



Clinical trial results:

A Randomized, Double-Blind, Placebo-Controlled, Phase 2 Trial to Evaluate the Efficacy and Safety of a Vaccine, ASP0113, in Cytomegalovirus (CMV)-Seronegative Kidney Transplant Recipients Receiving an Organ from a CMV-Seropositive Donor

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2013-000464-29 |
| Trial protocol | DE ES |
| Global end of trial date | 05 November 2020 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v2 |
| This version publication date | 06 November 2021 |
| First version publication date | 29 April 2017 |
| Version creation reason | |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | 0113-CL-2001 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01974206 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Astellas Pharma Global Development, Inc. |
| Sponsor organisation address | 1 Astellas Way, Northbrook, United States, 60062 |
| Public contact | Clinical Transparency, Astellas Pharma Global Development, Inc., astellas.resultsdisclosure@astellas.com |
| Scientific contact | Clinical Transparency, Astellas Pharma Global Development, Inc., astellas.resultsdisclosure@astellas.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 | 05 November 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 05 November 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate efficacy and safety of ASP0113 compared to placebo in reducing the incidence of Cytomegalovirus (CMV) viremia through 1 year post first study drug injection in CMV-seronegative participants who received a kidney from a CMV-seropositive donor.

Protection of trial subjects:

This clinical study was written, conducted and reported in accordance with the protocol, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Guidelines, and applicable local regulations, including the European Directive 2001/20/EC, on the protection of human rights, and with the ethical principles that have their origin in the Declaration of Helsinki. Astellas ensures that the use and disclosure of protected health information (PHI) obtained during a research study complies with the federal, national and/or regional legislation related to the privacy and protection of personal information.

Background therapy:

In the first 10 days after the transplant, patients received prophylactic valganciclovir or ganciclovir (dose per package insert) from the day of randomization to prevent Cytomegalovirus (CMV) disease. After randomization, patients continued to receive valganciclovir or ganciclovir until 100 days post-transplant. Valganciclovir or ganciclovir could be interrupted, dose adjusted or replaced by other CMV-specific antiviral prophylaxis (AVP) per standard of care after the day of randomization.

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 20 November 2013 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 4 Years |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Spain: 8 |
| Country: Number of subjects enrolled | United States: 93 |
| Country: Number of subjects enrolled | Australia: 11 |
| Country: Number of subjects enrolled | Canada: 7 |
| Country: Number of subjects enrolled | France: 15 |
| Country: Number of subjects enrolled | Germany: 16 |
| Worldwide total number of subjects | 150 |
| EEA total number of subjects | 39 |

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) | 129 |
| From 65 to 84 years | 21 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

A total of 150 participants were enrolled into the study from 6 countries. Eligible participants were ≥ 18 years of age, CMV-seronegative at the time of the transplant and had a kidney allograft from a CMV-seropositive living or deceased donor. After the primary period completion, 149 participants entered the long-term follow-up period.

Pre-assignment

Screening details:

Screening assessments were performed from 14-30 days after the transplant. Patients were randomized at day 30, in relation to the day of the transplant, in a 1:1 ratio to ASP0113 or placebo. Participants were stratified by the use of antithymocyte globulin (ATG) prior to randomization and by the receipt of a kidney from a living or deceased donor.

Period 1

| | |
|------------------------------|---------------------------------------|
| Period 1 title | Primary Study Period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Assessor |

Blinding implementation details:

This was a double-blind study. Participants were randomized to receive ASP0113 or placebo in a double-blind fashion such that the investigator, sponsor's study management team, clinical staff nor the participant knew which agent was being administered.

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description:

Participants received 1 mL of 5 mg/mL of placebo via injection in the deltoid muscle alternating sides with each dose on days 30, 60, 90, 120 and 180 in relation to the day of transplant (Day 0).

| | |
|--|-------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Participants received Placebo in 2-mL vials containing phosphate-buffered saline.

| | |
|------------------|-------------|
| Arm title | ASP0113 5mg |
|------------------|-------------|

Arm description:

Participants received 1 mL of 5 mg/mL of ASP0113 via injection in the deltoid muscle alternating sides with each dose on days 30, 60, 90, 120 and 180 in relation to the day of transplant (Day 0).

| | |
|--|-------------------|
| Arm type | Experimental |
| Investigational medicinal product name | ASP0113 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Participants received ASP0113 in single dose 2-ml vials containing 1.3 ml of 5 mg/mL of ASP0113.

| Number of subjects in period 1 | Placebo | ASP0113 5mg |
|---------------------------------------|---------|-------------|
| Started | 74 | 76 |
| Received Treatment | 74 | 75 |
| Completed | 68 | 75 |
| Not completed | 6 | 1 |
| Consent withdrawn by subject | 3 | - |
| Physician decision | 1 | - |
| Patient did not take study drug | - | 1 |
| Death | 1 | - |
| Lost to follow-up | 1 | - |

Baseline characteristics

Reporting groups

| | |
|---|-------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received 1 mL of 5 mg/mL of placebo via injection in the deltoid muscle alternating sides with each dose on days 30, 60, 90, 120 and 180 in relation to the day of transplant (Day 0). | |
| Reporting group title | ASP0113 5mg |
| Reporting group description: | |
| Participants received 1 mL of 5 mg/mL of ASP0113 via injection in the deltoid muscle alternating sides with each dose on days 30, 60, 90, 120 and 180 in relation to the day of transplant (Day 0). | |

| Reporting group values | Placebo | ASP0113 5mg | Total |
|---|---------|-------------|-------|
| Number of subjects | 74 | 76 | 150 |
| Age categorical Units: Subjects | | | |
| Age continuous Units: years | | | |
| arithmetic mean | 47.9 | 50.8 | |
| standard deviation | ± 13.3 | ± 13.6 | - |
| Gender categorical Units: Participants | | | |
| Male | 55 | 55 | 110 |
| Female | 19 | 21 | 40 |
| Ethnicity Units: Subjects | | | |
| Hispanic or Latino | 2 | 70 | 72 |
| Not Hispanic or Latino | 72 | 6 | 78 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Race Units: Subjects | | | |
| American Indian or Alaska Native | 1 | 0 | 1 |
| Asian | 0 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 14 | 11 | 25 |
| White | 57 | 61 | 118 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 2 | 4 | 6 |
| Use of ATG Units: Subjects | | | |
| Use of ATG = No | 44 | 44 | 88 |
| Use of ATG = Yes | 30 | 32 | 62 |
| Source of Current Transplant Units: Subjects | | | |
| Living Unrelated Donor | 10 | 17 | 27 |
| Living Related Donor | 16 | 9 | 25 |
| Deceased Donor | 48 | 49 | 97 |

| Not Recorded | 0 | 1 | 1 |
|--------------------------------|----|----|----|
| Randomization Strata | | | |
| Units: Subjects | | | |
| Living Donor & ATG Use = No | 18 | 16 | 34 |
| Living Donor & ATG Use = Yes | 8 | 10 | 18 |
| Deceased Donor & ATG Use = Yes | 22 | 22 | 44 |
| Deceased Donor & ATG Use = No | 26 | 27 | 53 |
| Not Recorded | 0 | 1 | 1 |

End points

End points reporting groups

| | |
|---|-------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received 1 mL of 5 mg/mL of placebo via injection in the deltoid muscle alternating sides with each dose on days 30, 60, 90, 120 and 180 in relation to the day of transplant (Day 0). | |
| Reporting group title | ASP0113 5mg |
| Reporting group description: | |
| Participants received 1 mL of 5 mg/mL of ASP0113 via injection in the deltoid muscle alternating sides with each dose on days 30, 60, 90, 120 and 180 in relation to the day of transplant (Day 0). | |

Primary: Percentage of Participants with CMV Viremia Through One Year Post First Study Drug Injection. (Primary Study Period)

| | |
|--|--|
| End point title | Percentage of Participants with CMV Viremia Through One Year Post First Study Drug Injection. (Primary Study Period) |
| End point description: | |
| CMV viremia was defined as presence of cytomegalovirus as measured in plasma viral load of ≥ 1000 IU/mL by central laboratory assay. A participants who discontinued the study without a positive CMV viral load was imputed as having a CMV viremia. A participant who had more than one viral load ≥ 1000 IU/mL by central assay was counted once in this summary. CMV viral loads after first injection (Day 1) through Day 380 (scheduled or unscheduled) were included in the analysis. The analysis population was the Full Analysis Set (FAS) which consisted of all randomized patients who received at least 1 dose of randomized study drug and who had at least 1 post dose viral load assessment within 1 year post first injection by central laboratory. | |
| End point type | Primary |
| End point timeframe: | |
| From first study dose injection (Day 1) up to one year post study drug injection (up to Day 380) | |

| End point values | Placebo | ASP0113 5mg | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 73 | 73 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| Known CMV Viremia | 35.6 | 35.6 | | |
| Imputed CMV Viremia Due to Discontinuation | 5.5 | 0 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Common Odds Ratio for Patients With CMV |
| Statistical analysis description: | |
| The Cochran-Mantel-Haenszel (CMH) estimate of the common odds ratio (ASP0113 vs placebo) stratified by randomization strata, and the 90% CIs of the CMH odds ratio stratified by randomization group. | |
| Comparison groups | Placebo v ASP0113 5mg |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 146 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.307 ^[1] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Common Odds Ratio |
| Point estimate | 0.79 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.43 |
| upper limit | 1.47 |

Notes:

[1] - P-value (1-sided) of the CMH adjusted odds ratio stratified by randomization group.

Secondary: Percentage of Participants with Adjudicated CMV-Associated Disease, Including CMV Syndrome and CMV Tissue-Invasive Disease (Primary Study Period)

| | |
|-----------------|---|
| End point title | Percentage of Participants with Adjudicated CMV-Associated Disease, Including CMV Syndrome and CMV Tissue-Invasive Disease (Primary Study Period) |
|-----------------|---|

End point description:

An independent panel of medical experts reviewed/adjudicated events of CMV-associated disease including CMV syndrome and tissue invasive disease, which were defined according to the American Society of Transplantation Recommendations for Screening, Monitoring and Reporting of Infectious Complications in Immunosuppression Trials in Recipients of Organ Transplantation 2006. The analysis population was the FAS.

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

End point timeframe:

From first study dose injection (Day 1) up to one year post study drug injection (up to Day 380)

| End point values | Placebo | ASP0113 5mg | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 73 | 73 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 19.18 | 19.18 | | |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Common Odds Ratio for CMV-Associated Disease |
|----------------------------|--|

Statistical analysis description:

The exact Cochran-Mantel-Haenszel (CMH) estimate of the common odds ratio (ASP0113 vs placebo) stratified by randomization group, and the 90% CI of the exact CMH odds ratio stratified by randomization group.

| | |
|-------------------|-----------------------|
| Comparison groups | Placebo v ASP0113 5mg |
|-------------------|-----------------------|

| | |
|---|-------------------------|
| Number of subjects included in analysis | 146 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.576 ^[2] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Common Odds Ratio |
| Point estimate | 0.99 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.46 |
| upper limit | 2.15 |

Notes:

[2] - P-value (1-sided) of the exact CMH method adjusted odds ratio stratified by randomization group.

Secondary: Percentage of Participants with CMV Viremia Defined as Plasma Viral Load \geq the Lower Limit of Quantification (LLOQ) Assessed by Central Laboratory (Primary Study Period)

| | |
|-----------------|--|
| End point title | Percentage of Participants with CMV Viremia Defined as Plasma Viral Load \geq the Lower Limit of Quantification (LLOQ) Assessed by Central Laboratory (Primary Study Period) |
|-----------------|--|

End point description:

The central laboratory had the LLOQ level for CMV viral load assessment. When the viral load was below the LLOQ the actual reading was not possible and was denoted as \leq LLOQ. If the participant had any CMV viral load assessments greater than the LLOQ, set up by the central laboratory, participant was classified as viremic and was included in the analysis. The analysis population was the FAS.

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

End point timeframe:

From first study dose injection (Day 1) up to one year post study drug injection (up to Day 380)

| End point values | Placebo | ASP0113 5mg | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 73 | 73 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 49.32 | 46.58 | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Common Odds Ratio for Participants w/ CMV Viremia |
|----------------------------|---|

Statistical analysis description:

The exact Cochran-Mantel-Haenszel (CMH) estimate of the common odds ratio (ASP0113 vs placebo) stratified by randomization group, and the 90% CI of the exact CMH odds ratio stratified by randomization group.

| | |
|-------------------|-----------------------|
| Comparison groups | Placebo v ASP0113 5mg |
|-------------------|-----------------------|

| | |
|---|-------------------------|
| Number of subjects included in analysis | 146 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.408 ^[3] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Common Odds Ratio |
| Point estimate | 0.88 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.48 |
| upper limit | 1.59 |

Notes:

[3] - P-value (1-sided) of the exact CMH method adjusted odds ratio stratified by randomization group.

Secondary: Percentage of Participants Who Took Adjudicated CMV-specific antiviral therapy (AVT) for the Treatment of CMV Viremia or Disease (Primary Study Period)

| | |
|-----------------|---|
| End point title | Percentage of Participants Who Took Adjudicated CMV-specific antiviral therapy (AVT) for the Treatment of CMV Viremia or Disease (Primary Study Period) |
|-----------------|---|

End point description:

An independent panel of medical experts reviewed/adjudicated events of CMV-specific AVT for treatment of CMV viremia or disease. The analysis population was the FAS.

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

End point timeframe:

From first study dose injection (Day 1) up to one year post study drug injection (up to Day 380)

| End point values | Placebo | ASP0113 5mg | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 73 | 73 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 45.21 | 42.47 | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Common Odds Ratio for Participants With CMV-AVT |
|----------------------------|---|

Statistical analysis description:

The exact Cochran-Mantel-Haenszel (CMH) estimate of the common odds ratio (ASP0113 vs placebo) stratified by randomization group, and the 90% CI of the exact CMH odds ratio stratified by randomization group.

| | |
|-------------------|-----------------------|
| Comparison groups | Placebo v ASP0113 5mg |
|-------------------|-----------------------|

| | |
|---|-------------------------|
| Number of subjects included in analysis | 146 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.419 ^[4] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Common Odds Ratio |
| Point estimate | 0.88 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.48 |
| upper limit | 1.61 |

Notes:

[4] - P-value (1-sided) of the exact CMH method adjusted odds ratio stratified by randomization group.

Secondary: Percentage of Participants with Graft Survival (Primary Study Period)

| | |
|-----------------|---|
| End point title | Percentage of Participants with Graft Survival (Primary Study Period) |
|-----------------|---|

End point description:

Graft survival was defined for any participants that did not fit the definition of graft loss. Graft loss was defined as participant death, re-transplant, nephrectomy, or return to permanent dialysis (i.e., for > 30 days). Missing values for graft survival were not included in the denominator when making the proportion. The analysis population was the FAS.

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

End point timeframe:

From first study dose injection (Day 1) up to one year post study drug injection (up to Day 380)

| End point values | Placebo | ASP0113 5mg | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 74 | 76 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 98.53 | 100 | | |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Common Odds Ratio of Participants w/Graft Survival |
|----------------------------|--|

Statistical analysis description:

Exact Cochran-Mantel-Haenszel estimate of the common odds ratio (ASP0113 versus Placebo) could not be estimated and is denoted as "9999." Moreover, upper limit of 90% CI of odds ratio is an infinity value and is also denoted as "9999."

| | |
|-------------------|-----------------------|
| Comparison groups | Placebo v ASP0113 5mg |
|-------------------|-----------------------|

| | |
|---|-------------------------|
| Number of subjects included in analysis | 150 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.5 ^[5] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Common Odds Ratio |
| Point estimate | 9999 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.11 |
| upper limit | 9999 |

Notes:

[5] - P-value (1-sided) of the Exact Cochran-Mantel-Haenszel method adjusted odds ratio stratified by randomization group.

Secondary: Percentage of Participants with Graft Survival (Long-term Follow up)

| | |
|-----------------|--|
| End point title | Percentage of Participants with Graft Survival (Long-term Follow up) |
|-----------------|--|

End point description:

Graft survival was defined for any participants that did not fit the definition of graft loss. Graft loss was defined as participant death, re-transplant, nephrectomy, or return to permanent dialysis (i.e., for > 30 days). The analysis population was FAS.

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

End point timeframe:

From Day 395 to next 4.5 years

| End point values | Placebo | ASP0113 5mg | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 74 | 76 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| Long-term Follow up Month 18 | 91.9 | 94.7 | | |
| Long-term Follow up Month 30 | 83.8 | 81.6 | | |
| Long-term Follow up Month 42 | 85.1 | 80.3 | | |
| Long-term Follow up Month 54 | 78.4 | 77.6 | | |
| Long-term Follow up Month 66 | 82.4 | 84.2 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 to Day 380

Adverse event reporting additional description:

Treatment Emergent Adverse Event (TEAE) was defined as an AE observed after the first study drug injection Day 1 through Day 380. No AEs were collected/reported during the long-term follow-up period.

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

Dictionary used

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

| | |
|--------------------|-----|
| Dictionary version | v16 |
|--------------------|-----|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | ASP0113 |
|-----------------------|---------|

Reporting group description:

Participants received 1 mL of 5 mg/mL of ASP0113 via injection in the deltoid muscle alternating sides with each dose on days 30, 60, 90, 120 and 180 in relation to the day of transplant (Day 0).

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Participants received 1 mL of 5 mg/mL of placebo via injection in the deltoid muscle alternating sides with each dose on days 30, 60, 90, 120 and 180 in relation to the day of transplant (Day 0).

| Serious adverse events | ASP0113 | Placebo | |
|---|------------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 44 / 75 (58.67%) | 36 / 74 (48.65%) | |
| number of deaths (all causes) | 7 | 5 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 2 / 75 (2.67%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colorectal cancer | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Invasive lobular breast carcinoma | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Metastases to peritoneum | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Prostate cancer | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 2 / 74 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Aortic aneurysm | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| 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 | 0 / 75 (0.00%) | 2 / 74 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 2 / 74 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jugular vein thrombosis | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (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 | 1 / 75 (1.33%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombophlebitis superficial | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (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 | 1 / 75 (1.33%) | 0 / 74 (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 | | | |
| Nephrectomy | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transurethral prostatectomy | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ureteral stent removal | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urostomy | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (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 | | | |
| Malaise | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Pyrexia | | | |
| subjects affected / exposed | 3 / 75 (4.00%) | 3 / 74 (4.05%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Kidney transplant rejection | | | |
| subjects affected / exposed | 3 / 75 (4.00%) | 4 / 74 (5.41%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (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 | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 5 / 75 (6.67%) | 4 / 74 (5.41%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood glucose increased | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HLA marker study positive | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immunosuppressant drug level increased | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Bone fissure | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Graft haemorrhage | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Graft thrombosis | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Lumbar vertebral fracture | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Perinephric collection | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural haematuria | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Seroma | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal compression fracture | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bradycardia | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Convulsion | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| 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 | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 2 / 75 (2.67%) | 2 / 74 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leukopenia | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 2 / 75 (2.67%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Angle closure glaucoma | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aphthous stomatitis | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Constipation | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 75 (2.67%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal toxicity | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subileus | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Umbilical hernia | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 75 (1.33%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Bile duct stone | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Diabetic foot | | | |
| subjects affected / exposed | 2 / 75 (2.67%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Calculus urinary | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematuria | | | |
| subjects affected / exposed | 2 / 75 (2.67%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|------------------|----------------|--|
| Nephropathy | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (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 | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal cyst | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure acute | | | |
| subjects affected / exposed | 10 / 75 (13.33%) | 6 / 74 (8.11%) | |
| occurrences causally related to treatment / all | 0 / 12 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal impairment | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal tubular necrosis | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 2 / 74 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ureteric stenosis | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary bladder atrophy | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary retention | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract disorder | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinoma | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Hyperparathyroidism tertiary | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Rhabdomyolysis | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (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 | | | |
| Abscess soft tissue | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BK virus infection | | | |
| subjects affected / exposed | 2 / 75 (2.67%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacterial pyelonephritis | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cytomegalovirus colitis | | | |
| subjects affected / exposed | 2 / 75 (2.67%) | 0 / 74 (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 | 7 / 75 (9.33%) | 2 / 74 (2.70%) | |
| occurrences causally related to treatment / all | 1 / 7 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cytomegalovirus mucocutaneous ulcer | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cytomegalovirus oesophagitis | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cytomegalovirus syndrome | | | |
| subjects affected / exposed | 2 / 75 (2.67%) | 5 / 74 (6.76%) | |
| occurrences causally related to treatment / all | 2 / 2 | 3 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cytomegalovirus viraemia | | | |
| subjects affected / exposed | 5 / 75 (6.67%) | 3 / 74 (4.05%) | |
| occurrences causally related to treatment / all | 3 / 7 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterococcal bacteraemia | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterocolitis bacterial | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epstein-Barr viraemia | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia bacteraemia | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia sepsis | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 5 / 75 (6.67%) | 2 / 74 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis clostridial | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis norovirus | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis viral | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematoma infection | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infected lymphocele | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Orchitis | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pneumocystis jiroveci pneumonia | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 2 / 75 (2.67%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia cytomegaloviral | | | |
| subjects affected / exposed | 3 / 75 (4.00%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia necrotising | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Polyomavirus-associated nephropathy | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 2 / 74 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal sepsis | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Streptococcal bacteraemia | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 75 (2.67%) | 2 / 74 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 3 / 75 (4.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection enterococcal | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection pseudomonal | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (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 | 3 / 75 (4.00%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetes mellitus | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetes mellitus inadequate control | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Failure to thrive | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 1 / 74 (1.35%) | |
| 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 | 1 / 75 (1.33%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 2 / 74 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 2 / 75 (2.67%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 2 / 75 (2.67%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypovolaemia | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | ASP0113 | Placebo | |
|---|-------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 75 / 75 (100.00%) | 72 / 74 (97.30%) | |
| Vascular disorders | | | |
| Arteriosclerosis | | | |
| subjects affected / exposed | 4 / 75 (5.33%) | 1 / 74 (1.35%) | |
| occurrences (all) | 4 | 1 | |
| Hypertension | | | |
| subjects affected / exposed | 12 / 75 (16.00%) | 9 / 74 (12.16%) | |
| occurrences (all) | 12 | 14 | |
| Hypotension | | | |
| subjects affected / exposed | 11 / 75 (14.67%) | 8 / 74 (10.81%) | |
| occurrences (all) | 16 | 10 | |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 4 / 74 (5.41%) | |
| occurrences (all) | 0 | 5 | |
| Surgical and medical procedures | | | |
| Ureteral stent removal | | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 6 / 74 (8.11%) | |
| occurrences (all) | 1 | 6 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 5 / 75 (6.67%) | 8 / 74 (10.81%) | |
| occurrences (all) | 5 | 8 | |
| Chills | | | |
| subjects affected / exposed | 2 / 75 (2.67%) | 4 / 74 (5.41%) | |
| occurrences (all) | 2 | 4 | |
| Fatigue | | | |
| subjects affected / exposed | 27 / 75 (36.00%) | 24 / 74 (32.43%) | |
| occurrences (all) | 59 | 38 | |
| Injection site erythema | | | |
| subjects affected / exposed | 8 / 75 (10.67%) | 2 / 74 (2.70%) | |
| occurrences (all) | 14 | 2 | |
| Injection site pain | | | |

| | | | |
|--|-------------------------|------------------------|--|
| subjects affected / exposed occurrences (all) | 47 / 75 (62.67%) 277 | 18 / 74 (24.32%) 46 | |
| Oedema subjects affected / exposed occurrences (all) | 5 / 75 (6.67%) 5 | 3 / 74 (4.05%) 3 | |
| Oedema peripheral subjects affected / exposed occurrences (all) | 9 / 75 (12.00%) 13 | 5 / 74 (6.76%) 8 | |
| Pyrexia subjects affected / exposed occurrences (all) | 9 / 75 (12.00%) 11 | 13 / 74 (17.57%) 14 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 7 / 75 (9.33%) 8 | 4 / 74 (5.41%) 4 | |
| Dyspnoea subjects affected / exposed occurrences (all) | 5 / 75 (6.67%) 9 | 8 / 74 (10.81%) 10 | |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 4 / 75 (5.33%) 4 | 5 / 74 (6.76%) 5 | |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 8 / 75 (10.67%) 11 | 6 / 74 (8.11%) 8 | |
| Investigations Blood creatinine increased subjects affected / exposed occurrences (all) | 11 / 75 (14.67%) 17 | 16 / 74 (21.62%) 19 | |
| Weight increased subjects affected / exposed occurrences (all) | 4 / 75 (5.33%) 4 | 3 / 74 (4.05%) 3 | |
| White blood cell count decreased subjects affected / exposed occurrences (all) | 1 / 75 (1.33%) 1 | 4 / 74 (5.41%) 12 | |
| Injury, poisoning and procedural complications | | | |

| | | | |
|---|------------------------|------------------------|--|
| Complications of transplant surgery subjects affected / exposed occurrences (all) | 2 / 75 (2.67%) 2 | 4 / 74 (5.41%) 4 | |
| Complications of transplanted kidney subjects affected / exposed occurrences (all) | 4 / 75 (5.33%) 4 | 4 / 74 (5.41%) 4 | |
| Procedural pain subjects affected / exposed occurrences (all) | 6 / 75 (8.00%) 10 | 2 / 74 (2.70%) 2 | |
| Cardiac disorders Bradycardia subjects affected / exposed occurrences (all) | 5 / 75 (6.67%) 5 | 3 / 74 (4.05%) 3 | |
| Tachycardia subjects affected / exposed occurrences (all) | 5 / 75 (6.67%) 5 | 3 / 74 (4.05%) 3 | |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) | 3 / 75 (4.00%) 3 | 9 / 74 (12.16%) 12 | |
| Headache subjects affected / exposed occurrences (all) | 13 / 75 (17.33%) 13 | 12 / 74 (16.22%) 14 | |
| Tremor subjects affected / exposed occurrences (all) | 10 / 75 (13.33%) 11 | 7 / 74 (9.46%) 9 | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 7 / 75 (9.33%) 7 | 4 / 74 (5.41%) 4 | |
| Leukopenia subjects affected / exposed occurrences (all) | 29 / 75 (38.67%) 32 | 19 / 74 (25.68%) 23 | |
| Neutropenia subjects affected / exposed occurrences (all) | 10 / 75 (13.33%) 11 | 6 / 74 (8.11%) 6 | |
| Thrombocytopenia | | | |

| | | | |
|--|------------------------|------------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 75 (1.33%) 1 | 5 / 74 (6.76%) 6 | |
| Eye disorders Vision blurred subjects affected / exposed occurrences (all) | 5 / 75 (6.67%) 5 | 1 / 74 (1.35%) 1 | |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) | 8 / 75 (10.67%) 9 | 6 / 74 (8.11%) 7 | |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 5 / 75 (6.67%) 5 | 3 / 74 (4.05%) 3 | |
| Constipation subjects affected / exposed occurrences (all) | 4 / 75 (5.33%) 4 | 6 / 74 (8.11%) 7 | |
| Diarrhoea subjects affected / exposed occurrences (all) | 23 / 75 (30.67%) 33 | 24 / 74 (32.43%) 38 | |
| Dyspepsia subjects affected / exposed occurrences (all) | 5 / 75 (6.67%) 6 | 3 / 74 (4.05%) 3 | |
| Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) | 1 / 75 (1.33%) 1 | 6 / 74 (8.11%) 7 | |
| Nausea subjects affected / exposed occurrences (all) | 13 / 75 (17.33%) 22 | 14 / 74 (18.92%) 19 | |
| Vomiting subjects affected / exposed occurrences (all) | 9 / 75 (12.00%) 12 | 9 / 74 (12.16%) 13 | |
| Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) | 3 / 75 (4.00%) 3 | 8 / 74 (10.81%) 9 | |
| Rash | | | |

| | | | |
|--|---------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 4 / 75 (5.33%) 4 | 2 / 74 (2.70%) 2 | |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 5 / 75 (6.67%) | 6 / 74 (8.11%) | |
| occurrences (all) | 5 | 6 | |
| Haematuria | | | |
| subjects affected / exposed | 6 / 75 (8.00%) | 7 / 74 (9.46%) | |
| occurrences (all) | 8 | 7 | |
| Kidney fibrosis | | | |
| subjects affected / exposed | 7 / 75 (9.33%) | 4 / 74 (5.41%) | |
| occurrences (all) | 7 | 4 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 5 / 75 (6.67%) | 8 / 74 (10.81%) | |
| occurrences (all) | 7 | 10 | |
| Back pain | | | |
| subjects affected / exposed | 5 / 75 (6.67%) | 8 / 74 (10.81%) | |
| occurrences (all) | 6 | 9 | |
| Muscle spasms | | | |
| subjects affected / exposed | 3 / 75 (4.00%) | 5 / 74 (6.76%) | |
| occurrences (all) | 3 | 6 | |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 75 (0.00%) | 4 / 74 (5.41%) | |
| occurrences (all) | 0 | 4 | |
| Musculoskeletal discomfort | | | |
| subjects affected / exposed | 4 / 75 (5.33%) | 6 / 74 (8.11%) | |
| occurrences (all) | 11 | 7 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 4 / 75 (5.33%) | 2 / 74 (2.70%) | |
| occurrences (all) | 4 | 2 | |
| Myalgia | | | |
| subjects affected / exposed | 21 / 75 (28.00%) | 15 / 74 (20.27%) | |
| occurrences (all) | 38 | 22 | |
| Pain in extremity | | | |

| | | | |
|--|---------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 4 / 75 (5.33%) 5 | 8 / 74 (10.81%) 9 | |
| Infections and infestations | | | |
| BK virus infection | | | |
| subjects affected / exposed | 16 / 75 (21.33%) | 16 / 74 (21.62%) | |
| occurrences (all) | 17 | 18 | |
| Cytomegalovirus infection | | | |
| subjects affected / exposed | 3 / 75 (4.00%) | 5 / 74 (6.76%) | |
| occurrences (all) | 4 | 7 | |
| Cytomegalovirus syndrome | | | |
| subjects affected / exposed | 7 / 75 (9.33%) | 6 / 74 (8.11%) | |
| occurrences (all) | 7 | 6 | |
| Cytomegalovirus viraemia | | | |
| subjects affected / exposed | 22 / 75 (29.33%) | 19 / 74 (25.68%) | |
| occurrences (all) | 30 | 22 | |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 6 / 75 (8.00%) | 5 / 74 (6.76%) | |
| occurrences (all) | 9 | 5 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 8 / 75 (10.67%) | 8 / 74 (10.81%) | |
| occurrences (all) | 10 | 10 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 8 / 75 (10.67%) | 7 / 74 (9.46%) | |
| occurrences (all) | 9 | 7 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 10 / 75 (13.33%) | 4 / 74 (5.41%) | |
| occurrences (all) | 17 | 5 | |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 8 / 75 (10.67%) | 3 / 74 (4.05%) | |
| occurrences (all) | 11 | 5 | |
| Metabolism and nutrition disorders | | | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 4 / 75 (5.33%) | 1 / 74 (1.35%) | |
| occurrences (all) | 4 | 1 | |
| Decreased appetite | | | |

| | | |
|-----------------------------|------------------|-----------------|
| subjects affected / exposed | 3 / 75 (4.00%) | 5 / 74 (6.76%) |
| occurrences (all) | 3 | 5 |
| Hypercalcaemia | | |
| subjects affected / exposed | 4 / 75 (5.33%) | 5 / 74 (6.76%) |
| occurrences (all) | 4 | 5 |
| Hyperglycaemia | | |
| subjects affected / exposed | 2 / 75 (2.67%) | 5 / 74 (6.76%) |
| occurrences (all) | 2 | 6 |
| Hyperkalaemia | | |
| subjects affected / exposed | 12 / 75 (16.00%) | 8 / 74 (10.81%) |
| occurrences (all) | 16 | 8 |
| Hyperlipidaemia | | |
| subjects affected / exposed | 4 / 75 (5.33%) | 3 / 74 (4.05%) |
| occurrences (all) | 4 | 3 |
| Hypomagnesaemia | | |
| subjects affected / exposed | 7 / 75 (9.33%) | 6 / 74 (8.11%) |
| occurrences (all) | 13 | 6 |
| Hypoglycaemia | | |
| subjects affected / exposed | 1 / 75 (1.33%) | 6 / 74 (8.11%) |
| occurrences (all) | 1 | 7 |
| Hyponatraemia | | |
| subjects affected / exposed | 5 / 75 (6.67%) | 1 / 74 (1.35%) |
| occurrences (all) | 7 | 1 |
| Hypophosphataemia | | |
| subjects affected / exposed | 7 / 75 (9.33%) | 7 / 74 (9.46%) |
| occurrences (all) | 8 | 8 |
| Metabolic acidosis | | |
| subjects affected / exposed | 11 / 75 (14.67%) | 4 / 74 (5.41%) |
| occurrences (all) | 12 | 4 |
| Vitamin D deficiency | | |
| subjects affected / exposed | 7 / 75 (9.33%) | 4 / 74 (5.41%) |
| occurrences (all) | 7 | 4 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 13 August 2013 | Key changes in Substantial Amendment 1, dated 13 Aug 2013, are summarized below. • Patients with graft failure would be discontinued from treatment • 1-sided P value (not 2-sided) would be used for testing the hypothesis • Urinalysis with microscopic evaluation was added to the safety labs • Vital signs for reactogenicity assessments were added • Screening laboratory tests could be repeated once • Collect creatinine values during the long-term follow-up period, if available |
| 06 January 2014 | Key changes in Substantial Amendment 2, dated 06 Jan 2014, are summarized below. • Screening period could begin -14 days from transplant to day of randomization • Redefined CMV viremia as plasma viral load ≥ 1000 IU/mL • Expanded stratification criteria for ATG to day of randomization • Revised CMV AVP period of adjustment to after the day of randomization • Added vital signs and evaluation of patients 15 minutes after study drug injection • Inclusion Criterion 5 - clarified patients received valganciclovir or ganciclovir per regulatory label (package insert) • Exclusion Criteria: Excluded patients who required dialysis on day of randomization, Deleted criterion that excluded patients who had an episode of hyperacute or acute rejection prior to Randomization, Excluded patients who received eculizumab, bortezomib, and intravenous immunoglobulin (IVIG) and/or plasmapheresis from day of transplantation through day of randomization, Clarified contraindications to prophylaxis of CMV viremia/disease with valganciclovir and ganciclovir, Clarified a contraindication to an intramuscular injection also included those who were expected to have a contraindication to the injection, Clarified aspartate aminotransferase (AST) or alanine aminotransferase (ALT) criteria was within 3 days prior to randomization, Concomitant medications – included several clarifications (dose adjustments, interruptions to therapy, time periods for prohibited medications, recording) and additional prohibited medications, Spontaneously reported SAEs during long-term follow-up that were possibly or probably related to study drug should be reported. • Patients with a temperature $\geq 100.4^{\circ}\text{F}$ should not receive study drug • Transplant surgery on day 0 would not be considered an AE or SAE |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

N/A

Notes: