Clinical trial results:
A pivotal study of SGN-35 in treatment of patients with relapsed or refractory systemic anaplastic large cell lymphoma (ALCL)

Summary

EudraCT number	2008-006035-12
Trial protocol	BE DE IT FR GB
Global end of trial date	06 June 2016

Results information

Result version number	v1 (current)
This version publication date	05 January 2017
First version publication date	05 January 2017

Trial information

Trial identification

Sponsor protocol code	SG035-0004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00866047
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Seattle Genetics, Inc.
Sponsor organisation address	21823 30th Drive SE, Bothell, United States, 98021
Public contact	Chief Medical Officer, Seattle Genetics, Inc. , 1 855 473-2436, medinfo@seagen.com
Scientific contact	Chief Medical Officer, Seattle Genetics, Inc. , 1 855 473-2436, medinfo@seagen.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 October 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 August 2010
Global end of trial reached?	Yes
Global end of trial date	06 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the antitumor efficacy of single-agent SGN-35 (1.8 mg/kg administered intravenously every 3 weeks) as measured by the overall objective response rate in patients with relapsed or refractory systemic anaplastic large cell lymphoma following front-line chemotherapy (CHOP or equivalent)

Protection of trial subjects:

The protocol for this study was designed in accordance with the general ethical principles outlined in the Declaration of Helsinki. The conduct of all aspects of the study, including methods for obtaining informed consent, were also in accordance with principles enunciated in the declaration, the International Conference on Harmonisation (ICH) Good Clinical Practices (GCP), and applicable Food and Drug Administration (FDA) regulations/guidelines set forth in Title 21 CFR Parts 11, 50, 54, 56, and 312. The consent form approved by each IRB/IEC included all elements required by the applicable regional laws and regulations, including a statement that Seattle Genetics, Inc. and authorities had access to patient records. Consent was obtained from all patients before any protocol-required procedures were performed, including any procedure not part of normal patient care.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 March 2009
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	United Kingdom: 3
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	United States: 43
Worldwide total number of subjects	58
EEA total number of subjects	12

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	4
Adults (18-64 years)	45
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Enrollment period: March 2009 - May 2010

Pre-assignment

Screening details:

Patients with relapsed or refractory systemic ALCL who have previously received front line chemotherapy.

Period 1

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

Arms

Arm title	Brentuximab vedotin

Arm description:

Brentuximab vedotin 1.8 mg/kg every 3 weeks by IV infusion

Arm type	Experimental
Investigational medicinal product name	Brentuximab vedotin
Investigational medicinal product code	
Other name	ADCETRIS, SGN-35
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Brentuximab vedotin 1.8 mg/kg every 3 weeks by IV infusion

Number of subjects in period 1	Brentuximab vedotin
Started	58
Completed	10
Not completed	48
Adverse event, serious fatal	6
Physician decision	14
Patient decision	5
Adverse event, non-fatal	10
Progressive disease	13

Baseline characteristics

Reporting groups

Reporting group title	Treatment

Reporting group description: -

Reporting group values	Treatment	Total	
Number of subjects	58	58	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	4	4	
Adults (18-64 years)	45	45	
From 65-84 years	9	9	
85 years and over	0	0	
Age continuous Units: years			
median	52		
full range (min-max)	14 to 76	-	
Gender categorical Units: Subjects			
Female	25	25	
Male	33	33	
Race Units: Subjects			
Asian	1	1	
Black or African American	7	7	
White	48	48	
Other	2	2	
Eastern Cooperative Oncology Group Performance Status			
0 = Normal activity 1 = Symptoms but ambulatory 2 = In bed <50% of the time 3 = In bed >50% of the time 4 = 100% bedridden 5 = Dead			
Units: Subjects			
Zero	19	19	
One	38	38	
Two to Five	1	1	
ALK Status Units: Subjects			
Positive	16	16	
Negative	42	42	

End points

End points reporting groups

Reporting group title	Brentuximab vedotin

Reporting group description:

Brentuximab vedotin 1.8 mg/kg every 3 weeks by IV infusion

Primary: Objective Response Rate by Independent Review Group

End point title	Objective Response Rate by Independent Review Group[1]

End point description:

Percentage of participants who achieved a best response of complete remission (CR, disappearance of all evidence of disease) or partial remission (PR, regression of greater than or equal to 50% of measurable disease and no new sites) per Cheson 2007 Revised Response Criteria for Malignant Lymphoma.

End point type	Primary

End point timeframe:

Up to 12 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The primary efficacy hypothesis was specified. H0: ORR <20% versus Ha: ORR ≥20%

End point values	Brentuximab vedotin			
Subject group type	Reporting group			
Number of subjects analysed	58[2]			
Units: Percent of Participants				
number (confidence interval 95%)				
ORR by Independent Review Group	86 (74.6 to 93.9)			

Notes:

[2] - The primary efficacy hypothesis was specified. H0: ORR <20% versus Ha: ORR ≥20%

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Remission Rate by Independent Review Group

End point title	Complete Remission Rate by Independent Review Group

End point description:

Percentage of participants who achieved a best response of CR (disappearance of all evidence of disease) per Cheson 2007 Revised Response Criteria for Malignant Lymphoma

End point type	Secondary

End point timeframe:

up to 12 months

End point values	Brentuximab vedotin			
Subject group type	Reporting group			
Number of subjects analysed	58[3]			
Units: Percent of Participants				
number (confidence interval 95%)				
CR Rate by Independent Review Group	59 (44.9 to 71.4)			

Notes:

[3] - Intention to treat

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Objective Response by Kaplan-Meier Analysis

End point title	Duration of Objective Response by Kaplan-Meier Analysis

End point description:

Duration of objective response (CR + PR) by independent review group, defined as time of initial response until disease progression or death

End point type	Secondary

End point timeframe:

up to approximately 4 years

End point values	Brentuximab vedotin			
Subject group type	Reporting group			
Number of subjects analysed	50[4]			
Units: Months				
number (confidence interval 95%)				
Duration of OR by Kaplan-Meier Analysis	13.2 (5.7 to 26.3)			

Notes:

[4] - Participants with objective response among the intention to treat population

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Objective Response in Participants with Complete Remission by Kaplan-Meier Analysis

End point title	Duration of Objective Response in Participants with Complete Remission by Kaplan-Meier Analysis

End point description:

Duration of response from start of first objective tumor response (CR or PR) by independent review group to disease progression or death due to any cause in participants with CR

End point type	Secondary

End point timeframe:

up to approximately 4 years

End point values	Brentuximab vedotin			
Subject group type	Reporting group			
Number of subjects analysed	34[5]			
Units: Months				
number (confidence interval 95%)				
Duration of OR in Participants with CR	26.3 (13.2 to 999)			

Notes:

[5] - Participants w/CR (ITT population)
999 = NA; insufficient number of events to estimate upper bound

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival by Kaplan-Meier Analysis

End point title	Progression-free Survival by Kaplan-Meier Analysis

End point description:

Time from start of study treatment to disease progression per independent review group or death due to any cause

End point type	Secondary

End point timeframe:

up to approximately 4 years

End point values	Brentuximab vedotin			
Subject group type	Reporting group			
Number of subjects analysed	58			
Units: Months				
number (confidence interval 95%)				
Progression-free Survival by Kaplan-Meier Analysis	14.6 (6.9 to 20.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Time from start of study treatment to date of death due to any cause

End point type	Secondary

End point timeframe:

up to approximately 7 years

End point values	Brentuximab vedotin			
Subject group type	Reporting group			
Number of subjects analysed	58[6]			
Units: Months				
number (confidence interval 95%)				
Overall Survival	999 (21.3 to 999)			

Notes:

[6] - Intention to treat
999 = NA; insufficient number of events to estimate

Statistical analyses

No statistical analyses for this end point

Secondary: Adverse Events by Severity, Seriousness, and Relationship to Treatment

End point title	Adverse Events by Severity, Seriousness, and Relationship to Treatment

End point description:

Counts of participants who had adverse events or treatment-emergent adverse events (TEAE, defined as newly occurring or worsening after first dose). Serious adverse events are reported from the time of informed consent. National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE version 3.0) were used to assess severity (1=mild, 2=moderate, 3=severe, 4=life threatening/disabling, 5=death). Relatedness to study drug was assessed by the investigator (Yes/No). Participants with multiple occurrences of an adverse event within a category are counted once within the category.

End point type	Secondary

End point timeframe:

up to 12 months

End point values	Brentuximab vedotin			
Subject group type	Reporting group			
Number of subjects analysed	58[7]			
Units: Participants				
number (not applicable)				
Any TEAE	58			
TEAE related to study drug	53			
TEAE with severity grade >/=3	36			
Serious adverse event	25			
Serious adverse event related to study drug	11			
Discontinued treatment due to adverse event	16			

Notes:

[7] - All participants who received treatment

Statistical analyses

No statistical analyses for this end point

Secondary: Hematology Laboratory Abnormalities >/= Grade 3

End point title	Hematology Laboratory Abnormalities >/= Grade 3

End point description:

Counts of study participants with pose-baseline hematology laboratory abnormalities of Grade 3 or greater per NCI CTCAE version 3.0. Participants with multiple occurrences of a laboratory abnormality within a category are counted once in that category.

End point type	Secondary

End point timeframe:

up to 12 months

End point values	Brentuximab vedotin			
Subject group type	Reporting group			
Number of subjects analysed	58[8]			
Units: Participants				
number (not applicable)				
Any >/= Grade 3 hematology laboratory abnormality	17			
Leukocytes (low)	3			
Lymphocytes (low)	10			
Neutrophils (low)	7			
Platelets (low)	3			

Notes:

[8] - All participants who received treatment

Statistical analyses

No statistical analyses for this end point

Secondary: Chemistry Laboratory Abnormalities >/= Grade 3

End point title	Chemistry Laboratory Abnormalities >/= Grade 3

End point description:

Counts of study participants with post-baseline chemistry laboratory abnormalities of Grade 3 or greater per NCI CTCAE version 3.0. Participants with multiple occurrences of a laboratory abnormality within a category are counted once in that category.

End point type	Secondary

End point timeframe:

up to 12 months

End point values	Brentuximab vedotin			
Subject group type	Reporting group			
Number of subjects analysed	58[9]			
Units: Participants				
number (not applicable)				
Any >/= Grade 3 chemistry laboratory abnormality	13			
Aspartate Aminotransferase (High)	1			
Calcium (Low)	3			
Glucose (High)	4			
Potassium (Low)	1			
Sodium (Low)	1			
Urate (High)	3			

Notes:

[9] - All participants who received treatment

Statistical analyses

No statistical analyses for this end point

Other pre-specified: B Symptom Resolution

End point title	B Symptom Resolution

End point description:

Percentage of participants with lymphoma-related symptoms (B symptoms: fever, night sweats, or weight loss > 10%) at baseline who achieved resolution of all B symptoms at any time during the treatment period.

End point type	Other pre-specified

End point timeframe:

up to 12 months

End point values	Brentuximab vedotin			
Subject group type	Reporting group			
Number of subjects analysed	17[10]			
Units: Percent of Participants				
number (confidence interval 95%)				
B Symptom Resolution	82 (56.6 to 96.2)			

Notes:

[10] - Participants with B symptoms at baseline

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
up to 12 months	
Adverse event reporting additional description:	
Treatment-emergent adverse events (TEAE) defined as newly occurring (not present at baseline) or worsening after first dose of investigational product	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	13

Reporting groups	
Reporting group title	Brentuximab vedotin
Reporting group description:	
Brentuximab vedotin	

Serious adverse events	Brentuximab vedotin		
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 58 (43.10%)		
number of deaths (all causes)	25		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anaplastic large cell lymphoma T- and null-cell types recurrent			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 3		
Mycosis fungoides			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tumour flare			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Generalised oedema			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sudden death			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary oedema			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Tracheal disorder			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Psychiatric disorders			
Mental status changes			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Lower limb fracture			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Arrhythmia supraventricular			
subjects affected / exposed	2 / 58 (3.45%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block complete			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bradycardia			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Demyelinating polyneuropathy			

subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Encephalopathy				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemorrhage intracranial				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neuralgia				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral motor neuropathy				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral sensory neuropathy				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal cord compression				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				

subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Retinal vein occlusion				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Rash papular				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal Failure Acute			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Musculoskeletal and connective tissue disorders			
Myositis			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pain in extremity			
subjects affected / exposed	2 / 58 (3.45%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocarditis staphylococcal			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis viral			

subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Klebsiella bacteraemia				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	2 / 58 (3.45%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Superinfection bacterial				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	2 / 58 (3.45%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Decreased appetite				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fluid overload				
subjects affected / exposed	1 / 58 (1.72%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				

subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tumour lysis syndrome			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Brentuximab vedotin		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	58 / 58 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anaplastic large cell lymphoma T- and null-cell types recurrent			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	3		
Tumour flare			
subjects affected / exposed	4 / 58 (6.90%)		
occurrences (all)	4		
Vascular disorders			
Hot flush			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	4		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	5		
Chills			
subjects affected / exposed	8 / 58 (13.79%)		
occurrences (all)	11		
Fatigue			
subjects affected / exposed	22 / 58 (37.93%)		
occurrences (all)	27		
Oedema peripheral			

subjects affected / exposed	8 / 58 (13.79%)		
occurrences (all)	9		
Pain			
subjects affected / exposed	6 / 58 (10.34%)		
occurrences (all)	7		
Pyrexia			
subjects affected / exposed	20 / 58 (34.48%)		
occurrences (all)	25		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 58 (17.24%)		
occurrences (all)	10		
Dyspnoea			
subjects affected / exposed	11 / 58 (18.97%)		
occurrences (all)	12		
Oropharyngeal pain			
subjects affected / exposed	4 / 58 (6.90%)		
occurrences (all)	4		
Productive cough			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	3		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 58 (6.90%)		
occurrences (all)	4		
Confusional state			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	3		
Depression			
subjects affected / exposed	4 / 58 (6.90%)		
occurrences (all)	4		
Insomnia			
subjects affected / exposed	9 / 58 (15.52%)		
occurrences (all)	10		
Investigations			

Weight decreased subjects affected / exposed occurrences (all)	8 / 58 (13.79%) 10		
Injury, poisoning and procedural complications Excoriation subjects affected / exposed occurrences (all)	3 / 58 (5.17%) 3		
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	3 / 58 (5.17%) 3		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	9 / 58 (15.52%) 9		
Headache subjects affected / exposed occurrences (all)	11 / 58 (18.97%) 15		
Memory impairment subjects affected / exposed occurrences (all)	3 / 58 (5.17%) 3		
Neuralgia subjects affected / exposed occurrences (all)	3 / 58 (5.17%) 5		
Paraesthesia subjects affected / exposed occurrences (all)	5 / 58 (8.62%) 6		
Peripheral motor neuropathy subjects affected / exposed occurrences (all)	3 / 58 (5.17%) 4		
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	24 / 58 (41.38%) 43		
Blood and lymphatic system disorders Anaemia			

subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	6		
Lymphadenopathy			
subjects affected / exposed	6 / 58 (10.34%)		
occurrences (all)	9		
Neutropenia			
subjects affected / exposed	11 / 58 (18.97%)		
occurrences (all)	14		
Thrombocytopenia			
subjects affected / exposed	8 / 58 (13.79%)		
occurrences (all)	10		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	3		
Abdominal pain			
subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	5		
Constipation			
subjects affected / exposed	12 / 58 (20.69%)		
occurrences (all)	12		
Diarrhoea			
subjects affected / exposed	16 / 58 (27.59%)		
occurrences (all)	19		
Dyspepsia			
subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	5		
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	3		
Haemorrhoids			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	3		
Nausea			
subjects affected / exposed	23 / 58 (39.66%)		
occurrences (all)	28		

Oral pain			
subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	5		
Vomiting			
subjects affected / exposed	9 / 58 (15.52%)		
occurrences (all)	11		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	8 / 58 (13.79%)		
occurrences (all)	8		
Dermatitis			
subjects affected / exposed	4 / 58 (6.90%)		
occurrences (all)	5		
Dry skin			
subjects affected / exposed	6 / 58 (10.34%)		
occurrences (all)	10		
Night sweats			
subjects affected / exposed	4 / 58 (6.90%)		
occurrences (all)	4		
Pruritus			
subjects affected / exposed	11 / 58 (18.97%)		
occurrences (all)	12		
Rash			
subjects affected / exposed	14 / 58 (24.14%)		
occurrences (all)	23		
Rash pruritic			
subjects affected / exposed	4 / 58 (6.90%)		
occurrences (all)	6		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	7		
Back pain			
subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	5		
Groin pain			

subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	5		
Muscle spasms			
subjects affected / exposed	8 / 58 (13.79%)		
occurrences (all)	9		
Musculoskeletal pain			
subjects affected / exposed	4 / 58 (6.90%)		
occurrences (all)	4		
Myalgia			
subjects affected / exposed	9 / 58 (15.52%)		
occurrences (all)	10		
Neck pain			
subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	5		
Pain in extremity			
subjects affected / exposed	6 / 58 (10.34%)		
occurrences (all)	6		
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	5		
Folliculitis			
subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	6		
Nasopharyngitis			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	4		
Sinusitis			
subjects affected / exposed	4 / 58 (6.90%)		
occurrences (all)	4		
Upper respiratory tract infection			
subjects affected / exposed	11 / 58 (18.97%)		
occurrences (all)	14		
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	8 / 58 (13.79%)		
occurrences (all)	8		
Dehydration			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	3		
Hyperglycaemia			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	3		
Hypokalaemia			
subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	5		
Hypomagnesaemia			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 December 2008	Increased sample size from 30 to 55 patients. CD30 assessment was to be centrally confirmed. Explained why no formal interim efficacy and/or futility analyses were planned. Specified how patients who do not have the correct histological cancer type will be handled in the analysis.
13 February 2009	Allowed patients 12 years or older to enroll at sites in Canada. Refined entry criteria to ensure that all patients have active relapsed or refractory systemic ALCL at study entry. Increased the time since immunotherapy before study entry to ensure any therapeutic benefit is realized. Added descriptions of interim analyses that may be conducted for scientific meetings and/or regulatory submissions.
16 November 2009	Allowed patients who have previously received treatment with non-anthracycline or anthracendione-based multi-agent chemotherapy regimens to enroll in the study provided they had received a frontline multi-agent chemotherapy regimen with curative intent. Removed the requirement for central pathology review to confirm CD30-positivity at the time of enrollment. Slides were to be submitted for central review prior to initiation of treatment with brentuximab vedotin. Clarified that prior treatments must have been completed in the protocol-specified timeframe unless patient was progressing on therapy. Updated baseline platelet and bilirubin requirements for patients with bone marrow and hepatic lymphoma involvement. Clarified that patients with active infections Grade 3 or higher are not eligible for the study.
03 October 2011	Added a section to the protocol regarding the management of suspected progressive multifocal leukoencephalopathy (PML).
30 January 2012	Revised the timing of assessments during the study follow-up period.
10 October 2013	Removed the requirement for CT scanning during the long-term follow-up period. CT scans will only be done if progression is suspected based on clinical signs and symptoms. Added a long-term follow-up questionnaire to be taken by patients who remain in remission.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/22614995