



Clinical trial results:

A Phase 2, Open-Label Study of BGB-A317 in Patients with Relapsed or Refractory Mature T- and NK-cell Neoplasms

Summary

EudraCT number	2017-003700-44
Trial protocol	DE FR IT
Global end of trial date	21 April 2021

Results information

Result version number	v1 (current)
This version publication date	18 April 2022
First version publication date	18 April 2022

Trial information

Trial identification

Sponsor protocol code	BGB-A317-207
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03493451
WHO universal trial number (UTN)	-
Other trial identifiers	-: -

Notes:

Sponsors

Sponsor organisation name	BeiGene, Ltd., c/o BeiGene USA, Inc.
Sponsor organisation address	2955 Campus Drive, Suite 200, San Mateo, United States, 94403
Public contact	BeiGene Clinical Support, BeiGene, Ltd., 1 877-828-5568, clinicaltrials@beigene.com
Scientific contact	BeiGene Clinical Support, BeiGene, Ltd., 1 877-828-5568, clinicaltrials@beigene.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	16 July 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	21 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate efficacy of BGB-A317 in subjects with relapsed or refractory mature T- and NK-cell neoplasms as measured by overall response rate and determined by investigator.

- For cohorts 1 and 2, overall response rate will be measured using the Lugano criteria (Cheson et al 2014) with Lymphoma Response to Immunomodulatory Therapy Criteria (LYRIC) modification for immunomodulatory drugs (Cheson et al 2016).
- For cohort 3, overall response rate will be measured using the International Society for Cutaneous Lymphomas/European Organization of Research and Treatment of Cancer (ISCL/EORTC) guidelines (Olsen et al 2011).

Protection of trial subjects:

This trial was designed and monitored in accordance with Sponsor procedures, which comply with the ethical principles of GCP as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki. The IEC/IRB-approved ICF was signed and dated by the subject or the subject's legally authorized representative before his or her participation in the study. A copy of each signed ICF was provided to the subject or the subject's legally authorized representative. All signed and dated ICFs were retained in each patient's study file or in the site file. For any updated or revised ICFs, written informed consent was obtained using the IEC/IRB-approved updated/revised ICFs for continued participation in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 April 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	China: 41
Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Italy: 28
Worldwide total number of subjects	77
EEA total number of subjects	33

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)	55
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled from study centers in Canada, China, France, Italy, and Taiwan, China.

Pre-assignment

Screening details:

Subjects were enrolled into 1 of 3 cohorts in this study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	Cohort 1: ENKTL
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Arm description:

Subjects with relapsed or refractory (R/R) extranodal natural killer-/T-cell lymphoma (ENKTL; nasal or non-nasal type) were treated with tislelizumab 200 mg intravenously (IV) on Day 1 of each cycle until disease progression, intolerable toxicity, or treatment discontinuation for any other reason (21 days per cycle)

Arm type	Experimental
Investigational medicinal product name	Tislelizumab
Investigational medicinal product code	
Other name	BGB-A317
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Tislelizumab 200 mg intravenously (IV) on Day 1 of each cycle until disease progression, intolerable toxicity, or treatment discontinuation for any other reason (21 days per cycle)

Arm title	Cohort 2: PTCL-NOS, AITL, and ALCL
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Arm description:

Subjects with other R/R mature T-cell neoplasms [limited to peripheral T-cell lymphoma-not otherwise specified (PTCL-NOS), angioimmunoblastic T-cell lymphoma (AITL), and anaplastic large-cell lymphoma (ALCL)] were treated with tislelizumab 200 mg intravenously (IV) on Day 1 of each cycle until disease progression, intolerable toxicity, or treatment discontinuation for any other reason (21 days per cycle)

Arm type	Experimental
Investigational medicinal product name	Tislelizumab
Investigational medicinal product code	
Other name	BGB-A317
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Tislelizumab 200 mg intravenously (IV) on Day 1 of each cycle until disease progression, intolerable toxicity, or treatment discontinuation for any other reason (21 days per cycle)

Arm title	Cohort 3: MF and SS
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Arm description:

Subjects with R/R cutaneous T-cell lymphoma [limited to mycosis fungoides (MF) and Sèzary syndrome (SS)] were treated with tislelizumab 200 mg intravenously (IV) on Day 1 of each cycle until disease progression, intolerable toxicity, or treatment discontinuation for any other reason (21 days per cycle)

Arm type	Experimental
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Investigational medicinal product name	Tislelizumab
Investigational medicinal product code	
Other name	BGB-A317
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Tislelizumab 200 mg intravenously (IV) on Day 1 of each cycle until disease progression, intolerable toxicity, or treatment discontinuation for any other reason (21 days per cycle)

Number of subjects in period 1	Cohort 1: ENKTL	Cohort 2: PTCL-NOS, AITL, and ALCL	Cohort 3: MF and SS
Started	22	44	11
Completed	0	0	0
Not completed	22	44	11
Consent withdrawn by subject	1	1	2
Death	11	26	3
Transferred to long term extension study	8	13	5
Lost to follow-up	1	4	1
Progressive disease	1	-	-

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1: ENKTL
Reporting group description: Subjects with relapsed or refractory (R/R) extranodal natural killer-/T-cell lymphoma (ENKTL; nasal or non-nasal type) were treated with tislelizumab 200 mg intravenously (IV) on Day 1 of each cycle until disease progression, intolerable toxicity, or treatment discontinuation for any other reason (21 days per cycle)	
Reporting group title	Cohort 2: PTCL-NOS, AITL, and ALCL
Reporting group description: Subjects with other R/R mature T-cell neoplasms [limited to peripheral T-cell lymphoma-not otherwise specified (PTCL-NOS), angioimmunoblastic T-cell lymphoma (AITL), and anaplastic large-cell lymphoma (ALCL)] were treated with tislelizumab 200 mg intravenously (IV) on Day 1 of each cycle until disease progression, intolerable toxicity, or treatment discontinuation for any other reason (21 days per cycle)	
Reporting group title	Cohort 3: MF and SS
Reporting group description: Subjects with R/R cutaneous T-cell lymphoma [limited to mycosis fungoides (MF) and Sèzary syndrome (SS)] were treated with tislelizumab 200 mg intravenously (IV) on Day 1 of each cycle until disease progression, intolerable toxicity, or treatment discontinuation for any other reason (21 days per cycle)	

Reporting group values	Cohort 1: ENKTL	Cohort 2: PTCL-NOS, AITL, and ALCL	Cohort 3: MF and SS
Number of subjects	22	44	11
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean	51.5	55.8	59.4
standard deviation	± 16.24	± 15.03	± 12.45
Gender categorical Units: Subjects			
Female	8	15	3
Male	14	29	8
Race/Ethnicity Units: Subjects			
Asian	19	23	2
White	2	18	8
Not reported	1	3	1

Reporting group values	Total		
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Number of subjects	77		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	26		
Male	51		
Race/Ethnicity			
Units: Subjects			
Asian	44		
White	28		
Not reported	5		

End points

End points reporting groups

Reporting group title	Cohort 1: ENKTL
Reporting group description: Subjects with relapsed or refractory (R/R) extranodal natural killer-/T-cell lymphoma (ENKTL; nasal or non-nasal type) were treated with tislelizumab 200 mg intravenously (IV) on Day 1 of each cycle until disease progression, intolerable toxicity, or treatment discontinuation for any other reason (21 days per cycle)	
Reporting group title	Cohort 2: PTCL-NOS, AITL, and ALCL
Reporting group description: Subjects with other R/R mature T-cell neoplasms [limited to peripheral T-cell lymphoma-not otherwise specified (PTCL-NOS), angioimmunoblastic T-cell lymphoma (AITL), and anaplastic large-cell lymphoma (ALCL)] were treated with tislelizumab 200 mg intravenously (IV) on Day 1 of each cycle until disease progression, intolerable toxicity, or treatment discontinuation for any other reason (21 days per cycle)	
Reporting group title	Cohort 3: MF and SS
Reporting group description: Subjects with R/R cutaneous T-cell lymphoma [limited to mycosis fungoides (MF) and Sèzary syndrome (SS)] were treated with tislelizumab 200 mg intravenously (IV) on Day 1 of each cycle until disease progression, intolerable toxicity, or treatment discontinuation for any other reason (21 days per cycle)	

Primary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR) ^[1]
End point description: ORR is defined as the percentage of subjects achieving a best overall response of complete response or partial response as determined by the investigator using Lugano criteria with Lymphoma Response to Immunomodulatory Therapy Criteria (LYRIC) modification for cohorts 1 and 2 and International Society for Cutaneous Lymphomas/European Organization of Research and Treatment of Cancer (ISCL/EORTC) guidelines for cohort 3.	
End point type	Primary
End point timeframe: Up to approximately 3 years and 1 week	

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: Two-sided Clopper-Pearson 95% Confidence Intervals are provided for this endpoint

End point values	Cohort 1: ENKTL	Cohort 2: PTCL-NOS, AITL, and ALCL	Cohort 3: MF and SS	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	44	11	
Units: Percentage of subjects				
number (confidence interval 95%)	31.8 (13.9 to 54.9)	20.5 (9.8 to 35.3)	45.5 (16.7 to 76.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)
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End point description:

DOR defined as the time from the first determination of an objective response until progression or death, whichever occurs first, as assessed by the investigator using Lugano criteria with LYRIC modification for cohorts 1 and 2 and ISCL/EORTC guidelines for cohort 3. Duration of response analysis only included responders (those who achieved partial or complete response).

End point type	Secondary
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End point timeframe:

Up to approximately 3 years and 1 week

End point values	Cohort 1: ENKTL	Cohort 2: PTCL-NOS, AITL, and ALCL	Cohort 3: MF and SS	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7 ^[2]	9 ^[3]	5	
Units: Months				
median (confidence interval 95%)	9999 (2.66 to 9999)	8.2 (2.50 to 9999)	11.3 (2.76 to 11.30)	

Notes:

[2] - 9999 = Not estimable due to insufficient number of subjects with events

[3] - 9999 = Not estimable due to insufficient number of subjects with events

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS)

End point title	Progression-free Survival (PFS)
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End point description:

PFS is defined as the time from first study drug administration to the date of disease progression or death, whichever occurs first, as assessed by the investigator using Lugano criteria with LYRIC modification for cohorts 1 and 2 and ISCL/EORTC guidelines for cohort 3.

End point type	Secondary
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End point timeframe:

Up to approximately 3 years and 1 week

End point values	Cohort 1: ENKTL	Cohort 2: PTCL-NOS, AITL, and ALCL	Cohort 3: MF and SS	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	44	11	
Units: Months				
median (confidence interval 95%)	2.7 (1.45 to 5.32)	2.7 (2.56 to 4.76)	16.8 (2.60 to 16.82)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS) ^[4]
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End point description:

OS defined as the time from first study drug administration to the date of death due to any reason for cohorts 1 and 2.

End point type	Secondary
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End point timeframe:

Up to approximately 3 years and 1 week

Notes:

[4] - 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: Only Cohorts 1 and 2 were analysed for this endpoint

End point values	Cohort 1: ENKTL	Cohort 2: PTCL-NOS, AITL, and ALCL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22 ^[5]	44		
Units: Months				
median (confidence interval 95%)	8.8 (3.25 to 9999)	13.3 (7.66 to 26.22)		

Notes:

[5] - 9999 = Not estimable due to insufficient number of subjects with events

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Response Rate (CRR)

End point title	Complete Response Rate (CRR)
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End point description:

CRR is defined as the percentage of subjects who achieve complete response or complete metabolic response as best overall response as assessed by the investigator using Lugano criteria with LYRIC modification for cohorts 1 and 2 and ISCL/EORTC guidelines for cohort 3.

End point type	Secondary
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End point timeframe:

Up to approximately 3 years and 1 week

End point values	Cohort 1: ENKTL	Cohort 2: PTCL-NOS, AITL, and ALCL	Cohort 3: MF and SS	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	44	11	
Units: Percentage of subjects				
number (confidence interval 95%)	18.2 (5.2 to 40.3)	9.1 (2.5 to 21.7)	9.1 (0.2 to 41.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response (TTR)

End point title	Time to Response (TTR)
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End point description:

Time to response defined as the time from first study drug administration to the time the response criteria (complete response or partial response) are first met as assessed by the investigator using Lugano criteria with LYRIC modification for cohorts 1 and 2 and ISCL/EORTC guidelines for cohort 3. Duration of response analysis only included responders (those who achieved partial or complete response).

End point type	Secondary
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End point timeframe:

Up to approximately 3 years and 1 week

End point values	Cohort 1: ENKTL	Cohort 2: PTCL-NOS, AITL, and ALCL	Cohort 3: MF and SS	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	9	5	
Units: Months				
median (full range (min-max))	5.75 (2.1 to 13.9)	2.86 (2.1 to 5.5)	6.83 (2.6 to 11.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life Assessment: EQ-5D-5L Change from Baseline in Visual Analogue Score

End point title	Quality of Life Assessment: EQ-5D-5L Change from Baseline in Visual Analogue Score
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End point description:

Mean change from baseline at safety follow-up visit in EQ-5D-5L visual analogue score (VAS). The EQ-5D-5L measures health outcomes using a VAS to record a participant's self-rated health on a scale from 0 to 100, where 100 is 'the best health you can imagine' and 0 is 'the worst health you can imagine.' An increasing score indicates improvements from baseline.

End point type	Secondary
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End point timeframe:

Baseline and on Day 1 in Cycles 5, 9, 13, 17, 21, 25, 29, and 33 (21 days per cycle) and safety follow-up visit (up to 30 days after end of treatment; up to approximately 3 years and 1 week)

End point values	Cohort 1: ENKTL	Cohort 2: PTCL-NOS, AITL, and ALCL	Cohort 3: MF and SS	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22 ^[6]	44 ^[7]	11 ^[8]	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Cycle 5, Day 1; n=12, 19, 8	4.42 (± 10.273)	1.11 (± 13.884)	0.25 (± 22.276)	
Cycle 9, Day 1; n=6, 9, 6	1.17 (± 4.916)	5.56 (± 21.279)	-0.83 (± 17.713)	
Cycle 13, Day 1; n=7, 5, 6	-3.29 (± 16.650)	15.00 (± 19.685)	1.33 (± 21.398)	
Cycle 17, Day 1; n= 6, 6, 6	0.17 (± 9.326)	10.00 (± 17.889)	3.67 (± 23.551)	
Cycle 21, Day 1; n=4, 3, 4	4.25 (± 10.905)	8.33 (± 22.546)	5.50 (± 18.285)	
Cycle 25, Day 1; n=3, 2, 2	4.00 (± 14.422)	-2.50 (± 10.607)	5.00 (± 7.071)	
Cycle 29, Day 1; n=3, 2, 0	-2.67 (± 4.619)	-5.00 (± 7.071)	9999 (± 9999)	
Cycle 33, Day 1; n=1, 1, 0	-3.00 (± 9999)	0.00 (± 9999)	9999 (± 9999)	
Safety Follow-up; n=14, 23, 2	-1.50 (± 8.546)	-9.52 (± 21.047)	12.50 (± 3.536)	

Notes:

[6] - 9999 = Not estimable due to sample size

[7] - 9999 = Not estimable due to sample size

[8] - 9999 = Not estimable due to sample size or no subjects analysed

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life Assessment: EORTC QLQ-C30 Change from Baseline in Global Health Status Score

End point title	Quality of Life Assessment: EORTC QLQ-C30 Change from Baseline in Global Health Status Score
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End point description:

Mean change from baseline at safety follow-up visit in EORTC QLQ-C30 Global Health Status/Quality of Life score. The EORTC QLQ-C30 v3.0 is a questionnaire that assesses quality of life of cancer patients and includes global health status and quality of life questions related to their overall health in which participants respond based on a 7-point scale, where 1 is very poor and 7 is excellent. A increasing score indicates improvements from baseline.

End point type	Secondary
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End point timeframe:

Baseline and on Day 1 in Cycles 5, 9, 13, 17, 21, 25, 29, and 33 (21 days per cycle) and safety follow-up visit (up to 30 days after end of treatment; up to approximately 3 years and 1 week)

End point values	Cohort 1: ENKTL	Cohort 2: PTCL-NOS, AITL, and ALCL	Cohort 3: MF and SS	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22 ^[9]	44 ^[10]	11 ^[11]	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Cycle 5, Day 1; n=12, 20, 8	7.64 (± 24.220)	6.67 (± 19.041)	10.42 (± 24.296)	
Cycle 9, Day 1; n=6, 9, 6	8.33 (± 10.541)	12.04 (± 28.294)	1.39 (± 21.995)	
Cycle 13, Day 1; n=7, 5, 6	4.76 (± 11.644)	-1.67 (± 19.003)	2.78 (± 15.516)	
Cycle 17, Day 1; n=6, 6, 6	2.78 (± 12.546)	6.94 (± 30.008)	4.17 (± 21.570)	
Cycle 21, Day 1; n=4, 3, 4	12.50 (± 14.434)	0.00 (± 33.333)	0.00 (± 20.412)	
Cycle 25, Day 1; n=4, 2, 2	14.58 (± 25.797)	-8.33 (± 11.785)	-4.17 (± 5.893)	
Cycle 29, Day 1; n=3, 2, 0	16.67 (± 16.667)	-8.33 (± 11.785)	9999 (± 9999)	
Cycle 33, Day 1; n=1, 1, 0	0.00 (± 9999)	0.00 (± 9999)	9999 (± 9999)	
Safety Follow-up; n=14, 24, 2	7.74 (± 27.045)	-14.93 (± 26.917)	20.83 (± 17.678)	

Notes:

[9] - 9999 = Not estimable due to sample size

[10] - 9999 = Not estimable due to sample size

[11] - 9999 = Not estimable due to sample size or no subjects analysed

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life Assessment: EORTC QLQ-C30 Change from Baseline in Fatigue Score

End point title	Quality of Life Assessment: EORTC QLQ-C30 Change from Baseline in Fatigue Score
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End point description:

Mean change from baseline at safety follow-up visit in EORTC QLQ-C30 Fatigue score. The EORTC QLQ-C30 v3.0 is a questionnaire that assesses quality of life of cancer patients and includes questions related to fatigue symptoms in which participants respond based on a 7-point scale, where 1 is very poor and 7 is excellent. A increasing score indicates improvements from baseline.

End point type	Secondary
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End point timeframe:

Baseline and on Day 1 in Cycles 5, 9, 13, 17, 21, 25, 29, and 33 (21 days per cycle) and safety follow-up visit (up to 30 days after end of treatment; up to approximately 3 years and 1 week)

End point values	Cohort 1: ENKTL	Cohort 2: PTCL-NOS, AITL, and ALCL	Cohort 3: MF and SS	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22 ^[12]	44 ^[13]	11 ^[14]	
Units: Score on a scale				
arithmetic mean (standard deviation)				

Cycle 5, Day 1; n=12, 19, 8	-2.78 (± 14.312)	7.02 (± 14.912)	1.39 (± 41.335)	
Cycle 9, Day 1; n=6, 8, 6	0.00 (± 12.172)	-1.39 (± 11.011)	-22.22 (± 41.574)	
Cycle 13, Day 1; n=7, 5, 6	-1.59 (± 11.878)	-6.67 (± 12.669)	-5.56 (± 18.257)	
Cycle 17, Day 1; n=6, 6, 6	9.26 (± 16.355)	1.85 (± 10.924)	-12.96 (± 16.355)	
Cycle 21, Day 1; n=4, 3, 4	0.00 (± 12.830)	11.11 (± 11.111)	-16.67 (± 14.344)	
Cycle 25, Day 1; n=4, 2, 2	0.00 (± 15.713)	27.78 (± 7.857)	-5.56 (± 7.857)	
Cycle 29, Day 1; n=3, 2, 0	3.70 (± 27.962)	22.22 (± 15.713)	9999 (± 9999)	
Cycle 33, Day 1; n=1, 1, 0	11.11 (± 9999)	33.33 (± 9999)	9999 (± 9999)	
Safety Follow-up; n=14, 24, 2	-1.59 (± 19.903)	7.87 (± 30.820)	-44.44 (± 31.427)	

Notes:

[12] - 9999 = Not estimable due to sample size

[13] - 9999 = Not estimable due to sample size

[14] - 9999 = Not estimable due to sample size or no subjects analysed

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Adverse Events

End point title	Number of Subjects with Adverse Events
End point description:	
Number of subjects with treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs), including clinically relevant changes in laboratory tests, physical examination, electrocardiogram, and vital signs	
End point type	Secondary
End point timeframe:	
Up to approximately 3 years and 1 week	

End point values	Cohort 1: ENKTL	Cohort 2: PTCL-NOS, AITL, and ALCL	Cohort 3: MF and SS	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	44	11	
Units: Subjects				
At least one TEAE	22	41	10	
SAEs	9	21	5	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 3 years and 1 week

Adverse event reporting additional description:

Adverse events were graded by the investigators using Common Terminology Criteria for Adverse Events (CTCAE) v4.03.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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Reporting groups

Reporting group title	Cohort 1: ENKTL
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Reporting group description:

Subjects with relapsed or refractory (R/R) extranodal natural killer-/T-cell lymphoma (ENKTL; nasal or non-nasal type) were treated with tislelizumab 200 mg intravenously (IV) on Day 1 of each cycle until disease progression, intolerable toxicity, or treatment discontinuation for any other reason (21 days per cycle)

Reporting group title	Cohort 3: MF and SS
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Reporting group description:

Subjects with R/R cutaneous T-cell lymphoma [limited to mycosis fungoides (MF) and Sèzary syndrome (SS)] were treated with tislelizumab 200 mg intravenously (IV) on Day 1 of each cycle until disease progression, intolerable toxicity, or treatment discontinuation for any other reason (21 days per cycle)

Reporting group title	Cohort 2: PTCL-NOS, AITL, and ALCL
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Reporting group description:

Subjects with other R/R mature T-cell neoplasms [limited to peripheral T-cell lymphoma-not otherwise specified (PTCL-NOS), angioimmunoblastic T-cell lymphoma (AITL), and anaplastic large-cell lymphoma (ALCL)] were treated with tislelizumab 200 mg intravenously (IV) on Day 1 of each cycle until disease progression, intolerable toxicity, or treatment discontinuation for any other reason (21 days per cycle)

Serious adverse events	Cohort 1: ENKTL	Cohort 3: MF and SS	Cohort 2: PTCL-NOS, AITL, and ALCL
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 22 (40.91%)	5 / 11 (45.45%)	21 / 44 (47.73%)
number of deaths (all causes)	11	3	26
number of deaths resulting from adverse events	1	1	3
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour flare			

subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour rupture			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (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
Tumour ulceration			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arterial haemorrhage			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
General physical health deterioration			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	2 / 44 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pyrexia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	4 / 44 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (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
Immune-mediated lung disease			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (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
Interstitial lung disease			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
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 failure			
subjects affected / exposed	1 / 22 (4.55%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 0
Psychiatric disorders			
Depression			

subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Epstein-Barr virus test positive			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
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			
Cardiac failure			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (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
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (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
Syncope			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	2 / 44 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			

subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (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
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspepsia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (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
Intussusception			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (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
Nausea			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (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
Vomiting			

subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (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			
Skin ulcer			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (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
Renal impairment			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			

subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis staphylococcal			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (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
Oral infection			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (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
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 22 (9.09%)	0 / 11 (0.00%)	4 / 44 (9.09%)
occurrences causally related to treatment / all	5 / 5	0 / 0	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia cryptococcal			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (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
Pseudomonal sepsis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (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
Varicella zoster virus infection			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (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
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (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
Hypercalcaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	2 / 44 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (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

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Cohort 1: ENKTL	Cohort 3: MF and SS	Cohort 2: PTCL-NOS, AITL, and ALCL
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 22 (95.45%)	10 / 11 (90.91%)	39 / 44 (88.64%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	4	0
Tumour flare			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	1 / 44 (2.27%)
occurrences (all)	0	1	1
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	0 / 22 (0.00%)	2 / 11 (18.18%)	2 / 44 (4.55%)
occurrences (all)	0	2	2
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 22 (4.55%)	2 / 11 (18.18%)	8 / 44 (18.18%)
occurrences (all)	2	2	9
Chest discomfort			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Face oedema			
subjects affected / exposed	1 / 22 (4.55%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	1	1	0
Fatigue			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	2 / 44 (4.55%)
occurrences (all)	0	2	3
Influenza like illness			
subjects affected / exposed	0 / 22 (0.00%)	3 / 11 (27.27%)	1 / 44 (2.27%)
occurrences (all)	0	3	2

Malaise subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3	0 / 11 (0.00%) 0	1 / 44 (2.27%) 1
Non-cardiac chest pain subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 11 (9.09%) 2	0 / 44 (0.00%) 0
Oedema peripheral subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2	4 / 11 (36.36%) 6	3 / 44 (6.82%) 3
Pyrexia subjects affected / exposed occurrences (all)	6 / 22 (27.27%) 13	4 / 11 (36.36%) 7	13 / 44 (29.55%) 25
Swelling face subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 11 (0.00%) 0	0 / 44 (0.00%) 0
Reproductive system and breast disorders Benign prostatic hyperplasia subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 11 (9.09%) 1	0 / 44 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 11 (0.00%) 0	0 / 44 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	4 / 22 (18.18%) 4	0 / 11 (0.00%) 0	7 / 44 (15.91%) 10
Dyspnoea subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 11 (9.09%) 1	2 / 44 (4.55%) 3
Epistaxis subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 11 (0.00%) 0	0 / 44 (0.00%) 0
Hiccups subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	2 / 44 (4.55%) 3
Nasal congestion			

subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Nasal obstruction			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences (all)	1	0	1
Pharyngeal ulceration			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Respiratory acidosis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	4 / 44 (9.09%)
occurrences (all)	0	1	4
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	2	0	0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	3 / 44 (6.82%)
occurrences (all)	1	0	5
Alpha hydroxybutyrate dehydrogenase increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	2 / 44 (4.55%)
occurrences (all)	0	0	3
Aspartate aminotransferase increased			

subjects affected / exposed	3 / 22 (13.64%)	0 / 11 (0.00%)	3 / 44 (6.82%)
occurrences (all)	4	0	3
Blood albumin decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	2 / 44 (4.55%)
occurrences (all)	0	0	3
Blood bilirubin increased			
subjects affected / exposed	2 / 22 (9.09%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences (all)	5	0	2
Blood creatine phosphokinase MB increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences (all)	1	0	1
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 22 (9.09%)	1 / 11 (9.09%)	1 / 44 (2.27%)
occurrences (all)	5	4	1
Blood creatinine increased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	3 / 44 (6.82%)
occurrences (all)	0	1	6
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	4 / 44 (9.09%)
occurrences (all)	1	0	7
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences (all)	2	0	1
C-reactive protein increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	2 / 44 (4.55%)
occurrences (all)	0	0	2
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences (all)	1	0	1
Haemoglobin decreased			

subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 11 (0.00%) 0	0 / 44 (0.00%) 0
Lymphocyte count decreased subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 9	0 / 11 (0.00%) 0	0 / 44 (0.00%) 0
Neutrophil count decreased subjects affected / exposed occurrences (all)	4 / 22 (18.18%) 16	0 / 11 (0.00%) 0	2 / 44 (4.55%) 2
Platelet count decreased subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 10	0 / 11 (0.00%) 0	4 / 44 (9.09%) 5
Tri-iodothyronine free decreased subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 11 (0.00%) 0	0 / 44 (0.00%) 0
Weight decreased subjects affected / exposed occurrences (all)	4 / 22 (18.18%) 8	0 / 11 (0.00%) 0	4 / 44 (9.09%) 5
Weight increased subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 11	0 / 11 (0.00%) 0	2 / 44 (4.55%) 2
White blood cell count decreased subjects affected / exposed occurrences (all)	4 / 22 (18.18%) 21	0 / 11 (0.00%) 0	3 / 44 (6.82%) 6
Injury, poisoning and procedural complications			
Contusion subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 11 (0.00%) 0	0 / 44 (0.00%) 0
Procedural pain subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 11 (9.09%) 1	0 / 44 (0.00%) 0
Cardiac disorders			
Angina pectoris subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 11 (9.09%) 1	0 / 44 (0.00%) 0
Atrial fibrillation			

subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Conduction disorder			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Extrasystoles			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Sinus tachycardia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences (all)	1	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	2 / 44 (4.55%)
occurrences (all)	0	0	2
Peripheral sensorimotor neuropathy			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	3 / 44 (6.82%)
occurrences (all)	0	0	3
Syncope			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 22 (27.27%)	0 / 11 (0.00%)	7 / 44 (15.91%)
occurrences (all)	14	0	8
Lymph node pain			

subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	2 / 44 (4.55%) 4
Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	2 / 44 (4.55%) 4
Neutropenia subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	5 / 44 (11.36%) 13
Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	7 / 44 (15.91%) 11
Ear and labyrinth disorders			
Deafness subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 11 (9.09%) 1	0 / 44 (0.00%) 0
Deafness unilateral subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 11 (9.09%) 2	0 / 44 (0.00%) 0
Tinnitus subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 11 (0.00%) 0	2 / 44 (4.55%) 2
Vertigo subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	0 / 11 (0.00%) 0	2 / 44 (4.55%) 2
Eye disorders			
Blepharitis subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 11 (9.09%) 1	0 / 44 (0.00%) 0
Cataract subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	1 / 11 (9.09%) 2	0 / 44 (0.00%) 0
Eversion of lacrimal punctum subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 11 (9.09%) 1	0 / 44 (0.00%) 0
Eyelid oedema			

subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	1 / 44 (2.27%)
occurrences (all)	0	1	1
Lacrimation increased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Periorbital oedema			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Retinal disorder			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	2	0	0
Retinopathy			
subjects affected / exposed	3 / 22 (13.64%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	3	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	2 / 22 (9.09%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	2	0	0
Abdominal pain			
subjects affected / exposed	1 / 22 (4.55%)	2 / 11 (18.18%)	2 / 44 (4.55%)
occurrences (all)	2	2	2
Abdominal pain upper			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences (all)	1	0	2
Constipation			
subjects affected / exposed	0 / 22 (0.00%)	2 / 11 (18.18%)	4 / 44 (9.09%)
occurrences (all)	0	2	4
Diarrhoea			
subjects affected / exposed	3 / 22 (13.64%)	4 / 11 (36.36%)	4 / 44 (9.09%)
occurrences (all)	3	5	4
Dyspepsia			
subjects affected / exposed	1 / 22 (4.55%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	1	1	0
Dysphagia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0

Haemorrhoids			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Mouth ulceration			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	3 / 44 (6.82%)
occurrences (all)	0	0	4
Nausea			
subjects affected / exposed	3 / 22 (13.64%)	2 / 11 (18.18%)	1 / 44 (2.27%)
occurrences (all)	3	2	1
Oral cavity fistula			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	2 / 22 (9.09%)	2 / 11 (18.18%)	1 / 44 (2.27%)
occurrences (all)	3	2	1
Toothache			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	2 / 44 (4.55%)
occurrences (all)	0	0	2
Vomiting			
subjects affected / exposed	2 / 22 (9.09%)	3 / 11 (27.27%)	0 / 44 (0.00%)
occurrences (all)	2	3	0
Skin and subcutaneous tissue disorders			
Actinic keratosis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Blood blister			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Circumoral oedema			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Dermatitis			

subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Dermatitis psoriasiform			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	2	0
Dry skin			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	5 / 44 (11.36%)
occurrences (all)	0	1	10
Pruritus			
subjects affected / exposed	2 / 22 (9.09%)	3 / 11 (27.27%)	6 / 44 (13.64%)
occurrences (all)	3	4	9
Rash			
subjects affected / exposed	1 / 22 (4.55%)	3 / 11 (27.27%)	2 / 44 (4.55%)
occurrences (all)	1	4	2
Rash maculo-papular			
subjects affected / exposed	3 / 22 (13.64%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences (all)	3	0	1
Rash pruritic			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	2 / 44 (4.55%)
occurrences (all)	0	0	8
Skin mass			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	2 / 44 (4.55%)
occurrences (all)	0	0	2
Skin ulcer			
subjects affected / exposed	1 / 22 (4.55%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	1	3	0
Urticaria			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	1 / 44 (2.27%)
occurrences (all)	0	1	2
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0

Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 22 (0.00%)	0 / 11 (0.00%)	2 / 44 (4.55%)
occurrences (all)	0	0	3
Hypothyroidism			
subjects affected / exposed	1 / 22 (4.55%)	3 / 11 (27.27%)	5 / 44 (11.36%)
occurrences (all)	1	4	5
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 22 (13.64%)	3 / 11 (27.27%)	7 / 44 (15.91%)
occurrences (all)	5	5	18
Back pain			
subjects affected / exposed	1 / 22 (4.55%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	1	1	0
Intervertebral disc protrusion			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	1 / 22 (4.55%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Osteoporosis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Pain in jaw			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	2	0	0
Tendonitis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			

Bronchitis			
subjects affected / exposed	2 / 22 (9.09%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	2	1	0
COVID-19			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences (all)	1	0	1
Gingivitis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Herpes simplex			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Impetigo			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 22 (4.55%)	1 / 11 (9.09%)	2 / 44 (4.55%)
occurrences (all)	1	1	3
Pharyngitis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences (all)	1	0	1
Pneumonia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Pseudomonal skin infection			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	2 / 22 (9.09%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences (all)	2	0	1

Skin bacterial infection subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 11 (9.09%) 1	0 / 44 (0.00%) 0
Skin infection subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	1 / 11 (9.09%) 1	1 / 44 (2.27%) 1
Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2	0 / 11 (0.00%) 0	5 / 44 (11.36%) 8
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 11 (9.09%) 1	1 / 44 (2.27%) 1
Wound infection subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 11 (0.00%) 0	0 / 44 (0.00%) 0
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	1 / 11 (9.09%) 1	1 / 44 (2.27%) 1
Diabetes mellitus subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 11 (9.09%) 1	0 / 44 (0.00%) 0
Gout subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 11 (0.00%) 0	0 / 44 (0.00%) 0
Hyperglycaemia subjects affected / exposed occurrences (all)	4 / 22 (18.18%) 4	1 / 11 (9.09%) 1	4 / 44 (9.09%) 5
Hypertriglyceridaemia subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 11 (0.00%) 0	0 / 44 (0.00%) 0
Hypoalbuminaemia subjects affected / exposed occurrences (all)	5 / 22 (22.73%) 8	1 / 11 (9.09%) 1	1 / 44 (2.27%) 1
Hypocalcaemia			

subjects affected / exposed	2 / 22 (9.09%)	0 / 11 (0.00%)	1 / 44 (2.27%)
occurrences (all)	3	0	1
Hypokalaemia			
subjects affected / exposed	4 / 22 (18.18%)	0 / 11 (0.00%)	2 / 44 (4.55%)
occurrences (all)	4	0	3
Hyponatraemia			
subjects affected / exposed	3 / 22 (13.64%)	0 / 11 (0.00%)	0 / 44 (0.00%)
occurrences (all)	7	0	0
Impaired fasting glucose			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0
Malnutrition			
subjects affected / exposed	0 / 22 (0.00%)	1 / 11 (9.09%)	0 / 44 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 December 2017	• Decreased the frequency of imaging studies to reduce the radiation exposure and burden to patients and sites • Added a guidance for enrollment holds for Cohorts 1 and 2 • Added LYRIC modification for immunomodulatory therapy for disease response assessment • Clarified some Inclusion and Exclusion Criteria • Added the section of exam of liver, spleen, and lymph nodes to clarify efficacy assessments • Corrected corticosteroid therapy usage and removed hormone replacement, bisphosphonates, and RANKL inhibitors to clarify permitted therapies • Clarified adverse event collection and safety monitoring guidance per guidance from the health authority • Added additional safety assessments (ie, ophthalmologic examinations, thyroid function tests, and pancreatic enzymes) per guidance from the health authority
23 August 2018	• Updated the compound name to the International Nonproprietary Name (ie, tislelizumab) throughout the protocol • Increased the sample size of Cohort 1 approximately 50 patients to approximately 70 patients for potential regulatory considerations and having adequate power • Updated the protocol according to administrative changes made to other tislelizumab protocols (eg, confidentiality statement and safety reporting language, etc) • Replaced the Safety Monitoring Committee with an IDMC per guidance from the health authority • Clarified that EBV circulating DNA testing were to be done if patients are EBV-positive by EBV encoded RNAs in situ hybridization at screening • Clarified tumor assessment per LYRIC guidelines regarding pseudoprogression and indeterminate response • Clarified that cohorts were to be analyzed separately for the primary efficacy analyses • Added additional requirements for safety assessments (ie, sensitivity requirement for HBV DNA test; inclusion of liver function, creatine kinase, and creatine kinase-cardiac muscle isoenzyme testing; performing pancreatic enzymes and coagulation profile testing when clinically indicated; and clarification of the frequency of ophthalmologic monitoring) per guidance from the health authority • Clarified procedures for patients who continue treatment after study termination • Clarified permitted and prohibited therapy during study treatment • Clarified adverse event collection and safety monitoring guidance per guidance from the health authority • Clarified some Inclusion and Exclusion Criteria

14 March 2019	• Added a Cohort 3 to enroll patients with MF or SS and updated the description throughout the protocol for the addition of Cohort 3 • Changed the tumor assessment for primary endpoint from “determined by an independent central review” to “by investigators” because the study was no longer a confirmatory study • Updated the protocol according to changes made to other tislelizumab protocols (ie, changed PK and immunogenicity objectives from secondary to exploratory and safety reporting language) • Updated sample size • Specified subtypes of Cohort 2 in the guidance for enrollment holds and efficacy analyses • Exclusion Criteria #4: Clarified that the chemotherapy was meant for systemic treatment and the required washout period for investigational treatment • Changed the minimum amount of time between doses from 14 days to 10 days • Added weekly visits during Cycle 1 for safety assessments per recommendation from IDMC • Clarified that a pump would not be required if infusion speed was controlled through alternative means and consistent with approved institutional procedures • Provided additional diagnostic and treatment recommendations for cytokine release syndrome
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported