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	-
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	65.73	56.68	
standard deviation	± 12.9	± 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

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 ≤ 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

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	5 / 38 (13.16%)	3 / 14 (21.43%)	1 / 11 (9.09%)
occurrences (all)	5	3	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 38 (2.63%)	1 / 14 (7.14%)	1 / 11 (9.09%)
occurrences (all)	1	1	1
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 38 (5.26%)	1 / 14 (7.14%)	1 / 11 (9.09%)
occurrences (all)	2	2	1
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 38 (2.63%)	2 / 14 (14.29%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
Blood bilirubin increased			
subjects affected / exposed	0 / 38 (0.00%)	3 / 14 (21.43%)	0 / 11 (0.00%)
occurrences (all)	0	6	0
Blood creatinine increased			
subjects affected / exposed	5 / 38 (13.16%)	5 / 14 (35.71%)	1 / 11 (9.09%)
occurrences (all)	5	6	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Blood urea increased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Blood uric acid increased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
CD4 lymphocytes decreased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Epstein-Barr virus test positive			
subjects affected / exposed	0 / 38 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	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	0 / 38 (0.00%)	2 / 14 (14.29%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	16 / 38 (42.11%)	10 / 14 (71.43%)	6 / 11 (54.55%)
occurrences (all)	32	17	9
Febrile neutropenia			
subjects affected / exposed	2 / 38 (5.26%)	1 / 14 (7.14%)	0 / 11 (0.00%)
occurrences (all)	2	1	0
Leukopenia			
subjects affected / exposed	1 / 38 (2.63%)	4 / 14 (28.57%)	0 / 11 (0.00%)
occurrences (all)	1	5	0
Lymphopenia			
subjects affected / exposed	1 / 38 (2.63%)	1 / 14 (7.14%)	1 / 11 (9.09%)
occurrences (all)	1	1	2
Neutropenia			
subjects affected / exposed	6 / 38 (15.79%)	4 / 14 (28.57%)	3 / 11 (27.27%)
occurrences (all)	11	5	9
Thrombocytopenia			
subjects affected / exposed	3 / 38 (7.89%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	8	0	1
Splenomegaly			
subjects affected / exposed	0 / 38 (0.00%)	1 / 14 (7.14%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 38 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Eye disorders			
Vision blurred			
subjects affected / exposed	2 / 38 (5.26%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Macular degeneration			
subjects affected / exposed	0 / 38 (0.00%)	1 / 14 (7.14%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Vitreous floaters			

subjects affected / exposed	0 / 38 (0.00%)	1 / 14 (7.14%)	0 / 11 (0.00%)
occurrences (all)	0	1	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	0 / 38 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 38 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Gingival pain			
subjects affected / exposed	0 / 38 (0.00%)	1 / 14 (7.14%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	12 / 38 (31.58%)	9 / 14 (64.29%)	4 / 11 (36.36%)
occurrences (all)	17	9	5
Stomatitis			
subjects affected / exposed	3 / 38 (7.89%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	3	0	1
Toothache			
subjects affected / exposed	1 / 38 (2.63%)	1 / 14 (7.14%)	1 / 11 (9.09%)
occurrences (all)	1	1	1
Vomiting			
subjects affected / exposed	6 / 38 (15.79%)	5 / 14 (35.71%)	3 / 11 (27.27%)
occurrences (all)	8	5	4
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 14 (7.14%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 38 (0.00%)	0 / 14 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Erythema multiforme			
subjects affected / exposed	2 / 38 (5.26%)	0 / 14 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 14 (7.14%)	0 / 11 (0.00%)
occurrences (all)	0	2	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
Streptoccocal 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	1 / 25 (4.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Decreased activity			
subjects affected / exposed	1 / 25 (4.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Influenza like illness			
subjects affected / exposed	2 / 25 (8.00%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Malaise			
subjects affected / exposed	3 / 25 (12.00%)	1 / 2 (50.00%)	
occurrences (all)	4	1	
Oedema peripheral			
subjects affected / exposed	7 / 25 (28.00%)	0 / 2 (0.00%)	
occurrences (all)	8	0	
Pain			
subjects affected / exposed	1 / 25 (4.00%)	1 / 2 (50.00%)	
occurrences (all)	1	1	
Medical device pain			
subjects affected / exposed	1 / 25 (4.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Non-cardiac chest pain			
subjects affected / exposed	2 / 25 (8.00%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Pyrexia			
subjects affected / exposed	5 / 25 (20.00%)	1 / 2 (50.00%)	
occurrences (all)	9	1	
Reproductive system and breast disorders			
Gynaecomastia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 25 (20.00%)	0 / 2 (0.00%)	
occurrences (all)	5	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	1 / 25 (4.00%)	0 / 2 (0.00%)	
occurrences (all)	1	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	1 / 25 (4.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 25 (4.00%)	1 / 2 (50.00%)	
occurrences (all)	1	1	
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 25 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Macular degeneration			
subjects affected / exposed	1 / 25 (4.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Vitreous floaters			
subjects affected / exposed	1 / 25 (4.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 25 (16.00%)	0 / 2 (0.00%)	
occurrences (all)	6	0	
Abdominal pain lower			
subjects affected / exposed	1 / 25 (4.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
subjects affected / exposed	1 / 25 (4.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Abdominal discomfort			
subjects affected / exposed	1 / 25 (4.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Abdominal distension			
subjects affected / exposed	3 / 25 (12.00%)	1 / 2 (50.00%)	
occurrences (all)	4	1	
Constipation			
subjects affected / exposed	6 / 25 (24.00%)	0 / 2 (0.00%)	
occurrences (all)	8	0	
Diarrhoea			

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	2 / 25 (8.00%)	0 / 2 (0.00%)	
occurrences (all)	5	0	
Urticaria			
subjects affected / exposed	0 / 25 (0.00%)	0 / 2 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 25 (12.00%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Haematuria			
subjects affected / exposed	1 / 25 (4.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Nocturia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Renal colic			
subjects affected / exposed	1 / 25 (4.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Urinary retention			
subjects affected / exposed	1 / 25 (4.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Urine abnormality			
subjects affected / exposed	1 / 25 (4.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 25 (24.00%)	0 / 2 (0.00%)	
occurrences (all)	7	0	
Back pain			
subjects affected / exposed	3 / 25 (12.00%)	1 / 2 (50.00%)	
occurrences (all)	3	1	
Bone pain			
subjects affected / exposed	2 / 25 (8.00%)	0 / 2 (0.00%)	
occurrences (all)	4	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	
Streptoccocal 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	0 / 25 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	9 / 25 (36.00%)	1 / 2 (50.00%)	
occurrences (all)	11	1	
Dehydration			
subjects affected / exposed	4 / 25 (16.00%)	0 / 2 (0.00%)	
occurrences (all)	5	0	
Hypercalcaemia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 2 (0.00%)	
occurrences (all)	4	0	
Hyperglycaemia			
subjects affected / exposed	2 / 25 (8.00%)	1 / 2 (50.00%)	
occurrences (all)	2	1	
Hyperkalaemia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Hyperuricaemia			
subjects affected / exposed	2 / 25 (8.00%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Hypoalbuminaemia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Hypocalcaemia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Hypokalaemia			
subjects affected / exposed	6 / 25 (24.00%)	0 / 2 (0.00%)	
occurrences (all)	8	0	
Hypomagnesaemia			
subjects affected / exposed	5 / 25 (20.00%)	0 / 2 (0.00%)	
occurrences (all)	6	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	Protocol Amendment 1 (dated 06 January 2016), implemented the following substantive changes: •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	Protocol Amendment 1 continued (dated 06 January 2016), implemented the following substantive changes: •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 Cmax, 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.

06 January 2016	Protocol Amendment 1 continued (dated 06 January 2016), implemented the following substantive changes: •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	Protocol Amendment 2 (dated 29 March 2016), implemented the following substantive changes: • 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. − 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	Protocol Amendment 3 (dated 25 August 2016), implemented the following substantive changes: •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.

08 March 2017	Protocol Amendment 4 (dated 08 March 2017), implemented the following substantive changes: • 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	Protocol Amendment 5 (dated 06 July 2017), implemented the following substantive changes: • 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	Protocol Amendment 5 continued (dated 06 July 2017), implemented the following substantive changes: • 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	Protocol Amendment 6 (dated 08 January 2018), implemented the following substantive changes: • 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.

12 July 2019	Protocol Amendment 7 (dated 12 July 2019), implemented the following substantive changes: • 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