Brentuximab Vedotin in Transplant-Naïve Patients with Relapsed or Refractory Hodgkin Lymphoma: Analysis of Two Phase I Studies

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ABSTRACT

Background. Brentuximab vedotin is an antibody-drug conjugate designed to selectively deliver monomethyl auristatin E, a microtubule-disrupting agent, to CD30-expressing cells. Brentuximab vedotin induces durable objective responses in patients with relapsed or refractory Hodgkin lymphoma (HL) after autologous stem cell transplantation (ASCT). The objective of this post-hoc analysis was to characterize the safety and efficacy of brentuximab vedotin for patients with relapsed or refractory HL who relapsed or were ineligible for ASCT.

Methods. This case series included 20 transplant-naïve patients who were enrolled in two phase I multicenter studies. Patients received brentuximab vedotin intravenously every 3 weeks or every week for 3 out of 4 weeks.

Results. The majority of patients were transplant-naïve because of chemorefractory disease. Median age was 31.5

years (range, 12–87 years). Treatment-emergent adverse events in >20% of patients were peripheral neuropathy, fatigue, nausea, pyrexia, diarrhea, weight decreased, anemia, back pain, decreased appetite, night sweats, and vomiting; most events were grade 1 or 2. Six patients obtained objective responses: two complete remissions and four partial remissions. Median duration of response was not met; censored durations ranged from >6.8 to >13.8 months. Three of six responders subsequently received ASCT.

Conclusion. Brentuximab vedotin was associated with manageable adverse events in transplant-naïve patients with relapsed or refractory HL. The objective responses observed demonstrate that antitumor activity is not limited to patients who received brentuximab vedotin after ASCT. The promising activity observed in this population warrants further study. *The Oncologist* 2012;17:1073–1080

INTRODUCTION

Despite modern treatment regimens, advanced Hodgkin lymphoma (HL) recurs after primary therapy in up to 40%

of patients [1–3]. Based on two prospective randomized phase III clinical trials [4, 5], the standard management for patients with relapsed or refractory HL is salvage chemo-

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therapy followed by high-dose chemotherapy with autologous stem cell rescue in the subset of patients with chemoresponsive disease. Interestingly, this consolidative treatment approach results in prolonged progression-free survival (PFS) but has not shown a significant overall survival advantage [4–6].

Multiple clinical trials evaluating different salvage chemotherapy regimens prior to autologous stem cell transplantation (ASCT) have been published; however, because of the lack of direct comparisons, there is no consensus on a standard second-line regimen [7–11]. Cumulatively, data from phase II clinical trials of multiagent chemotherapy deliver somewhat equivocal results, with overall response rates of approximately 75% and complete remission (CR) rates of 40% [12]. These multiagent chemotherapy regimens are associated with hematologic toxicities and often require inpatient admission for administration. Complicating interpretation of these data is the fact that these trials enrolled a mixed population of patients, including those with relapsed disease as well as patients with primary refractory HL, which confers a particularly poor prognosis and is less chemoresponsive.

There is also no consensus on additional salvage therapy for the approximately 30% of patients who fail to achieve a remission with second-line multiagent salvage chemotherapy, and the inability to secure a remission frequently prevents patients from receiving high-dose chemotherapy and ASCT [13]. In addition to patients with chemorefractory disease, there are populations who are not candidates for ASCT for a variety of reasons, including advanced age, comorbidities, personal preference, religious beliefs, and lack of access to centers with the ability to deliver ASCT. Patients with chemorefractory disease following salvage therapy and those who are not candidates for ASCT have a very poor prognosis and the disease is considered incurable. Thus, new strategies are required to address the unmet need in these populations.

Brentuximab vedotin (Adcetris®, Seattle Genetics, Inc., Bothell, WA), an antibody drug conjugate, is an anti-CD30 monoclonal antibody conjugated by a protease-cleavable linker to the microtubule-disrupting agent, monomethyl auristatin E (MMAE). Binding of brentuximab vedotin to CD30 on the cell surface initiates internalization of the antibody drug conjugate CD30 complex, which then traffics to the lysosomal compartment, releasing MMAE via proteolytic cleavage [14]. Binding of MMAE to tubulin disrupts the microtubule network, induces cell cycle arrest, and results in apoptotic death of the CD30-expressing tumor cell [15].

Two phase I dose-escalation studies of brentuximab vedotin were conducted in patients with relapsed/refractory CD30-positive malignancies. SG035–0001 was a single-arm, open-label multicenter study of brentuximab vedotin administered every 3 weeks [16]. SG035–0002 was designed as a single-arm, open-label two-part study of weekly brentuximab vedotin alone and in combination with gemcitabine. However, after the brentuximab vedotin monotherapy arm was completed, the study was closed due to sponsor decision and the combination arm was not enrolled [17].

Based on the safety and activity profile of brentuximab vedotin in these phase I clinical trials [16, 17] a pivotal phase II clinical trial was conducted in patients with relapsed or refractory CD30-positive HL after ASCT [18]. A total of 102 patients were enrolled, with a primary endpoint of overall objective response rate (ORR) as determined by an independent review facility. The ORR was 75%, with CR in 34% of patients. The median PFS for all patients was 5.6 months and the median duration of response for those in CR was 20.5 months. Notably, 31 patients were alive and free of documented progressive disease after a median follow-up time of >1.5 years. As in the phase I clinical trials, brentuximab vedotin was well tolerated; the most common adverse events were neutropenia and peripheral sensory neuropathy. The composite of these results led to accelerated approval (subpart E) of brentuximab vedotin by the U.S. Food and Drug Administration (FDA) for patients with HL after failure of ASCT or after failure of at least two prior multiagent chemotherapy regimens in patients who are not candidates for ASCT.

In this article, we report the outcomes of 20 patients with HL who were enrolled in the phase I clinical trials of brentuximab vedotin and who were not candidates for ASCT (i.e., patients who refused or were ineligible for ASCT).

PATIENTS AND METHODS

Study Design and Treatment

This case series is a post-hoc analysis of a subset of patients who participated in two phase I studies that allowed enrollment of patients who were ineligible for or who had refused treatment with ASCT. Patients were enrolled at six centers within the U.S. (ClinicalTrials.gov numbers NCT00430846 and NCT00649584). Ten transplant-naïve patients with HL were enrolled in study SG035–0001 (total enrollment of 45 patients) and 10 transplant-naïve patients with HL were enrolled in study SG035–0002 (total enrollment of 44 patients). Study SG035–0001 was a single-arm, open-label, dose-escalation study of brentuximab vedotin administered intravenously every 3 weeks. Study SG035–0002 was a single-arm, open-label, dose-escalation study of brentuximab vedotin administered intravenously every week for 3 out of every 4 weeks.

The studies were approved by the Institutional Review Board at each study site. Written informed consent was obtained from all patients prior to any study-specific procedures, per the Declaration of Helsinki.

Patient Eligibility

Patients had failed systemic chemotherapy either as induction therapy for advanced stage disease or salvage therapy after initial radiotherapy for early-stage disease and had not previously received an autologous or allogeneic stem cell transplant. In addition, patients were required to have histologically confirmed CD30-positive measurable disease of at least 1.0 cm as documented by radiographic technique. Patients were age 12 years or older and had an Eastern Cooperative Oncology Group (ECOG) performance status score of 0, 1, or 2.

Other inclusion criteria were absolute neutrophil count $\geq 1,500/\mu\text{L}$, platelet count $\geq 75,000/\mu\text{L}$, serum creatinine ≤ 1.5 times the upper limit of normal, and alanine transaminase and aspartate transaminase ≤ 2.5 times the upper limit of normal.

Study Assessments

Safety monitoring included the assessment of adverse events, dose-limiting toxicities, and clinical laboratory values. Adverse events were summarized according to the Medical Dictionary for Regulatory Activities and graded according to the National Cancer Institute's Common Terminology Criteria for Adverse Events (version 3). Immunogenicity, physical examinations, vital signs, ECOG performance status, and electrocardiograms were also assessed.

For study SG035–0001, response was assessed after every two cycles (every 6 weeks) by the clinical investigators according to the 2007 Revised Response Criteria for Malignant Lymphoma [19]. Patients with CR, partial remission (PR), or stable disease (SD) with protocol-defined clinical benefit (improved performance status, decreased analgesic consumption, or decreased disease volume) could continue therapy. Study treatment was discontinued on confirmation of disease progression.

For study SG035–0002, response was assessed after every two cycles (every 8 weeks) by the clinical investigators according to the 2007 Revised Response Criteria for Malignant Lymphoma [19]. Patients who experienced clinical benefit with acceptable safety were eligible to receive up to 12 cycles of treatment.

For both studies, patients were monitored for a minimum of 30 days after the last dose of brentuximab vedotin or until they received another treatment for lymphoma.

Statistical Analysis

All analyses of data from this study were descriptive and calculations of confidence intervals were two-sided.

RESULTS

Recruitment occurred from November 2006 through February 2010. Twenty transplant-naïve patients with relapsed or refractory HL were enrolled in the two phase I clinical studies (Table 1). The median age was 31.5 years (range, 12–87 years); four of the patients (20%) were 70 years or older. Sixteen patients (80%) were white and 13 (65%) were men. Sixteen patients (80%) had a baseline ECOG performance status of 0 or 1; four patients (20%) had a baseline ECOG status of 2. Seven patients (35%) had systemic symptoms at baseline.

The median number of prior cancer-related systemic regimens was three (range, 1–7). Nine patients (45%) had received prior radiation therapy. Each patient was assessed for their status relative to frontline therapy and most recent therapy. Seven patients (35%) had disease that was refractory to frontline therapy and 13 patients (65%) had disease that was refractory to their most recent prior therapy (see Table 1 for definitions of response categories). The best responses achieved with the most recent regimen were as follows: complete remission,

Table 1. Demographics and baseline disease characteristics

Characteristic	Value
Age, median yrs (range)	31.5 (12–87)
Sex	
Male	13 (65)
Female	7 (35)
Race	
Black	4 (20)
White	16 (80)
ECOG performance status ^a	
0	10 (50)
1	6 (30)
2	4 (20)
Presence of systemic symptoms at baseline	7 (35)
Prior radiation	9 (45)
Median prior chemotherapy regimens (range)	3 (1–7)
No response to any prior therapy ^b	4 (20)
Refractory to frontline therapy ^c	7 (35)
Refractory to most recent prior therapy ^d	13 (65)
Best response with most recent systemic regimen	
Complete response	4 (20)
Partial response	3 (15)
Stable disease	5 (25)
Progressive disease	8 (40)

Data are *n* (%) unless noted.

^aECOG performance scores range from 0 (normal activity) to 5 (death), with higher scores indicating more severe disability.

^bDid not achieve partial remission or complete remission with prior therapy.

^cBest response of stable disease or progressive disease to frontline therapy.

^dBest response of partial remission, stable disease, or progressive disease if a patient only had one prior therapy, or best response of stable disease or progressive disease to most recent prior therapy if a patient had more than one prior therapy.

Abbreviation: ECOG, Eastern Cooperative Oncology Group.

20%; partial remission, 15%; stable disease, 25%; and progressive disease, 40%. Four patients (20%) had failed to achieve a remission with any prior therapy.

Thirteen patients (65%) had not received prior ASCT because of chemorefractory disease. Three patients had refused the procedure, including one who refused for religious reasons. For two patients, stem cell collection was not possible. Two patients were not candidates for ASCT because of advanced age and comorbidities.

Table 2. Adverse events reported by at least 20% of patients overall (regardless of relationship to brentuximab vedotin) and grade 3 incidence of these events

Adverse event	Received every 3 weeks		Received every week		Total	
	All grades	Grade 3	All grades	Grade 3	All grades	Grade 3
Any event	10 (100)	4 (40)	10 (100)	7 (70)	20 (100)	11 (55)
Fatigue	4 (40)	0 (0)	5 (50)	0 (0)	9 (45)	0 (0)
Peripheral neuropathy ^a	5 (50)	0 (0)	4 (40)	0 (0)	9 (45)	0 (0)
Nausea	1 (10)	0 (0)	7 (70)	1 (10)	8 (40)	1 (5)
Pyrexia	3 (30)	0 (0)	4 (40)	0 (0)	7 (35)	0 (0)
Diarrhea	1 (10)	0 (0)	5 (50)	1 (10)	6 (30)	1 (5)
Weight decreased	2 (20)	0 (0)	4 (40)	0 (0)	6 (30)	0 (0)
Anemia	4 (40)	2 (20)	1 (10)	1 (10)	5 (25)	3 (15)
Back pain	2 (20)	0 (0)	3 (30)	0 (0)	5 (25)	0 (0)
Decreased appetite	1 (10)	0 (0)	4 (40)	0 (0)	5 (25)	0 (0)
Night sweats	2 (20)	0 (0)	3 (30)	0 (0)	5 (25)	0 (0)
Vomiting	1 (10)	0 (0)	4 (40)	2 (20)	5 (25)	2 (10)
Chills	1 (10)	0 (0)	3 (30)	0 (0)	4 (20)	0 (0)
Dehydration	3 (30)	1 (10)	1 (10)	1 (10)	4 (20)	2 (10)

Data are *n* (%). None of these events occurred at a severity of grade 4 or 5.

^aIncidence calculated by grouping preferred terms peripheral neuropathy, peripheral sensory neuropathy, paresthesia, and gait disturbance.

Safety

All patients received at least one dose of brentuximab vedotin and were included in the safety population. Patients enrolled in study SG035-0001 received brentuximab vedotin administered intravenously every 3 weeks at the following dose levels: 0.1 mg/kg (*n* = 1), 0.2 mg/kg (*n* = 1), 0.6 mg/kg (*n* = 1), 1.2 mg/kg (*n* = 1), 1.8 mg/kg (*n* = 2), and 2.7 mg/kg (*n* = 4). The overall median duration of treatment was 12.5 weeks (range, 3.0–51.9 weeks). Patients enrolled in study SG035-0002 received brentuximab vedotin administered intravenously every week, for 3 out of 4 weeks, at the following dose levels: 0.4 mg/kg (*n* = 2), 0.8 mg/kg (*n* = 1), 1.0 mg/kg (*n* = 3), 1.2 mg/kg (*n* = 1), and 1.4 mg/kg (*n* = 3). The overall median duration of treatment was 11.0 weeks (range, 3.0–28.9 weeks).

The most common treatment-emergent adverse events (i.e., occurring in ≥20% of patients) are shown in Table 2. Most adverse events were grade 1 or 2. Eleven patients (55%) experienced grade 3 adverse events; 3 of the 11 patients experienced events that were considered related to study drug (diarrhea, vomiting, and neutropenia/decreased white blood cell count in a single patient). There were no deaths within 30 days of the last dose of brentuximab vedotin. The adverse event profiles were similar in patients treated either weekly or every 3 weeks; however, there was a higher overall incidence of grade 3 and higher events in patients who received the weekly dosing schedule (80% vs. 50%). There was no obvious relationship between brentuximab vedotin dose and the severity of adverse events.

Grouping of preferred terms of peripheral neuropathy (peripheral sensory neuropathy, peripheral neuropathy, gait disturbance, and paresthesia) indicated that nine patients (45%)

experienced adverse events of peripheral neuropathy. In this small case series, the incidence of peripheral neuropathy was similar in patients treated weekly or every 3 weeks. Five of the nine patients who experienced peripheral neuropathy had received brentuximab vedotin every 3 weeks at doses ranging from 0.1 mg/kg to 2.7 mg/kg. The other four patients received brentuximab vedotin on the weekly schedule at doses ranging from 0.8 mg/kg to 1.4 mg/kg. All peripheral neuropathy events were treatment emergent and of grade 1 or 2 in severity. No patients discontinued treatment because of peripheral neuropathy.

Efficacy

Objective responses were observed in 6 of the 20 patients, including two CRs and four PRs. For the remaining patients, the best response was stable disease (10 patients) and progressive disease (2 patients); two patients (both enrolled in study SG035-0002) were not evaluable because they discontinued the study before completing any post-baseline disease assessments. One of the two unevaluable patients received three doses of 1.0 mg/kg brentuximab vedotin before discontinuing treatment due to adverse events of grade 4 neutropenia and grade 3 vomiting. The patient subsequently died of progressive disease 63 days after his last dose of brentuximab vedotin. The second unevaluable patient received two doses of the study drug (one dose at 1.4 mg/kg and one reduced dose of 1.0 mg/kg) before discontinuing treatment because of grade 1 abdominal pain and grade 2 chills.

Table 3 provides a summary of patient demographics, disease characteristics, prior treatments, and brentuximab vedotin dosing for the six patients who achieved an objective response. The six responders varied in age from 22 to 87 years; four of the

Table 3. Characteristics of patients who achieved an objective response with brentuximab vedotin							
Sex/age (yrs)	Brentuximab vedotin dose	Best response	Duration of response (mos)	Prior therapies	Best response to prior therapies	Reason for being transplant naïve	Stem cell transplant after brentuximab vedotin
Male, 87	0.6 mg/kg, every 3 weeks	PR	0.6	ABVD	CR	Age and comorbidity	No
Female, 76	1.8 mg/kg, every 3 weeks	CR	>13.8	ABVD (2 cycles), R-ESHAP, GND (2 cycles), high-dose ifosfamide/VP-16, GND	CR	Unable to collect stem cells	No
Female, 30	2.7 mg/kg, every 3 weeks	PR	>11.5	Stanford V, ESHAP (4 cycles), IGEV (2 cycles), MGCD-0103 HDAC inhibitor	PR	Chemorefractory	Yes
Male, 22	1.0 mg/kg, every week	PR	>6.8	ABVD, escalated BEACOPP	SD	Chemorefractory	No
Male, 31	1.4 mg/kg, every week	PR	>7.9	ABVD, IGEV, ESHAP	SD	Chemorefractory	Yes
Male, 37	1.4 mg/kg, every week	CR	>10.7	ABVD (4 cycles), IGEV (3 cycles), MGCD-0103 HDAC inhibitor	PR	Chemorefractory	Yes

Abbreviations: ABVD, doxorubicin, bleomycin, vinblastine, dacarbazine; BEACOPP, cyclophosphamide, doxorubicin, etoposide, procarbazine, prednisone, bleomycin, vincristine; CR, complete remission; ESHAP, etoposide, methylprednisolone, high-dose cytarabine, cisplatin; GND, gemcitabine, vinorelbine, doxorubicin; HDAC, histone deacetylase; IGEV, ifosfamide, gemcitabine, vinorelbine; PR, partial remission; R-ESHAP, rituximab, etoposide, methylprednisolone, high-dose cytarabine, and cisplatin; SD, stable disease.

Figure 1. Duration of response in patients who achieved an objective response. ^aStudy SG035–0001, in which patients received brentuximab vedotin every 3 weeks at the indicated doses; ^bStudy SG035–0002, in which patients received brentuximab vedotin weekly for 3 out of every 4 weeks at the indicated doses. Abbreviations: CR, complete remission; PR, partial remission.

six patients were men and five of the six were white. Half of the responding patients received brentuximab vedotin every 3 weeks at doses of 0.6 mg/kg (one PR patient), 1.8 mg/kg (one CR patient), and 2.7 mg/kg (one PR patient). The other three responders received treatment with the weekly schedule at doses of 1.0 mg/kg (one PR patient) and 1.4 mg/kg (two patients: one PR and one CR). In this small case series, there did not appear to be a correlation between the dose or schedule of brentuximab vedotin and outcome. Four of the six responding patients were not previously eligible for ASCT because they were chemorefractory. Interestingly, three of these four patients were able to receive ASCT after achieving a response with brentuximab vedotin. One of the six responders was not previously eligible for ASCT because of age and associated comorbidity. This patient, an 87-year-old man, received 0.6 mg/kg brentuximab vedotin every 3 weeks; he achieved a PR but subsequently died of disease progression on study day 82. The final responding patient, a 76-year-old woman

who received 1.8 mg/kg brentuximab vedotin every 3 weeks and achieved a CR, had not previously received an ASCT because of insufficient stem cell collection (see Case Study 2 in the following section for more details).

The median duration of objective response was not met because only one of the six responding patients had progressed by the time of study closure. Censored response durations in the remaining five responders ranged from >6.8 to >13.8 months (Fig. 1, Table 3). The two patients who achieved a CR had the longest duration of response (>10.7 months and >13.8 months).

Case Studies

Case Study 1

A 37-year-old white man had stage II relapsed HL at initial diagnosis approximately 18 months prior to participating in study

Figure 2. Positron emission tomography (PET) and computed tomography (CT) images from the chemorefractory patient in Case Study 1 who received 12 weekly doses of 1.4 mg/kg brentuximab vedotin, achieved complete remission, and went on to receive an autologous stem cell transplantation. CT and PET scans are shown for baseline (**A and B**) and first assessment of complete remission (**C and D**).

SG035–0002. The patient was initially treated with doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD), but progressed after four cycles. He then participated in a clinical trial of MGCD-0103 (a histone deacetylase inhibitor) and again progressed before receiving three cycles of ifosfamide, gemcitabine, and vinorelbine and achieving a limited PR. He was considered ineligible for ASCT because of his chemorefractory disease. During his participation on the brentuximab vedotin clinical trial, he received 12 weekly doses of 1.4 mg/kg brentuximab vedotin and achieved a CR, which was maintained at the time of his last assessment before the study was closed (>10.7 months). The patient went on to receive an ASCT and remains in remission more than 2 years after discontinuing from the study (Fig. 2).

Case Study 2

A 76-year-old white woman was diagnosed with stage II HL more than 9 years prior to participating in study SG035–0001.

She was initially treated with ABVD and achieved a CR. Approximately 4 years later, she relapsed and was treated with rituximab, etoposide, methylprednisolone, high-dose cytarabine, and cisplatin (best response of SD), gemcitabine, vinorelbine, and doxorubicin (GND; best response of PR), stem cell mobilization with high dose ifosfamide/VP-16 (best response of CR), and two further cycles of GND (best response of CR). Unfortunately, the patient was not eligible for ASCT due to insufficient stem cell collection.

She decided to participate in the brentuximab vedotin clinical trial and received six cycles of 1.8 mg/kg brentuximab vedotin administered every 3 weeks. She achieved a CR that was maintained at the time of her last assessment on study (a response duration of >13.8 months). The patient did not receive an ASCT following brentuximab vedotin treatment. Three years after discontinuing from the study, the patient still has no evidence of disease.

DISCUSSION

Although frontline therapy for HL is associated with a high cure rate, advanced HL recurs after primary therapy in up to 40% of patients [1–3]. The majority of patients with relapsed or refractory HL will proceed to ASCT based on the results of two phase III clinical trials showing improvement in PFS for patients who received ASCT compared to those who received standard chemotherapy [4, 5]. Interestingly, these trials failed to show improvement in overall survival. New therapies are therefore needed for patients who are not considered suitable candidates for ASCT because of age, comorbidities, personal preference, or chemorefractory disease, as well as for patients who relapse after ASCT.

Brentuximab vedotin was approved by the FDA for patients with HL after failure of ASCT or after failure of at least two prior multiagent chemotherapy regimens in patients who are not candidates for ASCT. As described in the current report, transplant-naïve patients who were enrolled in the phase I trials of brentuximab vedotin had an ORR of 30% with a CR rate of 10%. Although the response rate observed in this case series is lower than that seen in the pivotal trial of brentuximab vedotin (ORR of 75% with a CR rate of 34%) [18], the activity is still notable considering the majority of patients enrolled in the phase I trials were transplant naïve due to chemorefractory disease.

Of the six transplant-naïve patients who achieved a response with brentuximab vedotin, four were not previously considered eligible for ASCT because of chemorefractory disease. Notably, three of these four patients were able to proceed to ASCT after receiving brentuximab vedotin. Previous reports by others have indicated that the proportion of patients who were able to receive ASCT after salvage chemotherapy ranged from 70% to 97% depending on the salvage chemotherapy regimen used [7–11]. Although the current case series represents a relatively small number of patients and the population was heterogeneous with respect to prior therapies, performance status, and brentuximab vedotin dose and schedule, the results are promising and merit further study in the transplant-naïve setting.

Furthermore, patients who received single-agent brentuximab vedotin achieved objective responses without the characteristic toxicity of combination chemotherapy regimens such as carmustine, etoposide, cytarabine, and melphalan [20];

ifosfamide, carboplatin, and etoposide [21]; GND [22]; gemcitabine, carboplatin, and dexamethasone [23] or dexamethasone, cytarabine, and cisplatin [9]. These regimens are associated with considerable grade 3 and 4 hematological toxicities. Most adverse events associated with brentuximab vedotin were managed with standard supportive care and were typically grade 1 and 2. The most significant adverse event was peripheral neuropathy, an anticipated class effect of microtubule-disrupting agents, such as brentuximab vedotin [24, 25]. Although 45% of patients experienced peripheral neuropathy, all events were grade 1 or 2 and no patients discontinued treatment as a result.

In summary, the data provided by this small case series show that brentuximab vedotin has activity in patients who are not candidates for ASCT and should be further evaluated in the salvage setting, either alone or in combination with other therapies. In addition, because patients who are not candidates for ASCT after salvage therapy do not have curative options, continued evaluation of brentuximab vedotin as maintenance therapy may be warranted.

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