



Clinical trial results:

A Phase II Clinical Trial of MK-3475 (Pembrolizumab) in Subjects with Relapsed or Refractory (R/R) Classical Hodgkin Lymphoma (cHL)

Summary

EudraCT number	2014-004482-24
Trial protocol	SE NO ES NL DE AT HU IE FR GB GR
Global end of trial date	18 September 2023

Results information

Result version number	v1 (current)
This version publication date	28 September 2024
First version publication date	28 September 2024

Trial information

Trial identification

Sponsor protocol code	3475-087
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02453594
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC
Sponsor organisation address	126 East Lincoln Avenue, Rahway, NJ, United States, P.O. Box 2000
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.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	18 September 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 September 2023
Global end of trial reached?	Yes
Global end of trial date	18 September 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a study of pembrolizumab (MK-3475) for participants with relapsed/refractory classical Hodgkin Lymphoma (RRcHL) who: 1) have failed to achieve a response or progressed after autologous stem cell transplant (auto-SCT) and have relapsed after treatment with or failed to respond to brentuximab vedotin (BV) post auto-SCT or 2) were unable to achieve a Complete Response (CR) or Partial Response (PR) to salvage chemotherapy and did not receive auto-SCT, but have relapsed after treatment with or failed to respond to BV or 3) have failed to achieve a response to or progressed after auto-SCT and have not received BV post auto-SCT.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 June 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	Australia: 5
Country: Number of subjects enrolled	Canada: 10
Country: Number of subjects enrolled	France: 25
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Greece: 9
Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Israel: 12
Country: Number of subjects enrolled	Italy: 23
Country: Number of subjects enrolled	Japan: 10
Country: Number of subjects enrolled	Norway: 3
Country: Number of subjects enrolled	Russian Federation: 14
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	Sweden: 11
Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	United States: 51
Country: Number of subjects enrolled	Netherlands: 1

Worldwide total number of subjects	211
EEA total number of subjects	94

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)	193
From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Males and females with relapsed or refractory de novo classical Hodgkin lymphoma (RRcHL) of at least 18 years of age were enrolled in this study.

Period 1

Period 1 title	Randomized
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1

Arm description:

Participants with RRcHL who failed to achieve a response or progressed after auto-stem cell transplant (SCT) and have relapsed after treatment with or failed to respond to brentuximab vedotin (BV) post auto-SCT received pembrolizumab, 200 mg, intravenously (IV) every 3 weeks (Q3W) on Day 1 of each 21-day cycle up to 35 cycles, for up to 24 months.

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	KEYTRUDA®
Pharmaceutical forms	Infusion
Routes of administration	Intracavernous use

Dosage and administration details:

200 mg every 3 weeks (Q3W) on Day 1 of each 21-day cycle for up to 24 months.

Arm title	Cohort 2
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Arm description:

Participants with RRcHL who were unable to achieve Complete Response (CR) or Partial Response (PR) to salvage chemotherapy and did not receive auto-SCT, but have relapsed after treatment with or failed to respond to BV received pembrolizumab, 200 mg, IV Q3W on Day 1 of each 21-day cycle up to 35 cycles, for up to 24 months.

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	KEYTRUDA®
Pharmaceutical forms	Infusion
Routes of administration	Intracavernous use

Dosage and administration details:

200 mg Q3W on Day 1 of each 21-day cycle for up to 24 months.

Arm title	Cohort 3
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Arm description:

Participants with RRcHL who failed to achieve a response to or progressed after auto-SCT and have not received BV post auto-SCT received pembrolizumab, 200 mg, IV Q3W on Day 1 of each 21-day cycle, up to 35 cycles for up to 24 months. These participants may or may not have received BV as part of primary treatment or salvage treatment.

Arm type	Experimental
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Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	KEYTRUDA®
Pharmaceutical forms	Infusion
Routes of administration	Intracavernous use

Dosage and administration details:

200 mg Q3W on Day 1 of each 21-day cycle for up to 24 months.

Number of subjects in period 1	Cohort 1	Cohort 2	Cohort 3
Started	69	81	61
Treated	69	81	60
Completed	69	81	60
Not completed	0	0	1
Protocol deviation	-	-	1

Period 2

Period 2 title	Treated
Is this the baseline period?	Yes ^[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

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

Participants with RRcHL who failed to achieve a response or progressed after auto-stem cell transplant (SCT) and have relapsed after treatment with or failed to respond to brentuximab vedotin (BV) post auto-SCT received pembrolizumab, 200 mg, intravenously (IV) every 3 weeks (Q3W) on Day 1 of each 21-day cycle up to 35 cycles, for up to 24 months.

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	KEYTRUDA®
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

200 mg Q3W on Day 1 of each 21-day cycle for up to 24 months.

Arm title	Cohort 2
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Arm description:

Participants with RRcHL who were unable to achieve Complete Response (CR) or Partial Response (PR) to salvage chemotherapy and did not receive auto-SCT, but have relapsed after treatment with or failed to respond to BV received pembrolizumab, 200 mg, IV Q3W on Day 1 of each 21-day cycle up to 35 cycles, for up to 24 months.

Arm type	Experimental
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Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	KEYTRUDA®
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 200 mg Q3W on Day 1 of each 21-day cycle for up to 24 months.	
Arm title	Cohort 3

Arm description:

Participants with RRcHL who failed to achieve a response to or progressed after auto-SCT and have not received BV post auto-SCT received pembrolizumab, 200 mg, IV Q3W on Day 1 of each 21-day cycle, up to 35 cycles for up to 24 months. These participants may or may not have received BV as part of primary treatment or salvage treatment.

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	KEYTRUDA®
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

200 mg Q3W on Day 1 of each 21-day cycle for up to 24 months.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Period 1 was enrolled participants which was not the baseline period. The baseline period was treated participants.

Number of subjects in period 2[2]	Cohort 1	Cohort 2	Cohort 3
Started	69	81	60
Second Course Pembrolizumab	10	7	3
Completed	0	0	0
Not completed	69	81	60
Adverse event, serious fatal	20	24	16
Consent withdrawn by subject	7	9	11
Physician decision	2	4	-
Cohort Was Closed	17	21	14
Site Terminated by Sponsor	1	-	1
Study Terminated by Sponsor	16	9	16
Lost to follow-up	6	14	2

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The baseline period was not the worldwide number enrolled; but rather the number treated.

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1
Reporting group description:	
Participants with RRcHL who failed to achieve a response or progressed after auto-stem cell transplant (SCT) and have relapsed after treatment with or failed to respond to brentuximab vedotin (BV) post auto-SCT received pembrolizumab, 200 mg, intravenously (IV) every 3 weeks (Q3W) on Day 1 of each 21-day cycle up to 35 cycles, for up to 24 months.	
Reporting group title	Cohort 2
Reporting group description:	
Participants with RRcHL who were unable to achieve Complete Response (CR) or Partial Response (PR) to salvage chemotherapy and did not receive auto-SCT, but have relapsed after treatment with or failed to respond to BV received pembrolizumab, 200 mg, IV Q3W on Day 1 of each 21-day cycle up to 35 cycles, for up to 24 months.	
Reporting group title	Cohort 3
Reporting group description:	
Participants with RRcHL who failed to achieve a response to or progressed after auto-SCT and have not received BV post auto-SCT received pembrolizumab, 200 mg, IV Q3W on Day 1 of each 21-day cycle, up to 35 cycles for up to 24 months. These participants may or may not have received BV as part of primary treatment or salvage treatment.	

Reporting group values	Cohort 1	Cohort 2	Cohort 3
Number of subjects	69	81	60
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	69	66	57
From 65-84 years	0	15	3
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	37.0	42.3	36.8
standard deviation	± 10.9	± 17.4	± 13.4
Sex: Female, Male			
Units: Participants			
Female	33	38	26
Male	36	43	34
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	7	4	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	2	3

White	57	73	55
More than one race	2	0	0
Unknown or Not Reported	1	1	1
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	7	5	3
Not Hispanic or Latino	43	63	48
Unknown or Not Reported	19	13	9

Reporting group values	Total		
Number of subjects	210		
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)	192		
From 65-84 years	18		
85 years and over	0		
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Participants			
Female	97		
Male	113		
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	1		
Asian	12		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	7		
White	185		
More than one race	2		
Unknown or Not Reported	3		
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	15		
Not Hispanic or Latino	154		
Unknown or Not Reported	41		

End points

End points reporting groups

Reporting group title	Cohort 1
Reporting group description: Participants with RRcHL who failed to achieve a response or progressed after auto-stem cell transplant (SCT) and have relapsed after treatment with or failed to respond to brentuximab vedotin (BV) post auto-SCT received pembrolizumab, 200 mg, intravenously (IV) every 3 weeks (Q3W) on Day 1 of each 21-day cycle up to 35 cycles, for up to 24 months.	
Reporting group title	Cohort 2
Reporting group description: Participants with RRcHL who were unable to achieve Complete Response (CR) or Partial Response (PR) to salvage chemotherapy and did not receive auto-SCT, but have relapsed after treatment with or failed to respond to BV received pembrolizumab, 200 mg, IV Q3W on Day 1 of each 21-day cycle up to 35 cycles, for up to 24 months.	
Reporting group title	Cohort 3
Reporting group description: Participants with RRcHL who failed to achieve a response to or progressed after auto-SCT and have not received BV post auto-SCT received pembrolizumab, 200 mg, IV Q3W on Day 1 of each 21-day cycle, up to 35 cycles for up to 24 months. These participants may or may not have received BV as part of primary treatment or salvage treatment.	
Reporting group title	Cohort 1
Reporting group description: Participants with RRcHL who failed to achieve a response or progressed after auto-stem cell transplant (SCT) and have relapsed after treatment with or failed to respond to brentuximab vedotin (BV) post auto-SCT received pembrolizumab, 200 mg, intravenously (IV) every 3 weeks (Q3W) on Day 1 of each 21-day cycle up to 35 cycles, for up to 24 months.	
Reporting group title	Cohort 2
Reporting group description: Participants with RRcHL who were unable to achieve Complete Response (CR) or Partial Response (PR) to salvage chemotherapy and did not receive auto-SCT, but have relapsed after treatment with or failed to respond to BV received pembrolizumab, 200 mg, IV Q3W on Day 1 of each 21-day cycle up to 35 cycles, for up to 24 months.	
Reporting group title	Cohort 3
Reporting group description: Participants with RRcHL who failed to achieve a response to or progressed after auto-SCT and have not received BV post auto-SCT received pembrolizumab, 200 mg, IV Q3W on Day 1 of each 21-day cycle, up to 35 cycles for up to 24 months. These participants may or may not have received BV as part of primary treatment or salvage treatment.	

Primary: Percentage of Participants Experiencing at Least One Adverse Event (AE)

End point title	Percentage of Participants Experiencing at Least One Adverse Event (AE) ^[1]
End point description: An adverse event (AE) is any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure, that occurs during the course of the study. The population analyzed was all allocated participants who received at least 1 dose of study treatment.	
End point type	Primary
End point timeframe: Up to 27 months	

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: Statistical analyses between treatment groups were neither planned nor performed for this primary endpoint.

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	81	60	
Units: Percentage of Participants				
number (not applicable)	98.6	98.8	95.0	

Statistical analyses

No statistical analyses for this end point

Primary: Overall Response Rate (ORR) by BICR based on IWG criteria

End point title	Overall Response Rate (ORR) by BICR based on IWG criteria ^[2]
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End point description:

ORR is the percentage of participants who had a complete response (CR) or partial response (PR) prior to disease progression based on the International Working Group (IWG) criteria using blinded independent central review (BICR). CR is the disappearance of all evidence of disease and PR is the regression of measurable disease and no new sites. The point estimate and 95% 2-sided exact confidence interval (CI) used the Clopper-Pearson method. An exact binomial test was conducted for each cohort versus a fixed control rate for each cohort. It is hypothesized that ORR will be greater than 20% in each of the 3 cohorts. The population analyzed was all allocated participants who received at least 1 dose of study treatment.

End point type	Primary
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End point timeframe:

Up to approximately 99 months

Notes:

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

Justification: Statistical analyses between treatment groups were neither planned nor performed for this primary endpoint.

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	81	60	
Units: Percentage of participants				
number (confidence interval 95%)	78.3 (66.7 to 87.3)	64.2 (52.8 to 74.6)	73.3 (60.3 to 83.9)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Discontinuing Study Drug Due to AEs

End point title	Percentage of Participants Discontinuing Study Drug Due to AEs ^[3]
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End point description:

An AE is any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure, that occurs during the course of the study. The population analyzed was all allocated participants who received at least 1 dose of study treatment.

End point type	Primary
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End point timeframe:

Up to 24 months

Notes:

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

Justification: Statistical analyses between treatment groups were neither planned nor performed for this primary endpoint.

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	81	60	
Units: Percentage of Participants				
number (not applicable)	11.6	6.2	8.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR) by BICR based on Lugano criteria

End point title	Overall Response Rate (ORR) by BICR based on Lugano criteria
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End point description:

ORR is the percentage of participants who had a CR or PR prior to disease progression based on the Lugano criteria using BICR. CR is the disappearance of all evidence of disease and PR is the regression of measurable disease and no new sites. The point estimate and 95% 2-sided exact confidence interval (CI) used the Clopper-Pearson method. An exact binomial test was conducted for each cohort versus a fixed control rate for each cohort. The population analyzed was all allocated participants who received at least 1 dose of study treatment.

End point type	Secondary
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End point timeframe:

Up to approximately 99 months

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	81	60	
Units: Percentage of participants				
number (confidence interval 95%)	82.6 (71.6 to 90.7)	67.9 (56.6 to 77.8)	68.3 (55.0 to 79.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR) assessed by investigator based on IWG criteria

End point title	Overall Response Rate (ORR) assessed by investigator based on IWG criteria
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End point description:

ORR is the percentage of participants who had a CR or PR prior to disease progression assessed by the investigator using IWG criteria. CR is the disappearance of all evidence of disease and PR is the regression of measurable disease and no new sites. The point estimate and 95% 2-sided exact confidence interval (CI) used the Clopper-Pearson method. An exact binomial test was conducted for each cohort versus a fixed control rate for each cohort. The population analyzed was all allocated participants who received at least 1 dose of study treatment.

End point type	Secondary
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End point timeframe:

Up to approximately 99 months

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	81	60	
Units: Percentage of participants				
number (confidence interval 95%)	72.5 (60.4 to 82.5)	66.7 (55.3 to 76.8)	71.7 (58.6 to 82.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Remission Rate (CRR) by BICR based on IWG criteria

End point title	Complete Remission Rate (CRR) by BICR based on IWG criteria
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End point description:

CRR is the percentage of participants with complete remission as demonstrated by disappearance of all evidence of disease in the bone marrow, spleen, liver, and lymph nodes based on the IWG criteria using BICR. The analysis consisted of the point estimate and 95% 2-sided exact CI, separately by Cohort using the Clopper-Pearson method. Additional analyses were based on site assessment and by central review using the Lugano (2014) criteria. The population analyzed was all allocated participants who received at least 1 dose of study treatment.

End point type	Secondary
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End point timeframe:

Up to approximately 99 months

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	81	60	
Units: Percentage of participants				
number (not applicable)	24.6	25.9	33.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Remission Rate (CRR) by BICR based on Lugano criteria

End point title	Complete Remission Rate (CRR) by BICR based on Lugano criteria
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End point description:

CRR is the percentage of participants with complete remission as demonstrated by disappearance of all evidence of disease in the bone marrow, spleen, liver, and lymph nodes based on the Lugano criteria using BICR. The analysis consisted of the point estimate and 95% 2-sided exact CI, separately by Cohort using the Clopper-Pearson method. Additional analyses were based on site assessment and by central review using the Lugano (2014) criteria. The population analyzed was all allocated participants who received at least 1 dose of study treatment.

End point type	Secondary
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End point timeframe:

Up to approximately 99 months

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	81	60	
Units: Percentage of participants				
number (not applicable)	34.8	28.4	35.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS) based on BICR

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

PFS is the time from first dose to the first documented progressive disease (PD) or death due to any cause, whichever occurs first based on BICR. For those who have PD, the true date of disease progression was approximated by the date of the first assessment at which PD is objectively documented per IWG criteria, regardless of discontinuation of study drug. Death is always considered as a confirmed PD event. The non-parametric Kaplan-Meier method was used to estimate the PFS curve with missing data censored at last assessment. The population analyzed was all allocated participants who received at least 1 dose of study treatment.

End point type	Secondary
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End point timeframe:
Up to approximately 99 months

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	81	60	
Units: Months				
median (confidence interval 95%)	16.5 (12.0 to 30.3)	11.1 (7.5 to 13.7)	19.7 (10.8 to 32.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Remission Rate (CRR) assessed by investigator based on IWG criteria

End point title	Complete Remission Rate (CRR) assessed by investigator based on IWG criteria
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End point description:

CRR is the percentage of participants with complete remission as demonstrated by disappearance of all evidence of disease in the bone marrow, spleen, liver, and lymph nodes assessed by the investigator using IWG criteria. The analysis consisted of the point estimate and 95% 2-sided exact CI, separately by Cohort using the Clopper-Pearson method. Additional analyses were based on site assessment and by central review using the Lugano (2014) criteria. The population analyzed was all allocated participants who received at least 1 dose of study treatment.

End point type	Secondary
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End point timeframe:

Up to approximately 99 months

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	81	60	
Units: Percentage of participants				
number (not applicable)	42.0	32.1	43.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS) assessed by the investigator

End point title	Progression-free Survival (PFS) assessed by the investigator
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End point description:

PFS is the time from first dose to the first documented progressive disease (PD) or death due to any cause, whichever occurs first assessed by the investigator based on the IWG criteria. For those who have PD, the true date of disease progression was approximated by the date of the first assessment at which PD is objectively documented per IWG criteria, regardless of discontinuation of study drug. Death is always considered as a confirmed PD event. The non-parametric Kaplan-Meier method was used to estimate the PFS curve with missing data censored at last assessment. The population analyzed was all allocated participants who received at least 1 dose of study treatment.

End point type	Secondary
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End point timeframe:

Up to approximately 99 months

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	81	60	
Units: Months				
median (confidence interval 95%)	24.9 (13.9 to 33.9)	13.9 (10.9 to 22.4)	22.0 (11.1 to 30.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) based on BICR

End point title	Duration of Response (DOR) based on BICR
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End point description:

DOR for the subgroup of participants who achieved a CR or PR by independent central review, is the time from start of the first documentation of objective tumor response (CR or PR) to the first documentation of PD or to death due to any cause, whichever comes first based on BICR. CR is the disappearance of all evidence of disease and PR is the regression of measurable disease and no new sites. The analysis used the Kaplan-Meier method, with participants with response censored at their last assessment, and there was no progressive disease at the time of the last disease assessment. The population analyzed was all allocated participants who received at least 1 dose of study treatment.

End point type	Secondary
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End point timeframe:

Up to approximately 99 months

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	52	44	
Units: Months				
median (full range (min-max))	25.0 (0.0 to 88.8)	11.1 (0.0 to 86.2)	24.4 (0.0 to 88.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) assessed by the investigator

End point title	Duration of Response (DOR) assessed by the investigator
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End point description:

DOR for the subgroup of participants who achieved a CR or PR by independent central review, is the time from start of the first documentation of objective tumor response (CR or PR) to the first documentation of PD or to death due to any cause, whichever comes first assessed by the investigator based on the IWG criteria. CR is the disappearance of all evidence of disease and PR is the regression of measurable disease and no new sites. The analysis used the Kaplan-Meier method, with participants with response censored at their last assessment, and there was no progressive disease at the time of the last disease assessment. The population analyzed was all allocated participants who received at least 1 dose of study treatment.

End point type	Secondary
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End point timeframe:

Up to approximately 99 months

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	54	43	
Units: Months				
median (full range (min-max))	25.0 (0.0 to 88.8)	16.4 (0.0 to 86.1)	24.7 (2.8 to 91.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
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End point description:

OS is the time from the first dose to death due to any cause. The Kaplan-Meier method was used to estimate the survival curve, separately by Cohort with missing data censored at last assessment. The population analyzed was all allocated participants who received at least 1 dose of study treatment.

End point type	Secondary
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End point timeframe:

Up to approximately 99 months

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69 ^[4]	81 ^[5]	60 ^[6]	
Units: Months				
median (full range (min-max))	9999 (9999 to 9999)	9999 (9999 to 9999)	9999 (9999 to 9999)	

Notes:

[4] - 9999 means median, upper limit, and lower limit not reached at time of data cut-off.

[5] - 9999 means median, upper limit, and lower limit not reached at time of data cut-off.

[6] - 9999 means median, upper limit, and lower limit not reached at time of data cut-off.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 99 months.

Adverse event reporting additional description:

The population analyzed for all-cause mortality consisted of all allocated participants. The population for AEs consisted of all allocated participants who received at least 1 dose of study treatment. The following AE preferred terms not related to the drug were excluded: Neoplasm progression, Malignant neoplasm progression and Disease progression.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.0
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Reporting groups

Reporting group title	Cohort 1 (First Course)
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Reporting group description:

Participants with RRcHL who failed to achieve a response or progressed after auto-stem cell transplant (SCT) and have relapsed after treatment with or failed to respond to brentuximab vedotin (BV) post auto-SCT received pembrolizumab, 200 mg, intravenously (IV) every 3 weeks (Q3W) on Day 1 of each 21-day cycle up to 35 cycles, for up to 24 months.

Reporting group title	Cohort 2 (First Course)
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Reporting group description:

Participants with RRcHL who were unable to achieve Complete Response (CR) or Partial Response (PR) to salvage chemotherapy and did not receive auto-SCT, but have relapsed after treatment with or failed to respond to BV received pembrolizumab, 200 mg, IV Q3W on Day 1 of each 21-day cycle up to 35 cycles, for up to 24 months.

Reporting group title	Cohort 3 (First Course)
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Reporting group description:

Participants with RRcHL who failed to achieve a response to or progressed after auto-SCT and have not received BV post auto-SCT received pembrolizumab, 200 mg, IV Q3W on Day 1 of each 21-day cycle up to 35 cycles, for up to 24 months. These participants may or may not have received BV as part of primary treatment or salvage treatment.

Reporting group title	Cohort 1 (Second Course)
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Reporting group description:

Eligible participants allocated to the pembrolizumab first course in Cohort 1 who stopped (or completed) initial treatment with pembrolizumab after attaining confirmed CR, initiated a second course of pembrolizumab at the investigator's discretion at 200 mg on Day 1 of each 3 week cycle (Q3W) for up to 17 cycles up to approximately an additional year.

Reporting group title	Cohort 2 (Second Course)
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Reporting group description:

Eligible participants allocated to the pembrolizumab first course in Cohort 2 who stopped (or completed) initial treatment with pembrolizumab after attaining confirmed CR, initiated a second course of pembrolizumab at the investigator's discretion at 200 mg on Day 1 Q3W for up to 17 cycles up to approximately an additional year.

Reporting group title	Cohort 3 (Second Course)
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Reporting group description:

Eligible participants allocated to the pembrolizumab first course in Cohort 3 who stopped (or completed) initial treatment with pembrolizumab after attaining confirmed CR, initiated a second course of pembrolizumab at the investigator's discretion at 200 mg on Day 1 Q3W for up to 17 cycles up to approximately an additional year.

Serious adverse events	Cohort 1 (First Course)	Cohort 2 (First Course)	Cohort 3 (First Course)
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 69 (21.74%)	18 / 81 (22.22%)	15 / 60 (25.00%)
number of deaths (all causes)	21	28	19
number of deaths resulting from adverse events	0	2	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Small cell lung cancer			
subjects affected / exposed	1 / 69 (1.45%)	0 / 81 (0.00%)	0 / 60 (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
Myelodysplastic syndrome			
subjects affected / exposed	1 / 69 (1.45%)	0 / 81 (0.00%)	0 / 60 (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
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 69 (0.00%)	1 / 81 (1.23%)	0 / 60 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 69 (0.00%)	1 / 81 (1.23%)	0 / 60 (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
Squamous cell carcinoma			
subjects affected / exposed	0 / 69 (0.00%)	1 / 81 (1.23%)	0 / 60 (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
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 69 (0.00%)	1 / 81 (1.23%)	0 / 60 (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
Vascular disorders			
Aortic stenosis			

subjects affected / exposed	0 / 69 (0.00%)	0 / 81 (0.00%)	1 / 60 (1.67%)
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			
Pyrexia			
subjects affected / exposed	0 / 69 (0.00%)	1 / 81 (1.23%)	3 / 60 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthermia			
subjects affected / exposed	0 / 69 (0.00%)	1 / 81 (1.23%)	0 / 60 (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 system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 69 (0.00%)	1 / 81 (1.23%)	0 / 60 (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
Acute graft versus host disease			
subjects affected / exposed	1 / 69 (1.45%)	1 / 81 (1.23%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	1 / 69 (1.45%)	1 / 81 (1.23%)	2 / 60 (3.33%)
occurrences causally related to treatment / all	1 / 1	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 69 (0.00%)	1 / 81 (1.23%)	0 / 60 (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
Pneumothorax			

subjects affected / exposed	0 / 69 (0.00%)	0 / 81 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Schizophrenia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 81 (0.00%)	1 / 60 (1.67%)
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			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 69 (0.00%)	1 / 81 (1.23%)	0 / 60 (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			
Infusion related reaction			
subjects affected / exposed	0 / 69 (0.00%)	1 / 81 (1.23%)	0 / 60 (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
Hip fracture			
subjects affected / exposed	1 / 69 (1.45%)	0 / 81 (0.00%)	0 / 60 (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 disorders			
Stress cardiomyopathy			
subjects affected / exposed	0 / 69 (0.00%)	1 / 81 (1.23%)	0 / 60 (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
Pericarditis			
subjects affected / exposed	2 / 69 (2.90%)	0 / 81 (0.00%)	0 / 60 (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
Myocarditis			

subjects affected / exposed	1 / 69 (1.45%)	0 / 81 (0.00%)	0 / 60 (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
Myocardial infarction			
subjects affected / exposed	0 / 69 (0.00%)	0 / 81 (0.00%)	1 / 60 (1.67%)
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			
Chronic inflammatory demyelinating polyradiculoneuropathy			
subjects affected / exposed	0 / 69 (0.00%)	1 / 81 (1.23%)	0 / 60 (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
Epilepsy			
subjects affected / exposed	0 / 69 (0.00%)	0 / 81 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyneuropathy			
subjects affected / exposed	1 / 69 (1.45%)	0 / 81 (0.00%)	0 / 60 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 69 (1.45%)	0 / 81 (0.00%)	0 / 60 (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			
Alcoholic pancreatitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 81 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 69 (1.45%)	0 / 81 (0.00%)	0 / 60 (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

Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 81 (0.00%)	0 / 60 (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
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 69 (0.00%)	0 / 81 (0.00%)	1 / 60 (1.67%)
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	1 / 69 (1.45%)	0 / 81 (0.00%)	0 / 60 (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
Musculoskeletal and connective tissue disorders			
Necrotising myositis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 81 (0.00%)	0 / 60 (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
Osteonecrosis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 81 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 81 (1.23%)	0 / 60 (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
Escherichia bacteraemia			
subjects affected / exposed	0 / 69 (0.00%)	1 / 81 (1.23%)	0 / 60 (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
Device related infection			

subjects affected / exposed	0 / 69 (0.00%)	1 / 81 (1.23%)	0 / 60 (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
Cystitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 81 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 81 (1.23%)	0 / 60 (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
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 81 (1.23%)	0 / 60 (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
Bronchitis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 81 (1.23%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 69 (0.00%)	0 / 81 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 69 (1.45%)	0 / 81 (0.00%)	0 / 60 (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
Herpes zoster			
subjects affected / exposed	0 / 69 (0.00%)	2 / 81 (2.47%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex			

subjects affected / exposed	1 / 69 (1.45%)	0 / 81 (0.00%)	0 / 60 (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
Gastroenteritis salmonella			
subjects affected / exposed	0 / 69 (0.00%)	1 / 81 (1.23%)	0 / 60 (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
Myelitis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 81 (0.00%)	0 / 60 (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
Gastroenteritis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 81 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	4 / 69 (5.80%)	1 / 81 (1.23%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 5	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	0 / 69 (0.00%)	1 / 81 (1.23%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 69 (0.00%)	0 / 81 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 69 (0.00%)	1 / 81 (1.23%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Respiratory tract infection			

subjects affected / exposed	1 / 69 (1.45%)	0 / 81 (0.00%)	0 / 60 (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 syncytial virus infection			
subjects affected / exposed	0 / 69 (0.00%)	0 / 81 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella zoster virus infection			
subjects affected / exposed	1 / 69 (1.45%)	0 / 81 (0.00%)	0 / 60 (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
Urosepsis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 81 (0.00%)	0 / 60 (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

Serious adverse events	Cohort 1 (Second Course)	Cohort 2 (Second Course)	Cohort 3 (Second Course)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
number of deaths (all causes)	2	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Small cell lung cancer			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelodysplastic syndrome			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Basal cell carcinoma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthermia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute graft versus host disease			

subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Schizophrenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			

subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Stress cardiomyopathy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Chronic inflammatory demyelinating polyradiculoneuropathy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyneuropathy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Alcoholic pancreatitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 7 (14.29%)	0 / 3 (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
Diarrhoea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Necrotising myositis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			

subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			

subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis salmonella			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			

subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella zoster virus infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Cohort 1 (First Course)	Cohort 2 (First Course)	Cohort 3 (First Course)
Total subjects affected by non-serious adverse events subjects affected / exposed	68 / 69 (98.55%)	76 / 81 (93.83%)	56 / 60 (93.33%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Tumour inflammation subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	0 / 81 (0.00%) 0	0 / 60 (0.00%) 0
Vascular disorders Hot flush subjects affected / exposed occurrences (all) Hypertension subjects affected / exposed occurrences (all)	1 / 69 (1.45%) 1 1 / 69 (1.45%) 1	1 / 81 (1.23%) 1 3 / 81 (3.70%) 3	3 / 60 (5.00%) 3 1 / 60 (1.67%) 1
General disorders and administration site conditions Catheter site erosion subjects affected / exposed occurrences (all) Asthenia subjects affected / exposed occurrences (all) Chest discomfort subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Chills subjects affected / exposed occurrences (all) Chest pain subjects affected / exposed occurrences (all) Influenza like illness subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0 6 / 69 (8.70%) 8 1 / 69 (1.45%) 1 15 / 69 (21.74%) 16 4 / 69 (5.80%) 4 3 / 69 (4.35%) 4 7 / 69 (10.14%) 9	0 / 81 (0.00%) 0 9 / 81 (11.11%) 11 1 / 81 (1.23%) 1 17 / 81 (20.99%) 19 5 / 81 (6.17%) 5 2 / 81 (2.47%) 3 2 / 81 (2.47%) 3	0 / 60 (0.00%) 0 2 / 60 (3.33%) 2 0 / 60 (0.00%) 0 16 / 60 (26.67%) 19 5 / 60 (8.33%) 5 5 / 60 (8.33%) 5 0 / 60 (0.00%) 0

Malaise subjects affected / exposed occurrences (all)	4 / 69 (5.80%) 4	2 / 81 (2.47%) 3	0 / 60 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	27 / 69 (39.13%) 48	18 / 81 (22.22%) 22	16 / 60 (26.67%) 17
Pain subjects affected / exposed occurrences (all)	3 / 69 (4.35%) 3	2 / 81 (2.47%) 2	3 / 60 (5.00%) 3
Oedema peripheral subjects affected / exposed occurrences (all)	3 / 69 (4.35%) 3	4 / 81 (4.94%) 4	5 / 60 (8.33%) 5
Immune system disorders Sarcoidosis subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	1 / 81 (1.23%) 1	0 / 60 (0.00%) 0
Reproductive system and breast disorders Vaginal haemorrhage subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	0 / 81 (0.00%) 0	0 / 60 (0.00%) 0
Pelvic pain subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	1 / 81 (1.23%) 1	0 / 60 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	7 / 69 (10.14%) 11	7 / 81 (8.64%) 8	9 / 60 (15.00%) 11
Nasal congestion subjects affected / exposed occurrences (all)	6 / 69 (8.70%) 8	8 / 81 (9.88%) 8	8 / 60 (13.33%) 14
Dyspnoea subjects affected / exposed occurrences (all)	8 / 69 (11.59%) 19	10 / 81 (12.35%) 16	7 / 60 (11.67%) 13
Cough subjects affected / exposed occurrences (all)	19 / 69 (27.54%) 26	22 / 81 (27.16%) 37	14 / 60 (23.33%) 19

Productive cough subjects affected / exposed occurrences (all)	10 / 69 (14.49%) 11	1 / 81 (1.23%) 1	4 / 60 (6.67%) 6
Tonsillar exudate subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	0 / 81 (0.00%) 0	0 / 60 (0.00%) 0
Rhinorrhoea subjects affected / exposed occurrences (all)	9 / 69 (13.04%) 10	4 / 81 (4.94%) 4	3 / 60 (5.00%) 3
Psychiatric disorders			
Insomnia subjects affected / exposed occurrences (all)	7 / 69 (10.14%) 7	6 / 81 (7.41%) 8	7 / 60 (11.67%) 7
Depression subjects affected / exposed occurrences (all)	1 / 69 (1.45%) 1	3 / 81 (3.70%) 3	3 / 60 (5.00%) 3
Anxiety subjects affected / exposed occurrences (all)	3 / 69 (4.35%) 3	4 / 81 (4.94%) 4	4 / 60 (6.67%) 4
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	7 / 69 (10.14%) 12	3 / 81 (3.70%) 3	0 / 60 (0.00%) 0
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	6 / 69 (8.70%) 12	3 / 81 (3.70%) 3	1 / 60 (1.67%) 1
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	5 / 69 (7.25%) 6	1 / 81 (1.23%) 1	1 / 60 (1.67%) 1
Blood creatinine increased subjects affected / exposed occurrences (all)	4 / 69 (5.80%) 6	2 / 81 (2.47%) 2	2 / 60 (3.33%) 2
Blood thyroid stimulating hormone increased subjects affected / exposed occurrences (all)	2 / 69 (2.90%) 2	4 / 81 (4.94%) 4	1 / 60 (1.67%) 1
Blood uric acid increased			

subjects affected / exposed occurrences (all)	1 / 69 (1.45%) 1	1 / 81 (1.23%) 1	1 / 60 (1.67%) 1
Platelet count decreased subjects affected / exposed occurrences (all)	3 / 69 (4.35%) 5	3 / 81 (3.70%) 4	0 / 60 (0.00%) 0
Weight increased subjects affected / exposed occurrences (all)	3 / 69 (4.35%) 3	5 / 81 (6.17%) 6	0 / 60 (0.00%) 0
Injury, poisoning and procedural complications			
Fall subjects affected / exposed occurrences (all)	3 / 69 (4.35%) 3	1 / 81 (1.23%) 1	1 / 60 (1.67%) 1
Infusion related reaction subjects affected / exposed occurrences (all)	6 / 69 (8.70%) 6	2 / 81 (2.47%) 2	2 / 60 (3.33%) 2
Ligament sprain subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	1 / 81 (1.23%) 1	0 / 60 (0.00%) 0
Limb injury subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	0 / 81 (0.00%) 0	0 / 60 (0.00%) 0
Skin laceration subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	0 / 81 (0.00%) 0	0 / 60 (0.00%) 0
Cardiac disorders			
Palpitations subjects affected / exposed occurrences (all)	4 / 69 (5.80%) 4	0 / 81 (0.00%) 0	3 / 60 (5.00%) 3
Pericarditis subjects affected / exposed occurrences (all)	2 / 69 (2.90%) 2	0 / 81 (0.00%) 0	0 / 60 (0.00%) 0
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	12 / 69 (17.39%) 19	6 / 81 (7.41%) 11	10 / 60 (16.67%) 11
Disturbance in attention			

subjects affected / exposed occurrences (all)	4 / 69 (5.80%) 4	1 / 81 (1.23%) 1	2 / 60 (3.33%) 2
Neuropathy peripheral subjects affected / exposed occurrences (all)	3 / 69 (4.35%) 4	5 / 81 (6.17%) 5	2 / 60 (3.33%) 2
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	4 / 69 (5.80%) 4	4 / 81 (4.94%) 4	1 / 60 (1.67%) 1
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	7 / 69 (10.14%) 8	8 / 81 (9.88%) 8	5 / 60 (8.33%) 6
Neutropenia subjects affected / exposed occurrences (all)	5 / 69 (7.25%) 6	4 / 81 (4.94%) 6	4 / 60 (6.67%) 5
Thrombocytopenia subjects affected / exposed occurrences (all)	4 / 69 (5.80%) 5	3 / 81 (3.70%) 3	3 / 60 (5.00%) 7
Ear and labyrinth disorders			
Ear pain subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	2 / 81 (2.47%) 2	1 / 60 (1.67%) 1
Ear congestion subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	0 / 81 (0.00%) 0	0 / 60 (0.00%) 0
Eye disorders			
Visual impairment subjects affected / exposed occurrences (all)	1 / 69 (1.45%) 1	0 / 81 (0.00%) 0	0 / 60 (0.00%) 0
Scleral hyperaemia subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	0 / 81 (0.00%) 0	0 / 60 (0.00%) 0
Iritis subjects affected / exposed occurrences (all)	1 / 69 (1.45%) 1	0 / 81 (0.00%) 0	0 / 60 (0.00%) 0
Gastrointestinal disorders			

Abdominal discomfort subjects affected / exposed occurrences (all)	1 / 69 (1.45%) 1	0 / 81 (0.00%) 0	1 / 60 (1.67%) 1
Abdominal pain subjects affected / exposed occurrences (all)	5 / 69 (7.25%) 6	5 / 81 (6.17%) 5	3 / 60 (5.00%) 4
Abdominal pain upper subjects affected / exposed occurrences (all)	3 / 69 (4.35%) 3	3 / 81 (3.70%) 3	1 / 60 (1.67%) 1
Constipation subjects affected / exposed occurrences (all)	9 / 69 (13.04%) 12	11 / 81 (13.58%) 11	3 / 60 (5.00%) 23
Vomiting subjects affected / exposed occurrences (all)	16 / 69 (23.19%) 22	9 / 81 (11.11%) 11	13 / 60 (21.67%) 20
Stomatitis subjects affected / exposed occurrences (all)	4 / 69 (5.80%) 5	2 / 81 (2.47%) 2	2 / 60 (3.33%) 2
Nausea subjects affected / exposed occurrences (all)	16 / 69 (23.19%) 25	11 / 81 (13.58%) 15	11 / 60 (18.33%) 32
Dyspepsia subjects affected / exposed occurrences (all)	2 / 69 (2.90%) 2	2 / 81 (2.47%) 3	4 / 60 (6.67%) 4
Diarrhoea subjects affected / exposed occurrences (all)	20 / 69 (28.99%) 37	12 / 81 (14.81%) 19	11 / 60 (18.33%) 17
Skin and subcutaneous tissue disorders			
Rash pruritic subjects affected / exposed occurrences (all)	1 / 69 (1.45%) 1	0 / 81 (0.00%) 0	0 / 60 (0.00%) 0
Rash maculo-papular subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	1 / 81 (1.23%) 4	4 / 60 (6.67%) 5
Rash			

subjects affected / exposed occurrences (all)	12 / 69 (17.39%) 15	9 / 81 (11.11%) 11	10 / 60 (16.67%) 14
Pruritus subjects affected / exposed occurrences (all)	12 / 69 (17.39%) 16	11 / 81 (13.58%) 18	7 / 60 (11.67%) 8
Erythema subjects affected / exposed occurrences (all)	4 / 69 (5.80%) 4	2 / 81 (2.47%) 2	1 / 60 (1.67%) 1
Dry skin subjects affected / exposed occurrences (all)	5 / 69 (7.25%) 6	5 / 81 (6.17%) 5	2 / 60 (3.33%) 2
Alopecia subjects affected / exposed occurrences (all)	3 / 69 (4.35%) 3	0 / 81 (0.00%) 0	4 / 60 (6.67%) 4
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all)	1 / 69 (1.45%) 1	1 / 81 (1.23%) 1	0 / 60 (0.00%) 0
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	8 / 69 (11.59%) 9	13 / 81 (16.05%) 14	12 / 60 (20.00%) 15
Musculoskeletal and connective tissue disorders Groin pain subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	1 / 81 (1.23%) 1	0 / 60 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	8 / 69 (11.59%) 11	12 / 81 (14.81%) 13	5 / 60 (8.33%) 6
Arthralgia subjects affected / exposed occurrences (all)	14 / 69 (20.29%) 20	12 / 81 (14.81%) 14	6 / 60 (10.00%) 10
Pain in extremity subjects affected / exposed occurrences (all)	4 / 69 (5.80%) 5	2 / 81 (2.47%) 2	2 / 60 (3.33%) 2
Neck pain			

subjects affected / exposed	0 / 69 (0.00%)	0 / 81 (0.00%)	1 / 60 (1.67%)
occurrences (all)	0	0	2
Myalgia			
subjects affected / exposed	6 / 69 (8.70%)	5 / 81 (6.17%)	5 / 60 (8.33%)
occurrences (all)	8	7	8
Muscular weakness			
subjects affected / exposed	4 / 69 (5.80%)	0 / 81 (0.00%)	1 / 60 (1.67%)
occurrences (all)	4	0	1
Muscle twitching			
subjects affected / exposed	0 / 69 (0.00%)	0 / 81 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	8 / 69 (11.59%)	1 / 81 (1.23%)	5 / 60 (8.33%)
occurrences (all)	12	2	5
Muscle contracture			
subjects affected / exposed	0 / 69 (0.00%)	0 / 81 (0.00%)	1 / 60 (1.67%)
occurrences (all)	0	0	1
Joint swelling			
subjects affected / exposed	0 / 69 (0.00%)	2 / 81 (2.47%)	0 / 60 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	3 / 69 (4.35%)	4 / 81 (4.94%)	1 / 60 (1.67%)
occurrences (all)	3	4	1
Folliculitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 81 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	4 / 69 (5.80%)	2 / 81 (2.47%)	2 / 60 (3.33%)
occurrences (all)	4	2	2
Bronchitis			
subjects affected / exposed	6 / 69 (8.70%)	4 / 81 (4.94%)	7 / 60 (11.67%)
occurrences (all)	6	8	11
Herpes zoster			
subjects affected / exposed	2 / 69 (2.90%)	4 / 81 (4.94%)	4 / 60 (6.67%)
occurrences (all)	2	4	4

Sinusitis			
subjects affected / exposed	7 / 69 (10.14%)	9 / 81 (11.11%)	5 / 60 (8.33%)
occurrences (all)	11	12	9
Upper respiratory tract infection			
subjects affected / exposed	23 / 69 (33.33%)	7 / 81 (8.64%)	12 / 60 (20.00%)
occurrences (all)	33	7	22
Urinary tract infection			
subjects affected / exposed	4 / 69 (5.80%)	6 / 81 (7.41%)	5 / 60 (8.33%)
occurrences (all)	10	6	7
Respiratory tract infection viral			
subjects affected / exposed	0 / 69 (0.00%)	0 / 81 (0.00%)	1 / 60 (1.67%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	5 / 69 (7.25%)	3 / 81 (3.70%)	2 / 60 (3.33%)
occurrences (all)	6	3	2
Pneumonia			
subjects affected / exposed	5 / 69 (7.25%)	5 / 81 (6.17%)	1 / 60 (1.67%)
occurrences (all)	5	5	2
Nasopharyngitis			
subjects affected / exposed	12 / 69 (17.39%)	16 / 81 (19.75%)	7 / 60 (11.67%)
occurrences (all)	15	16	11
Rhinitis			
subjects affected / exposed	8 / 69 (11.59%)	0 / 81 (0.00%)	2 / 60 (3.33%)
occurrences (all)	8	0	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 69 (4.35%)	6 / 81 (7.41%)	2 / 60 (3.33%)
occurrences (all)	4	6	3
Hypomagnesaemia			
subjects affected / exposed	2 / 69 (2.90%)	1 / 81 (1.23%)	2 / 60 (3.33%)
occurrences (all)	2	1	4
Hypokalaemia			
subjects affected / exposed	5 / 69 (7.25%)	5 / 81 (6.17%)	0 / 60 (0.00%)
occurrences (all)	7	6	0
Hypocalcaemia			

subjects affected / exposed	3 / 69 (4.35%)	0 / 81 (0.00%)	0 / 60 (0.00%)
occurrences (all)	4	0	0
Hyperuricaemia			
subjects affected / exposed	1 / 69 (1.45%)	2 / 81 (2.47%)	1 / 60 (1.67%)
occurrences (all)	1	2	1
Hypophosphataemia			
subjects affected / exposed	2 / 69 (2.90%)	1 / 81 (1.23%)	3 / 60 (5.00%)
occurrences (all)	5	1	3

Non-serious adverse events	Cohort 1 (Second Course)	Cohort 2 (Second Course)	Cohort 3 (Second Course)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)	7 / 7 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour inflammation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	1 / 10 (10.00%)	2 / 7 (28.57%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
General disorders and administration site conditions			
Catheter site erosion			
subjects affected / exposed	1 / 10 (10.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Asthenia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Chest discomfort			
subjects affected / exposed	1 / 10 (10.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	3 / 10 (30.00%)	1 / 7 (14.29%)	1 / 3 (33.33%)
occurrences (all)	3	2	2

Chills			
subjects affected / exposed	1 / 10 (10.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Chest pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 10 (0.00%)	1 / 7 (14.29%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Malaise			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	4 / 10 (40.00%)	1 / 7 (14.29%)	1 / 3 (33.33%)
occurrences (all)	5	1	1
Pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Oedema peripheral			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Sarcoidosis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pelvic pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 10 (10.00%)	1 / 7 (14.29%)	1 / 3 (33.33%)
occurrences (all)	1	1	1

Nasal congestion subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0
Dyspnoea subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 7 (14.29%) 1	1 / 3 (33.33%) 1
Cough subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 3	2 / 7 (28.57%) 2	0 / 3 (0.00%) 0
Productive cough subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0
Tonsillar exudate subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 7 (0.00%) 0	1 / 3 (33.33%) 1
Depression subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Anxiety subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 4	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 4	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0
Blood alkaline phosphatase increased			

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Blood creatinine increased subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0
Blood thyroid stimulating hormone increased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Blood uric acid increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0
Platelet count decreased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Weight increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0
Infusion related reaction subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Ligament sprain subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0
Limb injury subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0
Skin laceration subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 7 (0.00%) 0	1 / 3 (33.33%) 1
Cardiac disorders			

Palpitations subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Pericarditis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Disturbance in attention subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Neuropathy peripheral subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 7 (0.00%) 0	1 / 3 (33.33%) 1
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0
Neutropenia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Ear and labyrinth disorders			
Ear pain subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 7 (0.00%) 0	1 / 3 (33.33%) 1
Ear congestion subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0
Eye disorders			

Visual impairment subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0
Scleral hyperaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0
Iritis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 2	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Gastrointestinal disorders			
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 7 (0.00%) 0	1 / 3 (33.33%) 1
Constipation subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 7 (0.00%) 0	1 / 3 (33.33%) 1
Vomiting subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0
Stomatitis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	1 / 7 (14.29%) 2	0 / 3 (0.00%) 0
Dyspepsia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Diarrhoea			

subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2	4 / 7 (57.14%) 7	2 / 3 (66.67%) 2
Skin and subcutaneous tissue disorders			
Rash pruritic			
subjects affected / exposed	1 / 10 (10.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 10 (10.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Pruritus			
subjects affected / exposed	3 / 10 (30.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	3	1	0
Erythema			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Alopecia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 10 (10.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Groin pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Back pain			
subjects affected / exposed	3 / 10 (30.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Arthralgia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Pain in extremity			
subjects affected / exposed	0 / 10 (0.00%)	1 / 7 (14.29%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Neck pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle twitching			
subjects affected / exposed	0 / 10 (0.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	1 / 10 (10.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Muscle contracture			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Joint swelling			
subjects affected / exposed	1 / 10 (10.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Folliculitis			

subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Herpes zoster			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	1 / 10 (10.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 10 (20.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Urinary tract infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 7 (0.00%)	3 / 3 (100.00%)
occurrences (all)	1	0	4
Respiratory tract infection viral			
subjects affected / exposed	1 / 10 (10.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	2 / 10 (20.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Rhinitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			

Decreased appetite subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 7 (0.00%) 0	1 / 3 (33.33%) 1
Hypomagnesaemia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 2	0 / 7 (0.00%) 0	1 / 3 (33.33%) 1
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Hypocalcaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 7 (0.00%) 0	1 / 3 (33.33%) 1
Hyperuricaemia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 2	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Hypophosphataemia subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 January 2016	Amendment 3: Revised statistical section and added safety updates.
11 September 2016	Amendment 7: Clarified timing of efficacy analyses.
03 February 2017	Amendment 8: Added clarification on efficacy interim and posttreatment analyses.
26 August 2017	Amendment 10: Added clarification on allostem cell transplant data collection.
19 April 2021	Amendment 12: Updated the dose modification and toxicity management guidelines for irAEs.
23 August 2022	Amendment 14: Merck Sharp & Dohme Corp. underwent an entity name and address change to Merck Sharp & Dohme LLC, Rahway, NJ, USA. This conversion resulted only in an entity name change and update to the address.
08 December 2022	Amendment 16: To add language allowing eligible participants to enroll in an extension study, if available, following the end of MK-3475-087. To clarify that specific events will be collected as ECIs for 18 months from the date of the allogeneic transplant unless the trial closes earlier.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported