Clinical trial results:
Risk-based, response-adapted, Phase II open-label trial of nivolumab + brentuximab vedotin (N+ Bv) for children, adolescents, and young adults with relapsed/refractory (R/R) CD30 + classic Hodgkin lymphoma (cHL) after failure of first-line therapy, followed by brentuximab + bendamustine (Bv + B) for participants with a suboptimal response. CheckMate 744: CHECKpoint pathway and nivolumab clinical Trial Evaluation

Summary

EudraCT number	2016-002347-41
Trial protocol	CZ ES IE DE GB NL PL Outside EU/EEA IT
Global end of trial date	28 May 2024

Results information

Result version number	v1 (current)
This version publication date	17 November 2024
First version publication date	17 November 2024

Trial information

Trial identification

Sponsor protocol code	CA209-744

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02927769
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussee de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001407-PIP02-15
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 July 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 May 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the complete metabolic response (CMR) rate before radiation therapy/high-dose chemotherapy/autologous stem-cell transplant and event-free survival (EFS) rate at 3 years, as assessed by blinded independent central review (BICR), using Lugano 2014 response criteria.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 March 2017
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	France: 14
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Ireland: 2
Country: Number of subjects enrolled	Italy: 15
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	United States: 20
Worldwide total number of subjects	72
EEA total number of subjects	48

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	7
Adolescents (12-17 years)	42
Adults (18-64 years)	23
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All participants entered the Induction phase. Participants entered the Intensification phase if they received brentuximab + bendamustine (Bv + B). Participants entered the Consolidation Phase if they received radiation therapy (C1) or high-dose chemotherapy/autologous stem cell transplant (HDCT/ASCT) (C2).

Period 1

Period 1 title	Induction Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse

Arm description:

Participants started in the induction phase and received nivolumab + brentuximab vedotin (N+Bv) for 2 cycles (6 weeks). Participants with radiographic progression, by Investigator at Cycle 2 entered follow-up. The rest continued in the induction phase and received 2 more cycles of N+Bv (total 4 cycles = 12 weeks). - Participants who had a complete metabolic response (CMR) by BICR after a total of 4 cycles (12 weeks) of N+Bv received 2 more cycles of treatment of N+Bv (total of 6 cycles [18 weeks]), followed by Radiation Therapy (RT) (consolidation phase). - Participants without a CMR after 4 cycles of N+Bv, by BICR, entered the intensification phase and received 2 cycles of brentuximab + bendamustine (Bv+B); participants who achieved CMR after these 2 cycles proceeded with RT (consolidation phase). - Participants who had radiographic progression after Cycle 4 N+Bv, by BICR, or those who did not achieve CMR, after 2 cycles of Bv+B were taken off study treatment and entered follow-up.

Arm type	Experimental
Investigational medicinal product name	Brentuximab Vedotin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

1.8 mg/kg every 21 days

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	BMS-936558
Other name	
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

3 mg/kg every 21 days

Arm title	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse

Arm description:

Participants started in the induction phase and received nivolumab + brentuximab vedotin (N+Bv) for 2 cycles (6 weeks). Those with progression at Cycle 2 entered follow-up. The rest received 2 more cycles of N+Bv (total 4 cycles = 12 weeks). - Participants with complete metabolic response (CMR) after 4 cycles of N+Bv received high-dose chemotherapy and autologous stem cell transplant (HDCT/ASCT) (consolidation phase). Participants with CMR could receive up to 2 more cycles of N+Bv if their HDCT/ASCT was postponed. - Participants without CMR after 4 cycles of N+Bv received 2 cycles of brentuximab + bendamustine (Bv+B) (intensification phase). - Participants in CMR after 2 cycles of Bv+B received HDCT/ASCT. - Participants without CMR could receive 2 more cycles of Bv+B. If they had

CMR, they received HDCT/ASCT. - Participants with CMR could receive up to 2 more cycles of B+Bv if their HDCT/ASCT was postponed. - Participants with progression after Cycle 4 N+Bv were taken off treatment.

Arm type	Experimental
Investigational medicinal product name	Bendamustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

90 mg/m2/day, 21-day cycles (on Days1 and 2)

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	BMS-936558
Other name	
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

3 mg/kg every 21 days

Number of subjects in period 1	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse
Started	28	44
Completed	27	42
Not completed	1	2
Disease progression	-	1
Study drug toxicity	1	1

Period 2

Period 2 title	Consolidation Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse

Arm description:

Participants started in the induction phase and received nivolumab + brentuximab vedotin (N+Bv) for 2 cycles (6 weeks). Participants with radiographic progression, by Investigator at Cycle 2 entered follow-up. The rest continued in the induction phase and received 2 more cycles of N+Bv (total 4 cycles = 12 weeks). - Participants who had a complete metabolic response (CMR) by BICR after a total of 4 cycles (12 weeks) of N+Bv received 2 more cycles of treatment of N+Bv (total of 6 cycles [18 weeks]), followed by Radiation Therapy (RT) (consolidation phase). - Participants without a CMR after 4 cycles of N+Bv, by BICR, entered the intensification phase and received 2 cycles of brentuximab + bendamustine (Bv+B); participants who achieved CMR after these 2 cycles proceeded with RT (consolidation phase). - Participants who had radiographic progression after Cycle 4 N+Bv, by BICR, or those who did not

achieve CMR, after 2 cycles of Bv+B were taken off study treatment and entered follow-up.

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	BMS-936558
Other name	
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use
Dosage and administration details: 3 mg/kg every 21 days	
Investigational medicinal product name	Bendamustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous use
Dosage and administration details: 90 mg/m2/day, 21-day cycles (on Days1 and 2)	
Investigational medicinal product name	Brentuximab Vedotin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use
Dosage and administration details: 1.8 mg/kg every 21 days	
Arm title	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse

Arm description:

Participants started in the induction phase and received nivolumab + brentuximab vedotin (N+Bv) for 2 cycles (6 weeks). Those with progression at Cycle 2 entered follow-up. The rest received 2 more cycles of N+Bv (total 4 cycles = 12 weeks). - Participants with complete metabolic response (CMR) after 4 cycles of N+Bv received high-dose chemotherapy and autologous stem cell transplant (HDCT/ASCT) (consolidation phase). Participants with CMR could receive up to 2 more cycles of N+Bv if their HDCT/ASCT was postponed. - Participants without CMR after 4 cycles of N+Bv received 2 cycles of brentuximab + bendamustine (Bv+B) (intensification phase). - Participants in CMR after 2 cycles of Bv+B received HDCT/ASCT. - Participants without CMR could receive 2 more cycles of Bv+B. If they had CMR, they received HDCT/ASCT. - Participants with CMR could receive up to 2 more cycles of B+Bv if their HDCT/ASCT was postponed. - Participants with progression after Cycle 4 N+Bv were taken off treatment.

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	BMS-936558
Other name	
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use
Dosage and administration details: 3 mg/kg every 21 days	
Investigational medicinal product name	Bendamustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous use
Dosage and administration details: 90 mg/m2/day, 21-day cycles (on Days1 and 2)	
Investigational medicinal product name	Bendamustine
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

90 mg/m2/day, 21-day cycles (on Days1 and 2)

Number of subjects in period 2[1]	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse
Started	22	32
Completed	22	32

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Not all participants who started in the induction phase entered the intensification or consolidation phase.

Period 3

Period 3 title	Intensification Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse

Arm description:

Participants started in the induction phase and received nivolumab + brentuximab vedotin (N+Bv) for 2 cycles (6 weeks). Participants with radiographic progression, by Investigator at Cycle 2 entered follow-up. The rest continued in the induction phase and received 2 more cycles of N+Bv (total 4 cycles = 12 weeks). - Participants who had a complete metabolic response (CMR) by BICR after a total of 4 cycles (12 weeks) of N+Bv received 2 more cycles of treatment of N+Bv (total of 6 cycles [18 weeks]), followed by Radiation Therapy (RT) (consolidation phase). - Participants without a CMR after 4 cycles of N+Bv, by BICR, entered the intensification phase and received 2 cycles of brentuximab + bendamustine (Bv+B); participants who achieved CMR after these 2 cycles proceeded with RT (consolidation phase). - Participants who had radiographic progression after Cycle 4 N+Bv, by BICR, or those who did not achieve CMR, after 2 cycles of Bv+B were taken off study treatment and entered follow-up.

Arm type	Experimental
Investigational medicinal product name	Bendamustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

90 mg/m2/day, 21-day cycles (on Days1 and 2)

Investigational medicinal product name	Brentuximab Vedotin
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

1.8 mg/kg every 21 days

Arm title	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse

Arm description:

Participants started in the induction phase and received nivolumab + brentuximab vedotin (N+Bv) for 2 cycles (6 weeks). Those with progression at Cycle 2 entered follow-up. The rest received 2 more cycles of N+Bv (total 4 cycles = 12 weeks). - Participants with complete metabolic response (CMR) after 4 cycles of N+Bv received high-dose chemotherapy and autologous stem cell transplant (HDCT/ASCT) (consolidation phase). Participants with CMR could receive up to 2 more cycles of N+Bv if their HDCT/ASCT was postponed. - Participants without CMR after 4 cycles of N+Bv received 2 cycles of brentuximab + bendamustine (Bv+B) (intensification phase). - Participants in CMR after 2 cycles of Bv+B received HDCT/ASCT. - Participants without CMR could receive 2 more cycles of Bv+B. If they had CMR, they received HDCT/ASCT. - Participants with CMR could receive up to 2 more cycles of B+Bv if their HDCT/ASCT was postponed. - Participants with progression after Cycle 4 N+Bv were taken off treatment.

Arm type	Experimental
Investigational medicinal product name	Bendamustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

90 mg/m2/day, 21-day cycles (on Days1 and 2)

Investigational medicinal product name	Brentuximab Vedotin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

1.8 mg/kg every 21 days

Number of subjects in period 3[2]	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse
Started	6	11
Completed	5	11
Not completed	1	0
Study drug toxicity	1	-

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all participants who started in the induction phase entered the intensification or consolidation phase.

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse

Reporting group description:

Participants started in the induction phase and received nivolumab + brentuximab vedotin (N+Bv) for 2 cycles (6 weeks). Participants with radiographic progression, by Investigator at Cycle 2 entered follow-up. The rest continued in the induction phase and received 2 more cycles of N+Bv (total 4 cycles = 12 weeks). - Participants who had a complete metabolic response (CMR) by BICR after a total of 4 cycles (12 weeks) of N+Bv received 2 more cycles of treatment of N+Bv (total of 6 cycles [18 weeks]), followed by Radiation Therapy (RT) (consolidation phase). - Participants without a CMR after 4 cycles of N+Bv, by BICR, entered the intensification phase and received 2 cycles of brentuximab + bendamustine (Bv+B); participants who achieved CMR after these 2 cycles proceeded with RT (consolidation phase). - Participants who had radiographic progression after Cycle 4 N+Bv, by BICR, or those who did not achieve CMR, after 2 cycles of Bv+B were taken off study treatment and entered follow-up.

Reporting group title	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse

Reporting group description:

Participants started in the induction phase and received nivolumab + brentuximab vedotin (N+Bv) for 2 cycles (6 weeks). Those with progression at Cycle 2 entered follow-up. The rest received 2 more cycles of N+Bv (total 4 cycles = 12 weeks). - Participants with complete metabolic response (CMR) after 4 cycles of N+Bv received high-dose chemotherapy and autologous stem cell transplant (HDCT/ASCT) (consolidation phase). Participants with CMR could receive up to 2 more cycles of N+Bv if their HDCT/ASCT was postponed. - Participants without CMR after 4 cycles of N+Bv received 2 cycles of brentuximab + bendamustine (Bv+B) (intensification phase). - Participants in CMR after 2 cycles of Bv+B received HDCT/ASCT. - Participants without CMR could receive 2 more cycles of Bv+B. If they had CMR, they received HDCT/ASCT. - Participants with CMR could receive up to 2 more cycles of B+Bv if their HDCT/ASCT was postponed. - Participants with progression after Cycle 4 N+Bv were taken off treatment.

Reporting group values	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse	Total
Number of subjects	28	44	72
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)	3	4	7
Adolescents (12-17 years)	15	27	42
Adults (18-64 years)	10	13	23
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	17.0	16.2	
standard deviation	± 4.3	± 3.7	-
Sex: Female, Male Units: Participants			
Female	18	15	33
Male	10	29	39

Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	1
Native Hawaiian or Other Pacific Islander	0	1	1
Black or African American	1	1	2
White	25	41	66
More than one race	0	0	0
Unknown or Not Reported	1	1	2
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	3	1	4
Not Hispanic or Latino	8	20	28
Unknown or Not Reported	17	23	40

End points reporting groups

Reporting group title	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse

Reporting group description:

Participants started in the induction phase and received nivolumab + brentuximab vedotin (N+Bv) for 2 cycles (6 weeks). Participants with radiographic progression, by Investigator at Cycle 2 entered follow-up. The rest continued in the induction phase and received 2 more cycles of N+Bv (total 4 cycles = 12 weeks). - Participants who had a complete metabolic response (CMR) by BICR after a total of 4 cycles (12 weeks) of N+Bv received 2 more cycles of treatment of N+Bv (total of 6 cycles [18 weeks]), followed by Radiation Therapy (RT) (consolidation phase). - Participants without a CMR after 4 cycles of N+Bv, by BICR, entered the intensification phase and received 2 cycles of brentuximab + bendamustine (Bv+B); participants who achieved CMR after these 2 cycles proceeded with RT (consolidation phase). - Participants who had radiographic progression after Cycle 4 N+Bv, by BICR, or those who did not achieve CMR, after 2 cycles of Bv+B were taken off study treatment and entered follow-up.

Reporting group title	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse

Reporting group description:

Participants started in the induction phase and received nivolumab + brentuximab vedotin (N+Bv) for 2 cycles (6 weeks). Those with progression at Cycle 2 entered follow-up. The rest received 2 more cycles of N+Bv (total 4 cycles = 12 weeks). - Participants with complete metabolic response (CMR) after 4 cycles of N+Bv received high-dose chemotherapy and autologous stem cell transplant (HDCT/ASCT) (consolidation phase). Participants with CMR could receive up to 2 more cycles of N+Bv if their HDCT/ASCT was postponed. - Participants without CMR after 4 cycles of N+Bv received 2 cycles of brentuximab + bendamustine (Bv+B) (intensification phase). - Participants in CMR after 2 cycles of Bv+B received HDCT/ASCT. - Participants without CMR could receive 2 more cycles of Bv+B. If they had CMR, they received HDCT/ASCT. - Participants with CMR could receive up to 2 more cycles of B+Bv if their HDCT/ASCT was postponed. - Participants with progression after Cycle 4 N+Bv were taken off treatment.

Reporting group title	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse

Reporting group description:

Participants started in the induction phase and received nivolumab + brentuximab vedotin (N+Bv) for 2 cycles (6 weeks). Participants with radiographic progression, by Investigator at Cycle 2 entered follow-up. The rest continued in the induction phase and received 2 more cycles of N+Bv (total 4 cycles = 12 weeks). - Participants who had a complete metabolic response (CMR) by BICR after a total of 4 cycles (12 weeks) of N+Bv received 2 more cycles of treatment of N+Bv (total of 6 cycles [18 weeks]), followed by Radiation Therapy (RT) (consolidation phase). - Participants without a CMR after 4 cycles of N+Bv, by BICR, entered the intensification phase and received 2 cycles of brentuximab + bendamustine (Bv+B); participants who achieved CMR after these 2 cycles proceeded with RT (consolidation phase). - Participants who had radiographic progression after Cycle 4 N+Bv, by BICR, or those who did not achieve CMR, after 2 cycles of Bv+B were taken off study treatment and entered follow-up.

Reporting group title	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse

Reporting group description:

Participants started in the induction phase and received nivolumab + brentuximab vedotin (N+Bv) for 2 cycles (6 weeks). Those with progression at Cycle 2 entered follow-up. The rest received 2 more cycles of N+Bv (total 4 cycles = 12 weeks). - Participants with complete metabolic response (CMR) after 4 cycles of N+Bv received high-dose chemotherapy and autologous stem cell transplant (HDCT/ASCT) (consolidation phase). Participants with CMR could receive up to 2 more cycles of N+Bv if their HDCT/ASCT was postponed. - Participants without CMR after 4 cycles of N+Bv received 2 cycles of brentuximab + bendamustine (Bv+B) (intensification phase). - Participants in CMR after 2 cycles of Bv+B received HDCT/ASCT. - Participants without CMR could receive 2 more cycles of Bv+B. If they had CMR, they received HDCT/ASCT. - Participants with CMR could receive up to 2 more cycles of B+Bv if their HDCT/ASCT was postponed. - Participants with progression after Cycle 4 N+Bv were taken off treatment.

Reporting group title	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse

Reporting group description:

Participants started in the induction phase and received nivolumab + brentuximab vedotin (N+Bv) for 2 cycles (6 weeks). Participants with radiographic progression, by Investigator at Cycle 2 entered follow-up. The rest continued in the induction phase and received 2 more cycles of N+Bv (total 4 cycles = 12 weeks). - Participants who had a complete metabolic response (CMR) by BICR after a total of 4 cycles (12 weeks) of N+Bv received 2 more cycles of treatment of N+Bv (total of 6 cycles [18 weeks]), followed by Radiation Therapy (RT) (consolidation phase). - Participants without a CMR after 4 cycles of N+Bv, by BICR, entered the intensification phase and received 2 cycles of brentuximab + bendamustine (Bv+B); participants who achieved CMR after these 2 cycles proceeded with RT (consolidation phase). -

Participants who had radiographic progression after Cycle 4 N+Bv, by BICR, or those who did not achieve CMR, after 2 cycles of Bv+B were taken off study treatment and entered follow-up.

Reporting group title	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse

Reporting group description:

Participants started in the induction phase and received nivolumab + brentuximab vedotin (N+Bv) for 2 cycles (6 weeks). Those with progression at Cycle 2 entered follow-up. The rest received 2 more cycles of N+Bv (total 4 cycles = 12 weeks). - Participants with complete metabolic response (CMR) after 4 cycles of N+Bv received high-dose chemotherapy and autologous stem cell transplant (HDCT/ASCT) (consolidation phase). Participants with CMR could receive up to 2 more cycles of N+Bv if their HDCT/ASCT was postponed. - Participants without CMR after 4 cycles of N+Bv received 2 cycles of brentuximab + bendamustine (Bv+B) (intensification phase). - Participants in CMR after 2 cycles of Bv+B received HDCT/ASCT. - Participants without CMR could receive 2 more cycles of Bv+B. If they had CMR, they received HDCT/ASCT. - Participants with CMR could receive up to 2 more cycles of B+Bv if their HDCT/ASCT was postponed. - Participants with progression after Cycle 4 N+Bv were taken off treatment.

Primary: Event-free Survival (EFS) Rate at 3 Years by Blinded Independent Centralized Review (BICR) - Cohort 1

End point title	Event-free Survival (EFS) Rate at 3 Years by Blinded Independent Centralized Review (BICR) - Cohort 1[1][2]

End point description:

Event Free Survival (EFS) is the time from the first treatment to the earliest occurrence of composite events including: Disease progression (PD), Failure to achieve complete metabolic response (CMR) after 4 cycles of N+Bv and 2 cycles of Bv+B, Secondary malignancy, Death .
PD :
Lymph Nodes and Lesions: new growth or increase of >= 50% in size from nadir. New or growing lesions outside the lymph nodes.
Spleen: Significant increase in spleen size, either from a previously enlarged state or from normal size.
New Lesions: Yes
Bone Marrow: New or returning FDG-avid disease
CM):
Lymph nodes/extralymphatic sites: Score 1, 2, 3 with/without residual mass on 5-point scale •
New lesions: No
Bone marrow: No FDG-avid disease
Participants without an "event" were censored at the last tumor assessment. Those who started subsequent anticancer therapy without a prior "event" were censored at the last tumor assessment prior to or upon starting subsequent therapy.
Based on Kaplan-Meier Estimates.

End point type	Primary

End point timeframe:

At 3 years post first dose of study therapy

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: Only descriptive statistics were planned for this endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Prespecified to be collected for Cohort 1 only.

End point values	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: Percent of participants				
number (confidence interval 90%)	87.5 (70.6 to 95.0)			

Statistical analyses

No statistical analyses for this end point

Primary: Complete Metabolic Response (CMR) Rate at Any Time Prior to High Dose Chemotherapy Followed by Autologous Stem Cell Treatment (HDCT/ASCT) by Blinded Independent Centralized Review (BICR) - Cohort 2

End point title	Complete Metabolic Response (CMR) Rate at Any Time Prior to High Dose Chemotherapy Followed by Autologous Stem Cell Treatment (HDCT/ASCT) by Blinded Independent Centralized Review (BICR) - Cohort 2[3][4]

End point description:

The complete metabolic response (CMR) rate is defined as the percent of all response-evaluable participants who, assessed by the BICR, achieved best response of CMR.
Complete metabolic response (CMR):
• Lymph nodes/extralymphatic sites: Score 1, 2, 3 with/without residual mass on 5-point scale
• New lesions: No
• Bone marrow: No FDG-avid disease
Participants who came off study treatment early for toxicity without a CMR were evaluable.
Confidence interval is based on the Clopper and Pearson method

End point type	Primary

End point timeframe:

From first dose to complete metabolic response or the completion of six cycles of therapy (up to approximately 18 weeks)

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: Only descriptive statistics were planned for this endpoint.

[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: Prespecified to be collected for Cohort 1 only.

End point values	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: Percent of participants				
number (confidence interval 90%)	88.6 (77.6 to 95.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Complete Metabolic Response (CMR) Rate at Any Time Prior to Radiation

Therapy by Blinded Independent Centralized Review (BICR) - Cohort 1

End point title	Complete Metabolic Response (CMR) Rate at Any Time Prior to Radiation Therapy by Blinded Independent Centralized Review (BICR) - Cohort 1[5][6]

End point description:

The complete metabolic response (CMR) rate is defined as the percent of all response-evaluable participants who, assessed by the BICR, achieved best response of CMR.
Complete metabolic response (CMR):
• Lymph nodes/extralymphatic sites: Score 1, 2, 3 with/without residual mass on 5-point scale
• New lesions: No
• Bone marrow: No FDG-avid disease
Participants who stopped study treatment early for toxicity without a CMR were evaluable.
Confidence interval is based on the Clopper and Pearson method

End point type	Primary

End point timeframe:

From first dose to complete metabolic response or the completion of six cycles of therapy (up to approximately 18 weeks).

Notes:

[5] - 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: Only descriptive statistics were planned for this endpoint.

[6] - 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: Prespecified to be collected for Cohort 1 only.

End point values	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: Percent of participants				
number (confidence interval 90%)	92.9 (79.2 to 98.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR) Following 4 Cycles of Nivolumab + Brentuximab Vedotin Treatment by Blinded Independent Centralized Review (BICR)

End point title	Overall Response Rate (ORR) Following 4 Cycles of Nivolumab + Brentuximab Vedotin Treatment by Blinded Independent Centralized Review (BICR)

End point description:

Overall response rate (ORR) is defined as the percent of all response-evaluable participants who, assessed by the BICR, achieved a best response of complete metabolic response (CMR) or partial metabolic response (PMR).
Complete metabolic response (CMR):
• Lymph nodes/extralymphatic sites: Score 1, 2, 3 with/without residual mass on 5-point scale
• New lesions: No
• Bone marrow: No FDG-avid disease
Partial metabolic response (PMR):
• Lymph nodes/extralymphatic: Score 4 or 5, reduced uptake from baseline
• New lesions: None
• Bone marrow: Residual uptake higher than normal, reduced from baseline.
Participants who came off early for toxicity without CMR or PMR were evaluable.

End point type	Secondary

End point timeframe:

From first dose to PMR or CMR within 4 cycles of therapy, or the completion of four cycles of therapy (N+Bv x4) (up to approximately 12 weeks).

End point values	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	44		
Units: Percent of participants				
number (confidence interval 90%)	96.4 (84.1 to 99.8)	93.2 (83.3 to 98.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) by Blinded Independent Centralized Review (BICR)

End point title	Duration of Response (DOR) by Blinded Independent Centralized Review (BICR)

End point description:

Duration of response (DOR) is from first complete metabolic response or partial metabolic response (CMR or PMR) to event free survival EFS (Cohort 1)/progression free survival PFS (Cohort 2) event. For participants with no event, the DOR was censored on the date of last tumor assessment.
Participants who started subsequent anticancer therapy (not part of high-dose chemotherapy followed by autologous stem cell transplant HDCT/ASCT) without a prior reported EFS/PFS event were censored at the last tumor assessment prior to starting subsequent anticancer therapy.
Complete metabolic response (CMR):
• Lymph nodes/extralymphatic sites: Score 1, 2, 3 with/without residual mass on 5-point scale
• New lesions: No
• Bone marrow: No FDG-avid disease
Partial metabolic response:
• Lymph nodes/extralymphatic: Score 4 or 5, reduced uptake from baseline
• New lesions: None
• Bone marrow: Residual uptake higher than normal, reduced from baseline.
Based on Kaplan-Meier estimates. "99999 = N/A".

End point type	Secondary

End point timeframe:

From first dose until disease progression, start of subsequent anti-cancer therapy, or or death due to any cause (up to approximately 86 months)

End point values	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	39		
Units: Months				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) Rate at 3 Years by Blinded Independent Centralized Review (BICR)

End point title	Progression Free Survival (PFS) Rate at 3 Years by Blinded Independent Centralized Review (BICR)

End point description:

Progression Free Survival (PFS) is the time from the date of first treatment to the date of first documented disease progression by BICR or death.
Progressive Disease (PD):
Lymph Nodes and Lesions: new growth or increase of >= 50% in size from nadir. New or growing lesions outside the lymph nodes.
Spleen: Significant increase in spleen size, either from a previously enlarged state or from normal size.
New Lesions: Yes
Bone Marrow: New or returning FDG-avid disease.
Participants who neither progressed nor died were censored at the last adequate tumor assessment.
Participants who started subsequent anticancer therapy (that is not part of high dose chemotherapy followed by autologous stem cell transplant (HDCT/ASCT) Consolidation Therapy for R2 Cohort) without a prior reported progression or death were censored at the last tumor assessment prior to initiation of the subsequent anticancer therapy.
Based on Kaplan-Meier Estimates.

End point type	Secondary

End point timeframe:

At 3 years post first dose of study therapy

End point values	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	44		
Units: Percent of participants				
number (confidence interval 90%)	95.2 (77.7 to 99.1)	91.1 (78.4 to 96.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Metabolic Response (CMR) Rate at Any Time Prior to Radiation Therapy by Investigator - Cohort 1

End point title	Complete Metabolic Response (CMR) Rate at Any Time Prior to Radiation Therapy by Investigator - Cohort 1[7]

End point description:

The complete metabolic response (CMR) rate is defined as the percent of all response-evaluable participants who, assessed by the investigator, achieved best response of CMR.
Complete metabolic response (CMR):
• Lymph nodes/extralymphatic sites: Score 1, 2, 3 with/without residual mass on 5-point scale
• New lesions: No
• Bone marrow: No FDG-avid disease
Participants who come off early for toxicity without a CMR were evaluable.
Confidence interval is based on the Clopper and Pearson method

End point type	Secondary

End point timeframe:

From first dose to complete metabolic response or the completion of six cycles of therapy (up to approximately 18 weeks).

Notes:

[7] - 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: Prespecified to be collected for Cohort 1 only.

End point values	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: Percent of participants				
number (confidence interval 90%)	89.3 (74.6 to 97.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Event-free Survival (EFS) Rate at 3 Years by Investigator - Cohort 1

End point title	Event-free Survival (EFS) Rate at 3 Years by Investigator - Cohort 1[8]

End point description:

Event Free Survival (EFS) is the time from the first treatment to the earliest occurrence of composite events including: Disease progression (PD), Failure to achieve complete metabolic response (CMR) after 4 cycles of N+Bv and 2 cycles of Bv+B, Secondary malignancy, Death .
PD :
Lymph Nodes and Lesions: new growth or increase of >= 50% in size from nadir. New or growing lesions outside the lymph nodes.
Spleen: Significant increase in spleen size, either from a previously enlarged state or from normal size.
New Lesions: Yes
Bone Marrow: New or returning FDG-avid disease
CMR:
Lymph nodes/extralymphatic sites: Score 1, 2, 3 with/without residual mass on 5-point scale
New lesions: No
Bone marrow: No FDG-avid disease
Participants without an "event" were censored at the last tumor assessment. Those who started subsequent anticancer therapy without a prior "event" were censored at the last tumor assessment prior

to or upon starting subsequent therapy.
Based on Kaplan-Meier Estimates.

End point type	Secondary

End point timeframe:

At 3 years post first dose of study therapy

Notes:

[8] - 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: Prespecified to be collected for Cohort 1 only.

End point values	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: Percent of participants				
number (confidence interval 90%)	88.5 (72.8 to 95.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) Rate at 3 Years by Investigator

End point title	Progression Free Survival (PFS) Rate at 3 Years by Investigator

End point description:

Progression Free Survival (PFS) is the time from the date of first treatment to the date of first documented disease progression by investigator or death.
Progressive Disease (PD):
Lymph Nodes and Lesions: new growth or increase of >= 50% in size from nadir. New or growing lesions outside the lymph nodes.
Spleen: Significant increase in spleen size, either from a previously enlarged state or from normal size.
New Lesions: Yes
Bone Marrow: New or returning FDG-avid disease.
Participants who neither progressed nor died were be censored at the last adequate tumor assessment.
Participants who started subsequent anticancer therapy (that is not part of high dose chemotherapy followed by autologous stem cell transplant (HDCT/ASCT) Consolidation Therapy forR2 Cohort) without a prior reported progression or death were censored at the last tumor assessment prior to initiation of the subsequent anticancer therapy.
Based on Kaplan-Meier Estimates.

End point type	Secondary

End point timeframe:

At 3 years post first dose

End point values	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	44		
Units: Percent of participants				

number (confidence interval 90%)	95.8 (80.2 to 99.2)	88.1 (74.8 to 94.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Metabolic Response (CMR) Rate at Any Time Prior to High Dose Chemotherapy Followed by Autologous Stem Cell Treatment (HDCT/ASCT) by Investigator - Cohort 2

End point title	Complete Metabolic Response (CMR) Rate at Any Time Prior to High Dose Chemotherapy Followed by Autologous Stem Cell Treatment (HDCT/ASCT) by Investigator - Cohort 2[9]

End point description:

The complete metabolic response (CMR) rate is defined as the percent of all response-evaluable participants who, assessed by the investigator, achieved best response of CMR.
Complete metabolic response (CMR):
• Lymph nodes/extralymphatic sites: Score 1, 2, 3 with/without residual mass on 5-point scale
• New lesions: No
• Bone marrow: No FDG-avid disease
Participants who came off study treatment early for toxicity without a CMR were evaluable.
Confidence interval is based on the Clopper and Pearson method.

End point type	Secondary

End point timeframe:

From first dose to complete metabolic response or the completion of six cycles of therapy (up to approximately 18 weeks)

Notes:

[9] - 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: Prespecified to be collected for Cohort 2 only.

End point values	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: Percent of participants				
number (confidence interval 95%)	86.4 (74.8 to 93.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR) Following 4 Cycles of Nivolumab + Brentuximab Vedotin Treatment by Investigator

End point title	Overall Response Rate (ORR) Following 4 Cycles of Nivolumab + Brentuximab Vedotin Treatment by Investigator

End point description:

Overall response rate (ORR) is defined as the percent of all response-evaluable participants who, assessed by the investigator, achieve a best response of complete metabolic response (CMR) or partial metabolic response (PMR).
Complete metabolic response (CMR):
• Lymph nodes/extralymphatic sites: Score 1, 2, 3 with/without residual mass on 5-point scale
• New lesions: No
• Bone marrow: No FDG-avid disease
Partial metabolic response:
• Lymph nodes/extralymphatic: Score 4 or 5, reduced uptake from baseline
• New lesions: None
• Bone marrow: Residual uptake higher than normal, reduced from baseline
Participants who came off early for toxicity without CMR or PMR were evaluable.

End point type	Secondary

End point timeframe:

From first dose to PMR or CMR within 4 cycles of therapy, or the completion of four cycles of therapy (N+Bv x4) (up to approximately 12 weeks).

End point values	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	44		
Units: Percent of participants				
number (confidence interval 90%)	100.0 (89.9 to 100.0)	90.9 (80.4 to 96.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) by Investigator

End point title	Duration of Response (DOR) by Investigator

End point description:

Duration of response (DOR) is from first complete metabolic response or partial metabolic response (CMR or PMR) to event free survival EFS (Cohort 1)/progression free survival PFS (Cohort 2) event. For participants with no event, the DOR was censored on the date of last tumor assessment.
Participants who started subsequent anticancer therapy (not part of high-dose chemotherapy followed by autologous stem cell transplant HDCT/ASCT) without a prior reported EFS/PFS event were censored at the last tumor assessment before starting subsequent anticancer therapy.
Complete metabolic response (CMR):
• Lymph nodes/extralymphatic sites: Score 1, 2, 3 with/without residual mass on 5-point scale
• New lesions: No
• Bone marrow: No FDG-avid disease
Partial metabolic response:
• Lymph nodes/extralymphatic: Score 4 or 5, reduced uptake from baseline
• New lesions: None
• Bone marrow: Residual uptake higher than normal, reduced from baseline.
Based on Kaplan-Meier estimates. "99999=N/A".

End point type	Secondary

End point timeframe:

From first dose until disease progression, start of subsequent anti-cancer therapy, or or death due to any cause (up to approximately 86 months)

End point values	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	44		
Units: Months				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participants with Adverse Events (AEs)

End point title	The Number of Participants with Adverse Events (AEs)

End point description:

An Adverse Event (AE) is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation participant administered study drug and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (such as an abnormal laboratory finding), symptom, or disease temporally associated with the use of study drug, whether or not considered related to the study drug.

End point type	Secondary

End point timeframe:

From first dose to 30 days post last dose (an average of 4 months up until a maximum of 7 months).

End point values	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	44		
Units: Participants	26	42		

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participants with Serious Adverse Events (SAEs)

End point title	The Number of Participants with Serious Adverse Events (SAEs)

End point description:

A Serious Adverse Event (SAE) is defined as any untoward medical occurrence that, at any dose:

- Results in death
- Is life-threatening (defined as an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe)
- Requires inpatient hospitalization or causes prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect
- Is an important medical event.

End point type	Secondary

End point timeframe:

From first dose to 30 days post last dose (an average of 4 months up until a maximum of 7 months)

End point values	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	44		
Units: Participants	8	9		

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participants with Abnormal Laboratory Values for Specific Thyroid Tests

End point title	The Number of Participants with Abnormal Laboratory Values for Specific Thyroid Tests

End point description:

The Number of Participants with Abnormal Laboratory Values for Specific Thyroid Tests.

End point type	Secondary

End point timeframe:

From first dose to 30 days post last dose (an average of 4 months up until a maximum of 7 months)

End point values	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	44		
Units: Participants				
TSH > ULN	6	8		
TSH > ULN WITH TSH <= ULN AT BASELINE	5	4		
TSH >ULN WITH ATLEAST ONE FT3/FT4 TEST VALUE <LLN	1	0		

TSH >ULN WITH ALL OTHER FT3/FT4 TEST VALUES >= LLN	4	5		
TSH > ULN WITH FT3/FT4 TEST MISSING	1	3		
TSH < LLN	4	1		
TSH <LLN WITH TSH >= LLN AT BASELINE	4	1		
TSH <LLN WITH ATLEAST ONE FT3/FT4 TEST VALUE > ULN	3	1		
TSH <LLN WITH ALL OTHER FT3/FT4 TEST VALUES <= ULN	1	0		
TSH < LLN WITH FT3/FT4 TEST MISSING	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participants with Abnormal Laboratory Values for Liver Tests

End point title	The Number of Participants with Abnormal Laboratory Values for Liver Tests

End point description:

The Number of Participants with Abnormal Laboratory Values for Liver Tests.

End point type	Secondary

End point timeframe:

From first dose to 30 days post last dose (an average of 4 months up until a maximum of 7 months)

End point values	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	44		
Units: Participants				
ALT OR AST > 3XULN	8	5		
ALT OR AST> 5XULN	3	1		
ALT OR AST> 10XULN	0	0		
ALT OR AST > 20XULN	0	0		
TOTAL BILIRUBIN > 2XULN	1	0		
ALT/AST ELEV>3XULN;TOTAL BILIRUBIN>2XULN IN 1 DAY	0	0		
ALT/AST ELEV>3XULN;TOTAL BILIRUBIN>2XULN 30 DAYS	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Vital Sign Measurements

End point title	Vital Sign Measurements
End point description: Data not collected	
End point type	Secondary
End point timeframe: Data not collected	

End point values	Cohort 1: Relapsed/Refractory cHL - Low Risk Relapse	Cohort 2: Relapsed/Refractory cHL - Standard Risk Relapse		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[10]	0[11]		
Units: N/A				

Notes:

[10] - Data not collected

[11] - Data not collected

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

SAEs and Non-serious AEs were assessed from first dose to 30 days after last dose of study therapy (assessed for an average of 4 months up until a maximum of 7 months).

Adverse event reporting additional description:

Serious Adverse Events and Non-Serious Adverse Events represents all participants that received at least 1 dose of study medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Cohort 1: Nivo + Bv

Reporting group description:

Participants started in the induction phase and received nivolumab + brentuximab vedotin (N+Bv) for 2 cycles (6 weeks). Participants with radiographic progression, as assessed by Investigator at Cycle 2 entered follow-up. The rest of the participants continued in the induction phase and received 2 additional cycles of N+Bv study therapy (total 4 cycles = 12 weeks).
- Participants who had a complete metabolic response (CMR) by BICR after a total of 4 cycles (12 weeks) of N+Bv received an additional 2 cycles of treatment of N+Bv (for a total of 6 cycles [18 weeks]), followed by Radiation Therapy (RT) (consolidation phase).

Reporting group title	Cohort 2: Nivo + Bv

Reporting group description:

Participants started in the induction phase and received nivolumab + brentuximab vedotin (N+Bv) for 2 cycles (6 weeks). Participants with radiographic progression, as assessed by Investigator at Cycle 2 entered follow-up. The rest of the participants received 2 additional cycles of N+Bv study therapy (total 4 cycles = 12 weeks).
- Participants who had complete metabolic response (CMR), by BICR, after a total of 4 cycles (12 weeks) of N+Bv proceeded with high-dose chemotherapy followed by an autologous stem cell transplant (HDCT/ASCT) (consolidation phase). Participants with CMR had the option to receive up to 2 additional cycles of N+Bv if their HDCT/ASCT was postponed for any reason.

Reporting group title	Cohort 2: (Nivo + Bv) + (Bv + B)

Reporting group description:

Participants started in the induction phase with nivolumab and brentuximab vedotin (N+Bv) for 2 cycles (6 weeks). Those with radiographic progression at Cycle 2 entered follow-up. The rest received 2 more cycles of N+Bv (total 4 cycles, 12 weeks). Participants with complete metabolic response (CMR) after 4 cycles of N+Bv got with high-dose chemotherapy and autologous stem cell transplant (HDCT/ASCT). Those with CMR could receive up to 2 additional cycles of N+Bv if HDCT/ASCT was postponed. Participants without CMR after 4 cycles of N+Bv received 2 cycles of brentuximab and bendamustine (Bv+B). Those with CMR after 2 cycles of Bv+B got HDCT/ASCT. Participants without CMR could receive 2 more cycles of Bv+B and, if CMR was attained, got HDCT/ASCT. Those with CMR could receive up to 2 additional cycles of Bv+B if HDCT/ASCT was postponed. Participants with radiographic progression after Cycle 4 N+Bv or no CMR after final Bv+B were taken off study treatment and entered follow-up.

Reporting group title	Cohort 1: (Nivo + Bv) + (Bv + B)

Reporting group description:

Participants started in the induction phase and received nivolumab and brentuximab vedotin (N+Bv) for 2 cycles (6 weeks). Those with radiographic progression at Cycle 2 entered follow-up. The rest continued in the induction phase for 2 additional cycles of N+Bv (total 4 cycles, 12 weeks). Participants with a complete metabolic response (CMR) after 4 cycles of N+Bv received 2 more cycles of N+Bv (total 6 cycles, 18 weeks) followed by Radiation Therapy (RT) in the consolidation phase. Participants without a CMR after 4 cycles of N+Bv entered the intensification phase and received 2 cycles of brentuximab and bendamustine (Bv+B). Those who achieved CMR after these 2 cycles proceeded with RT consolidation. Participants with radiographic progression after Cycle 4 N+Bv or those who did not achieve CMR after 2 cycles of Bv+B were taken off study treatment and entered follow-up.

Serious adverse events	Cohort 1: Nivo + Bv	Cohort 2: Nivo + Bv	Cohort 2: (Nivo + Bv) + (Bv + B)
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 22 (27.27%)	11 / 33 (33.33%)	4 / 11 (36.36%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	2 / 22 (9.09%)	3 / 33 (9.09%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 22 (0.00%)	1 / 33 (3.03%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	1 / 22 (4.55%)	1 / 33 (3.03%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	1 / 1	3 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			

subjects affected / exposed	0 / 22 (0.00%)	1 / 33 (3.03%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthopnoea			
subjects affected / exposed	0 / 22 (0.00%)	1 / 33 (3.03%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary veno-occlusive disease			
subjects affected / exposed	0 / 22 (0.00%)	1 / 33 (3.03%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 22 (0.00%)	1 / 33 (3.03%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood phosphorus increased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 33 (3.03%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 22 (0.00%)	1 / 33 (3.03%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular access complication			
subjects affected / exposed	0 / 22 (0.00%)	1 / 33 (3.03%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Pericardial effusion			

subjects affected / exposed	0 / 22 (0.00%)	1 / 33 (3.03%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 22 (4.55%)	1 / 33 (3.03%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 22 (0.00%)	1 / 33 (3.03%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 33 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	0 / 11 (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
Rash			
subjects affected / exposed	1 / 22 (4.55%)	0 / 33 (0.00%)	0 / 11 (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
Renal and urinary disorders			
Acute kidney injury			

subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	0 / 11 (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			
Synovial cyst			
subjects affected / exposed	0 / 22 (0.00%)	1 / 33 (3.03%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	0 / 11 (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			
Sepsis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 33 (3.03%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	0 / 11 (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

Serious adverse events	Cohort 1: (Nivo + Bv) + (Bv + B)		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	3 / 6 (50.00%)			
occurrences causally related to treatment / all	4 / 5			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Anaphylactic reaction				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypersensitivity				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Hypoxia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Orthopnoea				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary veno-occlusive disease				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood phosphorus increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular access complication			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Enteritis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Stomatitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Rash			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Synovial cyst			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pain in extremity			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Sepsis			

subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Otitis media				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

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

Non-serious adverse events	Cohort 1: Nivo + Bv	Cohort 2: Nivo + Bv	Cohort 2: (Nivo + Bv) + (Bv + B)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 22 (81.82%)	33 / 33 (100.00%)	11 / 11 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 22 (0.00%)	3 / 33 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	4	1
Hypotension			
subjects affected / exposed	0 / 22 (0.00%)	4 / 33 (12.12%)	1 / 11 (9.09%)
occurrences (all)	0	4	1
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Asthenia			
subjects affected / exposed	4 / 22 (18.18%)	1 / 33 (3.03%)	1 / 11 (9.09%)
occurrences (all)	6	1	2
Fatigue			
subjects affected / exposed	4 / 22 (18.18%)	7 / 33 (21.21%)	1 / 11 (9.09%)
occurrences (all)	4	12	1
Oedema peripheral			
subjects affected / exposed	0 / 22 (0.00%)	2 / 33 (6.06%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Non-cardiac chest pain			

subjects affected / exposed	1 / 22 (4.55%)	1 / 33 (3.03%)	1 / 11 (9.09%)
occurrences (all)	1	2	1
Mucosal inflammation			
subjects affected / exposed	1 / 22 (4.55%)	10 / 33 (30.30%)	5 / 11 (45.45%)
occurrences (all)	1	11	6
Influenza like illness			
subjects affected / exposed	0 / 22 (0.00%)	1 / 33 (3.03%)	1 / 11 (9.09%)
occurrences (all)	0	1	4
Gait disturbance			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 22 (4.55%)	17 / 33 (51.52%)	5 / 11 (45.45%)
occurrences (all)	1	22	8
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 22 (4.55%)	6 / 33 (18.18%)	3 / 11 (27.27%)
occurrences (all)	1	6	3
Infusion related hypersensitivity reaction			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Drug hypersensitivity			
subjects affected / exposed	1 / 22 (4.55%)	2 / 33 (6.06%)	1 / 11 (9.09%)
occurrences (all)	1	2	2
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	2 / 22 (9.09%)	0 / 33 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Pharyngeal inflammation			
subjects affected / exposed	0 / 22 (0.00%)	2 / 33 (6.06%)	0 / 11 (0.00%)
occurrences (all)	0	2	0

Oropharyngeal pain			
subjects affected / exposed	5 / 22 (22.73%)	4 / 33 (12.12%)	1 / 11 (9.09%)
occurrences (all)	5	5	1
Nasal congestion			
subjects affected / exposed	1 / 22 (4.55%)	3 / 33 (9.09%)	0 / 11 (0.00%)
occurrences (all)	1	3	0
Cough			
subjects affected / exposed	2 / 22 (9.09%)	8 / 33 (24.24%)	0 / 11 (0.00%)
occurrences (all)	2	9	0
Dyspnoea			
subjects affected / exposed	1 / 22 (4.55%)	3 / 33 (9.09%)	0 / 11 (0.00%)
occurrences (all)	1	3	0
Epistaxis			
subjects affected / exposed	3 / 22 (13.64%)	4 / 33 (12.12%)	1 / 11 (9.09%)
occurrences (all)	3	6	1
Hypoxia			
subjects affected / exposed	0 / 22 (0.00%)	3 / 33 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	5	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 22 (0.00%)	3 / 33 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	3	0
Anxiety			
subjects affected / exposed	1 / 22 (4.55%)	1 / 33 (3.03%)	1 / 11 (9.09%)
occurrences (all)	1	1	1
Agitation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	5 / 22 (22.73%)	2 / 33 (6.06%)	3 / 11 (27.27%)
occurrences (all)	6	2	4
Amylase increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	2
Aspartate aminotransferase increased			

subjects affected / exposed	3 / 22 (13.64%)	3 / 33 (9.09%)	2 / 11 (18.18%)
occurrences (all)	6	5	3
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 33 (3.03%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Blood bilirubin increased			
subjects affected / exposed	2 / 22 (9.09%)	0 / 33 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Body temperature increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Heart rate increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Lipase decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Lipase increased			
subjects affected / exposed	2 / 22 (9.09%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	2
Lymphocyte count decreased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 33 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Neutrophil count decreased			
subjects affected / exposed	1 / 22 (4.55%)	2 / 33 (6.06%)	0 / 11 (0.00%)
occurrences (all)	2	2	0
Platelet count decreased			

subjects affected / exposed	0 / 22 (0.00%)	4 / 33 (12.12%)	2 / 11 (18.18%)
occurrences (all)	0	4	2
Weight decreased			
subjects affected / exposed	1 / 22 (4.55%)	2 / 33 (6.06%)	1 / 11 (9.09%)
occurrences (all)	1	2	1
White blood cell count decreased			
subjects affected / exposed	1 / 22 (4.55%)	2 / 33 (6.06%)	2 / 11 (18.18%)
occurrences (all)	1	4	2
Injury, poisoning and procedural complications			
Radiation skin injury			
subjects affected / exposed	1 / 22 (4.55%)	0 / 33 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Radiation associated pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Post procedural complication			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction			
subjects affected / exposed	4 / 22 (18.18%)	4 / 33 (12.12%)	5 / 11 (45.45%)
occurrences (all)	4	4	9
Vascular access site pruritus			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Cardiac disorders			
Tachycardia			
subjects affected / exposed	2 / 22 (9.09%)	1 / 33 (3.03%)	0 / 11 (0.00%)
occurrences (all)	2	1	0
Sinus bradycardia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
Nervous system disorders			

Presyncope			
subjects affected / exposed	1 / 22 (4.55%)	2 / 33 (6.06%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
Disturbance in attention			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	1 / 22 (4.55%)	4 / 33 (12.12%)	1 / 11 (9.09%)
occurrences (all)	1	5	1
Headache			
subjects affected / exposed	10 / 22 (45.45%)	6 / 33 (18.18%)	4 / 11 (36.36%)
occurrences (all)	12	7	7
Somnolence			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 22 (4.55%)	6 / 33 (18.18%)	3 / 11 (27.27%)
occurrences (all)	1	6	3
Febrile neutropenia			
subjects affected / exposed	0 / 22 (0.00%)	5 / 33 (15.15%)	4 / 11 (36.36%)
occurrences (all)	0	5	4
Thrombocytopenia			
subjects affected / exposed	1 / 22 (4.55%)	4 / 33 (12.12%)	2 / 11 (18.18%)
occurrences (all)	1	5	2
Neutropenia			
subjects affected / exposed	1 / 22 (4.55%)	2 / 33 (6.06%)	2 / 11 (18.18%)
occurrences (all)	1	2	2
Leukopenia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye pain			
subjects affected / exposed	0 / 22 (0.00%)	2 / 33 (6.06%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			

Abdominal pain upper			
subjects affected / exposed	1 / 22 (4.55%)	7 / 33 (21.21%)	1 / 11 (9.09%)
occurrences (all)	3	7	2
Abdominal pain			
subjects affected / exposed	1 / 22 (4.55%)	9 / 33 (27.27%)	4 / 11 (36.36%)
occurrences (all)	1	13	7
Vomiting			
subjects affected / exposed	2 / 22 (9.09%)	7 / 33 (21.21%)	6 / 11 (54.55%)
occurrences (all)	2	11	22
Stomatitis			
subjects affected / exposed	1 / 22 (4.55%)	7 / 33 (21.21%)	1 / 11 (9.09%)
occurrences (all)	1	7	1
Paraesthesia oral			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Oral pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	9 / 22 (40.91%)	19 / 33 (57.58%)	11 / 11 (100.00%)
occurrences (all)	11	32	22
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 22 (4.55%)	1 / 33 (3.03%)	1 / 11 (9.09%)
occurrences (all)	1	1	1
Enterocolitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Diarrhoea			
subjects affected / exposed	5 / 22 (22.73%)	13 / 33 (39.39%)	4 / 11 (36.36%)
occurrences (all)	6	24	8
Constipation			
subjects affected / exposed	4 / 22 (18.18%)	3 / 33 (9.09%)	1 / 11 (9.09%)
occurrences (all)	5	4	1

Coating in mouth			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 22 (4.55%)	3 / 33 (9.09%)	2 / 11 (18.18%)
occurrences (all)	1	3	3
Dry skin			
subjects affected / exposed	0 / 22 (0.00%)	3 / 33 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	4	1
Dermatitis allergic			
subjects affected / exposed	0 / 22 (0.00%)	3 / 33 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	3	1
Alopecia			
subjects affected / exposed	3 / 22 (13.64%)	5 / 33 (15.15%)	1 / 11 (9.09%)
occurrences (all)	3	5	1
Acne			
subjects affected / exposed	2 / 22 (9.09%)	0 / 33 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Pruritus			
subjects affected / exposed	4 / 22 (18.18%)	2 / 33 (6.06%)	3 / 11 (27.27%)
occurrences (all)	5	2	4
Night sweats			
subjects affected / exposed	0 / 22 (0.00%)	1 / 33 (3.03%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Hyperhidrosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Rash maculo-papular			
subjects affected / exposed	2 / 22 (9.09%)	6 / 33 (18.18%)	2 / 11 (18.18%)
occurrences (all)	3	8	4
Rash			
subjects affected / exposed	0 / 22 (0.00%)	3 / 33 (9.09%)	4 / 11 (36.36%)
occurrences (all)	0	3	6
Purpura			

subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Psoriasis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Haematuria			
subjects affected / exposed	0 / 22 (0.00%)	2 / 33 (6.06%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 22 (4.55%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Hyperthyroidism			
subjects affected / exposed	2 / 22 (9.09%)	0 / 33 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 22 (0.00%)	2 / 33 (6.06%)	3 / 11 (27.27%)
occurrences (all)	0	4	3
Back pain			
subjects affected / exposed	1 / 22 (4.55%)	5 / 33 (15.15%)	2 / 11 (18.18%)
occurrences (all)	1	7	2
Bone pain			
subjects affected / exposed	0 / 22 (0.00%)	4 / 33 (12.12%)	1 / 11 (9.09%)
occurrences (all)	0	4	1
Flank pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Groin pain			

subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	0 / 22 (0.00%)	2 / 33 (6.06%)	1 / 11 (9.09%)
occurrences (all)	0	2	1
Pain in extremity			
subjects affected / exposed	3 / 22 (13.64%)	2 / 33 (6.06%)	2 / 11 (18.18%)
occurrences (all)	4	2	2
Pain in jaw			
subjects affected / exposed	1 / 22 (4.55%)	2 / 33 (6.06%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Device related infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Epstein-Barr virus infection reactivation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 22 (4.55%)	1 / 33 (3.03%)	1 / 11 (9.09%)
occurrences (all)	3	1	1
Otitis media			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 22 (0.00%)	3 / 33 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	4	1
Rhinitis			

subjects affected / exposed	1 / 22 (4.55%)	3 / 33 (9.09%)	0 / 11 (0.00%)
occurrences (all)	1	3	0
Staphylococcal infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	2 / 22 (9.09%)	2 / 33 (6.06%)	2 / 11 (18.18%)
occurrences (all)	2	3	2
Urinary tract infection			
subjects affected / exposed	2 / 22 (9.09%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 22 (0.00%)	8 / 33 (24.24%)	1 / 11 (9.09%)
occurrences (all)	0	9	1
Hyperglycaemia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Hypochloraemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Hypoalbuminaemia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 33 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 33 (3.03%)	1 / 11 (9.09%)
occurrences (all)	0	1	4
Hypokalaemia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	2
Hyponatraemia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 33 (0.00%)	2 / 11 (18.18%)
occurrences (all)	1	0	2
Hypophosphataemia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1

Hypouricaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 33 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Hypocalcaemia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 33 (3.03%)	1 / 11 (9.09%)
occurrences (all)	0	1	1

Non-serious adverse events	Cohort 1: (Nivo + Bv) + (Bv + B)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Asthenia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	7		
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Mucosal inflammation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

Influenza like illness			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Gait disturbance			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	3		
Infusion related hypersensitivity reaction			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Drug hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pharyngeal inflammation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Nasal congestion			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Agitation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	3		
Amylase increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	4		
Blood alkaline phosphatase increased			

subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Blood bilirubin increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Body temperature increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Gamma-glutamyltransferase increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Heart rate increased				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
International normalised ratio increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Lipase decreased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Lipase increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Lymphocyte count decreased				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Neutrophil count decreased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Platelet count decreased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Weight decreased				

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
White blood cell count decreased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Radiation skin injury			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Radiation associated pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Procedural pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Post procedural complication			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Infusion related reaction			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Vascular access site pruritus			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Sinus bradycardia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Presyncope			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Disturbance in attention			

subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Somnolence subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 2 / 6 (33.33%) 2 1 / 6 (16.67%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Febrile neutropenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 2 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1		
Eye disorders Eye pain subjects affected / exposed occurrences (all)	 0 / 6 (0.00%) 0		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) Abdominal pain	 1 / 6 (16.67%) 1		

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	4		
Stomatitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Paraesthesia oral			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Oral pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	5		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Enterocolitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Coating in mouth			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			

Erythema				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Dry skin				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Dermatitis allergic				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	2			
Alopecia				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Acne				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Pruritus				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Night sweats				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Hyperhidrosis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Rash maculo-papular				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Rash				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Purpura				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Psoriasis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			

Urticaria			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hyperthyroidism			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Back pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Flank pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Groin pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

Pain in extremity			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Pain in jaw			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Device related infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Epstein-Barr virus infection reactivation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Otitis media			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Staphylococcal infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hyperglycaemia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Hypochloraemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hyperuricaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypouricaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypocalcaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 March 2017	Per Health Authority recommendations (eg,: Add additional Safety Assessments to provide more frequent safety monitoring for this patient population during Induction Phase, update an optional lab sample and revise Section 2 Tables-due to new Safety Labs, add futility rule for R2 Cohort, amend inclusion criteria language from Direct to Total Bilirubin, simplify nivolumab dose delay criteria language and formatting, include guidance for live vaccinations, and clarify the need to follow local guidelines for opportunistic infection prophylaxis). Additionally, clarifying: R1 Consolidation Therapy may be inclusive of all types of Radiation Therapy (RT) per institutional guidelines, adds up to 2 additional cycles of Bv+B with BMS MM approval for R2 cohort consolidation therapy delays (to be consistent with the approach taken for Induction Phase, N+Bv), deletes wording "for biomarker analysis" as the biopsy isrequired per Standard of Care and provided to BMS for histologic confirmation of disease and biomarker testing, modification of requirements for FDG-PET at screening and during treatment in alignment with Standard of Care practices, and LYRIC 2016 criteria will be added as an exploratory endpoint for future data analysis according to refinement of LUGANO classification in the era of immunomodulatory therapy.
26 March 2021	The response assessment by investigators using Lugano 2014 response criteria was added as a secondary endpoint to allow for a comprehensive interpretation of the study data. Guidance for collection and submission of tumor assessments was added to support the evaluation of this new secondary endpoint. Contraception requirements for female participants of child bearing potential were modified to properly align with Nivolumab clinical research standard guidelines and brentuximab label. Other minor edits were made, as described in the Summary of Key Changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported