



## Clinical trial results: An Open Label, Phase 2 Study to Evaluate Efficacy and Safety of Daratumumab in Relapsed or Refractory Mantle Cell Lymphoma, Diffuse Large B-Cell Lymphoma, and Follicular Lymphoma Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2014-005299-26 |
| Trial protocol           | BE NL          |
| Global end of trial date | 01 June 2017   |

### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 13 June 2018 |
| First version publication date | 13 June 2018 |

### Trial information

#### Trial identification

|                       |                 |
|-----------------------|-----------------|
| Sponsor protocol code | 54767414LYM2001 |
|-----------------------|-----------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02413489 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Janssen-Cilag International N.V   |
| Sponsor organisation address | Turnhoutseweg 30, Beerse, Belgium, B-2340   |
| Public contact               | Clinical Registry Group, Janssen-Cilag International N.V,<br>ClinicalTrialsEU@its.jnj.com |
| Scientific contact           | Clinical Registry Group, Janssen-Cilag International N.V,<br>ClinicalTrialsEU@its.jnj.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                       | 01 June 2017 |
| Is this the analysis of the primary completion data? | No           |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 01 June 2017 |
| Was the trial ended prematurely?                     | No           |

Notes:

## General information about the trial

Main objective of the trial:

The main objectives were to assess overall response rate (ORR), including complete response (CR) and partial response (PR), of daratumumab in subjects with non-Hodgkin's lymphoma (NHL) and to evaluate association between ORR and CD38 expression level in order to determine a threshold for CD38 expression level in each NHL subtype, above which daratumumab activity is enhanced.

Protection of trial subjects:

Safety evaluations included adverse event monitoring, physical examinations, electrocardiogram (ECG) monitoring, clinical laboratory parameters (hematology, urinalysis and chemistry), vital sign measurements, and Eastern Cooperative Oncology Group (ECOG) performance status.

Background therapy: -

Evidence for comparator: -

|   |                   |
|---|-------------------|
| Actual start date of recruitment                          | 25 September 2015 |
| Long term follow-up planned                               | No                |
| Independent data monitoring committee (IDMC) involvement? | No                |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                       |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Korea, Republic of: 6 |
| Country: Number of subjects enrolled | Netherlands: 7        |
| Country: Number of subjects enrolled | Turkey: 5             |
| Country: Number of subjects enrolled | Australia: 2          |
| Country: Number of subjects enrolled | Belgium: 2            |
| Country: Number of subjects enrolled | France: 6             |
| Country: Number of subjects enrolled | United States: 8      |
| Worldwide total number of subjects   | 36                    |
| EEA total number of subjects         | 15                    |

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          | 0 |

|                           |    |
|---------------------------|----|
| months)                   |    |
| Children (2-11 years)     | 0  |
| Adolescents (12-17 years) | 0  |
| Adults (18-64 years)      | 18 |
| From 65 to 84 years       | 18 |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

In total 36 subjects were treated (15 subjects in the diffuse large B-cell lymphoma {DLBCL} cohort, 16 subjects in the follicular lymphoma {FL} cohort, and 5 subjects in the mantle cell lymphoma {MCL} cohort).

### Period 1

|                              |                               |
|------------------------------|-------------------------------|
| Period 1 title               | End of Study (overall period) |
| Is this the baseline period? | Yes                           |
| Allocation method            | Non-randomised - controlled   |
| Blinding used                | Not blinded                   |

### Arms

|                              |                                       |
|------------------------------|---------------------------------------|
| Are arms mutually exclusive? | Yes                                   |
| <b>Arm title</b>             | Diffuse Large B-cell Lymphoma (DLBCL) |

Arm description:

Subjects received daratumumab 16 milligram per kilogram (mg/kg) as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.

|  |                                       |
|--|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | Daratumumab                           |
| Investigational medicinal product code |                                       |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

Dosage and administration details:

Subjects received daratumumab 16 mg/kg as intravenous infusion.

|                  |                          |
|------------------|--------------------------|
| <b>Arm title</b> | Follicular Lymphoma (FL) |
|------------------|--------------------------|

Arm description:

Subjects received daratumumab 16 mg/kg as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.

|  |                                       |
|--|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | Daratumumab                           |
| Investigational medicinal product code |                                       |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

Dosage and administration details:

Subjects received daratumumab 16 mg/kg as intravenous infusion.

|                  |                            |
|------------------|----------------------------|
| <b>Arm title</b> | Mantle Cell Lymphoma (MCL) |
|------------------|----------------------------|

Arm description:

Subjects received daratumumab 16 mg/kg as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |                                       |
|--|---------------------------------------|
| Investigational medicinal product name | Daratumumab                           |
| Investigational medicinal product code |                                       |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

Dosage and administration details:

Subjects received daratumumab 16 mg/kg as intravenous infusion.

| <b>Number of subjects in period 1</b> | Diffuse Large B-cell Lymphoma (DLBCL) | Follicular Lymphoma (FL) | Mantle Cell Lymphoma (MCL) |
|---------------------------------------|---------------------------------------|--------------------------|----------------------------|
| Started                               | 15                                    | 16                       | 5                          |
| Completed                             | 0                                     | 0                        | 0                          |
| Not completed                         | 15                                    | 16                       | 5                          |
| Consent withdrawn by subject          | 2                                     | -                        | -                          |
| Death                                 | 11                                    | 3                        | 4                          |
| Study terminated by sponsor           | 2                                     | 13                       | 1                          |

## Baseline characteristics

### Reporting groups

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | Diffuse Large B-cell Lymphoma (DLBCL) |
|-----------------------|---------------------------------------|

Reporting group description:

Subjects received daratumumab 16 milligram per kilogram (mg/kg) as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.

|                       |                          |
|-----------------------|--------------------------|
| Reporting group title | Follicular Lymphoma (FL) |
|-----------------------|--------------------------|

Reporting group description:

Subjects received daratumumab 16 mg/kg as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | Mantle Cell Lymphoma (MCL) |
|-----------------------|----------------------------|

Reporting group description:

Subjects received daratumumab 16 mg/kg as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.

| Reporting group values   | Diffuse Large B-cell Lymphoma (DLBCL) | Follicular Lymphoma (FL) | Mantle Cell Lymphoma (MCL) |
|--|---------------------------------------|--------------------------|----------------------------|
| Number of subjects   | 15                                    | 16                       | 5                          |
| Title for AgeCategorical<br>Units: subjects  |                                       |                          |                            |
| Children (2-11 years)  | 0                                     | 0                        | 0                          |
| Adolescents (12-17 years)  | 0                                     | 0                        | 0                          |
| Adults (18-64 years)   | 5                                     | 9                        | 4                          |
| From 65 to 84 years  | 10                                    | 7                        | 1                          |
| 85 years and over  | 0                                     | 0                        | 0                          |
| Title for AgeContinuous<br>Units: years  |                                       |                          |                            |
| arithmetic mean  | 66.7                                  | 62.3                     | 59.8                       |
| standard deviation   | ± 11.88                               | ± 9.77                   | ± 6.69                     |
| Title for Gender<br>Units: subjects  |                                       |                          |                            |
| Female   | 6                                     | 5                        | 0                          |
| Male   | 9                                     | 11                       | 5                          |
| CD38 expression value  |                                       |                          |                            |
| The expression levels of CD38 were used to do diagnosis of MCL, DLBCL, or FL and measurable disease. |                                       |                          |                            |
| Units: Percentage of CD38 expression   |                                       |                          |                            |
| arithmetic mean  | 76.3                                  | 70.3                     | 64                         |
| standard deviation   | ± 18.07                               | ± 16.78                  | ± 8.22                     |

| Reporting group values                      | Total |  |  |
|---|-------|--|--|
| Number of subjects                          | 36    |  |  |
| Title for AgeCategorical<br>Units: subjects |       |  |  |
| Children (2-11 years)                       | 0     |  |  |
| Adolescents (12-17 years)                   | 0     |  |  |
| Adults (18-64 years)                        | 18    |  |  |
| From 65 to 84 years                         | 18    |  |  |

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

|  |    |  |  |
|--|----|--|--|
| Title for AgeContinuous<br>Units: years<br>arithmetic mean<br>standard deviation                     | -  |  |  |
| Title for Gender<br>Units: subjects  |    |  |  |
| Female   | 11 |  |  |
| Male   | 25 |  |  |
| CD38 expression value  |    |  |  |
| The expression levels of CD38 were used to do diagnosis of MCL, DLBCL, or FL and measurable disease. |    |  |  |
| Units: Percentage of CD38 expression<br>arithmetic mean<br>standard deviation                        | -  |  |  |

## End points

### End points reporting groups

|  |                                       |
|--|---------------------------------------|
| Reporting group title  | Diffuse Large B-cell Lymphoma (DLBCL) |
| Reporting group description:<br>Subjects received daratumumab 16 milligram per kilogram (mg/kg) as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end. |                                       |
| Reporting group title  | Follicular Lymphoma (FL)              |
| Reporting group description:<br>Subjects received daratumumab 16 mg/kg as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.                          |                                       |
| Reporting group title  | Mantle Cell Lymphoma (MCL)            |
| Reporting group description:<br>Subjects received daratumumab 16 mg/kg as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.                          |                                       |

### Primary: Overall Response Rate (ORR)

|   |  |
|---|--|
| End point title   | Overall Response Rate (ORR) <sup>[1]</sup> |
| End point description:<br>ORR was defined as the percentage of subjects who achieved complete response (CR) or partial response (PR). As per Revised Response Criteria for Malignant Lymphoma, Lymph node measurements were taken from Computed Tomography (CT), CT portion of the Positron Emission Tomography/Computed Tomography (PET/CT), or Magnetic resonance imaging (MRI) scans where applicable. CR is defined as complete disappearance of all evidence of disease; PR as a > 50 % decrease in the sum of the products of the maximal perpendicular diameters of measured lesions (SPD) and no new sites. The analysis population was all subjects that were treated with daratumumab. Here "99999" indicates data was not estimable as no subjects had response. |  |
| End point type  | Primary                                    |
| End point timeframe:<br>After the first dose until disease progression, withdrawal of consent from study participation, or the end of study (approximately 1.9 years)   |  |
| Notes:<br>[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.<br>Justification: Descriptive statistics were done, no inferential statistical analyses were performed.   |  |

| End point values                 | Diffuse Large B-cell Lymphoma (DLBCL) | Follicular Lymphoma (FL) | Mantle Cell Lymphoma (MCL) |  |
|----------------------------------|---------------------------------------|--------------------------|----------------------------|--|
| Subject group type               | Reporting group                       | Reporting group          | Reporting group            |  |
| Number of subjects analysed      | 15                                    | 16                       | 5                          |  |
| Units: Percentage of subjects    |                                       |                          |                            |  |
| number (confidence interval 95%) | 6.7 (0.2 to 31.9)                     | 12.5 (1.6 to 38.3)       | 0 (0 to 99999)             |  |

### Statistical analyses



No statistical analyses for this end point

### Secondary: Duration of Response

|                 |                      |
|-----------------|----------------------|
| End point title | Duration of Response |
|-----------------|----------------------|

End point description:

Duration of response was the duration from the date of the initial documentation of a response to the date of first documented evidence of progressive disease (PD). PD is defined as any new lesion >1.5 centimeter (cm) in any axis or  $\geq 50\%$  increase in previously involved sites. The analysis population was all subjects that were treated with daratumumab and who achieved overall response. There was insufficient data to perform Kaplan Meier analysis, therefore individual data for each evaluable subject was reported.

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

End point timeframe:

Approximately 1.9 years

| End point values            | Diffuse Large B-cell Lymphoma (DLBCL) | Follicular Lymphoma (FL) | Mantle Cell Lymphoma (MCL) |  |
|-----------------------------|---------------------------------------|--------------------------|----------------------------|--|
| Subject group type          | Reporting group                       | Reporting group          | Reporting group            |  |
| Number of subjects analysed | 1                                     | 2                        | 0 <sup>[2]</sup>           |  |
| Units: Months               |                                       |                          |                            |  |
| number (not applicable)     |                                       |                          |                            |  |
| Subject 1                   | 1.6                                   | 0.7                      |                            |  |
| Subject 2                   | 0                                     | 7.4                      |                            |  |

Notes:

[2] - None of subjects achieved response for this particular arm.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Progression Free Survival (PFS)

|                 |                                 |
|-----------------|---------------------------------|
| End point title | Progression Free Survival (PFS) |
|-----------------|---------------------------------|

End point description:

PFS was defined as the duration from the date of the first daratumumab dose to the date of Progression or death, whichever comes first. The analysis population was all subjects that were treated with daratumumab.

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

End point timeframe:

Approximately 1.9 years

| End point values                 | Diffuse Large B-cell Lymphoma (DLBCL) | Follicular Lymphoma (FL) | Mantle Cell Lymphoma (MCL) |  |
|----------------------------------|---------------------------------------|--------------------------|----------------------------|--|
| Subject group type               | Reporting group                       | Reporting group          | Reporting group            |  |
| Number of subjects analysed      | 15                                    | 16                       | 5                          |  |
| Units: Months                    |                                       |                          |                            |  |
| number (confidence interval 95%) | 1.2 (0.6 to 1.7)                      | 3.3 (1.9 to 3.8)         | 1.3 (0.5 to 1.9)           |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Overall Survival (OS)

|                 |                       |
|-----------------|-----------------------|
| End point title | Overall Survival (OS) |
|-----------------|-----------------------|

End point description:

Overall survival was defined as the duration from the date of the first daratumumab dose to the date of death. The analysis population was all subjects that were treated with daratumumab. Here "99999" upper limit of CI was not estimable due to less number of subjects with events and "99999" for MCL group indicates that Upper limit of CI could not be estimated due to less number of subjects analyzed.

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

End point timeframe:

Approximately 1.9 years

| End point values                 | Diffuse Large B-cell Lymphoma (DLBCL) | Follicular Lymphoma (FL) | Mantle Cell Lymphoma (MCL) |  |
|----------------------------------|---------------------------------------|--------------------------|----------------------------|--|
| Subject group type               | Reporting group                       | Reporting group          | Reporting group            |  |
| Number of subjects analysed      | 15                                    | 16                       | 5                          |  |
| Units: Months                    |                                       |                          |                            |  |
| number (confidence interval 95%) | 4.9 (2.1 to 9.0)                      | 17.2 (15.0 to 99999)     | 4.8 (1.7 to 99999)         |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time to Response

|                 |                  |
|-----------------|------------------|
| End point title | Time to Response |
|-----------------|------------------|

End point description:

Time to response was defined as the duration from the date of the first dose of daratumumab to the earliest date that a response (CR/PR) is first documented. The analysis population was all subjects that were treated with daratumumab and who achieved overall response There was insufficient data to perform Kaplan Meier analysis, therefore individual data for each evaluable subject was reported.

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

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End point timeframe:  
Approximately 1.9 years

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| <b>End point values</b>     | Diffuse Large B-cell Lymphoma (DLBCL) | Follicular Lymphoma (FL) | Mantle Cell Lymphoma (MCL) |  |
|-----------------------------|---------------------------------------|--------------------------|----------------------------|--|
| Subject group type          | Reporting group                       | Reporting group          | Reporting group            |  |
| Number of subjects analysed | 1                                     | 2                        | 0 <sup>[3]</sup>           |  |
| Units: Months               |                                       |                          |                            |  |
| number (not applicable)     |                                       |                          |                            |  |
| Subject 1                   | 1.9                                   | 2.3                      |                            |  |
| Subject 2                   | 0                                     | 1.9                      |                            |  |

Notes:

[3] - None of subjects achieved response for this particular arm.

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 1.9 years

Adverse event reporting additional description:

Analysis set included all subjects who received at least 1 dose of study treatment, and contributed any safety data after the start of study treatment.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 19.1 |
|--------------------|------|

### Reporting groups

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | Diffuse Large B-cell Lymphoma (DLBCL) |
|-----------------------|---------------------------------------|

Reporting group description:

Subjects received daratumumab 16 milligram per kilogram (mg/kg) as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.

|                       |                          |
|-----------------------|--------------------------|
| Reporting group title | Follicular Lymphoma (FL) |
|-----------------------|--------------------------|

Reporting group description:

Subjects received daratumumab 16 mg/kg as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | Mantle Cell Lymphoma (MCL) |
|-----------------------|----------------------------|

Reporting group description:

Subjects received daratumumab 16 mg/kg as intravenous infusion once every week for 8 weeks; then once every other week for 16 weeks; thereafter once every 4 weeks until documented progression, unacceptable toxicity, or study end.

| Serious adverse events  | Diffuse Large B-cell Lymphoma (DLBCL) | Follicular Lymphoma (FL) | Mantle Cell Lymphoma (MCL) |
|---|---------------------------------------|--------------------------|----------------------------|
| Total subjects affected by serious adverse events                   |                                       |                          |                            |
| subjects affected / exposed   | 6 / 15 (40.00%)                       | 6 / 16 (37.50%)          | 3 / 5 (60.00%)             |
| number of deaths (all causes)                                       | 11                                    | 3                        | 4                          |
| number of deaths resulting from adverse events                      |                                       |                          |                            |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                       |                          |                            |
| Diffuse Large B-Cell Lymphoma                                       |                                       |                          |                            |
| subjects affected / exposed   | 0 / 15 (0.00%)                        | 1 / 16 (6.25%)           | 0 / 5 (0.00%)              |
| occurrences causally related to treatment / all                     | 0 / 0                                 | 0 / 1                    | 0 / 0                      |
| deaths causally related to treatment / all                          | 0 / 0                                 | 0 / 0                    | 0 / 0                      |
| Injury, poisoning and procedural complications                      |                                       |                          |                            |
| Spinal Fracture   |                                       |                          |                            |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                          | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 0 / 5 (0.00%)  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders                 |                |                |                |
| Febrile Neutropenia                                  |                |                |                |
| subjects affected / exposed                          | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 1 / 5 (20.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          | 1 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Lymphadenopathy                                      |                |                |                |
| subjects affected / exposed                          | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 0 / 5 (0.00%)  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Thrombocytopenia                                     |                |                |                |
| subjects affected / exposed                          | 1 / 15 (6.67%) | 0 / 16 (0.00%) | 0 / 5 (0.00%)  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions |                |                |                |
| General Physical Health Deterioration                |                |                |                |
| subjects affected / exposed                          | 1 / 15 (6.67%) | 0 / 16 (0.00%) | 1 / 5 (20.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 1          |
| Pyrexia  |                |                |                |
| subjects affected / exposed                          | 0 / 15 (0.00%) | 0 / 16 (0.00%) | 2 / 5 (40.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 2 / 2          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                           |                |                |                |
| Abdominal Pain Lower                                 |                |                |                |
| subjects affected / exposed                          | 1 / 15 (6.67%) | 0 / 16 (0.00%) | 0 / 5 (0.00%)  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                          |                |                |                |
| Acute Kidney Injury                                  |                |                |                |

|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 1 / 15 (6.67%) | 0 / 16 (0.00%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Chronic Kidney Disease                          |                |                |               |
| subjects affected / exposed                     | 1 / 15 (6.67%) | 0 / 16 (0.00%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0         |
| Musculoskeletal and connective tissue disorders |                |                |               |
| Musculoskeletal Pain                            |                |                |               |
| subjects affected / exposed                     | 1 / 15 (6.67%) | 0 / 16 (0.00%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Infections and infestations                     |                |                |               |
| Pneumonia                                       |                |                |               |
| subjects affected / exposed                     | 1 / 15 (6.67%) | 1 / 16 (6.25%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 1 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0         |
| Pneumonia Cytomegaloviral                       |                |                |               |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Urinary Tract Infection                         |                |                |               |
| subjects affected / exposed                     | 0 / 15 (0.00%) | 1 / 16 (6.25%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Metabolism and nutrition disorders              |                |                |               |
| Decreased Appetite                              |                |                |               |
| subjects affected / exposed                     | 1 / 15 (6.67%) | 0 / 16 (0.00%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |

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

| <b>Non-serious adverse events</b>                                   | <b>Diffuse Large B-cell Lymphoma (DLBCL)</b> | <b>Follicular Lymphoma (FL)</b> | <b>Mantle Cell Lymphoma (MCL)</b> |
|---|--|---------------------------------|-----------------------------------|
| Total subjects affected by non-serious adverse events               |  |                                 |                                   |
| subjects affected / exposed   | 15 / 15 (100.00%)                            | 16 / 16 (100.00%)               | 5 / 5 (100.00%)                   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |                                 |                                   |
| Tumour Pain   |  |                                 |                                   |
| subjects affected / exposed   | 0 / 15 (0.00%)                               | 1 / 16 (6.25%)                  | 0 / 5 (0.00%)                     |
| occurrences (all)   | 0  | 2                               | 0                                 |
| Vascular disorders  |  |                                 |                                   |
| Flushing  |  |                                 |                                   |
| subjects affected / exposed   | 0 / 15 (0.00%)                               | 2 / 16 (12.50%)                 | 1 / 5 (20.00%)                    |
| occurrences (all)   | 0  | 2                               | 1                                 |
| Hot Flush   |  |                                 |                                   |
| subjects affected / exposed   | 0 / 15 (0.00%)                               | 0 / 16 (0.00%)                  | 1 / 5 (20.00%)                    |
| occurrences (all)   | 0  | 0                               | 1                                 |
| Hypertension  |  |                                 |                                   |
| subjects affected / exposed   | 2 / 15 (13.33%)                              | 3 / 16 (18.75%)                 | 0 / 5 (0.00%)                     |
| occurrences (all)   | 2  | 3                               | 0                                 |
| Hypotension   |  |                                 |                                   |
| subjects affected / exposed   | 1 / 15 (6.67%)                               | 1 / 16 (6.25%)                  | 0 / 5 (0.00%)                     |
| occurrences (all)   | 1  | 1                               | 0                                 |
| General disorders and administration site conditions                |  |                                 |                                   |
| Asthenia  |  |                                 |                                   |
| subjects affected / exposed   | 0 / 15 (0.00%)                               | 1 / 16 (6.25%)                  | 0 / 5 (0.00%)                     |
| occurrences (all)   | 0  | 2                               | 0                                 |
| Catheter Site Erythema  |  |                                 |                                   |
| subjects affected / exposed   | 1 / 15 (6.67%)                               | 0 / 16 (0.00%)                  | 0 / 5 (0.00%)                     |
| occurrences (all)   | 1  | 0                               | 0                                 |
| Catheter Site Inflammation  |  |                                 |                                   |
| subjects affected / exposed   | 1 / 15 (6.67%)                               | 0 / 16 (0.00%)                  | 0 / 5 (0.00%)                     |
| occurrences (all)   | 1  | 0                               | 0                                 |
| Chest Discomfort  |  |                                 |                                   |
| subjects affected / exposed   | 0 / 15 (0.00%)                               | 1 / 16 (6.25%)                  | 0 / 5 (0.00%)                     |
| occurrences (all)   | 0  | 1                               | 0                                 |
| Chills  |  |                                 |                                   |
| subjects affected / exposed   | 2 / 15 (13.33%)                              | 1 / 16 (6.25%)                  | 1 / 5 (20.00%)                    |
| occurrences (all)   | 2  | 1                               | 1                                 |

|   |                 |                 |                |
|---|-----------------|-----------------|----------------|
| Fatigue   |                 |                 |                |
| subjects affected / exposed                     | 4 / 15 (26.67%) | 3 / 16 (18.75%) | 1 / 5 (20.00%) |
| occurrences (all)                               | 4               | 4               | 1              |
| General Physical Health Deterioration           |                 |                 |                |
| subjects affected / exposed                     | 1 / 15 (6.67%)  | 0 / 16 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                               | 1               | 0               | 0              |
| Influenza Like Illness                          |                 |                 |                |
| subjects affected / exposed                     | 0 / 15 (0.00%)  | 2 / 16 (12.50%) | 0 / 5 (0.00%)  |
| occurrences (all)                               | 0               | 2               | 0              |
| Malaise   |                 |                 |                |
| subjects affected / exposed                     | 3 / 15 (20.00%) | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)                               | 4               | 1               | 0              |
| Non-Cardiac Chest Pain                          |                 |                 |                |
| subjects affected / exposed                     | 0 / 15 (0.00%)  | 1 / 16 (6.25%)  | 1 / 5 (20.00%) |
| occurrences (all)                               | 0               | 1               | 1              |
| Oedema Peripheral                               |                 |                 |                |
| subjects affected / exposed                     | 1 / 15 (6.67%)  | 2 / 16 (12.50%) | 1 / 5 (20.00%) |
| occurrences (all)                               | 1               | 2               | 3              |
| Pain  |                 |                 |                |
| subjects affected / exposed                     | 1 / 15 (6.67%)  | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)                               | 1               | 1               | 0              |
| Pyrexia   |                 |                 |                |
| subjects affected / exposed                     | 2 / 15 (13.33%) | 4 / 16 (25.00%) | 1 / 5 (20.00%) |
| occurrences (all)                               | 2               | 6               | 1              |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                |
| Cough   |                 |                 |                |
| subjects affected / exposed                     | 7 / 15 (46.67%) | 6 / 16 (37.50%) | 4 / 5 (80.00%) |
| occurrences (all)                               | 7               | 9               | 5              |
| Dysphonia                                       |                 |                 |                |
| subjects affected / exposed                     | 0 / 15 (0.00%)  | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)                               | 0               | 1               | 0              |
| Dyspnoea  |                 |                 |                |
| subjects affected / exposed                     | 1 / 15 (6.67%)  | 2 / 16 (12.50%) | 2 / 5 (40.00%) |
| occurrences (all)                               | 1               | 2               | 3              |
| Hiccups   |                 |                 |                |



|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0              |
| Hypoxia                     |                |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0              |
| Laryngeal Oedema            |                |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0              |
| Nasal Congestion            |                |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%) | 3 / 16 (18.75%) | 1 / 5 (20.00%) |
| occurrences (all)           | 0              | 4               | 1              |
| Oropharyngeal Discomfort    |                |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0              |
| Oropharyngeal Pain          |                |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0              |
| Pharyngeal Oedema           |                |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 16 (0.00%)  | 1 / 5 (20.00%) |
| occurrences (all)           | 0              | 0               | 1              |
| Pleural Effusion            |                |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0              |
| Productive Cough            |                |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%) | 2 / 16 (12.50%) | 0 / 5 (0.00%)  |
| occurrences (all)           | 0              | 5               | 0              |
| Rales                       |                |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0              |
| Respiratory Failure         |                |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0              |
| Rhinorrhoea                 |                |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%) | 2 / 16 (12.50%) | 0 / 5 (0.00%)  |
| occurrences (all)           | 0              | 2               | 0              |
| Sinus Congestion            |                |                 |                |

|  |                      |                      |                     |
|--|----------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 15 (0.00%)<br>0  | 0 / 16 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |
| Sneezing<br>subjects affected / exposed<br>occurrences (all)   | 0 / 15 (0.00%)<br>0  | 2 / 16 (12.50%)<br>2 | 0 / 5 (0.00%)<br>0  |
| Throat Irritation<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 15 (0.00%)<br>0  | 2 / 16 (12.50%)<br>2 | 2 / 5 (40.00%)<br>3 |
| Upper-Airway Cough Syndrome<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 15 (0.00%)<br>0  | 0 / 16 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |
| Wheezing<br>subjects affected / exposed<br>occurrences (all)   | 0 / 15 (0.00%)<br>0  | 0 / 16 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |
| Psychiatric disorders<br>Anxiety<br>subjects affected / exposed<br>occurrences (all)                     | 2 / 15 (13.33%)<br>2 | 0 / 16 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  |
| Delirium<br>subjects affected / exposed<br>occurrences (all)   | 1 / 15 (6.67%)<br>1  | 0 / 16 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  |
| Depressed Mood<br>subjects affected / exposed<br>occurrences (all)                                       | 1 / 15 (6.67%)<br>1  | 0 / 16 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)   | 3 / 15 (20.00%)<br>3 | 2 / 16 (12.50%)<br>3 | 1 / 5 (20.00%)<br>1 |
| Product issues<br>Thrombosis in Device<br>subjects affected / exposed<br>occurrences (all)               | 0 / 15 (0.00%)<br>0  | 1 / 16 (6.25%)<br>1  | 0 / 5 (0.00%)<br>0  |
| Investigations<br>Alanine Aminotransferase Increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 15 (6.67%)<br>1  | 0 / 16 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |
| Aspartate Aminotransferase Increased   |                      |                      |                     |

|  |                 |                 |               |
|--|-----------------|-----------------|---------------|
| subjects affected / exposed                    | 2 / 15 (13.33%) | 0 / 16 (0.00%)  | 0 / 5 (0.00%) |
| occurrences (all)                              | 2               | 0               | 0             |
| C-Reactive Protein Increased                   |                 |                 |               |
| subjects affected / exposed                    | 1 / 15 (6.67%)  | 0 / 16 (0.00%)  | 0 / 5 (0.00%) |
| occurrences (all)                              | 1               | 0               | 0             |
| Cytomegalovirus Test Positive                  |                 |                 |               |
| subjects affected / exposed                    | 1 / 15 (6.67%)  | 0 / 16 (0.00%)  | 0 / 5 (0.00%) |
| occurrences (all)                              | 1               | 0               | 0             |
| Oxygen Saturation Decreased                    |                 |                 |               |
| subjects affected / exposed                    | 1 / 15 (6.67%)  | 1 / 16 (6.25%)  | 0 / 5 (0.00%) |
| occurrences (all)                              | 1               | 1               | 0             |
| Prostatic Specific Antigen Increased           |                 |                 |               |
| subjects affected / exposed                    | 0 / 15 (0.00%)  | 1 / 16 (6.25%)  | 0 / 5 (0.00%) |
| occurrences (all)                              | 0               | 1               | 0             |
| Weight Decreased                               |                 |                 |               |
| subjects affected / exposed                    | 3 / 15 (20.00%) | 2 / 16 (12.50%) | 0 / 5 (0.00%) |
| occurrences (all)                              | 3               | 2               | 0             |
| Weight Increased                               |                 |                 |               |
| subjects affected / exposed                    | 0 / 15 (0.00%)  | 1 / 16 (6.25%)  | 0 / 5 (0.00%) |
| occurrences (all)                              | 0               | 1               | 0             |
| Injury, poisoning and procedural complications |                 |                 |               |
| Contusion                                      |                 |                 |               |
| subjects affected / exposed                    | 1 / 15 (6.67%)  | 0 / 16 (0.00%)  | 0 / 5 (0.00%) |
| occurrences (all)                              | 1               | 0               | 0             |
| Hip Fracture                                   |                 |                 |               |
| subjects affected / exposed                    | 0 / 15 (0.00%)  | 1 / 16 (6.25%)  | 0 / 5 (0.00%) |
| occurrences (all)                              | 0               | 1               | 0             |
| Procedural Pain                                |                 |                 |               |
| subjects affected / exposed                    | 0 / 15 (0.00%)  | 1 / 16 (6.25%)  | 0 / 5 (0.00%) |
| occurrences (all)                              | 0               | 1               | 0             |
| Skin Abrasion                                  |                 |                 |               |
| subjects affected / exposed                    | 0 / 15 (0.00%)  | 1 / 16 (6.25%)  | 0 / 5 (0.00%) |
| occurrences (all)                              | 0               | 1               | 0             |
| Cardiac disorders                              |                 |                 |               |

|   |                     |                      |                     |
|---|---------------------|----------------------|---------------------|
| Sinus Bradycardia<br>subjects affected / exposed<br>occurrences (all)             | 0 / 15 (0.00%)<br>0 | 1 / 16 (6.25%)<br>1  | 0 / 5 (0.00%)<br>0  |
| Nervous system disorders  |                     |                      |                     |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 15 (6.67%)<br>1 | 1 / 16 (6.25%)<br>2  | 1 / 5 (20.00%)<br>1 |
| Dysarthria<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 15 (0.00%)<br>0 | 0 / 16 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |
| Headache<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 15 (0.00%)<br>0 | 5 / 16 (31.25%)<br>6 | 1 / 5 (20.00%)<br>1 |
| Nerve Compression<br>subjects affected / exposed<br>occurrences (all)             | 0 / 15 (0.00%)<br>0 | 1 / 16 (6.25%)<br>2  | 0 / 5 (0.00%)<br>0  |
| Neuralgia<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 15 (0.00%)<br>0 | 1 / 16 (6.25%)<br>1  | 0 / 5 (0.00%)<br>0  |
| Paraesthesia<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 15 (6.67%)<br>1 | 0 / 16 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  |
| Peripheral Sensory Neuropathy<br>subjects affected / exposed<br>occurrences (all) | 1 / 15 (6.67%)<br>1 | 0 / 16 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  |
| Post Herpetic Neuralgia<br>subjects affected / exposed<br>occurrences (all)       | 0 / 15 (0.00%)<br>0 | 1 / 16 (6.25%)<br>2  | 0 / 5 (0.00%)<br>0  |
| Sensory Disturbance<br>subjects affected / exposed<br>occurrences (all)           | 0 / 15 (0.00%)<br>0 | 0 / 16 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |
| Somnolence<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 15 (0.00%)<br>0 | 1 / 16 (6.25%)<br>1  | 0 / 5 (0.00%)<br>0  |
| Blood and lymphatic system disorders  |                     |                      |                     |

|                             |                 |                 |                |
|-----------------------------|-----------------|-----------------|----------------|
| Anaemia                     |                 |                 |                |
| subjects affected / exposed | 1 / 15 (6.67%)  | 5 / 16 (31.25%) | 1 / 5 (20.00%) |
| occurrences (all)           | 1               | 8               | 1              |
| Leukopenia                  |                 |                 |                |
| subjects affected / exposed | 1 / 15 (6.67%)  | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 1               | 1               | 0              |
| Lymph Node Pain             |                 |                 |                |
| subjects affected / exposed | 2 / 15 (13.33%) | 2 / 16 (12.50%) | 0 / 5 (0.00%)  |
| occurrences (all)           | 2               | 4               | 0              |
| Lymphadenopathy             |                 |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%)  | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0              |
| Lymphocytosis               |                 |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%)  | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0              |
| Lymphopenia                 |                 |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%)  | 2 / 16 (12.50%) | 0 / 5 (0.00%)  |
| occurrences (all)           | 0               | 8               | 0              |
| Neutropenia                 |                 |                 |                |
| subjects affected / exposed | 1 / 15 (6.67%)  | 1 / 16 (6.25%)  | 1 / 5 (20.00%) |
| occurrences (all)           | 1               | 4               | 2              |
| Thrombocytopenia            |                 |                 |                |
| subjects affected / exposed | 3 / 15 (20.00%) | 3 / 16 (18.75%) | 1 / 5 (20.00%) |
| occurrences (all)           | 4               | 7               | 4              |
| Ear and labyrinth disorders |                 |                 |                |
| Ear Pain                    |                 |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%)  | 2 / 16 (12.50%) | 0 / 5 (0.00%)  |
| occurrences (all)           | 0               | 2               | 0              |
| Eye disorders               |                 |                 |                |
| Diplopia                    |                 |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%)  | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0              |
| Erythema of Eyelid          |                 |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%)  | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0              |
| Eyelid Oedema               |                 |                 |                |

|   |                      |                      |                     |
|---|----------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                          | 0 / 15 (0.00%)<br>0  | 1 / 16 (6.25%)<br>1  | 0 / 5 (0.00%)<br>0  |
| Ocular Hyperaemia<br>subjects affected / exposed<br>occurrences (all)     | 0 / 15 (0.00%)<br>0  | 1 / 16 (6.25%)<br>1  | 1 / 5 (20.00%)<br>1 |
| Visual Acuity Reduced<br>subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0  | 0 / 16 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |
| Gastrointestinal disorders  |                      |                      |                     |
| Abdominal Discomfort<br>subjects affected / exposed<br>occurrences (all)  | 0 / 15 (0.00%)<br>0  | 1 / 16 (6.25%)<br>1  | 0 / 5 (0.00%)<br>0  |
| Abdominal Pain<br>subjects affected / exposed<br>occurrences (all)        | 2 / 15 (13.33%)<br>2 | 5 / 16 (31.25%)<br>5 | 1 / 5 (20.00%)<br>1 |
| Abdominal Pain Lower<br>subjects affected / exposed<br>occurrences (all)  | 1 / 15 (6.67%)<br>3  | 0 / 16 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  |
| Abdominal Pain Upper<br>subjects affected / exposed<br>occurrences (all)  | 1 / 15 (6.67%)<br>1  | 1 / 16 (6.25%)<br>1  | 0 / 5 (0.00%)<br>0  |
| Anal Incontinence<br>subjects affected / exposed<br>occurrences (all)     | 0 / 15 (0.00%)<br>0  | 1 / 16 (6.25%)<br>1  | 0 / 5 (0.00%)<br>0  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)          | 2 / 15 (13.33%)<br>2 | 2 / 16 (12.50%)<br>2 | 1 / 5 (20.00%)<br>1 |
| Dental Caries<br>subjects affected / exposed<br>occurrences (all)         | 0 / 15 (0.00%)<br>0  | 1 / 16 (6.25%)<br>1  | 0 / 5 (0.00%)<br>0  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)             | 1 / 15 (6.67%)<br>1  | 2 / 16 (12.50%)<br>2 | 0 / 5 (0.00%)<br>0  |
| Dry Mouth<br>subjects affected / exposed<br>occurrences (all)             | 0 / 15 (0.00%)<br>0  | 1 / 16 (6.25%)<br>1  | 0 / 5 (0.00%)<br>0  |

|  |                      |                      |                     |
|--|----------------------|----------------------|---------------------|
| Gastrooesophageal Reflux Disease<br>subjects affected / exposed<br>occurrences (all)               | 0 / 15 (0.00%)<br>0  | 0 / 16 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |
| Nausea<br>subjects affected / exposed<br>occurrences (all)   | 5 / 15 (33.33%)<br>7 | 1 / 16 (6.25%)<br>1  | 2 / 5 (40.00%)<br>3 |
| Paraesthesia Oral<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 15 (0.00%)<br>0  | 1 / 16 (6.25%)<br>1  | 0 / 5 (0.00%)<br>0  |
| Swollen Tongue<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 15 (0.00%)<br>0  | 0 / 16 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                                       | 4 / 15 (26.67%)<br>5 | 0 / 16 (0.00%)<br>0  | 1 / 5 (20.00%)<br>2 |
| Hepatobiliary disorders<br>Hyperbilirubinaemia<br>subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0  | 0 / 16 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |
| Skin and subcutaneous tissue disorders<br>Acne<br>subjects affected / exposed<br>occurrences (all) | 1 / 15 (6.67%)<br>1  | 0 / 16 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  |
| Blood Blister<br>subjects affected / exposed<br>occurrences (all)                                  | 1 / 15 (6.67%)<br>1  | 0 / 16 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  |
| Eczema<br>subjects affected / exposed<br>occurrences (all)   | 1 / 15 (6.67%)<br>2  | 0 / 16 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  |
| Erythema<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 15 (0.00%)<br>0  | 0 / 16 (0.00%)<br>0  | 1 / 5 (20.00%)<br>2 |
| Night Sweats<br>subjects affected / exposed<br>occurrences (all)                                   | 1 / 15 (6.67%)<br>1  | 2 / 16 (12.50%)<br>2 | 0 / 5 (0.00%)<br>0  |
| Pain of Skin   |                      |                      |                     |

|   |                     |                      |                     |
|---|---------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 1 / 15 (6.67%)<br>3 | 2 / 16 (12.50%)<br>3 | 0 / 5 (0.00%)<br>0  |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)  | 1 / 15 (6.67%)<br>1 | 0 / 16 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |
| Rash<br>subjects affected / exposed<br>occurrences (all)  | 1 / 15 (6.67%)<br>1 | 1 / 16 (6.25%)<br>1  | 0 / 5 (0.00%)<br>0  |
| Skin Burning Sensation<br>subjects affected / exposed<br>occurrences (all)  | 0 / 15 (0.00%)<br>0 | 1 / 16 (6.25%)<br>1  | 0 / 5 (0.00%)<br>0  |
| Urticaria<br>subjects affected / exposed<br>occurrences (all)   | 1 / 15 (6.67%)<br>2 | 3 / 16 (18.75%)<br>3 | 0 / 5 (0.00%)<br>0  |
| Renal and urinary disorders<br>Chronic Kidney Disease<br>subjects affected / exposed<br>occurrences (all)         | 1 / 15 (6.67%)<br>1 | 0 / 16 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  |
| Haematuria<br>subjects affected / exposed<br>occurrences (all)  | 0 / 15 (0.00%)<br>0 | 1 / 16 (6.25%)<br>1  | 0 / 5 (0.00%)<br>0  |
| Urinary Tract Obstruction<br>subjects affected / exposed<br>occurrences (all)                                     | 1 / 15 (6.67%)<br>1 | 0 / 16 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  |
| Urine Flow Decreased<br>subjects affected / exposed<br>occurrences (all)  | 0 / 15 (0.00%)<br>0 | 0 / 16 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0 | 2 / 16 (12.50%)<br>3 | 0 / 5 (0.00%)<br>0  |
| Back Pain<br>subjects affected / exposed<br>occurrences (all)   | 1 / 15 (6.67%)<br>2 | 4 / 16 (25.00%)<br>5 | 1 / 5 (20.00%)<br>1 |
| Flank Pain  |                     |                      |                     |



|                             |                 |                 |                |
|-----------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 15 (6.67%)  | 0 / 16 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0              |
| Mobility Decreased          |                 |                 |                |
| subjects affected / exposed | 1 / 15 (6.67%)  | 0 / 16 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0              |
| Muscle Spasms               |                 |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%)  | 1 / 16 (6.25%)  | 2 / 5 (40.00%) |
| occurrences (all)           | 0               | 3               | 2              |
| Musculoskeletal Chest Pain  |                 |                 |                |
| subjects affected / exposed | 1 / 15 (6.67%)  | 0 / 16 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0              |
| Musculoskeletal Pain        |                 |                 |                |
| subjects affected / exposed | 2 / 15 (13.33%) | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 2               | 1               | 0              |
| Myalgia                     |                 |                 |                |
| subjects affected / exposed | 1 / 15 (6.67%)  | 2 / 16 (12.50%) | 0 / 5 (0.00%)  |
| occurrences (all)           | 1               | 2               | 0              |
| Pain in Extremity           |                 |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%)  | 3 / 16 (18.75%) | 1 / 5 (20.00%) |
| occurrences (all)           | 0               | 4               | 1              |
| Pain in Jaw                 |                 |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%)  | 0 / 16 (0.00%)  | 1 / 5 (20.00%) |
| occurrences (all)           | 0               | 0               | 1              |
| Peripheral Arthritis        |                 |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%)  | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0              |
| Infections and infestations |                 |                 |                |
| Cellulitis                  |                 |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%)  | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0              |
| Fungal Skin Infection       |                 |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%)  | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0              |
| Gastroenteritis             |                 |                 |                |
| subjects affected / exposed | 0 / 15 (0.00%)  | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0              |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| Genital Herpes                          |                |                 |                |
| subjects affected / exposed             | 0 / 15 (0.00%) | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)                       | 0              | 1               | 0              |
| Groin Infection                         |                |                 |                |
| subjects affected / exposed             | 1 / 15 (6.67%) | 0 / 16 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                       | 1              | 0               | 0              |
| Herpes Zoster                           |                |                 |                |
| subjects affected / exposed             | 0 / 15 (0.00%) | 1 / 16 (6.25%)  | 1 / 5 (20.00%) |
| occurrences (all)                       | 0              | 1               | 1              |
| Lower Respiratory Tract Infection       |                |                 |                |
| subjects affected / exposed             | 0 / 15 (0.00%) | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)                       | 0              | 1               | 0              |
| Nasopharyngitis                         |                |                 |                |
| subjects affected / exposed             | 1 / 15 (6.67%) | 1 / 16 (6.25%)  | 1 / 5 (20.00%) |
| occurrences (all)                       | 2              | 1               | 1              |
| Pneumonia                               |                |                 |                |
| subjects affected / exposed             | 0 / 15 (0.00%) | 0 / 16 (0.00%)  | 1 / 5 (20.00%) |
| occurrences (all)                       | 0              | 0               | 1              |
| Rhinitis                                |                |                 |                |
| subjects affected / exposed             | 0 / 15 (0.00%) | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)                       | 0              | 1               | 0              |
| Sinusitis                               |                |                 |                |
| subjects affected / exposed             | 0 / 15 (0.00%) | 2 / 16 (12.50%) | 0 / 5 (0.00%)  |
| occurrences (all)                       | 0              | 2               | 0              |
| Upper Respiratory Tract Infection       |                |                 |                |
| subjects affected / exposed             | 1 / 15 (6.67%) | 3 / 16 (18.75%) | 0 / 5 (0.00%)  |
| occurrences (all)                       | 1              | 3               | 0              |
| Urinary Tract Infection                 |                |                 |                |
| subjects affected / exposed             | 1 / 15 (6.67%) | 0 / 16 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                       | 1              | 0               | 0              |
| Viral Upper Respiratory Tract Infection |                |                 |                |
| subjects affected / exposed             | 0 / 15 (0.00%) | 1 / 16 (6.25%)  | 0 / 5 (0.00%)  |
| occurrences (all)                       | 0              | 1               | 0              |
| Metabolism and nutrition disorders      |                |                 |                |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| Decreased Appetite<br>subjects affected / exposed<br>occurrences (all)     | 1 / 15 (6.67%)<br>1 | 1 / 16 (6.25%)<br>1 | 0 / 5 (0.00%)<br>0  |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)         | 0 / 15 (0.00%)<br>0 | 0 / 16 (0.00%)<br>0 | 1 / 5 (20.00%)<br>1 |
| Hypertriglyceridaemia<br>subjects affected / exposed<br>occurrences (all)  | 0 / 15 (0.00%)<br>0 | 1 / 16 (6.25%)<br>1 | 0 / 5 (0.00%)<br>0  |
| Hypoalbuminaemia<br>subjects affected / exposed<br>occurrences (all)       | 1 / 15 (6.67%)<br>1 | 0 / 16 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  |
| Hyperuricaemia<br>subjects affected / exposed<br>occurrences (all)         | 0 / 15 (0.00%)<br>0 | 1 / 16 (6.25%)<br>1 | 0 / 5 (0.00%)<br>0  |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all)           | 1 / 15 (6.67%)<br>1 | 0 / 16 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  |
| Hyponatraemia<br>subjects affected / exposed<br>occurrences (all)          | 0 / 15 (0.00%)<br>0 | 1 / 16 (6.25%)<br>1 | 0 / 5 (0.00%)<br>0  |
| Vitamin B12 Deficiency<br>subjects affected / exposed<br>occurrences (all) | 1 / 15 (6.67%)<br>1 | 0 / 16 (0.00%)<br>0 | 0 / 5 (0.00%)<br>0  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment  |
|-----------------|--|
| 19 January 2015 | The main reason of this amendment was to Optimization of candidate screening potential, elaboration on Indirect Antiglobulin (Coombs) Testing (IAT) during the Screening Phase due to the risk of daratumumab interference with IAT, as well as updates throughout the protocol to align with the other daratumumab protocols, and some minor editorial changes. |

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.

The study was terminated due to 2 non-Hodgkin's lymphoma (NHL) subtypes ([DLBCL] and FL cohorts) meeting the futility criteria defined in the protocol, and the cell lymphoma (MCL) cohort not having adequate recruitment.

Notes: