



Clinical trial results:

Title: An Open-Label Phase 2 Study of Tipifarnib in Subjects with Relapsed or Refractory Peripheral T-Cell Lymphoma (PTCL)

Study design: This study utilised an open-label, nonrandomised design, a standard and appropriate approach for a Phase 2 study in subjects with relapsed or refractory PTCL. The primary objective was to determine the antitumour activity in terms of objective response rate (ORR) of tipifarnib in subjects with relapsed or refractory PTCL. Secondary objectives included antitumor activity in terms of progression-free survival (PFS) and duration of response (DOR), the safety and tolerability of tipifarnib, and the assessment of ORR, PFS, and DOR in subgroups defined according to genetic subtypes. Eligible subjects received tipifarnib administered at a starting dose of 300 mg, orally with food, twice daily (BID) on Days 1-21 in 28-day cycles (i.e., 3 weeks on/1 week off). In the absence of unmanageable toxicities, subjects may have continued to receive tipifarnib treatment for up to 12 months in the absence of disease progression. Tumour assessments were performed at screening, at the Day 22 visit (± 5 days), during Cycles 2, 4, 6, and once every approximately 12 weeks (Cycles 9, 12, 15, etc.) thereafter, until disease progression. Determination of objective tumour response was performed based on the Lugano Classification. Upon disease progression, subjects were followed approximately every 12 weeks for survival until either death or 12 months after accrual of the last study subject, whichever occurred first. All subjects were followed-up for safety during treatment and for approximately 30 additional days after treatment discontinuation.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2016-001396-69 |
| Trial protocol | ES |
| Global end of trial date | 31 March 2021 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 12 August 2022 |
| First version publication date | 12 August 2022 |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | KO-TIP-002 |
|-----------------------|------------|

Additional study identifiers

| | |
|---------------|---|
| ISRCTN number | - |
|---------------|---|

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|------------------------------------|---|
| ClinicalTrials.gov id (NCT number) | - |
|------------------------------------|---|

| | |
|----------------------------------|---|
| WHO universal trial number (UTN) | - |
|----------------------------------|---|

Notes:

Sponsors

| | |
|---------------------------|--------------------|
| Sponsor organisation name | Kura Oncology, Inc |
|---------------------------|--------------------|

| | |
|------------------------------|--|
| Sponsor organisation address | 12730 High Bluff Drive, San Diego, United States, CA 92130 |
|------------------------------|--|

| | |
|----------------|---|
| Public contact | Information desk, Kura Oncology, Inc, 001 8585008800, info@kuraoncology.com |
|----------------|---|

| | |
|--------------------|---|
| Scientific contact | Information desk, Kura Oncology, Inc, 001 8585008800, info@kuraoncology.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 | 31 March 2021 |
|--------------------------------|---------------|

| | |
|--|-----|
| Is this the analysis of the primary completion data? | Yes |
|--|-----|

| | |
|-------------------------|---------------|
| Primary completion date | 31 March 2021 |
|-------------------------|---------------|

| | |
|------------------------------|-----|
| Global end of trial reached? | Yes |
|------------------------------|-----|

| | |
|--------------------------|---------------|
| Global end of trial date | 31 March 2021 |
|--------------------------|---------------|

| | |
|----------------------------------|----|
| Was the trial ended prematurely? | No |
|----------------------------------|----|

Notes:

General information about the trial

Main objective of the trial:

To determine the antitumour activity in terms of ORR of tipifarnib in subjects with relapsed or refractory PTCL.

Subjects were enrolled into 4 cohorts based on the type of lymphoma: angioimmunoblastic T-cell lymphoma (AITL), PTCL not otherwise specified (PTCL-NOS), PTCL-NOS with CXCL12+ (C-X-C motif chemokine 12+), and Other. For the purposes of the analysis an additional reporting group was defined combining patients from both the PTCL-NOS and PTCL-NOS CXCL12+ groups.

Protection of trial subjects:

This trial was designed and monitored in accordance with sponsor procedures, which comply with the

ethical principles of Good Clinical Practice (GCP) as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki. The protocol, informed consent form (ICF), and other relevant study documentation were approved by the independent ethics committee (IEC)/institutional review boards (IRBs) before initiation of the study.

Background therapy:

All prescription and over-the-counter medications taken by a subject within 28 days before the first study drug administration were recorded in the electronic case report form (eCRF).

Supportive care medications considered necessary for the subject's safety and well-being may have been given at the discretion of the investigator. Any concomitant medications added or discontinued during the study were recorded on the eCRF. Best supportive care (BSC) was provided by the clinical study sites according to local guidelines and standard practices.

Furthermore, the following treatments were allowed during the trial:

- Intravenous hydration
- Correction of electrolyte deficiencies
- Haematopoietic growth factors and transfusions of blood or blood products in subjects who were experiencing haematological toxicity in accordance with standard institutional practice
- Radiotherapy for pain control against non-target lesions as long as it did not influence bone marrow function
- Total tumour resection in responding subjects who had become candidates for curative resection

Any additional concomitant therapy that became necessary during the trial and any change to concomitant drugs were recorded in the corresponding section of the eCRF, noting the name, dose, duration, and indication of each drug.

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 08 October 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 | Spain: 13 |
| Country: Number of subjects enrolled | Korea, Republic of: 12 |
| Country: Number of subjects enrolled | United States: 40 |
| Worldwide total number of subjects | 65 |
| EEA total number of subjects | 13 |

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) | 26 |
| From 65 to 84 years | 37 |
| 85 years and over | 2 |

Subject disposition

Recruitment

Recruitment details:

The first patient was enrolled on 25 Feb 2016 (13 in Europe; 52 outside Europe) and the date of the last visit was 31 Mar 2021. Overall, 65 patients were enrolled into cohorts with AITL, PTCL-NOS, PTCL-NOS CXCL12+, and Other (ALCL-ALK neg and PTCL-subtype not spec). For the analysis, a combined group of PTCL-NOS and PTCL-NOS CXCL12+ was defined.

Pre-assignment

Screening details:

Only consented subjects who met all the eligibility criteria were enrolled in the study. All screening evaluations were to be completed within 4 weeks (28 days) of Cycle 1 Day 1. Screen failure reasons were not included in the database.

Period 1

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

Blinding implementation details:

No blinding was used; this was an open-label study with no placebo or comparators.

Arms

| | |
|------------------------------|-------------|
| Are arms mutually exclusive? | No |
| Arm title | Cohort AITL |

Arm description:

Subjects with angioimmunoblastic T-cell lymphoma (AITL).

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Tipifarnib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received tipifarnib as monotherapy. Tipifarnib was administered with food at a starting dose of 300 mg administered orally BID on Days 1 – 21 of 28 -day treatment cycles. Subjects who received tipifarnib 300 mg administered orally BID on Days 1 – 7 and Days 15 – 21 during the conduct of earlier versions of this protocol may have remained on that dose regimen at the discretion of the investigator. Alternatively, the subject may have transitioned to receive a dose of 300 mg administered orally BID on Days 1 – 21 of 28-day treatment cycles beginning on Day 1 of their next cycle.

The first study dosing (Cycle 1 Day 1) took place in the study clinic. Subjects were provided with diaries with instructions to record the date and time of each dose and were asked to bring the diaries and tablet bottles to each clinic visit for subject compliance and drug accountability review by the site staff.

| | |
|------------------|-----------------|
| Arm title | Cohort PTCL-NOS |
|------------------|-----------------|

Arm description:

Subjects with peripheral T-cell lymphoma-not otherwise specified (PTCL-NOS).

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

| | |
|--|--------------------|
| Investigational medicinal product name | Tipifarnib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received tipifarnib as monotherapy. Tipifarnib was administered with food at a starting dose of 300 mg administered orally BID on Days 1 – 21 of 28 -day treatment cycles. Subjects who received tipifarnib 300 mg administered orally BID on Days 1 – 7 and Days 15 – 21 during the conduct of earlier versions of this protocol may have remained on that dose regimen at the discretion of the investigator. Alternatively, the subject may have transitioned to receive a dose of 300 mg administered orally BID on Days 1 – 21 of 28-day treatment cycles beginning on Day 1 of their next cycle.

The first study dosing (Cycle 1 Day 1) took place in the study clinic. Subjects were provided with diaries with instructions to record the date and time of each dose and were asked to bring the diaries and tablet bottles to each clinic visit for subject compliance and drug accountability review by the site staff.

| | |
|------------------|--------------------------|
| Arm title | Cohort PTCL-NOS, CXCL12+ |
|------------------|--------------------------|

Arm description:

Subjects with peripheral T-cell lymphoma-not otherwise specified (PTCL-NOS) whose tumours expressed high levels of C-X-C motif chemokine 12 (CXCL12).

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Tipifarnib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received tipifarnib as monotherapy. Tipifarnib was administered with food at a starting dose of 300 mg administered orally BID on Days 1 – 21 of 28 -day treatment cycles. Subjects who received tipifarnib 300 mg administered orally BID on Days 1 – 7 and Days 15 – 21 during the conduct of earlier versions of this protocol may have remained on that dose regimen at the discretion of the investigator. Alternatively, the subject may have transitioned to receive a dose of 300 mg administered orally BID on Days 1 – 21 of 28-day treatment cycles beginning on Day 1 of their next cycle.

The first study dosing (Cycle 1 Day 1) took place in the study clinic. Subjects were provided with diaries with instructions to record the date and time of each dose and were asked to bring the diaries and tablet bottles to each clinic visit for subject compliance and drug accountability review by the site staff.

| | |
|------------------|--------------------------|
| Arm title | Cohort PTCL-NOS, Overall |
|------------------|--------------------------|

Arm description:

All subjects with peripheral T-cell lymphoma-not otherwise specified (PTCL-NOS) from the PTCL-NOS and PTCL-NOS CXCL12+ cohorts combined. For the purposes of the analysis an additional reporting group was defined combining patients from both the PTCL-NOS and PTCL-NOS CXCL12+ groups.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Tipifarnib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received tipifarnib as monotherapy. Tipifarnib was administered with food at a starting dose of 300 mg administered orally BID on Days 1 – 21 of 28 -day treatment cycles. Subjects who received tipifarnib 300 mg administered orally BID on Days 1 – 7 and Days 15 – 21 during the conduct of earlier versions of this protocol may have remained on that dose regimen at the discretion of the investigator. Alternatively, the subject may have transitioned to receive a dose of 300 mg administered orally BID on Days 1 – 21 of 28-day treatment cycles beginning on Day 1 of their next cycle.

The first study dosing (Cycle 1 Day 1) took place in the study clinic. Subjects were provided with diaries with instructions to record the date and time of each dose and were asked to bring the diaries and tablet bottles to each clinic visit for subject compliance and drug accountability review by the site staff.

| | |
|---|--------------------|
| Arm title | Cohort Other |
| Arm description: | |
| Subjects with Other, including anaplastic large cell lymphoma-anaplastic lymphoma kinase (ALCL-ALK) negative and PTCL-subtype not specified per protocol. | |
| Arm type | Experimental |
| Investigational medicinal product name | Tipifarnib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received tipifarnib as monotherapy. Tipifarnib was administered with food at a starting dose of 300 mg administered orally BID on Days 1 – 21 of 28 -day treatment cycles. Subjects who received tipifarnib 300 mg administered orally BID on Days 1 – 7 and Days 15 – 21 during the conduct of earlier versions of this protocol may have remained on that dose regimen at the discretion of the investigator. Alternatively, the subject may have transitioned to receive a dose of 300 mg administered orally BID on Days 1 – 21 of 28-day treatment cycles beginning on Day 1 of their next cycle.

The first study dosing (Cycle 1 Day 1) took place in the study clinic. Subjects were provided with diaries with instructions to record the date and time of each dose and were asked to bring the diaries and tablet bottles to each clinic visit for subject compliance and drug accountability review by the site staff.

| Number of subjects in period 1 | Cohort AITL | Cohort PTCL-NOS | Cohort PTCL-NOS, CXCL12+ |
|---|-------------|-----------------|--------------------------|
| Started | 38 | 14 | 11 |
| Completed | 2 | 0 | 0 |
| Not completed | 36 | 14 | 11 |
| Consent withdrawn by subject | 1 | 1 | 1 |
| Disease progression | 22 | 12 | 5 |
| PI decision | 2 | - | 1 |
| Adverse event, non-fatal | 9 | - | 3 |
| Not specified | 1 | - | 1 |
| Termination for symptomatic deterioration | 1 | 1 | - |

| Number of subjects in period 1 | Cohort PTCL-NOS, Overall | Cohort Other |
|---------------------------------------|--------------------------|--------------|
| Started | 25 | 2 |
| Completed | 0 | 0 |
| Not completed | 25 | 2 |
| Consent withdrawn by subject | 2 | - |
| Disease progression | 17 | 2 |
| PI decision | 1 | - |

| | | |
|---|---|---|
| Adverse event, non-fatal | 3 | - |
| Not specified | 1 | - |
| Termination for symptomatic deterioration | 1 | - |

Baseline characteristics

| Reporting groups | |
|--|--------------------------|
| Reporting group title | Cohort AITL |
| Reporting group description: Subjects with angioimmunoblastic T-cell lymphoma (AITL). | |
| Reporting group title | Cohort PTCL-NOS |
| Reporting group description: Subjects with peripheral T-cell lymphoma-not otherwise specified (PTCL-NOS). | |
| Reporting group title | Cohort PTCL-NOS, CXCL12+ |
| Reporting group description: Subjects with peripheral T-cell lymphoma-not otherwise specified (PTCL-NOS) whose tumours expressed high levels of C-X-C motif chemokine 12 (CXCL12). | |
| Reporting group title | Cohort PTCL-NOS, Overall |
| Reporting group description: All subjects with peripheral T-cell lymphoma-not otherwise specified (PTCL-NOS) from the PTCL-NOS and PTCL-NOS CXCL12+ cohorts combined. For the purposes of the analysis an additional reporting group was defined combining patients from both the PTCL-NOS and PTCL-NOS CXCL12+ groups. | |
| Reporting group title | Cohort Other |
| Reporting group description: Subjects with Other, including anaplastic large cell lymphoma-anaplastic lymphoma kinase (ALCL-ALK) negative and PTCL-subtype not specified per protocol. | |

| Reporting group values | Cohort AITL | Cohort PTCL-NOS | Cohort PTCL-NOS, CXCL12+ |
|------------------------------------|-------------|-----------------|--------------------------|
| Number of subjects | 38 | 14 | 11 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|--------|--------|--------|
| Age continuous Units: years | | | |
| arithmetic mean | 65.50 | 65.73 | 65.74 |
| standard deviation | ± 10.7 | ± 13.7 | ± 12.6 |
| Gender categorical Units: Subjects | | | |
| Female | 16 | 2 | 5 |
| Male | 22 | 12 | 6 |
| ECOG performance score Units: Subjects | | | |
| Performance score 0 | 18 | 3 | 5 |
| Performance score 1 | 13 | 10 | 6 |
| Performance score 2 | 7 | 1 | 0 |
| Other | 0 | 0 | 0 |

| Reporting group values | Cohort PTCL-NOS, Overall | Cohort Other | Total |
|------------------------------------|--------------------------|--------------|-------|
| Number of subjects | 25 | 2 | 65 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|-----------------|-----------------|----|
| Age continuous Units: years arithmetic mean standard deviation | 65.73 ± 12.9 | 56.68 ± 12.0 | - |
| Gender categorical Units: Subjects | | | |
| Female | 7 | 1 | 24 |
| Male | 18 | 1 | 41 |
| ECOG performance score Units: Subjects | | | |
| Performance score 0 | 8 | 0 | 26 |
| Performance score 1 | 16 | 2 | 31 |
| Performance score 2 | 1 | 0 | 8 |
| Other | 0 | 0 | 0 |

End points

End points reporting groups

| | |
|--|--------------------------|
| Reporting group title | Cohort AITL |
| Reporting group description: Subjects with angioimmunoblastic T-cell lymphoma (AITL). | |
| Reporting group title | Cohort PTCL-NOS |
| Reporting group description: Subjects with peripheral T-cell lymphoma-not otherwise specified (PTCL-NOS). | |
| Reporting group title | Cohort PTCL-NOS, CXCL12+ |
| Reporting group description: Subjects with peripheral T-cell lymphoma-not otherwise specified (PTCL-NOS) whose tumours expressed high levels of C-X-C motif chemokine 12 (CXCL12). | |
| Reporting group title | Cohort PTCL-NOS, Overall |
| Reporting group description: All subjects with peripheral T-cell lymphoma-not otherwise specified (PTCL-NOS) from the PTCL-NOS and PTCL-NOS CXCL12+ cohorts combined. For the purposes of the analysis an additional reporting group was defined combining patients from both the PTCL-NOS and PTCL-NOS CXCL12+ groups. | |
| Reporting group title | Cohort Other |
| Reporting group description: Subjects with Other, including anaplastic large cell lymphoma-anaplastic lymphoma kinase (ALCL-ALK) negative and PTCL-subtype not specified per protocol. | |

Primary: Antitumor activity by overall objective response rate

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|--|--|
| End point title | Antitumor activity by overall objective response rate ^[1] |
| End point description: The objective response rate (ORR) of tipifarnib was based on response assessments according to the Lugano Classification. Either complete responses (CRs) or partial responses (PRs) contributed to an objective response. 2-sided 95% CIs were based on either Wilson approximation ($N > 4$) or Clopper-Pearson method ($N \leq 4$). P-value was calculated testing an overall response of 10% using a 2-sided binomial test. P- values by cohort: AITL = 0.000 PTCL-NOS = 1.000 PTCL, CXCL12+ = 0.026 PTCL-NOS, Overall = 0.077 Other = 1.000 | |
| End point type | Primary |
| End point timeframe: From baseline to end of follow-up. | |
| 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: There were no between group comparisons for the primary endpoint. Each group was compared against a target rate of 10%. The statistical analysis is therefore described under 'Description of the endpoint'.

| End point values | Cohort AITL | Cohort PTCL-NOS | Cohort PTCL-NOS, CXCL12+ | Cohort PTCL-NOS, Overall |
|---|---------------------|-------------------|--------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 32 | 14 | 10 | 24 |
| Units: percent | | | | |
| arithmetic mean (confidence interval 95%) | 56.3 (39.3 to 71.8) | 7.1 (0.2 to 33.9) | 40.0 (12.2 to 73.8) | 20.8 (9.2 to 40.5) |

| End point values | Cohort Other | | | |
|---|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 2 | | | |
| Units: percent | | | | |
| arithmetic mean (confidence interval 95%) | 0.0 (0.0 to 84.2) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival

| | |
|-----------------|---------------------------|
| End point title | Progression-free survival |
|-----------------|---------------------------|

End point description:

Progression-free survival (PFS) was defined as the time (in months) from first dose (Cycle 1 Day 1) to either first observation of progressive disease (PD) or occurrence of death due to any cause within 126 days (approximately 2 time-intervals for tumour assessments) of either first administration of tipifarnib or the last tumour assessment. Observation of PD could have been by either documented radiographic progression (i.e., scan results) or documentation of symptomatic or clinical progression agreed upon and documented by investigators. In subjects without a progression date or with a death date more than 126 days after the first administration of study drugs or the last tumour assessment, the PFS time should have been censored on the date of last tumour assessment or date of first administration of study tipifarnib. 95% CI was calculated using Hall-Wellner Method.

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

End point timeframe:

From baseline to end of follow-up.

| End point values | Cohort AITL | Cohort PTCL-NOS | Cohort PTCL-NOS, CXCL12+ | Cohort PTCL-NOS, Overall |
|----------------------------------|------------------|------------------|--------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 32 | 14 | 10 | 24 |
| Units: Months | | | | |
| median (confidence interval 95%) | 3.6 (1.9 to 8.3) | 2.1 (1.4 to 4.0) | 5.3 (1.8 to 11.1) | 3.5 (1.8 to 5.3) |

| End point values | Cohort Other | | | |
|------------------|--------------|--|--|--|
|------------------|--------------|--|--|--|

| | | | | |
|----------------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 2 | | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 1.4 (1.1 to 1.6) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response

| | |
|-----------------|-------------------------------------|
| End point title | Duration of response ^[2] |
|-----------------|-------------------------------------|

End point description:

The duration of the objective response (DOR) was defined as the time (in months) from the start date of the objective response to the first date of either documented PD or death. All efforts were made to objectively define the endpoint by collecting the necessary data and reducing the likelihood of missing data. No data imputations were conducted for missing data. In the event of a maintained response, the DOR was censored at the last evaluable non-PD assessment.

Data are presented for cohorts for which median and 95% CI were calculable (Kaplan-Meier analysis). 95% CI was calculated using Hall-Wellner Method. Where not calculable (NC), median (95% CI) listed below; N = number of responders:

PTCL-NOS (N = 1): 1.0 (NC, NC)
PTCL-NOS, CXCL12+ (N = 4): 2.8 (2.0, NC)
PTCL-NOS, Overall (N = 5): 2.0 (1.0, NC)
Other (N = 0): NC (NC, NC)

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

End point timeframe:

From baseline to end of follow-up.

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: For several cohorts, 95% CI were not estimable for median duration of response, therefore statistical analysis could only be described under 'Description of the endpoint'.

| | | | | |
|----------------------------------|-------------------|--|--|--|
| End point values | Cohort AITL | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 18 | | | |
| Units: months | | | | |
| median (confidence interval 95%) | 7.8 (2.0 to 16.3) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Antitumor activity - best overall response

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|-----------------|--|
| End point title | Antitumor activity - best overall response |
|-----------------|--|

End point description:

Best overall response according to the Lugano Classification was summarised using descriptive statistics.

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

End point timeframe:

From baseline to end of follow-up.

| End point values | Cohort AITL | Cohort PTCL- NOS | Cohort PTCL- NOS, CXCL12+ | Cohort PTCL- NOS, Overall |
|-----------------------------|-----------------|---------------------|------------------------------|------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 32 | 14 | 10 | 24 |
| Units: Subjects | | | | |
| Complete response | 9 | 0 | 1 | 1 |
| Partial response | 9 | 1 | 3 | 4 |
| Stable disease | 3 | 4 | 5 | 9 |
| Progressive disease | 11 | 8 | 1 | 9 |
| Not evaluable | 0 | 1 | 0 | 1 |

| End point values | Cohort Other | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 2 | | | |
| Units: Subjects | | | | |
| Complete response | 0 | | | |
| Partial response | 0 | | | |
| Stable disease | 0 | | | |
| Progressive disease | 2 | | | |
| Not evaluable | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the date of first signature of informed consent through the post-treatment follow-up period, defined as 30 days from final administration of study drug or immediately before initiation of any other anticancer therapy, whichever came first.

Adverse event reporting additional description:

The 5% cut-off for reporting of non-serious AEs (non-SAEs) was based on the percentages within individual cohorts.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | Cohort AITL |
|-----------------------|-------------|

Reporting group description:

Subjects with angioimmunoblastic T-cell lymphoma (AITL).

| | |
|-----------------------|-----------------|
| Reporting group title | Cohort PTCL-NOS |
|-----------------------|-----------------|

Reporting group description:

Subjects with peripheral T-cell lymphoma-not otherwise specified (PTCL-NOS).

| | |
|-----------------------|--------------------------|
| Reporting group title | Cohort PTCL-NOS, CXCL12+ |
|-----------------------|--------------------------|

Reporting group description:

Subjects with peripheral T-cell lymphoma-not otherwise specified (PTCL-NOS) whose tumours expressed high levels of C-X-C motif chemokine 12 (CXCL12).

| | |
|-----------------------|--------------------------|
| Reporting group title | Cohort PTCL-NOS, Overall |
|-----------------------|--------------------------|

Reporting group description:

All subjects with peripheral T-cell lymphoma-not otherwise specified (PTCL-NOS) from the other cohorts combined.

| | |
|-----------------------|--------------|
| Reporting group title | Cohort Other |
|-----------------------|--------------|

Reporting group description:

Subjects with Other, including ALCL-ALK Negative and PTCL-subtype not specified per protocol.

| Serious adverse events | Cohort AITL | Cohort PTCL-NOS | Cohort PTCL-NOS, CXCL12+ |
|---|------------------|-----------------|--------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 21 / 38 (55.26%) | 8 / 14 (57.14%) | 8 / 11 (72.73%) |
| number of deaths (all causes) | 13 | 8 | 4 |
| number of deaths resulting from adverse events | 4 | 1 | 1 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute myeloid leukaemia | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myelodysplastic syndrome | | | |

| | | | |
|--|----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (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 |
| Squamous cell carcinoma of lung | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (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 |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Death | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (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 |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 3 / 14 (21.43%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (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 |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (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 |

| | | | |
|---|----------------|----------------|----------------|
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Psychiatric disorders | | | |
| Delirium | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (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 |
| Confusional state | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (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 | | | |
| Fall | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femoral neck fracture | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Overdose | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (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 |
| Atrioventricular block second degree | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (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 |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (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 |
| Cardiopulmonary failure | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (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 |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Encephalopathy | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (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 |
| Syncope | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (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 |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 3 / 38 (7.89%) | 4 / 14 (28.57%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 2 / 3 | 4 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemolytic anaemia | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (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 |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancytopenia | | | |
| subjects affected / exposed | 3 / 38 (7.89%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaemia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (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 |
| Cytopenia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Histiocytosis haematophagic | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Colitis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (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 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (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 |
| Skin and subcutaneous tissue disorders | | | |
| Stevens-Johnson syndrome | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urticaria | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Toxic skin eruption | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (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 |
| Joint effusion | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (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 |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Kidney infection | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (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 |
| Lung infection | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (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 |
| Sepsis | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Urinary tract infection | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (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 |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 0 / 11 (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 |
| Failure to thrive | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (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 |

| Serious adverse events | Cohort PTCL-NOS, Overall | Cohort Other | |
|---|--------------------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 16 / 25 (64.00%) | 1 / 2 (50.00%) | |
| number of deaths (all causes) | 12 | 1 | |
| number of deaths resulting from adverse events | 2 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute myeloid leukaemia | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myelodysplastic syndrome | | | |

| | | | |
|--|-----------------|---------------|--|
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous cell carcinoma of lung | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tumour pain | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (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 | | | |
| Death | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 4 / 25 (16.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malaise | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|---------------|--|
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Psychiatric disorders | | | |
| Delirium | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Confusional state | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Overdose | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |

| | | | |
|---|-----------------|----------------|--|
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrioventricular block second degree | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiopulmonary failure | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (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 | | | |
| Encephalopathy | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 4 / 25 (16.00%) | 1 / 2 (50.00%) | |
| occurrences causally related to treatment / all | 4 / 4 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemolytic anaemia | | | |

| | | | |
|---|----------------|---------------|--|
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cytopenia | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Histiocytosis haematophagic | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Colitis | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |

| | | | |
|---|----------------|---------------|--|
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Stevens-Johnson syndrome | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urticaria | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Toxic skin eruption | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (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 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint effusion | | | |

| | | | |
|---|----------------|---------------|--|
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacteraemia | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Kidney infection | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung infection | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Urinary tract infection | | | |

| | | | |
|---|----------------|---------------|--|
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Failure to thrive | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Cohort AITL | Cohort PTCL-NOS | Cohort PTCL-NOS, CXCL12+ |
|--|-------------------|-------------------|--------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 38 / 38 (100.00%) | 14 / 14 (100.00%) | 11 / 11 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 2 |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|--|------------------|-----------------|-----------------|
| Haematoma | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Hypotension | | | |
| subjects affected / exposed | 8 / 38 (21.05%) | 2 / 14 (14.29%) | 1 / 11 (9.09%) |
| occurrences (all) | 8 | 2 | 2 |
| Peripheral coldness | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 3 / 38 (7.89%) | 3 / 14 (21.43%) | 3 / 11 (27.27%) |
| occurrences (all) | 3 | 3 | 4 |
| Chest pain | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Chills | | | |
| subjects affected / exposed | 4 / 38 (10.53%) | 1 / 14 (7.14%) | 2 / 11 (18.18%) |
| occurrences (all) | 5 | 2 | 3 |
| Fatigue | | | |
| subjects affected / exposed | 19 / 38 (50.00%) | 7 / 14 (50.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 23 | 7 | 2 |
| Gait disturbance | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Decreased activity | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 1 / 14 (7.14%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 2 | 1 |
| Malaise | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 1 / 14 (7.14%) | 2 / 11 (18.18%) |
| occurrences (all) | 1 | 1 | 3 |
| Oedema peripheral | | | |

| | | | |
|---|------------------|-----------------|-----------------|
| subjects affected / exposed | 3 / 38 (7.89%) | 3 / 14 (21.43%) | 4 / 11 (36.36%) |
| occurrences (all) | 4 | 3 | 5 |
| Pain | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 2 | 0 | 1 |
| Medical device pain | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 1 | 1 |
| Pyrexia | | | |
| subjects affected / exposed | 13 / 38 (34.21%) | 2 / 14 (14.29%) | 3 / 11 (27.27%) |
| occurrences (all) | 17 | 2 | 7 |
| Reproductive system and breast disorders | | | |
| Gynaecomastia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 8 / 38 (21.05%) | 3 / 14 (21.43%) | 2 / 11 (18.18%) |
| occurrences (all) | 9 | 3 | 2 |
| Dysphonia | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 4 / 38 (10.53%) | 6 / 14 (42.86%) | 0 / 11 (0.00%) |
| occurrences (all) | 5 | 6 | 0 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Hiccups | | | |

| | | | |
|-----------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 3 / 38 (7.89%) | 1 / 14 (7.14%) | 1 / 11 (9.09%) |
| occurrences (all) | 3 | 1 | 1 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 3 / 38 (7.89%) | 1 / 14 (7.14%) | 1 / 11 (9.09%) |
| occurrences (all) | 3 | 1 | 1 |
| Pleural effusion | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Pulmonary mass | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Psychiatric disorders | | | |
| Abnormal dreams | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 2 / 14 (14.29%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Agitation | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 2 / 14 (14.29%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Anxiety | | | |
| subjects affected / exposed | 3 / 38 (7.89%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Confusional state | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 2 / 14 (14.29%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 2 | 1 |
| Disorientation | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|----------------------|----------------------|---------------------|
| Insomnia subjects affected / exposed occurrences (all) | 5 / 38 (13.16%) 5 | 3 / 14 (21.43%) 3 | 1 / 11 (9.09%) 1 |
| Investigations | | | |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 1 / 38 (2.63%) 1 | 1 / 14 (7.14%) 1 | 1 / 11 (9.09%) 1 |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 2 / 38 (5.26%) 2 | 1 / 14 (7.14%) 2 | 1 / 11 (9.09%) 1 |
| Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) | 1 / 38 (2.63%) 1 | 2 / 14 (14.29%) 2 | 0 / 11 (0.00%) 0 |
| Blood bilirubin increased subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 3 / 14 (21.43%) 6 | 0 / 11 (0.00%) 0 |
| Blood creatinine increased subjects affected / exposed occurrences (all) | 5 / 38 (13.16%) 5 | 5 / 14 (35.71%) 6 | 1 / 11 (9.09%) 1 |
| Blood lactate dehydrogenase increased subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 0 / 14 (0.00%) 0 | 1 / 11 (9.09%) 1 |
| Blood urea increased subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 0 / 14 (0.00%) 0 | 1 / 11 (9.09%) 1 |
| Blood uric acid increased subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 0 / 14 (0.00%) 0 | 1 / 11 (9.09%) 1 |
| CD4 lymphocytes decreased subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 0 / 14 (0.00%) 0 | 1 / 11 (9.09%) 2 |
| Epstein-Barr virus test positive subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 0 / 14 (0.00%) 0 | 1 / 11 (9.09%) 1 |
| Gamma-glutamyltransferase increased | | | |

| | | | |
|--|------------------|------------------|-----------------|
| subjects affected / exposed | 2 / 38 (5.26%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Human rhinovirus test positive | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 1 / 14 (7.14%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 1 | 2 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 4 / 38 (10.53%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 8 | 2 | 0 |
| Lymphocyte count increased | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 2 |
| Monocyte count decreased | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 11 / 38 (28.95%) | 8 / 14 (57.14%) | 1 / 11 (9.09%) |
| occurrences (all) | 37 | 25 | 3 |
| Platelet count decreased | | | |
| subjects affected / exposed | 15 / 38 (39.47%) | 10 / 14 (71.43%) | 4 / 11 (36.36%) |
| occurrences (all) | 35 | 14 | 8 |
| Urine output increased | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 4 / 38 (10.53%) | 6 / 14 (42.86%) | 2 / 11 (18.18%) |
| occurrences (all) | 4 | 6 | 3 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 4 / 38 (10.53%) | 3 / 14 (21.43%) | 2 / 11 (18.18%) |
| occurrences (all) | 11 | 8 | 2 |
| Injury, poisoning and procedural complications | | | |

| | | | |
|-----------------------------|----------------|-----------------|-----------------|
| Contusion | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 0 / 14 (0.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 3 | 0 | 2 |
| Eye injury | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Fall | | | |
| subjects affected / exposed | 3 / 38 (7.89%) | 2 / 14 (14.29%) | 0 / 11 (0.00%) |
| occurrences (all) | 3 | 2 | 0 |
| Humerus fracture | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Joint injury | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Periorbital haemorrhage | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Radiation pneumonitis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Thermal burn | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 3 / 38 (7.89%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Tachycardia | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Palpitations | | | |

| | | | |
|-------------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 8 / 38 (21.05%) | 2 / 14 (14.29%) | 0 / 11 (0.00%) |
| occurrences (all) | 9 | 2 | 0 |
| Dysarthria | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Dysgeusia | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 1 / 14 (7.14%) | 1 / 11 (9.09%) |
| occurrences (all) | 2 | 1 | 1 |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Headache | | | |
| subjects affected / exposed | 5 / 38 (13.16%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 2 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 4 / 38 (10.53%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 6 | 2 | 0 |
| Sciatica | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sinus headache | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|--|------------------------|------------------------|----------------------|
| Tremor subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 2 / 14 (14.29%) 2 | 0 / 11 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 16 / 38 (42.11%) 32 | 10 / 14 (71.43%) 17 | 6 / 11 (54.55%) 9 |
| Febrile neutropenia subjects affected / exposed occurrences (all) | 2 / 38 (5.26%) 2 | 1 / 14 (7.14%) 1 | 0 / 11 (0.00%) 0 |
| Leukopenia subjects affected / exposed occurrences (all) | 1 / 38 (2.63%) 1 | 4 / 14 (28.57%) 5 | 0 / 11 (0.00%) 0 |
| Lymphopenia subjects affected / exposed occurrences (all) | 1 / 38 (2.63%) 1 | 1 / 14 (7.14%) 1 | 1 / 11 (9.09%) 2 |
| Neutropenia subjects affected / exposed occurrences (all) | 6 / 38 (15.79%) 11 | 4 / 14 (28.57%) 5 | 3 / 11 (27.27%) 9 |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 3 / 38 (7.89%) 8 | 0 / 14 (0.00%) 0 | 1 / 11 (9.09%) 1 |
| Splenomegaly subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 1 / 14 (7.14%) 1 | 0 / 11 (0.00%) 0 |
| Ear and labyrinth disorders | | | |
| Ear pain subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 0 / 14 (0.00%) 0 | 1 / 11 (9.09%) 1 |
| Eye disorders | | | |
| Vision blurred subjects affected / exposed occurrences (all) | 2 / 38 (5.26%) 2 | 0 / 14 (0.00%) 0 | 0 / 11 (0.00%) 0 |
| Macular degeneration subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 1 / 14 (7.14%) 1 | 0 / 11 (0.00%) 0 |
| Vitreous floaters | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 1 / 14 (7.14%) 1 | 0 / 11 (0.00%) 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 5 / 38 (13.16%) | 2 / 14 (14.29%) | 2 / 11 (18.18%) |
| occurrences (all) | 5 | 3 | 3 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 2 / 14 (14.29%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 2 | 2 |
| Constipation | | | |
| subjects affected / exposed | 5 / 38 (13.16%) | 5 / 14 (35.71%) | 1 / 11 (9.09%) |
| occurrences (all) | 5 | 7 | 1 |
| Diarrhoea | | | |
| subjects affected / exposed | 14 / 38 (36.84%) | 8 / 14 (57.14%) | 2 / 11 (18.18%) |
| occurrences (all) | 28 | 9 | 5 |
| Dyspepsia | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 0 / 14 (0.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 2 | 0 | 2 |
| Dysphagia | | | |
| subjects affected / exposed | 5 / 38 (13.16%) | 0 / 14 (0.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 5 | 0 | 2 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |

| | | | |
|--|------------------------|----------------------|----------------------|
| Gastrointestinal wall thickening subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 0 / 14 (0.00%) 0 | 1 / 11 (9.09%) 1 |
| Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 0 / 14 (0.00%) 0 | 1 / 11 (9.09%) 1 |
| Gingival pain subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 1 / 14 (7.14%) 1 | 0 / 11 (0.00%) 0 |
| Nausea subjects affected / exposed occurrences (all) | 12 / 38 (31.58%) 17 | 9 / 14 (64.29%) 9 | 4 / 11 (36.36%) 5 |
| Stomatitis subjects affected / exposed occurrences (all) | 3 / 38 (7.89%) 3 | 0 / 14 (0.00%) 0 | 1 / 11 (9.09%) 1 |
| Toothache subjects affected / exposed occurrences (all) | 1 / 38 (2.63%) 1 | 1 / 14 (7.14%) 1 | 1 / 11 (9.09%) 1 |
| Vomiting subjects affected / exposed occurrences (all) | 6 / 38 (15.79%) 8 | 5 / 14 (35.71%) 5 | 3 / 11 (27.27%) 4 |
| Hepatobiliary disorders Cholecystitis subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 1 / 14 (7.14%) 1 | 0 / 11 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Dermatitis acneiform subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 0 / 14 (0.00%) 0 | 1 / 11 (9.09%) 1 |
| Erythema multiforme subjects affected / exposed occurrences (all) | 2 / 38 (5.26%) 2 | 0 / 14 (0.00%) 0 | 0 / 11 (0.00%) 0 |
| Hyperhidrosis subjects affected / exposed occurrences (all) | 0 / 38 (0.00%) 0 | 1 / 14 (7.14%) 2 | 0 / 11 (0.00%) 0 |
| Ingrowing nail | | | |

| | | | |
|-----------------------------|------------------|-----------------|-----------------|
| subjects affected / exposed | 2 / 38 (5.26%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Onychomadesis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Pruritus | | | |
| subjects affected / exposed | 10 / 38 (26.32%) | 0 / 14 (0.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 11 | 0 | 4 |
| Rash | | | |
| subjects affected / exposed | 9 / 38 (23.68%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 11 | 0 | 0 |
| Rash macular | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 5 / 38 (13.16%) | 0 / 14 (0.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 7 | 0 | 6 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 1 | 4 |
| Urticaria | | | |
| subjects affected / exposed | 5 / 38 (13.16%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 3 / 14 (21.43%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Haematuria | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Nocturia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Renal colic | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Urinary retention | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Urine abnormality | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 3 / 38 (7.89%) | 4 / 14 (28.57%) | 2 / 11 (18.18%) |
| occurrences (all) | 4 | 4 | 3 |
| Back pain | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 1 / 14 (7.14%) | 2 / 11 (18.18%) |
| occurrences (all) | 1 | 1 | 2 |
| Bone pain | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 1 / 14 (7.14%) | 1 / 11 (9.09%) |
| occurrences (all) | 2 | 1 | 3 |
| Flank pain | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Groin pain | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 2 / 14 (14.29%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 7 / 38 (18.42%) | 0 / 14 (0.00%) | 3 / 11 (27.27%) |
| occurrences (all) | 10 | 0 | 3 |
| Myalgia | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Neck pain | | | |

| | | | |
|---------------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 2 | 0 | 1 |
| Scoliosis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Synovitis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Infections and infestations | | | |
| Bacterial infection | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 2 |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dermatitis infected | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Epstein-Barr virus infection | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Oral candidiasis | | | |
| subjects affected / exposed | 4 / 38 (10.53%) | 0 / 14 (0.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 4 | 0 | 2 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 0 | 0 | 2 |

| | | | |
|---------------------------------------|------------------|-----------------|-----------------|
| Pneumonia | | | |
| subjects affected / exposed | 4 / 38 (10.53%) | 1 / 14 (7.14%) | 1 / 11 (9.09%) |
| occurrences (all) | 4 | 1 | 1 |
| Rash pustular | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Sepsis | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Streptococcal urinary tract infection | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 5 / 38 (13.16%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 38 (7.89%) | 1 / 14 (7.14%) | 1 / 11 (9.09%) |
| occurrences (all) | 3 | 1 | 1 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 13 / 38 (34.21%) | 7 / 14 (50.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 16 | 8 | 3 |
| Dehydration | | | |
| subjects affected / exposed | 5 / 38 (13.16%) | 4 / 14 (28.57%) | 0 / 11 (0.00%) |
| occurrences (all) | 6 | 5 | 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 3 / 38 (7.89%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 3 | 4 | 0 |
| Hyperglycaemia | | | |

| | | | |
|-----------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 38 (2.63%) | 2 / 14 (14.29%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 2 / 14 (14.29%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 9 / 38 (23.68%) | 5 / 14 (35.71%) | 1 / 11 (9.09%) |
| occurrences (all) | 15 | 7 | 1 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 5 / 38 (13.16%) | 5 / 14 (35.71%) | 0 / 11 (0.00%) |
| occurrences (all) | 7 | 6 | 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 7 / 14 (50.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 3 | 10 | 1 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Hypovolaemia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lactic acidosis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 14 (7.14%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vitamin B1 deficiency | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 14 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |

| Non-serious adverse events | Cohort PTCL-NOS, Overall | Cohort Other | |
|---|-----------------------------|-----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 25 / 25 (100.00%) | 2 / 2 (100.00%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Tumour pain | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Haematoma | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypotension | | | |
| subjects affected / exposed | 3 / 25 (12.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Peripheral coldness | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 6 / 25 (24.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 7 | 0 | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Chills | | | |
| subjects affected / exposed | 3 / 25 (12.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 5 | 1 | |
| Fatigue | | | |
| subjects affected / exposed | 9 / 25 (36.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 9 | 0 | |

| | | | |
|---|----------------------|---------------------|--|
| Gait disturbance subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | 0 / 2 (0.00%) 0 | |
| Decreased activity subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | 0 / 2 (0.00%) 0 | |
| Influenza like illness subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 3 | 0 / 2 (0.00%) 0 | |
| Malaise subjects affected / exposed occurrences (all) | 3 / 25 (12.00%) 4 | 1 / 2 (50.00%) 1 | |
| Oedema peripheral subjects affected / exposed occurrences (all) | 7 / 25 (28.00%) 8 | 0 / 2 (0.00%) 0 | |
| Pain subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | 1 / 2 (50.00%) 1 | |
| Medical device pain subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | 0 / 2 (0.00%) 0 | |
| Non-cardiac chest pain subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 2 | 0 / 2 (0.00%) 0 | |
| Pyrexia subjects affected / exposed occurrences (all) | 5 / 25 (20.00%) 9 | 1 / 2 (50.00%) 1 | |
| Reproductive system and breast disorders Gynaecomastia subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | 0 / 2 (0.00%) 0 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 5 / 25 (20.00%) 5 | 0 / 2 (0.00%) 0 | |
| Dysphonia | | | |

| | | | |
|-----------------------------|-----------------|----------------|--|
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 6 / 25 (24.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 6 | 1 | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hiccups | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nasal congestion | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 2 | 1 | |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Productive cough | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Pulmonary mass | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Psychiatric disorders | | | |
| Abnormal dreams | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |

| | | | |
|---------------------------------------|-----------------|----------------|--|
| Agitation | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Confusional state | | | |
| subjects affected / exposed | 3 / 25 (12.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Disorientation | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Insomnia | | | |
| subjects affected / exposed | 4 / 25 (16.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 4 | 1 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 3 / 25 (12.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 6 | 0 | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 6 / 25 (24.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 7 | 0 | |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blood urea increased | | | |

| | | | |
|--|-----------------|---------------|--|
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blood uric acid increased | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| CD4 lymphocytes decreased | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Epstein-Barr virus test positive | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Human rhinovirus test positive | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| International normalised ratio increased | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Lymphocyte count increased | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Monocyte count decreased | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 9 / 25 (36.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 28 | 0 | |
| Platelet count decreased | | | |

| | | | |
|--|------------------|----------------|--|
| subjects affected / exposed | 14 / 25 (56.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 22 | 1 | |
| Urine output increased | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Weight decreased | | | |
| subjects affected / exposed | 8 / 25 (32.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 9 | 0 | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 5 / 25 (20.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 10 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Eye injury | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Fall | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Humerus fracture | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Joint injury | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Periorbital haemorrhage | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Radiation pneumonitis | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Thermal burn | | | |

| | | | |
|--|---------------------|--------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | 0 / 2 (0.00%) 0 | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tachycardia | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 1 | 1 | |
| Palpitations | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 2 | 1 | |
| Dysarthria | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dysgeusia | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Headache | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 2 / 2 (100.00%) | |
| occurrences (all) | 0 | 2 | |
| Paraesthesia | | | |

| | | | |
|--------------------------------------|------------------|----------------|--|
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Sciatica | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Sinus headache | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Somnolence | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tremor | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 16 / 25 (64.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 26 | 1 | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Leukopenia | | | |
| subjects affected / exposed | 4 / 25 (16.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 5 | 1 | |
| Lymphopenia | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 7 / 25 (28.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 14 | 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| | | | |
|---|---|---|--|
| Splenomegaly subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | 0 / 2 (0.00%) 0 | |
| Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | 1 / 2 (50.00%) 1 | |
| Eye disorders Vision blurred subjects affected / exposed occurrences (all) Macular degeneration subjects affected / exposed occurrences (all) Vitreous floaters subjects affected / exposed occurrences (all) | 0 / 25 (0.00%) 0 1 / 25 (4.00%) 1 1 / 25 (4.00%) 1 | 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 | |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain lower subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Abdominal discomfort subjects affected / exposed occurrences (all) Abdominal distension subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea | 4 / 25 (16.00%) 6 1 / 25 (4.00%) 1 1 / 25 (4.00%) 1 1 / 25 (4.00%) 1 3 / 25 (12.00%) 4 6 / 25 (24.00%) 8 | 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 1 / 2 (50.00%) 1 0 / 2 (0.00%) 0 | |

| | | | |
|----------------------------------|------------------|----------------|--|
| subjects affected / exposed | 10 / 25 (40.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 14 | 1 | |
| Dyspepsia | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Dysphagia | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 0 | 1 | |
| Gastritis | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Gastrointestinal wall thickening | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gingival pain | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nausea | | | |
| subjects affected / exposed | 13 / 25 (52.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 14 | 1 | |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Toothache | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Vomiting | | | |
| subjects affected / exposed | 8 / 25 (32.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 9 | 0 | |
| Hepatobiliary disorders | | | |

| | | | |
|--|----------------|----------------|--|
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Erythema multiforme | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 0 | 1 | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Ingrowing nail | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Night sweats | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Onychomadesis | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pruritus | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Rash | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Rash macular | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 6 | 1 | |
| Skin lesion | | | |

| | | | |
|---|----------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 5 | 0 / 2 (0.00%) 0 | |
| Urticaria subjects affected / exposed occurrences (all) | 0 / 25 (0.00%) 0 | 0 / 2 (0.00%) 0 | |
| Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all) | 3 / 25 (12.00%) 3 | 0 / 2 (0.00%) 0 | |
| Haematuria subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | 0 / 2 (0.00%) 0 | |
| Nocturia subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | 0 / 2 (0.00%) 0 | |
| Renal colic subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | 0 / 2 (0.00%) 0 | |
| Urinary retention subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | 0 / 2 (0.00%) 0 | |
| Urine abnormality subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | 0 / 2 (0.00%) 0 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 6 / 25 (24.00%) 7 | 0 / 2 (0.00%) 0 | |
| Back pain subjects affected / exposed occurrences (all) | 3 / 25 (12.00%) 3 | 1 / 2 (50.00%) 1 | |
| Bone pain subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 4 | 0 / 2 (0.00%) 0 | |
| Flank pain | | | |

| | | | |
|---------------------------------|-----------------|----------------|--|
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Groin pain | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 1 | 1 | |
| Muscle spasms | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Muscular weakness | | | |
| subjects affected / exposed | 3 / 25 (12.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Myalgia | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Neck pain | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 0 | 1 | |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 1 | 1 | |
| Scoliosis | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Synovitis | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Infections and infestations | | | |
| Bacterial infection | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| | | |
|---------------------------------------|----------------|----------------|
| Dermatitis infected | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 |
| Epstein-Barr virus infection | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 |
| Herpes zoster | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all) | 0 | 1 |
| Oral candidiasis | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 2 | 0 |
| Pharyngitis | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 2 | 0 |
| Pneumonia | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 2 | 0 |
| Rash pustular | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 2 | 0 |
| Sepsis | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 |
| Sinusitis | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 |
| Streptococcal urinary tract infection | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 1 | 0 |
| Upper respiratory tract infection | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 0 | 0 |
| Urinary tract infection | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 2 | 0 |

| | | | |
|--|-----------------------|---------------------|--|
| Skin infection subjects affected / exposed occurrences (all) | 0 / 25 (0.00%) 0 | 1 / 2 (50.00%) 1 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite subjects affected / exposed occurrences (all) | 9 / 25 (36.00%) 11 | 1 / 2 (50.00%) 1 | |
| Dehydration subjects affected / exposed occurrences (all) | 4 / 25 (16.00%) 5 | 0 / 2 (0.00%) 0 | |
| Hypercalcaemia subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 4 | 0 / 2 (0.00%) 0 | |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 2 | 1 / 2 (50.00%) 1 | |
| Hyperkalaemia subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | 0 / 2 (0.00%) 0 | |
| Hyperuricaemia subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 2 | 0 / 2 (0.00%) 0 | |
| Hypoalbuminaemia subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 2 | 0 / 2 (0.00%) 0 | |
| Hypocalcaemia subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 3 | 0 / 2 (0.00%) 0 | |
| Hypokalaemia subjects affected / exposed occurrences (all) | 6 / 25 (24.00%) 8 | 0 / 2 (0.00%) 0 | |
| Hypomagnesaemia subjects affected / exposed occurrences (all) | 5 / 25 (20.00%) 6 | 0 / 2 (0.00%) 0 | |
| Hyponatraemia | | | |

| | | | |
|-----------------------------|-----------------|----------------|--|
| subjects affected / exposed | 8 / 25 (32.00%) | 1 / 2 (50.00%) | |
| occurrences (all) | 11 | 1 | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypovolaemia | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Lactic acidosis | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Metabolic acidosis | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vitamin B1 deficiency | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 0 / 2 (0.00%) | |
| occurrences (all) | 1 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 06 January 2016 | <p>Protocol Amendment 1 (dated 06 January 2016), implemented the following substantive changes:</p> <ul style="list-style-type: none"> •Modified dosing regimen of tipifarnib to 900 mg po BID on Days 1 – 7 and 15 – 21 of 28-day treatment cycles •Indicated that if treatment-related treatment-emergent adverse event (TEAE) Common Terminology Criteria for Adverse Events (CTCAE) Grade > 3 haematological toxicity or CTCAE Grade 3 or 4 non-haematological toxicity was observed that could not be managed with supportive care measures, treatment with tipifarnib would be discontinued until recovery to CTCAE Grade ≤ 3 or CTCAE Grade ≤ 2 respectively. •Included (specifically for renal toxicity): If TEAE CTCAE Grade ≥ 2 renal toxicity was observed, treatment with tipifarnib was to be discontinued until recovery to Grade 1 or resolution. Upon recovery to Grade 1 or resolution, tipifarnib should have been restarted at a reduced dose level. •Dose re-escalation was clarified. Unless otherwise indicated (e.g., dosing discontinuation), reduced doses may have been re-escalated to the original dose at the judgement of the investigator. However, subjects who experienced SAEs or a recurrence of Grade ≥ 3 toxicity deemed to be related to tipifarnib would not have the dose re-escalated following dose reduction. In addition, subjects experiencing more than 1 dose delay of ≥ 14 days would not have the dose re-escalated. •The option for dose escalation to 1200 mg BID was clarified. At the discretion of the investigator, the dose of tipifarnib may have been increased to 1200 mg BID if the subject did not experience at dose limiting toxicity (DLT) at the 900 mg BID dose. However, the tipifarnib dose would not be escalated to 1200 mg BID in subjects who developed SAEs or experienced Grade ≥ 2 TEAEs that were deemed related to tipifarnib and lasted ≥ 14 days or in those subjects who had required dose reductions or dose delays ≥ 14 days for TEAEs deemed related to tipifarnib. |
| 06 January 2016 | <p>Protocol Amendment 1 continued (dated 06 January 2016), implemented the following substantive changes:</p> <ul style="list-style-type: none"> •Inclusion criteria 11 (acceptable haematological status) was updated to remove the exclusion of growth factor support or transfusion dependency. •Clarified the exclusion of subjects with hypersensitivity to structural compounds similar to tipifarnib. Subjects with hypersensitivity to imidazoles, such as clotrimazole, ketoconazole, miconazole, and others in this drug class were excluded from enrolment. •Defined non-tolerable Grade 2 toxicities as those with moderate symptoms that the subject was not able to endure for the conduct of instrumental activities of daily life or that persisted ≥ 7 days. •Added electrocardiogram (ECG) testing at Cycle 1 Day 1 and Day 7 at the projected time of C_{max}, 2 – 4 hours postdose. Replaced Day 15 procedures with Day 7 procedures in order to allow collection of ECG and laboratory safety evaluations at steady state. •Included the following statement: Subjects should not use enzyme-inducing anticonvulsants (e.g., phenytoin, phenobarbital, and carbamazepine) while taking tipifarnib. If needed, subjects may have used non-enzyme-inducing anticonvulsants (e.g., gabapentin, topiramate, valproate) while taking tipifarnib. •Detailed the exploratory objective to include oncogene panel sequencing from tumour tissue samples, immune cytokine profiling from serum samples, and Killer cell Immunoglobulin-like receptor (KIR) genotyping. •Updated protocol Section 9.5 Dose Modification and Management of Toxicity to align with the change in dose and schedule. •Added a blood sample for biomarkers as well as additional details on serum biomarker collections. |

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| 06 January 2016 | <p>Protocol Amendment 1 continued (dated 06 January 2016), implemented the following substantive changes:</p> <ul style="list-style-type: none"> • Added the following: Subjects may have used proton pump inhibitors or H2 antagonists during the treatment portion of this study. However, subjects were instructed to use antacids (magnesium or aluminium containing products) at least 2 hours before or after taking study drug. • Removed the need to perform urinalysis (based on absence of prior findings). • Clarified the tumour assessment schedule. • To facilitate the scheduling of subjects, assessments on Day 22 were removed (ECOG, physical examination, vital signs) and allowed a window (± 1 day) for Cycle 2 Day 1. |
| 29 March 2016 | <p>Protocol Amendment 2 (dated 29 March 2016), implemented the following substantive changes:</p> <ul style="list-style-type: none"> • Reduced the number of required tumour slides from 12 to 6 and clarified that if no slides were available, a formalin-fixed paraffin-embedded block could have been provided for biomarker testing. • Included a serum biomarker collection at Cycle 1 Day 7. • Clarified that baseline samples for biomarkers were 2 distinct samples (1 blood and 1 serum sample). • Allowed (in exceptional circumstances), dosing delays or skipping of doses for reasons other than management of toxicity. This was allowed at the judgement of the investigator as long as 50% of the total dose was maintained for a given cycle. • To facilitate the scheduling of subjects, allowed a window (± 2 day) for Cycle 2 Day 1. • Provided clarity to the sample size determination. <ul style="list-style-type: none"> – At least 4 out of 18 subjects would need to be observed for rejection of the null hypothesis. In a prior tipifarnib study, 4 responses were observed in 8 PTCL subjects. If this high level of activity were to be observed, provisions were to be made to address the unmet medical need of this patient population. – If 5 or more objective responses are observed in initial 11 subjects, enrolment would continue until a new study was initiated or until a maximum of 30 subjects were enrolled, whichever occurred first. – No specific statistical hypothesis was to be tested in this extension cohort and descriptive statistics would be employed to define the response rate and its 95% confidence interval of the overall set of treated subjects. • Included newly acquired EudraCT number. |
| 25 August 2016 | <p>Protocol Amendment 3 (dated 25 August 2016), implemented the following substantive changes:</p> <ul style="list-style-type: none"> • Reduced tipifarnib starting dose to 600 mg on Days 1 – 7 and 15 – 21 of a 28-day cycle. Additionally, the dose of tipifarnib may have been increased to 800 mg BID if the subject had not experienced DLTs at the 600 mg dose level. Subjects who received a starting dose of 900 mg BID during the conduct of the original version of the protocol may have been dose reduced to the 600 mg BID dose at the investigators discretion. • Incorporated 200 mg dose reductions as part of the management of TEAE toxicities. Incorporated dose modification (200 mg dose reduction) upon occurrence of Grade 3 haematological toxicities and clarified treatment interruption and reinitiation of tipifarnib at each dose level. • Clarified that for inclusion into the study, the site had to confirm that sufficient archival tumour tissue was available during screening, or the subject must have had a biopsy performed prior to initiation of tipifarnib. Allowed replacement of subjects who were unable to provide archival tumour tissue by the end of Cycle 1 and who had not had a tumour biopsy prior to initiation of tipifarnib therapy. • Clarified the response assessment to be used in the study was the Lugano Classification. In line with these response criteria, additional guidance was provided on the selection of imaging method (PET-CT or Spiral CT) and bone marrow (BM) evaluation (biopsy or PET). • Allowed for continuation of enrolment up to a maximum of 30 subjects if 5 or more responses were observed in the first 18 evaluable subjects. • Clarified that the visit schedule should have been maintained regardless of dose delays or additional assessments performed. • Reduced the frequency of coagulation testing and collection of vital signs. • Clarified that pregnancy testing could have been urine or serum. • Aligned the description of TEAE grading with CTCAE v4.03; moved “disabling” from Grade 4 to Grade 3. |

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| 08 March 2017 | <p>Protocol Amendment 4 (dated 08 March 2017), implemented the following substantive changes:</p> <ul style="list-style-type: none"> • Added AITL expansion cohort (N = 12) and statistical rationale for the selected sample size. • Added a buccal swab collection at screening and included markers for herpes virus infection as potential biomarkers for evaluation • Added a plasma sample in addition to the already included serum sample for the assessment of circulating biomarkers. • Provided additional clarification under which circumstances subjects may have been replaced. |
| 06 July 2017 | <p>Protocol Amendment 5 (dated 06 July 2017), implemented the following substantive changes:</p> <ul style="list-style-type: none"> • Changed the tipifarnib dose and regimen from 600 mg BID for 7 days in alternating weeks to 300 mg BID administered for 21 days in 28-day treatment cycles and allowed for stepwise 100 mg dose reductions to control treatment-related, treatment-emergent toxicities. Dose modifications guidelines were adjusted to account for the new dose regimen. In addition, guidance was included to allow subjects who received tipifarnib BID on Days 1 – 7 and Days 15 – 21 in 28-day cycles during the conduct of earlier versions of the protocol to remain on that dose regimen at the discretion of the investigator. Alternatively, the subject may have transitioned to receive a dose of 300 mg, orally with food, BID on Days 1 – 21 of 28-day treatment cycles beginning on Day 1 of the next cycle. • Adjusted contraception requirements for inclusion in the study, provided further information on the potential effects of tipifarnib on reproduction and fertility, and provided guidance on sperm cryopreservation in male subjects wishing to preserve their fertility after tipifarnib treatment. • Clarified that a negative pregnancy test must have been obtained during screening within 72 hours of the first dose of tipifarnib in women of childbearing potential. • Updated information on the study drug characteristics and the 300 mg tablet, which may have been used as clinical trial material. Revised guidance on crushing or chewing tablets. • Removed the limit on the number of allowable dose reductions prior to removing the subject from the study. Subjects should have been removed from the study based on criteria outlined in the protocol. • Provided additional clarification on how to define the cycle and day when tipifarnib is restarted following a treatment interruption. |
| 06 July 2017 | <p>Protocol Amendment 5 continued (dated 06 July 2017), implemented the following substantive changes:</p> <ul style="list-style-type: none"> • Provided additional emphasis that tumour assessments, including radiological assessments, should have maintained actual time schedule regardless of treatment delays or interruptions. In other words, subjects should have had their tumour assessed approximately every 8 weeks from starting tipifarnib treatment through the first 6 months of study participation. Thereafter, tumour assessments were to be performed every 12 weeks. • Provided additional details on the definition of End of Study. • Removed erroneously placed "x" for tumour assessment on Cycle 1 Day 7 in Schedule of Activities table. |
| 08 January 2018 | <p>Protocol Amendment 6 (dated 08 January 2018), implemented the following substantive changes:</p> <ul style="list-style-type: none"> • Added a CXCL12+ PTCL expansion cohort (N = 12) and statistical rationale for the selected sample size. • Clarified that pregnancy testing on Day 1 of each cycle was to begin at Cycle 2 as the screening pregnancy testing was to be done within 72 hours of first dose on Cycle 1 Day 1. |

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| 12 July 2019 | <p>Protocol Amendment 7 (dated 12 July 2019), implemented the following substantive changes:</p> <ul style="list-style-type: none"> • Based on the high antitumor activity observed in AITL subjects in the AITL cohort and other portions of the study, enrolment in the AITL cohort was expanded to include up to 20 additional subjects with tumours of AITL and related T follicular helper cell histologies in order to gather further experience with tipifarnib in this relatively rare patient population. The selection of 20 subjects was empirical and no statistical hypotheses were tested. Descriptive statistics were to be used to report response rate. • Expanded the buccal swab genomic assessments to allow for the determination of germinal/somatic status of gene variations in tumour samples. • Included supplementary clinical experience data, which supported the expansion of the study. |
|--------------|---|

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported