertension  |                                  |  |  |
| subjects affected / exposed                           | 230 / 1012<br>(22.73%)           | 240 / 1014<br>(23.67%)                 |  |
| occurrences (all)                                     | 264                              | 275                                    |  |

|  |   |   |  |
|--|---|---|--|
| Hypotension<br>subjects affected / exposed<br>occurrences (all)  | 78 / 1012 (7.71%)<br>83                                   | 62 / 1014 (6.11%)<br>67                                   |  |
| General disorders and administration site conditions<br>Fatigue<br>subjects affected / exposed<br>occurrences (all)<br><br>Oedema peripheral<br>subjects affected / exposed<br>occurrences (all) | 64 / 1012 (6.32%)<br>77<br><br>244 / 1012 (24.11%)<br>339 | 59 / 1014 (5.82%)<br>63<br><br>347 / 1014 (34.22%)<br>512 |  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)  | 132 / 1012 (13.04%)<br>162                                | 112 / 1014 (11.05%)<br>130                                |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)   | 102 / 1012 (10.08%)<br>110                                | 86 / 1014 (8.48%)<br>100                                  |  |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)   | 70 / 1012 (6.92%)<br>85                                   | 73 / 1014 (7.20%)<br>84                                   |  |
| Psychiatric disorders<br>Anxiety<br>subjects affected / exposed<br>occurrences (all)<br><br>Insomnia<br>subjects affected / exposed<br>occurrences (all)   | 59 / 1012 (5.83%)<br>66<br><br>138 / 1012 (13.64%)<br>155 | 51 / 1014 (5.03%)<br>57<br><br>100 / 1014 (9.86%)<br>113  |  |
| Investigations<br>Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)   | 133 / 1012 (13.14%)<br>160                                | 141 / 1014 (13.91%)<br>167                                |  |
| Weight increased<br>subjects affected / exposed<br>occurrences (all)   | 66 / 1012 (6.52%)<br>67                                   | 38 / 1014 (3.75%)<br>39                                   |  |
| Injury, poisoning and procedural complications   |   |   |  |

|   |                               |                               |  |
|---|-------------------------------|-------------------------------|--|
| Complications of transplanted kidney<br>subjects affected / exposed<br>occurrences (all)            | 54 / 1012 (5.34%)<br>65       | 63 / 1014 (6.21%)<br>67       |  |
| Incision site pain<br>subjects affected / exposed<br>occurrences (all)                              | 61 / 1012 (6.03%)<br>65       | 51 / 1014 (5.03%)<br>55       |  |
| Procedural pain<br>subjects affected / exposed<br>occurrences (all)                                 | 99 / 1012 (9.78%)<br>117      | 90 / 1014 (8.88%)<br>100      |  |
| Cardiac disorders<br>Tachycardia<br>subjects affected / exposed<br>occurrences (all)                | 52 / 1012 (5.14%)<br>59       | 53 / 1014 (5.23%)<br>62       |  |
| Nervous system disorders<br>Dizziness<br>subjects affected / exposed<br>occurrences (all)           | 54 / 1012 (5.34%)<br>62       | 51 / 1014 (5.03%)<br>58       |  |
| Headache<br>subjects affected / exposed<br>occurrences (all)  | 113 / 1012<br>(11.17%)<br>144 | 133 / 1014<br>(13.12%)<br>172 |  |
| Tremor<br>subjects affected / exposed<br>occurrences (all)  | 145 / 1012<br>(14.33%)<br>161 | 100 / 1014 (9.86%)<br>103     |  |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all) | 238 / 1012<br>(23.52%)<br>267 | 227 / 1014<br>(22.39%)<br>260 |  |
| Leukocytosis<br>subjects affected / exposed<br>occurrences (all)                                    | 58 / 1012 (5.73%)<br>59       | 24 / 1014 (2.37%)<br>26       |  |
| Leukopenia<br>subjects affected / exposed<br>occurrences (all)                                      | 194 / 1012<br>(19.17%)<br>234 | 94 / 1014 (9.27%)<br>108      |  |
| Polycythaemia<br>subjects affected / exposed<br>occurrences (all)                                   | 42 / 1012 (4.15%)<br>44       | 52 / 1014 (5.13%)<br>58       |  |

|  |                            |                            |  |
|--|----------------------------|----------------------------|--|
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)     | 41 / 1012 (4.05%)<br>45    | 74 / 1014 (7.30%)<br>85    |  |
| Gastrointestinal disorders   |                            |                            |  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)       | 104 / 1012 (10.28%)<br>126 | 94 / 1014 (9.27%)<br>107   |  |
| Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all) | 62 / 1012 (6.13%)<br>69    | 39 / 1014 (3.85%)<br>45    |  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)         | 242 / 1012 (23.91%)<br>286 | 245 / 1014 (24.16%)<br>282 |  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)            | 318 / 1012 (31.42%)<br>437 | 242 / 1014 (23.87%)<br>315 |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)               | 225 / 1012 (22.23%)<br>271 | 191 / 1014 (18.84%)<br>238 |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)             | 140 / 1012 (13.83%)<br>172 | 120 / 1014 (11.83%)<br>144 |  |
| Skin and subcutaneous tissue disorders                                   |                            |                            |  |
| Acne<br>subjects affected / exposed<br>occurrences (all)                 | 37 / 1012 (3.66%)<br>39    | 56 / 1014 (5.52%)<br>58    |  |
| Alopecia<br>subjects affected / exposed<br>occurrences (all)             | 59 / 1012 (5.83%)<br>59    | 27 / 1014 (2.66%)<br>28    |  |
| Renal and urinary disorders  |                            |                            |  |
| Dysuria<br>subjects affected / exposed<br>occurrences (all)              | 74 / 1012 (7.31%)<br>78    | 60 / 1014 (5.92%)<br>66    |  |
| Haematuria   |                            |                            |  |



|   |                     |                     |  |
|---|---------------------|---------------------|--|
| subjects affected / exposed                     | 101 / 1012 (9.98%)  | 102 / 1014 (10.06%) |  |
| occurrences (all)                               | 110                 | 117                 |  |
| Proteinuria                                     |                     |                     |  |
| subjects affected / exposed                     | 69 / 1012 (6.82%)   | 131 / 1014 (12.92%) |  |
| occurrences (all)                               | 80                  | 145                 |  |
| Musculoskeletal and connective tissue disorders |                     |                     |  |
| Arthralgia                                      |                     |                     |  |
| subjects affected / exposed                     | 65 / 1012 (6.42%)   | 63 / 1014 (6.21%)   |  |
| occurrences (all)                               | 74                  | 72                  |  |
| Back pain                                       |                     |                     |  |
| subjects affected / exposed                     | 98 / 1012 (9.68%)   | 93 / 1014 (9.17%)   |  |
| occurrences (all)                               | 106                 | 103                 |  |
| Pain in extremity                               |                     |                     |  |
| subjects affected / exposed                     | 61 / 1012 (6.03%)   | 66 / 1014 (6.51%)   |  |
| occurrences (all)                               | 68                  | 77                  |  |
| Infections and infestations                     |                     |                     |  |
| BK virus infection                              |                     |                     |  |
| subjects affected / exposed                     | 101 / 1012 (9.98%)  | 56 / 1014 (5.52%)   |  |
| occurrences (all)                               | 118                 | 68                  |  |
| Cytomegalovirus infection                       |                     |                     |  |
| subjects affected / exposed                     | 93 / 1012 (9.19%)   | 24 / 1014 (2.37%)   |  |
| occurrences (all)                               | 107                 | 26                  |  |
| Nasopharyngitis                                 |                     |                     |  |
| subjects affected / exposed                     | 117 / 1012 (11.56%) | 110 / 1014 (10.85%) |  |
| occurrences (all)                               | 152                 | 135                 |  |
| Upper respiratory tract infection               |                     |                     |  |
| subjects affected / exposed                     | 102 / 1012 (10.08%) | 81 / 1014 (7.99%)   |  |
| occurrences (all)                               | 125                 | 95                  |  |
| Urinary tract infection                         |                     |                     |  |
| subjects affected / exposed                     | 249 / 1012 (24.60%) | 219 / 1014 (21.60%) |  |
| occurrences (all)                               | 471                 | 373                 |  |
| Metabolism and nutrition disorders              |                     |                     |  |
| Diabetes mellitus                               |                     |                     |  |
| subjects affected / exposed                     | 120 / 1012 (11.86%) | 133 / 1014 (13.12%) |  |
| occurrences (all)                               | 126                 | 136                 |  |

|                             |                     |                     |  |
|-----------------------------|---------------------|---------------------|--|
| Dyslipidaemia               |                     |                     |  |
| subjects affected / exposed | 57 / 1012 (5.63%)   | 98 / 1014 (9.66%)   |  |
| occurrences (all)           | 59                  | 104                 |  |
| Hypercalcaemia              |                     |                     |  |
| subjects affected / exposed | 67 / 1012 (6.62%)   | 39 / 1014 (3.85%)   |  |
| occurrences (all)           | 74                  | 42                  |  |
| Hypercholesterolaemia       |                     |                     |  |
| subjects affected / exposed | 61 / 1012 (6.03%)   | 103 / 1014 (10.16%) |  |
| occurrences (all)           | 63                  | 110                 |  |
| Hyperglycaemia              |                     |                     |  |
| subjects affected / exposed | 144 / 1012 (14.23%) | 140 / 1014 (13.81%) |  |
| occurrences (all)           | 162                 | 155                 |  |
| Hyperkalaemia               |                     |                     |  |
| subjects affected / exposed | 184 / 1012 (18.18%) | 164 / 1014 (16.17%) |  |
| occurrences (all)           | 230                 | 192                 |  |
| Hyperlipidaemia             |                     |                     |  |
| subjects affected / exposed | 75 / 1012 (7.41%)   | 135 / 1014 (13.31%) |  |
| occurrences (all)           | 77                  | 140                 |  |
| Hypertriglyceridaemia       |                     |                     |  |
| subjects affected / exposed | 24 / 1012 (2.37%)   | 58 / 1014 (5.72%)   |  |
| occurrences (all)           | 25                  | 63                  |  |
| Hyperuricaemia              |                     |                     |  |
| subjects affected / exposed | 64 / 1012 (6.32%)   | 49 / 1014 (4.83%)   |  |
| occurrences (all)           | 69                  | 55                  |  |
| Hypocalcaemia               |                     |                     |  |
| subjects affected / exposed | 98 / 1012 (9.68%)   | 109 / 1014 (10.75%) |  |
| occurrences (all)           | 106                 | 118                 |  |
| Hypokalaemia                |                     |                     |  |
| subjects affected / exposed | 87 / 1012 (8.60%)   | 148 / 1014 (14.60%) |  |
| occurrences (all)           | 108                 | 180                 |  |
| Hypomagnesaemia             |                     |                     |  |
| subjects affected / exposed | 168 / 1012 (16.60%) | 134 / 1014 (13.21%) |  |
| occurrences (all)           | 190                 | 153                 |  |
| Hypophosphataemia           |                     |                     |  |

|                             |                        |                        |  |
|-----------------------------|------------------------|------------------------|--|
| subjects affected / exposed | 167 / 1012<br>(16.50%) | 190 / 1014<br>(18.74%) |  |
| occurrences (all)           | 178                    | 210                    |  |
| Metabolic acidosis          |                        |                        |  |
| subjects affected / exposed | 98 / 1012 (9.68%)      | 77 / 1014 (7.59%)      |  |
| occurrences (all)           | 109                    | 93                     |  |
| Vitamin D deficiency        |                        |                        |  |
| subjects affected / exposed | 57 / 1012 (5.63%)      | 53 / 1014 (5.23%)      |  |
| occurrences (all)           | 58                     | 54                     |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date         | Amendment  |
|--------------|--|
| 14 July 2016 | In response to the French Health Authorities (HA) request, the protocol was updated with the recent notifications for use of mycophenolate based on European Medicines Agency's (EMA) recommendation published on 23-Oct-2015, and the Dear Health Care Professional Letter (DHCPL) for CellCept that was distributed by Roche by 10-Nov-2015. Mycophenolate (mycophenolate mofetil or mycophenolic acid) is a confirmed teratogen associated with an increased rate of spontaneous abortion and congenital malformation compared with other immunosuppressants. Therefore, investigators should ensure that female and male patients taking mycophenolate understand the risk of harm to the baby, the need for effective contraception, and the need to immediately consult responsible investigator if there is a possibility of pregnancy or a suspected gap of contraception. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

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| NA |
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Notes: