



## Clinical trial results:

**Prospective, open-label, randomised, two-arm, controlled, multicentre clinical trial, phase I/IIa, for the evaluation of safety and efficacy of an adoptive immunotherapy with allogeneic CMV-/EBV-specific peptide-stimulated T-cells (CD3+) for the prevention or treatment of reactivation of 'CMV and/or EBV in patients after allogeneic HLA-identical stem cell transplantation**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2012-004240-30 |
| Trial protocol           | DE             |
| Global end of trial date | 26 April 2019  |

### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 03 July 2020 |
| First version publication date | 03 July 2020 |

### Trial information

#### Trial identification

|                       |                 |
|-----------------------|-----------------|
| Sponsor protocol code | AIT-MULTIVIR-01 |
|-----------------------|-----------------|

#### Additional study identifiers

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

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Universitätsklinikum Erlangen   |
| Sponsor organisation address | Maximiliansplatz 2, Erlangen, Germany, 91054  |
| Public contact               | Direktion Medizinische Klinik 5, Medizinische Klinik 5, Universitätsklinikum Erlangen, +49 09131 85 35954, andreas.mackensen@uk-erlangen.de |
| Scientific contact           | Direktion Medizinische Klinik 5, Medizinische Klinik 5, Universitätsklinikum Erlangen, +49 09131 85 35954, andreas.mackensen@uk-erlangen.de |

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                       | 26 April 2019 |
| Is this the analysis of the primary completion data? | Yes           |
| Primary completion date                              | 26 April 2019 |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 26 April 2019 |
| Was the trial ended prematurely?                     | Yes           |

Notes:

## General information about the trial

Main objective of the trial:

Evaluation of the safety and tolerability of an adoptive immunotherapy with CMV-/EBV-specific peptide-stimulated T-cells (CD3+) for prevention or treatment of the reactivation of CMV or EBV infection in patients after allogeneic HLA-identical stem cell transplantation.

Protection of trial subjects:

IMP sterility and purity testing, Premedication with antihistaminics, cardiopulmonal Monitoring

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 01 July 2014 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | Yes          |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Germany: 29 |
| Worldwide total number of subjects   | 29          |
| EEA total number of subjects         | 29          |

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)                      | 23 |
| From 65 to 84 years                       | 6  |

|                   |   |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Screening and randomization -> SCT -> Eligibility check Prior to IMP Administration -> final enrollment -> IMP admin. (Verum)/watch and wait (Control)

### Period 1

|                              |                         |
|------------------------------|-------------------------|
| Period 1 title               | Baseline 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>             | Verum1 |

Arm description:

Subjects randomized to IMP

|  |  |
|--|--|
| Arm type                               | Experimental   |
| Investigational medicinal product name | Allogeneic CMV-/EBV-specific peptide-stimulated T-cells (CD3+) |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection   |
| Routes of administration               | Intravenous use  |

Dosage and administration details:

20.000 - 50.000 cells per kg BW, 3 applications (day 1/30/60 = day 30/60/90 after stem cell Transplantation)

|                  |          |
|------------------|----------|
| <b>Arm title</b> | Control1 |
|------------------|----------|

Arm description:

Subjects randomized to Control

|   |                 |
|---|-----------------|
| Arm type  | No intervention |
| No investigational medicinal product assigned in this arm |                 |

| Number of subjects in period 1 | Verum1 | Control1 |
|--------------------------------|--------|----------|
| Started                        | 16     | 13       |
| Completed                      | 16     | 13       |

|  |  |
|--|--|
| <b>Period 2</b>  |  |
| Period 2 title   | Pre-Treatment period   |
| Is this the baseline period?   | No   |
| Allocation method  | Randomised - controlled  |
| Blinding used  | Not blinded  |
| <b>Arms</b>  |  |
| Are arms mutually exclusive?   | Yes  |
| <b>Arm title</b>   | Verum2   |
| Arm description:   |  |
| Subjects randomized to IMP who passed eligibility Evaluation (V2) and for whom IMP could be produced         |  |
| Arm type   | Experimental   |
| Investigational medicinal product name   | Allogeneic CMV-/EBV-specific peptide-stimulated T-cells (CD3+) |
| Investigational medicinal product code   |  |
| Other name   |  |
| Pharmaceutical forms   | Solution for injection   |
| Routes of administration   | Intravenous use  |
| Dosage and administration details:   |  |
| 20.000 - 50.000 cells per kg BW, 3 applications (day 1/30/60 = day 30/60/90 after stem cell Transplantation) |  |
| <b>Arm title</b>   | Control2   |
| Arm description:   |  |
| Subjects randomized to Control plus subjects randomized to Verum but IMP could not be produced               |  |
| Arm type   | No intervention  |
| No investigational medicinal product assigned in this arm  |  |

| Number of subjects in period 2      | Verum2 | Control2 |
|-------------------------------------|--------|----------|
| Started                             | 16     | 13       |
| Completed                           | 9      | 16       |
| Not completed                       | 7      | 0        |
| Consent withdrawn by subject        | 2      | -        |
| Physician decision                  | 2      | -        |
| Transferred to other arm/group      | 3      | -        |
| Joined                              | 0      | 3        |
| Transferred in from other group/arm | -      | 3        |

|  |  |
|--|--|
| <b>Period 3</b>  |  |
| Period 3 title   | Treatment and Follow up  |
| Is this the baseline period?   | No   |
| Allocation method  | Randomised - controlled  |
| Blinding used  | Not blinded  |
| <b>Arms</b>  |  |
| Are arms mutually exclusive?   | Yes  |
| <b>Arm title</b>   | Verum3   |
| Arm description:   |  |
| Subjects with at least one IMP administered  |  |
| Arm type   | Experimental   |
| Investigational medicinal product name   | Allogeneic CMV-/EBV-specific peptide-stimulated T-cells (CD3+) |
| Investigational medicinal product code   |  |
| Other name   |  |
| Pharmaceutical forms   | Solution for injection   |
| Routes of administration   | Intravenous use  |
| Dosage and administration details:   |  |
| 20.000 - 50.000 cells per kg BW, 3 applications (day 1/30/60 = day 30/60/90 after stem cell Transplantation) |  |
| <b>Arm title</b>   | Control3   |
| Arm description:   |  |
| Subjects from Control2 who reached EoS (day 204)   |  |
| Arm type   | No intervention  |
| No investigational medicinal product assigned in this arm  |  |

| Number of subjects in period 3  | Verum3 | Control3 |
|---------------------------------|--------|----------|
| Started                         | 9      | 16       |
| Completed                       | 9      | 14       |
| Not completed                   | 0      | 2        |
| Adverse event, non-fatal        | -      | 1        |
| Relaps underlying disease (AML) | -      | 1        |

## Baseline characteristics

### Reporting groups

|  |          |
|--|----------|
| Reporting group title  | Verum1   |
| Reporting group description:<br>Subjects randomized to IMP     |          |
| Reporting group title  | Control1 |
| Reporting group description:<br>Subjects randomized to Control |          |

| Reporting group values                                | Verum1   | Control1 | Total |
|---|----------|----------|-------|
| Number of subjects                                    | 16       | 13       | 29    |
| Age categorical<br>Units: Subjects                    |          |          |       |
| In utero  |          |          | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) |          |          | 0     |
| Newborns (0-27 days)                                  |          |          | 0     |
| Infants and toddlers (28 days-23 months)              |          |          | 0     |
| Children (2-11 years)                                 |          |          | 0     |
| Adolescents (12-17 years)                             |          |          | 0     |
| Adults (18-64 years)                                  |          |          | 0     |
| From 65-84 years                                      |          |          | 0     |
| 85 years and over                                     |          |          | 0     |
| Age continuous<br>Units: years                        |          |          |       |
| arithmetic mean                                       | 57.2     | 56.3     |       |
| full range (min-max)                                  | 29 to 75 | 25 to 74 | -     |
| Gender categorical<br>Units: Subjects                 |          |          |       |
| Female  | 3        | 1        | 4     |
| Male  | 13       | 12       | 25    |

## End points

### End points reporting groups

|  |          |
|--|----------|
| Reporting group title  | Verum1   |
| Reporting group description:<br>Subjects randomized to IMP   |          |
| Reporting group title  | Control1 |
| Reporting group description:<br>Subjects randomized to Control   |          |
| Reporting group title  | Verum2   |
| Reporting group description:<br>Subjects randomized to IMP who passed eligibility Evaluation (V2) and for whom IMP could be produced |          |
| Reporting group title  | Control2 |
| Reporting group description:<br>Subjects randomized to Control plus subjects randomized to Verum but IMP could not be produced       |          |
| Reporting group title  | Verum3   |
| Reporting group description:<br>Subjects with at least one IMP administered  |          |
| Reporting group title  | Control3 |
| Reporting group description:<br>Subjects from Control2 who reached EoS (day 204)   |          |

### Primary: Occurrence of acute toxicity

|  |   |
|--|---|
| End point title  | Occurrence of acute toxicity <sup>[1]</sup> |
| End point description:<br>e.g. allergic or anaphylactic reaction CTCAE ≥ 2 |   |
| End point type   | Primary                                     |
| End point timeframe:<br>within 72 Hours after Administration of the IMP    |   |

Notes:

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

Justification: Toxicity could occur only in Verum Group (Control: no IMP given); as no toxicity was reported, no statistical Analysis necessary

|                             |                 |  |  |  |
|-----------------------------|-----------------|--|--|--|
| <b>End point values</b>     | Verum3          |  |  |  |
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 9               |  |  |  |
| Units: events               | 0               |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: De novo onset of acute GvHD within 14 days after administration of the IMP



|                 |   |
|-----------------|---|
| End point title | De novo onset of acute GvHD within 14 days after administration of the IMP <sup>[2]</sup> |
|-----------------|---|

End point description:

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

End point timeframe:

at all visits during Treatment and follow up period

Notes:

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

Justification: Acute GvHD within 14 days after IMP administration could occur only in Verum Group (Control: no IMP given); as no Acute GvHD within 14 days after IMP administration was reported, no statistical Analysis necessary

|                             |                 |  |  |  |
|-----------------------------|-----------------|--|--|--|
| <b>End point values</b>     | Verum3          |  |  |  |
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 9               |  |  |  |
| Units: events               | 0               |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Occurrence of an aggravation of pre-existing acute GvHD (persistent acute GvHD) within 14 days after administratin of the IMP

|                 |  |
|-----------------|--|
| End point title | Occurrence of an aggravation of pre-existing acute GvHD (persistent acute GvHD) within 14 days after administratin of the IMP <sup>[3]</sup> |
|-----------------|--|

End point description:

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

End point timeframe:

at all visits during Treatment and follow-up period

Notes:

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

Justification: Endpoint could occur only in Verum Group (Control: no IMP given); as no Aggravation of a pre-existing acute GvHD was reported, no statistical Analysis necessary

|                             |                 |  |  |  |
|-----------------------------|-----------------|--|--|--|
| <b>End point values</b>     | Verum3          |  |  |  |
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 9               |  |  |  |
| Units: events               | 0               |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Occurrence of at least one CMV reactivation

|   |   |
|---|---|
| End point title   | Occurrence of at least one CMV reactivation |
| End point description:                                  |   |
| End point type  | Primary                                     |
| End point timeframe:                                    |   |
| at all visits during the Treatment and follow-up period |   |

|                             |                 |                 |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| <b>End point values</b>     | Verum3          | Control3        |  |  |
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 9               | 14              |  |  |
| Units: event                | 4               | 9               |  |  |

|                                   |   |
|-----------------------------------|---|
| <b>Attachments (see zip file)</b> | Cum incid CMV reactivation/Graph_CMV_reactivation.png |
|-----------------------------------|---|

### Statistical analyses

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | CMV reactivation Chi squared |
| Comparison groups                       | Verum3 v Control3            |
| Number of subjects included in analysis | 23                           |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | superiority                  |
| P-value                                 | = 0.349                      |
| Method                                  | Chi-squared                  |

|   |                                |
|---|--------------------------------|
| <b>Statistical analysis title</b>       | CMV reactivation log-rank test |
| Comparison groups                       | Verum3 v Control3              |
| Number of subjects included in analysis | 23                             |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | superiority                    |
| P-value                                 | = 0.17                         |
| Method                                  | Logrank                        |

### Secondary: Occurrence of at least one EBV reactivation

|   |   |
|---|---|
| End point title   | Occurrence of at least one EBV reactivation |
| End point description:                                  |   |
| End point type  | Secondary                                   |
| End point timeframe:                                    |   |
| at all visits during the Treatment and follow-up period |   |

|                             |                 |                 |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| <b>End point values</b>     | Verum3          | Control3        |  |  |
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 9               | 14              |  |  |
| Units: event                | 7               | 6               |  |  |

### Statistical analyses

|   |                   |
|---|-------------------|
| <b>Statistical analysis title</b>       | EBV reactivation  |
| Comparison groups                       | Verum3 v Control3 |
| Number of subjects included in analysis | 23                |
| Analysis specification                  | Pre-specified     |
| Analysis type                           | superiority       |
| P-value                                 | = 0.099           |
| Method                                  | Chi-squared       |

### Secondary: Occurrence of CMV viral load requiring treatment, cumulative dose valganciclovir

|   |  |
|---|--|
| End point title   | Occurrence of CMV viral load requiring treatment, cumulative dose valganciclovir |
| End point description:                                  |  |
| End point type  | Secondary  |
| End point timeframe:                                    |  |
| at all visits during the Treatment and follow-up period |  |

|                                      |                 |                  |  |  |
|--------------------------------------|-----------------|------------------|--|--|
| <b>End point values</b>              | Verum3          | Control3         |  |  |
| Subject group type                   | Reporting group | Reporting group  |  |  |
| Number of subjects analysed          | 4               | 6 <sup>[4]</sup> |  |  |
| Units: mg                            |                 |                  |  |  |
| arithmetic mean (standard deviation) | 26550 (± 20238) | 32721 (± 18680)  |  |  |

Notes:

[4] - Control Group: 14 subjects; cmv reactivation: 9 subjects; Treatment with valganciclovir: 6 subjects

### Statistical analyses

|                                   |                   |
|-----------------------------------|-------------------|
| <b>Statistical analysis title</b> | T-test            |
| Comparison groups                 | Verum3 v Control3 |

|   |                 |
|---|-----------------|
| Number of subjects included in analysis | 10              |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority     |
| P-value                                 | = 0.621         |
| Method                                  | t-test, 2-sided |

### Secondary: Occurrence of EBV viral load requiring treatment

|   |  |
|---|--|
| End point title   | Occurrence of EBV viral load requiring treatment |
| End point description:                                  |  |
| End point type  | Secondary  |
| End point timeframe:                                    |  |
| at all visits during the Treatment and follow-up period |  |

| End point values            | Verum3           | Control3         |  |  |
|-----------------------------|------------------|------------------|--|--|
| Subject group type          | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed | 7 <sup>[5]</sup> | 6 <sup>[6]</sup> |  |  |
| Units: subjects             | 3                | 3                |  |  |

Notes:

[5] - Verum Group: 9 subjects, EBV reactivation: 7 subjects, Treatment with Rituximab: 3 subjects

[6] - Control Group: 14 subjects, EBV reactivation: 6 subjects, Treatment with Rituximab: 3 subjects

### Statistical analyses

|   |                   |
|---|-------------------|
| Statistical analysis title              | Chi squared       |
| Comparison groups                       | Verum3 v Control3 |
| Number of subjects included in analysis | 13                |
| Analysis specification                  | Pre-specified     |
| Analysis type                           | superiority       |
| P-value                                 | = 0.343           |
| Method                                  | Chi-squared       |

### Secondary: De novo onset of acute GvHD

|   |                             |
|---|-----------------------------|
| End point title                                     | De novo onset of acute GvHD |
| End point description:                              |                             |
| End point type                                      | Secondary                   |
| End point timeframe:                                |                             |
| at all visits during Treatment and follow up period |                             |

| End point values            | Verum3          | Control3        |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 9               | 14              |  |  |
| Units: event                | 3               | 7               |  |  |

|                                   |   |
|-----------------------------------|---|
| <b>Attachments (see zip file)</b> | Logrank_cumulative_incidence_acute_GvHD.pdf |
|-----------------------------------|---|

### Statistical analyses

|   |                   |
|---|-------------------|
| <b>Statistical analysis title</b>       | Logrank           |
| Comparison groups                       | Verum3 v Control3 |
| Number of subjects included in analysis | 23                |
| Analysis specification                  | Post-hoc          |
| Analysis type                           | superiority       |
| P-value                                 | = 0.55            |
| Method                                  | Logrank           |

### Secondary: Occurrence of CMV viral load requiring treatment, days of valganciclovir treatment

|                 |  |
|-----------------|--|
| End point title | Occurrence of CMV viral load requiring treatment, days of valganciclovir treatment |
|-----------------|--|

End point description:

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

End point timeframe:

at all visits during the Treatment and follow-up period

| End point values                     | Verum3          | Control3        |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 4               | 6               |  |  |
| Units: days                          |                 |                 |  |  |
| arithmetic mean (standard deviation) | 22.00 (± 17.5)  | 37.14 (± 28.4)  |  |  |

### Statistical analyses

|                                   |                   |
|-----------------------------------|-------------------|
| <b>Statistical analysis title</b> | t-test            |
| Comparison groups                 | Verum3 v Control3 |

|   |                 |
|---|-----------------|
| Number of subjects included in analysis | 10              |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority     |
| P-value                                 | = 0.365         |
| Method                                  | t-test, 2-sided |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

from day 1 (day of first IMP Administration, for Control Group day 1 = day 28 after SCT) until day 204 after SCT

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 22.1   |

### Reporting groups

|                       |                          |
|-----------------------|--------------------------|
| Reporting group title | Verum (IMP administered) |
|-----------------------|--------------------------|

Reporting group description:

patients who switched from Verum to Control Group without any IMP administered were assigned to the reporting group "Control (no IMP administered)"

|                       |                               |
|-----------------------|-------------------------------|
| Reporting group title | Control (no IMP administered) |
|-----------------------|-------------------------------|

Reporting group description:

Patients who were randomized to the Verum Group but switched to the Control Group without any IMP Administration were assigned to the reporting Group "Control (no IMP administered)"

| Serious adverse events                            | Verum (IMP administered) | Control (no IMP administered) |  |
|---|--------------------------|-------------------------------|--|
| Total subjects affected by serious adverse events |                          |                               |  |
| subjects affected / exposed                       | 7 / 9 (77.78%)           | 10 / 16 (62.50%)              |  |
| number of deaths (all causes)                     | 0                        | 0                             |  |
| number of deaths resulting from adverse events    | 0                        | 0                             |  |
| Surgical and medical procedures                   |                          |                               |  |
| Joint arthroplasty                                |                          |                               |  |
| subjects affected / exposed                       | 1 / 9 (11.11%)           | 0 / 16 (0.00%)                |  |
| occurrences causally related to treatment / all   | 0 / 1                    | 0 / 0                         |  |
| deaths causally related to treatment / all        | 0 / 0                    | 0 / 0                         |  |
| Nervous system disorders                          |                          |                               |  |
| Radiculopathy                                     |                          |                               |  |
| subjects affected / exposed                       | 0 / 9 (0.00%)            | 1 / 16 (6.25%)                |  |
| occurrences causally related to treatment / all   | 0 / 0                    | 0 / 1                         |  |
| deaths causally related to treatment / all        | 0 / 0                    | 0 / 0                         |  |
| Transient ischaemic attack                        |                          |                               |  |
| subjects affected / exposed                       | 1 / 9 (11.11%)           | 0 / 16 (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                                 |                |                |  |
| Pyrexia   |                |                |  |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 1 / 16 (6.25%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Immune system disorders                         |                |                |  |
| Acute graft versus host disease                 |                |                |  |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 0 / 16 (0.00%) |  |
| occurrences causally related to treatment / all | 2 / 2          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Acute graft versus host disease in liver        |                |                |  |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 0 / 16 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Graft versus host disease                       |                |                |  |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 1 / 16 (6.25%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastrointestinal disorders                      |                |                |  |
| Diverticular perforation                        |                |                |  |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 1 / 16 (6.25%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pancreatitis                                    |                |                |  |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 0 / 16 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Renal and urinary disorders                     |                |                |  |
| Acute kidney injury                             |                |                |  |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 1 / 16 (6.25%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Infections and infestations                     |                |                |  |
| Bronchitis                                      |                |                |  |



|   |                |                 |  |
|---|----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Cytomegalovirus infection                       |                |                 |  |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 3 / 16 (18.75%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 3           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Device related infection                        |                |                 |  |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Epstein-Barr virus infection                    |                |                 |  |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 1 / 16 (6.25%)  |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Infection                                       |                |                 |  |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Large intestine infection                       |                |                 |  |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Respiratory tract infection                     |                |                 |  |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Sepsis  |                |                 |  |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Urinary tract infection                         |                |                 |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 3 / 9 (33.33%) | 1 / 16 (6.25%) |  |
| occurrences causally related to treatment / all | 0 / 4          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Metabolism and nutrition disorders              |                |                |  |
| Hypokalaemia                                    |                |                |  |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 1 / 16 (6.25%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| 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>                                   | Verum (IMP administered) | Control (no IMP administered) |  |
|---|--------------------------|-------------------------------|--|
| Total subjects affected by non-serious adverse events               |                          |                               |  |
| subjects affected / exposed   | 9 / 9 (100.00%)          | 16 / 16 (100.00%)             |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                          |                               |  |
| Chloroma  |                          |                               |  |
| subjects affected / exposed   | 0 / 9 (0.00%)            | 1 / 16 (6.25%)                |  |
| occurrences (all)   | 0                        | 1                             |  |
| Plasma cell myeloma   |                          |                               |  |
| subjects affected / exposed   | 1 / 9 (11.11%)           | 0 / 16 (0.00%)                |  |
| occurrences (all)   | 1                        | 0                             |  |
| Vascular disorders  |                          |                               |  |
| Flushing  |                          |                               |  |
| subjects affected / exposed   | 0 / 9 (0.00%)            | 2 / 16 (12.50%)               |  |
| occurrences (all)   | 0                        | 3                             |  |
| Haematoma   |                          |                               |  |
| subjects affected / exposed   | 1 / 9 (11.11%)           | 0 / 16 (0.00%)                |  |
| occurrences (all)   | 1                        | 0                             |  |
| hypertension  |                          |                               |  |
| subjects affected / exposed   | 1 / 9 (11.11%)           | 2 / 16 (12.50%)               |  |
| occurrences (all)   | 1                        | 3                             |  |
| Hypotension   |                          |                               |  |
| subjects affected / exposed   | 1 / 9 (11.11%)           | 0 / 16 (0.00%)                |  |
| occurrences (all)   | 1                        | 0                             |  |
| Circulatory collapse  |                          |                               |  |

|  |                |                 |  |
|--|----------------|-----------------|--|
| subjects affected / exposed                          | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |  |
| occurrences (all)                                    | 1              | 0               |  |
| Lymphoedema  |                |                 |  |
| subjects affected / exposed                          | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                                    | 0              | 1               |  |
| General disorders and administration site conditions |                |                 |  |
| Chest discomfort                                     |                |                 |  |
| subjects affected / exposed                          | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                                    | 0              | 1               |  |
| Fatigue  |                |                 |  |
| subjects affected / exposed                          | 4 / 9 (44.44%) | 1 / 16 (6.25%)  |  |
| occurrences (all)                                    | 8              | 1               |  |
| Pyrexia  |                |                 |  |
| subjects affected / exposed                          | 0 / 9 (0.00%)  | 6 / 16 (37.50%) |  |
| occurrences (all)                                    | 0              | 7               |  |
| Oedema peripheral                                    |                |                 |  |
| subjects affected / exposed                          | 2 / 9 (22.22%) | 1 / 16 (6.25%)  |  |
| occurrences (all)                                    | 5              | 2               |  |
| Chills   |                |                 |  |
| subjects affected / exposed                          | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                                    | 0              | 1               |  |
| Swelling   |                |                 |  |
| subjects affected / exposed                          | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                                    | 0              | 1               |  |
| Peripheral swelling                                  |                |                 |  |
| subjects affected / exposed                          | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                                    | 0              | 1               |  |
| Mucosal inflammation                                 |                |                 |  |
| subjects affected / exposed                          | 0 / 9 (0.00%)  | 2 / 16 (12.50%) |  |
| occurrences (all)                                    | 0              | 2               |  |
| Systemic inflammatory response syndrome              |                |                 |  |
| subjects affected / exposed                          | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                                    | 0              | 1               |  |
| Immune system disorders                              |                |                 |  |

|  |                     |                      |  |
|--|---------------------|----------------------|--|
| Acute graft versus host disease<br>subjects affected / exposed<br>occurrences (all)                                | 1 / 9 (11.11%)<br>4 | 3 / 16 (18.75%)<br>4 |  |
| Acute graft versus host disease in<br>skin<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 9 (11.11%)<br>2 | 5 / 16 (31.25%)<br>6 |  |
| Acute graft versus host disease in<br>intestine<br>subjects affected / exposed<br>occurrences (all)                | 0 / 9 (0.00%)<br>0  | 2 / 16 (12.50%)<br>2 |  |
| Chronic graft versus host disease<br>subjects affected / exposed<br>occurrences (all)                              | 2 / 9 (22.22%)<br>3 | 3 / 16 (18.75%)<br>4 |  |
| Chronic graft versus host disease in<br>skin<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 9 (11.11%)<br>1 | 2 / 16 (12.50%)<br>2 |  |
| Chronic graft versus host disease in<br>intestine<br>subjects affected / exposed<br>occurrences (all)              | 1 / 9 (11.11%)<br>1 | 0 / 16 (0.00%)<br>0  |  |
| Graft versus host disease in liver<br>subjects affected / exposed<br>occurrences (all)                             | 1 / 9 (11.11%)<br>2 | 1 / 16 (6.25%)<br>1  |  |
| Graft versus host disease<br>subjects affected / exposed<br>occurrences (all)                                      | 2 / 9 (22.22%)<br>2 | 0 / 16 (0.00%)<br>0  |  |
| Secondary immunodeficiency<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 9 (0.00%)<br>0  | 1 / 16 (6.25%)<br>3  |  |
| Reproductive system and breast<br>disorders<br>Balanoposthitis<br>subjects affected / exposed<br>occurrences (all) | 0 / 9 (0.00%)<br>0  | 1 / 16 (6.25%)<br>1  |  |
| Respiratory, thoracic and mediastinal<br>disorders   |                     |                      |  |

|  |                     |                       |  |
|--|---------------------|-----------------------|--|
| Dyspnoea exertional<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 9 (0.00%)<br>0  | 1 / 16 (6.25%)<br>1   |  |
| Oral mucosal blistering<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 9 (0.00%)<br>0  | 1 / 16 (6.25%)<br>1   |  |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)   | 0 / 9 (0.00%)<br>0  | 1 / 16 (6.25%)<br>1   |  |
| Cough<br>subjects affected / exposed<br>occurrences (all)  | 1 / 9 (11.11%)<br>1 | 2 / 16 (12.50%)<br>2  |  |
| Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)                                   | 1 / 9 (11.11%)<br>1 | 1 / 16 (6.25%)<br>1   |  |
| Psychiatric disorders<br>Insomnia<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 9 (0.00%)<br>0  | 2 / 16 (12.50%)<br>2  |  |
| Sleep disorder<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 9 (0.00%)<br>0  | 2 / 16 (12.50%)<br>2  |  |
| Confusional state<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 9 (0.00%)<br>0  | 1 / 16 (6.25%)<br>1   |  |
| Investigations<br>Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 9 (0.00%)<br>0  | 3 / 16 (18.75%)<br>10 |  |
| Hypoalbuminaemia<br>subjects affected / exposed<br>occurrences (all)                                     | 1 / 9 (11.11%)<br>3 | 0 / 16 (0.00%)<br>0   |  |
| Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all)                 | 2 / 9 (22.22%)<br>3 | 1 / 16 (6.25%)<br>1   |  |
| Alpha hydroxybutyrate<br>dehydrogenase increased   |                     |                       |  |

|                                      |                |                 |
|--------------------------------------|----------------|-----------------|
| subjects affected / exposed          | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |
| occurrences (all)                    | 0              | 2               |
| Amylase increased                    |                |                 |
| subjects affected / exposed          | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |
| occurrences (all)                    | 1              | 0               |
| Aspartate aminotransferase increased |                |                 |
| subjects affected / exposed          | 0 / 9 (0.00%)  | 3 / 16 (18.75%) |
| occurrences (all)                    | 0              | 10              |
| Blood pressure increased             |                |                 |
| subjects affected / exposed          | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |
| occurrences (all)                    | 0              | 1               |
| Clostridium test positive            |                |                 |
| subjects affected / exposed          | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |
| occurrences (all)                    | 1              | 0               |
| C-reactive protein increased         |                |                 |
| subjects affected / exposed          | 2 / 9 (22.22%) | 0 / 16 (0.00%)  |
| occurrences (all)                    | 2              | 0               |
| Electrolyte depletion                |                |                 |
| subjects affected / exposed          | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |
| occurrences (all)                    | 0              | 1               |
| Electrophoresis abnormal             |                |                 |
| subjects affected / exposed          | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |
| occurrences (all)                    | 0              | 1               |
| Serum ferritin increased             |                |                 |
| subjects affected / exposed          | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |
| occurrences (all)                    | 0              | 1               |
| Blood folate decreased               |                |                 |
| subjects affected / exposed          | 0 / 9 (0.00%)  | 3 / 16 (18.75%) |
| occurrences (all)                    | 0              | 3               |
| Gamma-glutamyltransferase increased  |                |                 |
| subjects affected / exposed          | 2 / 9 (22.22%) | 3 / 16 (18.75%) |
| occurrences (all)                    | 11             | 10              |
| Protein total decreased              |                |                 |

|  |                |                 |
|--|----------------|-----------------|
| subjects affected / exposed              | 1 / 9 (11.11%) | 1 / 16 (6.25%)  |
| occurrences (all)                        | 1              | 1               |
| Weight decreased                         |                |                 |
| subjects affected / exposed              | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |
| occurrences (all)                        | 4              | 0               |
| Blood immunoglobulin G decreased         |                |                 |
| subjects affected / exposed              | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |
| occurrences (all)                        | 0              | 1               |
| Immunoglobulins decreased                |                |                 |
| subjects affected / exposed              | 1 / 9 (11.11%) | 2 / 16 (12.50%) |
| occurrences (all)                        | 1              | 3               |
| International normalised ratio increased |                |                 |
| subjects affected / exposed              | 1 / 9 (11.11%) | 1 / 16 (6.25%)  |
| occurrences (all)                        | 1              | 1               |
| Blood potassium increased                |                |                 |
| subjects affected / exposed              | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |
| occurrences (all)                        | 0              | 1               |
| Blood potassium decreased                |                |                 |
| subjects affected / exposed              | 1 / 9 (11.11%) | 3 / 16 (18.75%) |
| occurrences (all)                        | 4              | 5               |
| Body temperature increased               |                |                 |
| subjects affected / exposed              | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |
| occurrences (all)                        | 1              | 0               |
| Blood creatine increased                 |                |                 |
| subjects affected / exposed              | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |
| occurrences (all)                        | 5              | 0               |
| Blood creatinine increased               |                |                 |
| subjects affected / exposed              | 3 / 9 (33.33%) | 3 / 16 (18.75%) |
| occurrences (all)                        | 12             | 12              |
| Blood lactate dehydrogenase increased    |                |                 |
| subjects affected / exposed              | 1 / 9 (11.11%) | 1 / 16 (6.25%)  |
| occurrences (all)                        | 1              | 2               |
| Hepatic enzyme increased                 |                |                 |

|  |                |                 |  |
|--|----------------|-----------------|--|
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                              | 0              | 1               |  |
| White blood cell count decreased               |                |                 |  |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 2 / 16 (12.50%) |  |
| occurrences (all)                              | 0              | 8               |  |
| Lipase increased                               |                |                 |  |
| subjects affected / exposed                    | 2 / 9 (22.22%) | 0 / 16 (0.00%)  |  |
| occurrences (all)                              | 12             | 0               |  |
| Carbon monoxide diffusing capacity decreased   |                |                 |  |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 2 / 16 (12.50%) |  |
| occurrences (all)                              | 0              | 2               |  |
| Lymphocyte count decreased                     |                |                 |  |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                              | 0              | 2               |  |
| Blood magnesium decreased                      |                |                 |  |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                              | 0              | 1               |  |
| Monoclonal immunoglobulin present              |                |                 |  |
| subjects affected / exposed                    | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |  |
| occurrences (all)                              | 1              | 0               |  |
| Neutrophil count decreased                     |                |                 |  |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                              | 0              | 3               |  |
| Sensory level abnormal                         |                |                 |  |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                              | 0              | 1               |  |
| Staphylococcus test positive                   |                |                 |  |
| subjects affected / exposed                    | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |  |
| occurrences (all)                              | 1              | 0               |  |
| Platelet count decreased                       |                |                 |  |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 3 / 16 (18.75%) |  |
| occurrences (all)                              | 0              | 16              |  |
| Injury, poisoning and procedural complications |                |                 |  |



|   |                     |                      |  |
|---|---------------------|----------------------|--|
| Femoral neck fracture<br>subjects affected / exposed<br>occurrences (all)     | 1 / 9 (11.11%)<br>1 | 0 / 16 (0.00%)<br>0  |  |
| Infusion related reaction<br>subjects affected / exposed<br>occurrences (all) | 0 / 9 (0.00%)<br>0  | 1 / 16 (6.25%)<br>1  |  |
| Fall<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 9 (11.11%)<br>1 | 2 / 16 (12.50%)<br>2 |  |
| Cardiac disorders   |                     |                      |  |
| Bradycardia<br>subjects affected / exposed<br>occurrences (all)               | 1 / 9 (11.11%)<br>1 | 0 / 16 (0.00%)<br>0  |  |
| Pericardial effusion<br>subjects affected / exposed<br>occurrences (all)      | 0 / 9 (0.00%)<br>0  | 1 / 16 (6.25%)<br>1  |  |
| Tachycardia<br>subjects affected / exposed<br>occurrences (all)               | 1 / 9 (11.11%)<br>1 | 0 / 16 (0.00%)<br>0  |  |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)       | 0 / 9 (0.00%)<br>0  | 1 / 16 (6.25%)<br>1  |  |
| Nervous system disorders  |                     |                      |  |
| Burning sensation feet<br>subjects affected / exposed<br>occurrences (all)    | 0 / 9 (0.00%)<br>0  | 1 / 16 (6.25%)<br>1  |  |
| Hypertension<br>subjects affected / exposed<br>occurrences (all)              | 3 / 9 (33.33%)<br>6 | 0 / 16 (0.00%)<br>0  |  |
| Dysgeusia<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 9 (0.00%)<br>0  | 1 / 16 (6.25%)<br>1  |  |
| Headache<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 9 (0.00%)<br>0  | 2 / 16 (12.50%)<br>2 |  |
| Paresis   |                     |                      |  |

|                                      |                |                 |  |
|--------------------------------------|----------------|-----------------|--|
| subjects affected / exposed          | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                    | 0              | 1               |  |
| Polyneuropathy                       |                |                 |  |
| subjects affected / exposed          | 0 / 9 (0.00%)  | 2 / 16 (12.50%) |  |
| occurrences (all)                    | 0              | 2               |  |
| Dizziness                            |                |                 |  |
| subjects affected / exposed          | 0 / 9 (0.00%)  | 2 / 16 (12.50%) |  |
| occurrences (all)                    | 0              | 2               |  |
| Syncope                              |                |                 |  |
| subjects affected / exposed          | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |  |
| occurrences (all)                    | 1              | 0               |  |
| Transient ischaemic attack           |                |                 |  |
| subjects affected / exposed          | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |  |
| occurrences (all)                    | 1              | 0               |  |
| Tremor                               |                |                 |  |
| subjects affected / exposed          | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |  |
| occurrences (all)                    | 1              | 0               |  |
| Blood and lymphatic system disorders |                |                 |  |
| Anaemia                              |                |                 |  |
| subjects affected / exposed          | 2 / 9 (22.22%) | 7 / 16 (43.75%) |  |
| occurrences (all)                    | 18             | 19              |  |
| Granulocytopenia                     |                |                 |  |
| subjects affected / exposed          | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                    | 0              | 1               |  |
| Immune thrombocytopenic purpura      |                |                 |  |
| subjects affected / exposed          | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                    | 0              | 10              |  |
| Splenic infarction                   |                |                 |  |
| subjects affected / exposed          | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                    | 0              | 1               |  |
| Leukopenia                           |                |                 |  |
| subjects affected / exposed          | 1 / 9 (11.11%) | 4 / 16 (25.00%) |  |
| occurrences (all)                    | 1              | 6               |  |
| Lymphadenopathy                      |                |                 |  |
| subjects affected / exposed          | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                    | 0              | 1               |  |

|  |                      |                       |  |
|--|----------------------|-----------------------|--|
| Monocytosis<br>subjects affected / exposed<br>occurrences (all)  | 1 / 9 (11.11%)<br>1  | 0 / 16 (0.00%)<br>0   |  |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)                                   | 2 / 9 (22.22%)<br>2  | 3 / 16 (18.75%)<br>11 |  |
| Ear and labyrinth disorders<br>Middle ear effusion<br>subjects affected / exposed<br>occurrences (all) | 0 / 9 (0.00%)<br>0   | 1 / 16 (6.25%)<br>1   |  |
| Vertigo<br>subjects affected / exposed<br>occurrences (all)  | 0 / 9 (0.00%)<br>0   | 1 / 16 (6.25%)<br>1   |  |
| Eye disorders<br>Erythema of eyelid<br>subjects affected / exposed<br>occurrences (all)                | 1 / 9 (11.11%)<br>1  | 0 / 16 (0.00%)<br>0   |  |
| Visual acuity reduced<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 9 (0.00%)<br>0   | 1 / 16 (6.25%)<br>1   |  |
| Dry eye<br>subjects affected / exposed<br>occurrences (all)  | 1 / 9 (11.11%)<br>1  | 1 / 16 (6.25%)<br>1   |  |
| Gastrointestinal disorders<br>Abdominal pain<br>subjects affected / exposed<br>occurrences (all)       | 1 / 9 (11.11%)<br>2  | 0 / 16 (0.00%)<br>0   |  |
| Chronic gastritis<br>subjects affected / exposed<br>occurrences (all)                                  | 1 / 9 (11.11%)<br>1  | 0 / 16 (0.00%)<br>0   |  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)  | 3 / 9 (33.33%)<br>13 | 1 / 16 (6.25%)<br>3   |  |
| Diverticular perforation<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 9 (0.00%)<br>0   | 1 / 16 (6.25%)<br>1   |  |
| Vomiting   |                      |                       |  |

|                             |                |                 |
|-----------------------------|----------------|-----------------|
| subjects affected / exposed | 2 / 9 (22.22%) | 4 / 16 (25.00%) |
| occurrences (all)           | 4              | 4               |
| Mucosal inflammation oral   |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |
| occurrences (all)           | 0              | 1               |
| Flatulence                  |                |                 |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |
| occurrences (all)           | 1              | 0               |
| Gastric disorder            |                |                 |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |
| occurrences (all)           | 1              | 0               |
| Gastric mucosa erythema     |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |
| occurrences (all)           | 0              | 1               |
| Oral pain                   |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |
| occurrences (all)           | 0              | 1               |
| Dry mouth                   |                |                 |
| subjects affected / exposed | 1 / 9 (11.11%) | 4 / 16 (25.00%) |
| occurrences (all)           | 1              | 4               |
| Constipation                |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |
| occurrences (all)           | 0              | 1               |
| Pancreatitis acute          |                |                 |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |
| occurrences (all)           | 1              | 0               |
| Proctalgia                  |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |
| occurrences (all)           | 0              | 1               |
| Oral mucosal erythema       |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |
| occurrences (all)           | 0              | 1               |
| Abdominal pain upper        |                |                 |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 16 (6.25%)  |
| occurrences (all)           | 1              | 1               |
| Stomatitis                  |                |                 |

|  |                |                 |  |
|--|----------------|-----------------|--|
| subjects affected / exposed            | 0 / 9 (0.00%)  | 2 / 16 (12.50%) |  |
| occurrences (all)                      | 0              | 2               |  |
| Nausea                                 |                |                 |  |
| subjects affected / exposed            | 4 / 9 (44.44%) | 5 / 16 (31.25%) |  |
| occurrences (all)                      | 6              | 9               |  |
| Tongue coated                          |                |                 |  |
| subjects affected / exposed            | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                      | 0              | 1               |  |
| Hepatobiliary disorders                |                |                 |  |
| Cholestasis                            |                |                 |  |
| subjects affected / exposed            | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |  |
| occurrences (all)                      | 1              | 0               |  |
| Cholecystitis chronic                  |                |                 |  |
| subjects affected / exposed            | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                      | 0              | 1               |  |
| Hyperbilirubinaemia                    |                |                 |  |
| subjects affected / exposed            | 1 / 9 (11.11%) | 1 / 16 (6.25%)  |  |
| occurrences (all)                      | 1              | 1               |  |
| Skin and subcutaneous tissue disorders |                |                 |  |
| Rash                                   |                |                 |  |
| subjects affected / exposed            | 2 / 9 (22.22%) | 3 / 16 (18.75%) |  |
| occurrences (all)                      | 3              | 3               |  |
| Erythema                               |                |                 |  |
| subjects affected / exposed            | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |  |
| occurrences (all)                      | 1              | 0               |  |
| Skin atrophy                           |                |                 |  |
| subjects affected / exposed            | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                      | 0              | 1               |  |
| Skin fissures                          |                |                 |  |
| subjects affected / exposed            | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                      | 0              | 1               |  |
| Skin hyperpigmentation                 |                |                 |  |
| subjects affected / exposed            | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                      | 0              | 1               |  |
| Sensitive skin                         |                |                 |  |

|                             |                |                 |  |
|-----------------------------|----------------|-----------------|--|
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)           | 0              | 1               |  |
| Papule                      |                |                 |  |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)           | 0              | 1               |  |
| Penile ulceration           |                |                 |  |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)           | 0              | 1               |  |
| Pruritus                    |                |                 |  |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 16 (6.25%)  |  |
| occurrences (all)           | 2              | 2               |  |
| stasis dermatitis           |                |                 |  |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |  |
| occurrences (all)           | 1              | 0               |  |
| Dry skin                    |                |                 |  |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)           | 0              | 1               |  |
| Renal and urinary disorders |                |                 |  |
| Acute kidney injury         |                |                 |  |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 16 (12.50%) |  |
| occurrences (all)           | 2              | 2               |  |
| Renal failure               |                |                 |  |
| subjects affected / exposed | 2 / 9 (22.22%) | 6 / 16 (37.50%) |  |
| occurrences (all)           | 3              | 9               |  |
| Pollakiuria                 |                |                 |  |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)           | 0              | 1               |  |
| Protein urine present       |                |                 |  |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |  |
| occurrences (all)           | 1              | 0               |  |
| Endocrine disorders         |                |                 |  |
| Cushing's syndrome          |                |                 |  |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)           | 0              | 1               |  |
| Hyperthyroidism             |                |                 |  |

|   |                |                 |  |
|---|----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                               | 0              | 1               |  |
| Hypothyroidism                                  |                |                 |  |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 2 / 16 (12.50%) |  |
| occurrences (all)                               | 1              | 2               |  |
| Musculoskeletal and connective tissue disorders |                |                 |  |
| Arthralgia                                      |                |                 |  |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                               | 0              | 1               |  |
| Muscle spasms                                   |                |                 |  |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 1 / 16 (6.25%)  |  |
| occurrences (all)                               | 1              | 1               |  |
| Muscular weakness                               |                |                 |  |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                               | 0              | 1               |  |
| Myalgia   |                |                 |  |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |  |
| occurrences (all)                               | 0              | 1               |  |
| Pain in extremity                               |                |                 |  |
| subjects affected / exposed                     | 2 / 9 (22.22%) | 1 / 16 (6.25%)  |  |
| occurrences (all)                               | 2              | 1               |  |
| Musculoskeletal pain                            |                |                 |  |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |  |
| occurrences (all)                               | 2              | 0               |  |
| Infections and infestations                     |                |                 |  |
| Respiratory tract infection                     |                |                 |  |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 1 / 16 (6.25%)  |  |
| occurrences (all)                               | 1              | 3               |  |
| Bacteriuria                                     |                |                 |  |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |  |
| occurrences (all)                               | 1              | 0               |  |
| Bronchitis                                      |                |                 |  |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 1 / 16 (6.25%)  |  |
| occurrences (all)                               | 1              | 1               |  |
| Bronchitis viral                                |                |                 |  |

|                                    |                |                 |
|------------------------------------|----------------|-----------------|
| subjects affected / exposed        | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |
| occurrences (all)                  | 1              | 0               |
| Clostridium difficile infection    |                |                 |
| subjects affected / exposed        | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |
| occurrences (all)                  | 1              | 0               |
| Diverticulitis                     |                |                 |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |
| occurrences (all)                  | 0              | 1               |
| Epstein-Barr virus infection       |                |                 |
| subjects affected / exposed        | 4 / 9 (44.44%) | 6 / 16 (37.50%) |
| occurrences (all)                  | 7              | 11              |
| Gastroenteritis Escherichia coli   |                |                 |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |
| occurrences (all)                  | 0              | 1               |
| Urinary tract infection            |                |                 |
| subjects affected / exposed        | 4 / 9 (44.44%) | 6 / 16 (37.50%) |
| occurrences (all)                  | 8              | 8               |
| Hepatitis infectious mononucleosis |                |                 |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |
| occurrences (all)                  | 0              | 1               |
| Enteritis infectious               |                |                 |
| subjects affected / exposed        | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |
| occurrences (all)                  | 1              | 0               |
| Infection                          |                |                 |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |
| occurrences (all)                  | 0              | 1               |
| Catheter site infection            |                |                 |
| subjects affected / exposed        | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |
| occurrences (all)                  | 1              | 0               |
| Upper respiratory tract infection  |                |                 |
| subjects affected / exposed        | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |
| occurrences (all)                  | 2              | 0               |
| Conjunctivitis                     |                |                 |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |
| occurrences (all)                  | 0              | 1               |
| Oral candidiasis                   |                |                 |



|                                    |                |                  |  |
|------------------------------------|----------------|------------------|--|
| subjects affected / exposed        | 1 / 9 (11.11%) | 5 / 16 (31.25%)  |  |
| occurrences (all)                  | 1              | 6                |  |
| Parvovirus B19 infection           |                |                  |  |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 2 / 16 (12.50%)  |  |
| occurrences (all)                  | 0              | 2                |  |
| Pneumonia                          |                |                  |  |
| subjects affected / exposed        | 1 / 9 (11.11%) | 1 / 16 (6.25%)   |  |
| occurrences (all)                  | 1              | 1                |  |
| Rhinitis                           |                |                  |  |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 1 / 16 (6.25%)   |  |
| occurrences (all)                  | 0              | 1                |  |
| Sepsis                             |                |                  |  |
| subjects affected / exposed        | 1 / 9 (11.11%) | 1 / 16 (6.25%)   |  |
| occurrences (all)                  | 1              | 1                |  |
| Sinusitis                          |                |                  |  |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 3 / 16 (18.75%)  |  |
| occurrences (all)                  | 0              | 3                |  |
| Systemic mycosis                   |                |                  |  |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 1 / 16 (6.25%)   |  |
| occurrences (all)                  | 0              | 1                |  |
| Viral infection                    |                |                  |  |
| subjects affected / exposed        | 1 / 9 (11.11%) | 0 / 16 (0.00%)   |  |
| occurrences (all)                  | 1              | 0                |  |
| Cystitis                           |                |                  |  |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 1 / 16 (6.25%)   |  |
| occurrences (all)                  | 0              | 1                |  |
| Cytomegalovirus infection          |                |                  |  |
| subjects affected / exposed        | 3 / 9 (33.33%) | 10 / 16 (62.50%) |  |
| occurrences (all)                  | 3              | 20               |  |
| Metabolism and nutrition disorders |                |                  |  |
| Decreased appetite                 |                |                  |  |
| subjects affected / exposed        | 1 / 9 (11.11%) | 3 / 16 (18.75%)  |  |
| occurrences (all)                  | 1              | 3                |  |
| Dehydration                        |                |                  |  |
| subjects affected / exposed        | 1 / 9 (11.11%) | 1 / 16 (6.25%)   |  |
| occurrences (all)                  | 1              | 1                |  |

|                             |                |                 |
|-----------------------------|----------------|-----------------|
| Folate deficiency           |                |                 |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 16 (6.25%)  |
| occurrences (all)           | 1              | 1               |
| Haemosiderosis              |                |                 |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 16 (0.00%)  |
| occurrences (all)           | 1              | 0               |
| Hypercholesterolaemia       |                |                 |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 16 (6.25%)  |
| occurrences (all)           | 5              | 1               |
| Hyperglycaemia              |                |                 |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 16 (6.25%)  |
| occurrences (all)           | 2              | 1               |
| Hyperuricaemia              |                |                 |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 16 (12.50%) |
| occurrences (all)           | 1              | 2               |
| Hypokalaemia                |                |                 |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 16 (6.25%)  |
| occurrences (all)           | 2              | 1               |
| Hypomagnesaemia             |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |
| occurrences (all)           | 0              | 2               |
| Hyponatraemia               |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |
| occurrences (all)           | 0              | 2               |
| Vitamin B12 deficiency      |                |                 |
| subjects affected / exposed | 3 / 9 (33.33%) | 0 / 16 (0.00%)  |
| occurrences (all)           | 4              | 0               |
| Vitamin D deficiency        |                |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 16 (6.25%)  |
| occurrences (all)           | 0              | 1               |
| Hypertriglyceridaemia       |                |                 |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 16 (6.25%)  |
| occurrences (all)           | 6              | 1               |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date          | Amendment   |
|---------------|---|
| 08 April 2016 | Clarification of preexisting safety endpoints, changes in forbidden/permitted concomitant medication, additional blood samples for immunomonitoring and Determination of viral load |

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.

|  |
|--|
| Small number of subjects recruited Limits informative value of results |
|--|

Notes: