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Results of a phase II trial of brentuximab vedotin for CD30 cutaneous T-cell lymphoma and lymphomatoid papulosis

Authors:

Duvic M et al.

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All authors: The University of Texas MD
Anderson Cancer Center, Houston, TX.

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Corresponding author: Madeleine
Duvic, MD, The University of Texas MD
Anderson Cancer Center, Pickens
Tower, FCT11.6078, 1515 Holcombe
Blvd, Unit # 1452, Houston, TX 77030-
4009; e-mail: mduvic@mdanderson.org.

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Results of a Phase II Trial of Brentuximab Vedotin for CD30⁺ Cutaneous T-Cell Lymphoma and Lymphomatoid Papulosis

Madeleine Duvic, Michael T. Tetzlaff, Pamela Gangar, Audra L. Clos, Dawen Sui, and Rakhshandra Talpur

See accompanying article doi:10.1200/JCO.2014.60.3969

A B S T R A C T

Purpose

Brentuximab vedotin, a monoclonal antibody (cAC10) conjugated to monomethyl auristatin E, targets CD30⁺ receptors. This phase II open-label trial was conducted to evaluate safety and efficacy in CD30⁺ cutaneous T-cell lymphomas.

Patients and Methods

Forty-eight patients with CD30⁺ lymphoproliferative disorders or mycosis fungoides (MF) received an infusion of 1.8 mg/kg every 21 days.

Results

Forty-eight evaluable patients (22 women and 26 men; median age, 59.5 years) had an overall response rate of 73% (95% CI, 60% to 86%; 35 of 48 patients) and complete response rate of 35% (95% CI, 22% to 49%; 17 of 48 patients). Fifteen (54%; 95% CI, 31% to 59%) of 28 patients with MF responded, independent of CD30 expression. In patients with MF/Sézary syndrome, the overall response rate was 50% (five of 10 patients) in patients with low CD30 expression (< 10%), 58% (seven of 12 patients) in patients with medium expression (10% to 50%), and 50% (three of six patients) in patients with high expression (≥ 50%). Time to response was 12 weeks (range, 3 to 39 weeks), and duration of response was 32 weeks (range, 3 to 93 weeks). All patients with lymphomatoid papulosis (n = 9) and primary cutaneous anaplastic T-cell lymphomas (n = 2) responded; time to response was 3 weeks (range, 3 to 9 weeks), and median duration of response was 26 weeks (range, 6 to 44 weeks). Soluble baseline CD30 levels were lowest in complete responders (P = .036). Grade 1 to 2 peripheral neuropathy was observed in 65% of patients (95% CI, 52% to 79%; 31 of 48 patients), is still ongoing in 55% of patients (95% CI, 41% to 69%; 17 of 31 patients), and resolved in 45% of patients (95% CI, 31% to 59%; 14 of 31 patients), with a median time to resolution of 41.5 weeks. Grade 3 to 4 events were neutropenia (n = 5), nausea (n = 2), chest pain (n = 2), deep vein thrombosis (n = 1), transaminitis (n = 1), and dehydration (n = 1). Dose reductions to 1.2 mg/kg were instituted as a result of grade 2 neuropathy (n = 6), transaminitis (n = 1), and arthralgias and fatigue (n = 2).

Conclusion

Brentuximab vedotin is both active and well tolerated in cutaneous T-cell lymphoma and lymphomatoid papulosis, with an overall response rate of 73% and complete response rate of 35%.

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INTRODUCTION

Cutaneous T-cell lymphomas are classified by clinical features and distinctive surface markers,¹ with some used as targets for therapy. CD30, or Ki-1 antigen, is a transmembrane glycoprotein tumor necrosis factor receptor superfamily member 8^{2,3} first identified in 1983 with Ki-1 antibody on Reed-Sternberg cells in Hodgkin lymphoma.^{4,5} CD30 is also present on activated or malignant T cells in the two CD30⁺ lymphoproliferative

disorders—self-regressing lymphomatoid papulosis (LyP) and primary cutaneous anaplastic large-cell lymphoma (pc-ALCL). The most common cutaneous T-cell lymphoma, mycosis fungoides (MF), can also express CD30 with or without the presence of tumors and large-cell transformation.⁶⁻⁹

LyP lesions, first described by Macaulay in 1968, are self-regressing papules, histologically identical to anaplastic T-cell lymphoma but clinically benign, associated with increased risk of anaplastic

large-cell lymphoma (ALCL; MF, or rarely, Hodgkin lymphoma).^{6,10,11} MF usually presents as limited patches and/or plaques in sun-shielded areas and, in early stages, can be controlled or cleared with skin-directed therapy.¹² Clinical progression to plaques, tumors, or blood negatively impacts overall survival.^{13,14} Large-cell transformation can be associated with expression of CD30 and poor overall survival.^{15,16} Treatment of advanced MF is currently unsatisfactory because complete responses are rare and serial chemotherapy leads to immunosuppression and infection.¹³

Brentuximab vedotin is an antibody-drug conjugate composed of an anti-CD30 monoclonal antibody (cAC10) conjugated to the microtubule-disrupting agent monomethyl auristatin E.³⁻⁵ It received accelerated approval for relapsed Hodgkin lymphoma and systemic ALCL with high overall response rates of 75% and 86%, respectively.¹⁷⁻²¹ In an exploratory phase II multicenter trial of naked cAC10 antibody, there was a 70% overall response rate in 16 of 23 patients with CD30⁺ cutaneous MF, pc-ALCL, and LyP and some long-standing complete responses.²² This phase II trial of brentuximab vedotin was conducted in CD30⁺ cutaneous T-cell lymphomas—CD30⁺ lymphoproliferative disorders (LyP and pc-ALCL) and MF.

PATIENTS AND METHODS

Study Design and Treatment

An open-label, single-center, phase II trial was designed to determine safety and preliminary activity of brentuximab vedotin in patients with LyP in need of systemic therapy or in previously treated patients with MF or pc-ALCL. The study was conducted in accordance with Good Clinical Practice and approved by the Institutional Review Board of The University of Texas MD Anderson Cancer Center. All patients gave written informed consent.

Brentuximab vedotin was administered intravenously at 1.8 mg/kg every 21 days for a maximum of eight doses. Patients with partial or stable response were eligible to receive up to eight additional doses. Patients with complete response could receive two additional doses. Patients with breakthrough lesions could receive 1.2 mg/kg every 2 weeks at the discretion of the principal investigator.

Patients

Patients were ≥ 18 years old with a clinical and histologically confirmed diagnosis of CD30⁺ LyP, CD30⁺ pc-ALCL, or MF. Eastern Cooperative Oncology Group performance status of ≤ 2 and adequate bone marrow and organ function were required. Lesional skin biopsies at baseline and during the study were graded for expression of CD30 by one dermatopathologist (M.T.T.). Skin lesions were required to have detectible CD30 present on malignant T cells. For LyP, more than 10 lesions, scarring, or active lesions on the face, hands, or feet requiring systemic treatment were required. Patients with active infection, HIV, positive hepatitis B or C status, or known or suspected CNS involvement were not eligible. Patients with MF or pc-ALCL must have failed at least one prior systemic therapy 4 or more weeks before study entry. Patients who had received monoclonal antibodies required a washout of 12 weeks.

Safety

All patients who received one or more doses of brentuximab vedotin were included in the safety analysis and evaluated throughout. Blood samples for chemistry and hematologic measurements and urine samples for urinalysis were taken at day 1 and every 21 days before each infusion. Toxicities were evaluated and reported using National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0. Patients were monitored for adverse events from initial infusion of study drug until 30 days after last dose. Neuropathy severity and duration and overall survival were monitored until resolution.

Efficacy Assessment and Response Criteria

Patients with CD30⁺ LyP, pc-ALCL, or MF who received at least two doses of brentuximab vedotin at baseline and at least one on-study assessment of response were evaluable for efficacy. Disease-specific assessments were performed on day 1 of each treatment. The Modified Severity-Weighted Assessment Tool (mSWAT) was used to determine the skin burden²³ for MF. pc-ALCL required a 50% reduction from baseline for partial response or 100% reduction and no disease elsewhere for complete response.^{1,23} Active LyP lesions were counted; complete response was considered to be zero lesions, whereas partial response was a reduction in lesions of 50%. For pc-ALCL, the sum of bidimensional measurements of index lesions and mSWAT were used. Positron emission tomography/computed tomography scans at baseline and at response assessed responses in bulky tumors or lymph nodes. Three-color flow cytometry monitored number of CD4⁺CD26[−]Sézary cells in blood.¹⁴ The overall global response score was a composite of responses from all compartments (skin, lymph nodes, blood $> 1,000$ cells/ μ L, and viscera).²³ Stable disease was defined as a failure to attain a complete or partial response and no evidence of disease progression in any compartment. Progressive disease was defined as a more than 25% increase from baseline mSWAT (nonresponders) or loss of response in partial or complete responders (increase in mSWAT greater than the sum of the nadir plus 50% of the baseline score).

CD30 Expression in Lesions

Biopsies from representative clinical lesions (LyP, ALCL, and/or MF) were stained by immunohistochemistry and evaluated by one dermatopathologist (M.T.T.). There was no specified amount of CD30 expression other than staining of tumor cells from skin biopsy specimens in paraffin tissue sections. Antibodies were CD3 (1:150; DakoCytomation, Glostrup, Denmark), CD4 (1:80; Novocastra, Buffalo Grove, IL), CD7 (1:100; Novocastra), CD8 (1:20; Thermo Scientific, Cheshire, United Kingdom), and CD30 (1:80; Covance, Princeton, NJ). CD30 positivity (membranous and/or cytoplasmic) was defined as follows: circumference of the cell membrane entirely positive or cytoplasm diffusely positive. Both membranous and cytoplasmic positivity were noted. CD30 expression was graded as percentage of the entire lymphocytic infiltrate seen in the tissue (low, $\leq 10\%$; medium, $\geq 10\%$ to $\leq 50\%$; or high, $\geq 50\%$). CD30 intensity was also graded as weak (1+), moderate (2+), or strong (3+). Interim and end-of-study skin biopsies were taken to assess complete response, progressive disease, and new lesions for level of expression. We assessed the configuration of the T-cell receptor (TCR) β chain (*TCRB*) and T-cell receptor γ chain (*TCRG*) genes using polymerase chain reaction–based methods to detect monoclonal *TCRB* and *TCRG* rearrangements. *TCRG* clonality assessment was performed using four fluorescently labeled consensus V β family-specific forward primers and common JH reverse primers as previously described.²⁴ *TCRB* gene rearrangements were performed as described previously using consensus primer sets in tubes A and B as established by the BIOMED-2 consortium.²⁵ Size of the clonal peaks was determined by capillary electrophoresis.

Statistical Analyses

Simon's optimum two-stage design discriminated between a true objective response rate of no more than 35% and at least 65%. With a maximum trial size of 48 evaluable patients, if at least 25 objective responses ($\geq 52\%$) were observed among the 48 evaluable patients, the regimen was considered worthy of further testing. If less than nine objective responses ($< 47\%$) were observed among the initial 19 patients, the study was to be terminated early and declared negative. Total sample size was 58 patients to ensure 48 evaluable patients. Safety was analyzed in a descriptive manner. Kaplan-Meier survival analysis was used to obtain the population survival curve and the median survival time estimation. The analyses were performed using SAS software, version 9.3 (SAS Institute, Cary, NC).

Table 1. Demographic and Clinical Characteristics of All Patients and the Eligible Patients Who Received Two or More Doses of Brentuximab Vedotin

Characteristic	No. (%)	
	All Patients (N = 54)	All Eligible Patients (n = 48)
Age, years		
Median	59.5	
Range	31-77	
Sex		
Male	27 (50)	26 (54)
Female	27 (50)	22 (46)
Race		
White	31 (57)	30 (63)
African American	15 (28)	13 (27)
Hispanic	8 (15)	5 (11)
Diagnosis		
MF	31	28
pc-ALCL	3	2
LyP	10	9
LyP and MF	8	7
ALCL/LyP/MF	2	2

Abbreviations: ALCL, anaplastic large-cell lymphoma; LyP, lymphomatoid papulosis; MF, mycosis fungoides; pc, primary cutaneous.

RESULTS

Patient Characteristics

Between June 2011 and April 2013, 48 eligible patients with histologically confirmed diagnosis and clinical criteria for one or both CD30⁺ lymphoproliferative disorders, CD30⁺ LyP or CD30⁺ pc-ALCL (n = 20), or CD30⁺ MF/Sézary syndrome (n = 28) consented and enrolled. Baseline demographic and diagnostic data are listed in [Tables 1](#) and [2](#). Twenty-eight patients had only MF, two patients had only pc-ALCL, two patients had pc-ALCL plus LyP or MF, nine patients had only LyP, and seven patients had both LyP and MF. The median age of all patients was 59.5 years (range, 31 to 77 years). Patients with MF were heavily pretreated, with a median of five prior therapies (range, one to 13 prior therapies). The median number of prior systemic therapies was two (range, one to 10 prior systemic therapies) for patients with MF and one (range, zero to five prior systemic therapies) for patients with LyP/pc-ALCL. The median num-

ber of cycles of brentuximab vedotin was seven (range, two to 19 cycles) for MF and 7.5 (range, two to 16 cycles) for LyP/pc-ALCL. Median time to follow-up from the first dose was 27 months (range, 2 to 36 months) for MF and 23 months (range, 4 to 37 months) for LyP/pc-ALCL.

Regarding clinical efficacy, response was evaluable in 48 of 54 patients. Six patients were excluded because they did not have at least one on-study response evaluation. The overall response rate for 48 evaluable patients was 73% (95% CI, 60% to 86%; 35 of 48 patients). Complete responses were observed in 35% of all evaluable patients (95% CI, 22% to 49%; 17 of 48 patients; [Table 2](#)). The response rate in the intent-to-treat population of 54 patients, including patients with ≤ two doses, was 65% (95% CI, 52% to 79%; 35 of 54 patients).

The overall response rate in 28 patients with MF was 54%, compared with a 100% response rate in patients with LyP/pc-ALCL. When patients with MF were divided according to CD30 expression in skin lesions at baseline, overall response rates were 50% in low, 58% in medium, and 50% in high CD30 expression ([Fig 1A](#)). Complete responses were seen in patients with medium and high expression; the only patient with progressive disease had low expression. [Figure 1B](#) shows the percent change in mSWAT and time of best response for patients with MF.

Five patients with MF had large-cell transformation in skin lesions at study entry. One patient had a complete response still ongoing at 30 months, two had partial responses, and two had stable disease. Three patients developed large-cell transformation during the study. One patient experienced transformation 6 months after stopping brentuximab vedotin for progression and receiving multiagent chemotherapy; two patients developed large-cell transformation while on study. Two of three patients with folliculotropic MF had partial responses ([Appendix Fig A1C](#), online only); one patient had a complete response. Ten patients with MF experienced relapse and had repeat biopsies. Six of 10 patients with more than 10% CD30 staining in baseline lesions had less than 10% expression in new lesions; four patients were low at baseline and remained low.

LyP and pc-ALCL lesions responded more rapidly than MF lesions ([Fig 1C](#)), but responses were of shorter duration ([Fig 1D](#)). Time to response for patients with LyP/pc-ALCL was 3 weeks (range, 3 to 9 weeks) compared with 12 weeks (range, 3 to 39 weeks) for patients with MF. Median duration of response was 26 weeks (range, 6 to 44) for patients with LyP/pc-ALCL versus 32 weeks (range, 3 to 93 weeks) for patients with MF. Although new LyP lesions appeared in eight of

Table 2. Response in Evaluable Patients

Diagnosis	Total No. of Patients (N = 48)	Response		Secondary Response (No.)
		No.	%	
All patients	48	35	73	
MF	28	13 PR, 2 CR	54	
LyP	9	5 CR, 4 PR	100	
pc-ALCL	2	2 CR	100	
LyP/MF	7	6 LyP CR, 1 LyP PR	100	6 MF PR, 1 MF SD
pc-ALCL/LyP	1	CR	100	1 LyP PD
pc-ALCL/MF	1	CR	100	1 MF PR

Abbreviations: ALCL, anaplastic large-cell lymphoma; CR, complete response; LyP, lymphomatoid papulosis; MF, mycosis fungoides; pc, primary cutaneous; PD, progressive disease; PR, partial response; SD, stable disease.

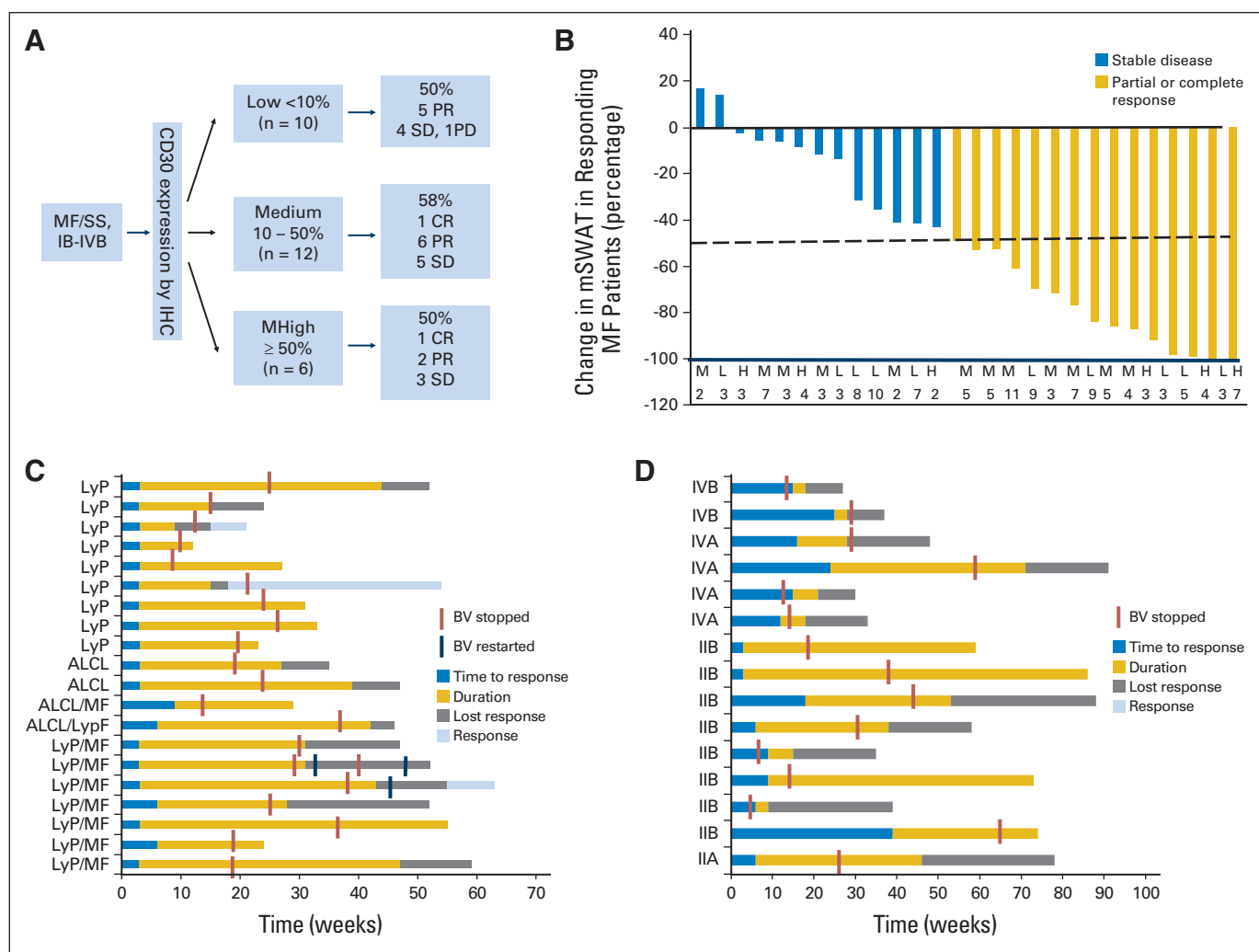


Fig 1. Responses to brentuximab vedotin (BV) in patients. (A) Clinical response in 28 evaluable patients with mycosis fungoides (MF) divided by level of baseline CD30 expression. (B) Waterfall plot of percent change in Modified Severity-Weighted Assessment Tool (mSWAT) in responding patients with MF. The first line in the bottom of the graph indicates the level of CD30 expression in skin lesions at baseline—low (L), medium (M), or high (H). The second line shows the number of cycles at the time of best response. (C) Duration of response in all responders whose primary disease was lymphomatoid papulosis (LyP) including LyP (n = 9), primary cutaneous anaplastic large-cell lymphoma (ALCL; n = 2), and combined LyP/MF (n = 7). Each horizontal bar represents the time on therapy. Blue bars show time to response, gold bars are the duration of response, and gray shows the relapse (loss of partial response). Vertical red bars show the week when BV was stopped. (D) Duration of response (DOR) in 28 responding patients with MF as the primary disease. Time to response was 12 weeks (range, 3 to 39 weeks), and DOR was 32 weeks (range, 3 to 93 weeks). CR, complete response; IHC, immunohistochemistry; PD, progressive disease; PR, partial response; SD, stable disease; SS, Sézary syndrome.

20 patients after treatment ended, two patients were re-treated off label and responded (Fig 1C).

Examples of clinical responses in patients with different variants of cutaneous T-cell lymphoma are shown in Figure A1. At baseline, a severely affected patient had more than 500 LyP lesions, multiple ALCL tumors greater than 1.5 cm, and widely diffuse MF patches (Fig A1A). He had complete resolution of LyP and ALCL tumors at cycle 5 with stable MF patches. A middle-aged female with long-standing patch/plaque MF with 5% expression of CD30 developed a tumor with 10% CD30 expression (Fig A1B). The tumor resolved completely by cycle 6, whereas the patch/plaque MF partially responded at cycle 11.

Some patients with MF experienced localized tumor lysis (flares) or hypersensitivity drug rash after one to two infusions. A 60-year-old male patient with folliculotropic, granulomatous MF developed a flare in his skin after one dose of brentuximab vedotin (Fig A1C). He continued on therapy for 18 courses and subsequently achieved an excellent durable

near complete response. A 71-year-old erythrodermic female with stage IVA Sézary syndrome experienced treatment failure with extracorporeal photopheresis, interferon alfa, and oral bexarotene (Fig A1D). Baseline 60% CD4⁺CD26[−] Sézary cells normalized at less than 35% and less than 200 cells/ μ L by cycle 4, but her erythroderma did not clear until cycle 7 (Fig A1E). At cycle 2, she developed a morbilliform hypersensitivity dermatitis with spongiosis that cleared with topical triamcinolone. In both cases, it was difficult to distinguish between transient tumor flares and drug reactions and progression of the underlying disease.

Survival

For all 48 evaluable patients, median overall survival (Figs 2A and 2B) was not reached when calculated from first dose (Fig 2A) and was 14.7 years (95% CI, 10.2 years to not reached) from date of first diagnosis (Fig 2B). Disease-specific survival was not reached when calculated either from first dose or from date of first diagnosis (Figs 2C

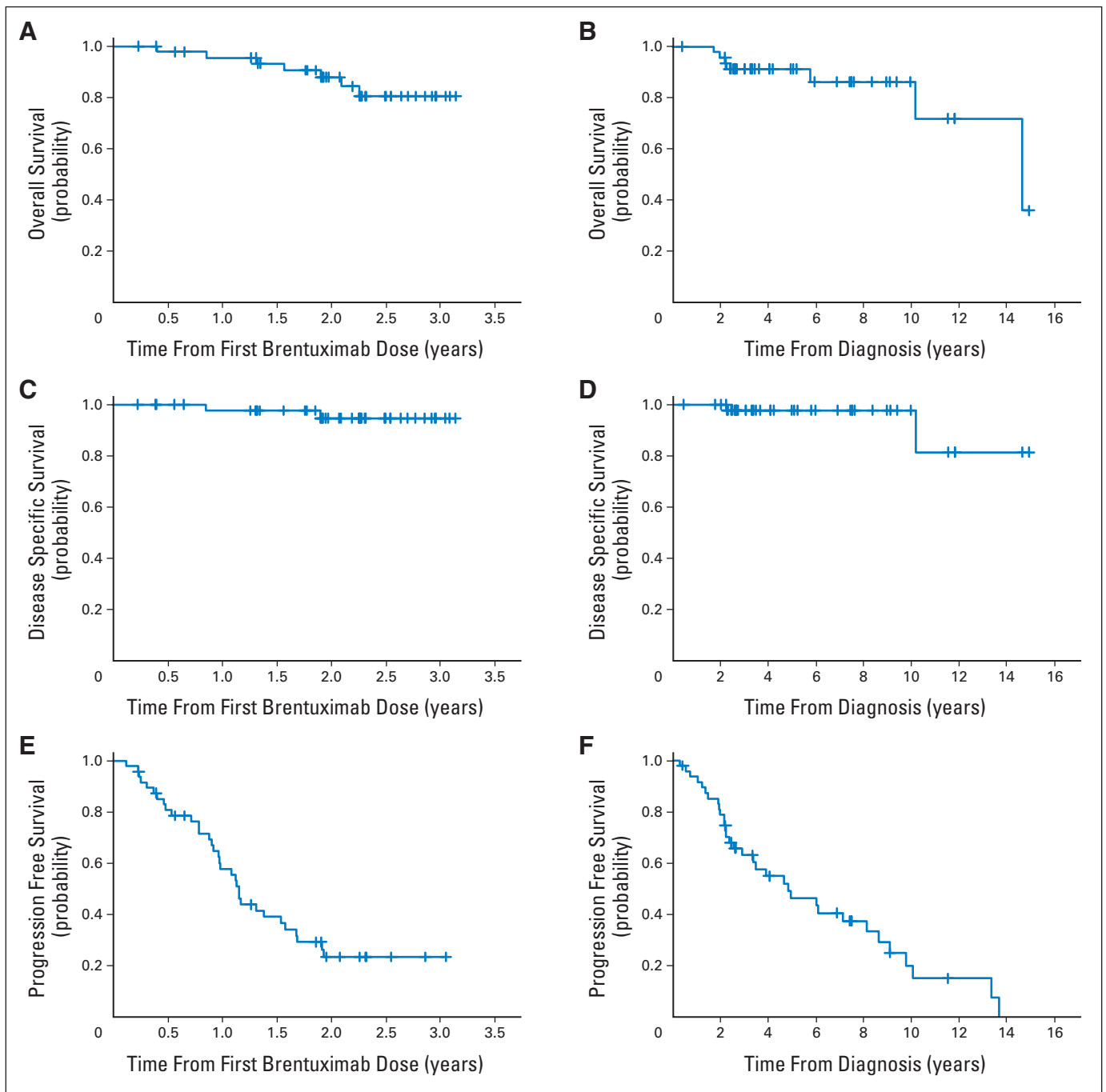


Fig 2. Kaplan-Meier plots of overall survival (OS), disease-specific survival (DSS), and progression-free survival (PFS) from (A, C, E) date of first treatment with brentuximab vedotin or (B, D, F) date of diagnosis for all 48 evaluable patients in the trial. OS from (A) date of first treatment and (B) date of diagnosis. DSS from (C) date of first treatment and (D) date of diagnosis. PFS from (E) date of first treatment and (F) date of diagnosis.

and 2D). Progression-free survival was 1.1 year (95% CI, 0.9 to 1.4 years; Fig 2E) from first dose and 4.8 years (95% CI, 3.1 to 7.1 years) from first diagnosis (Fig 2F).

Regarding expression of CD30 with response, CD30 expression in baseline MF skin lesion biopsies did not seem to correlate with response to brentuximab vedotin (Fig 1A). Overall response was 54% in all patients with MF, and the response rate did not significantly differ when patients were divided by CD30 expression in skin at baseline (< 10% expression, 50%; 10% to 50% expression, 58%; >

50% expression, 50%). There was a borderline significant difference between CD30 expression and duration of response ($P = .0463$).

Safety

Fifty-four patients who received at least one dose of brentuximab vedotin were included in the safety population. Figure 3A shows the most frequent treatment-related adverse events ($\geq 10\%$ and possibly related to brentuximab vedotin); these were peripheral neuropathy (67%), nausea (19%), fatigue (35%), rash (24%), diarrhea (15%),

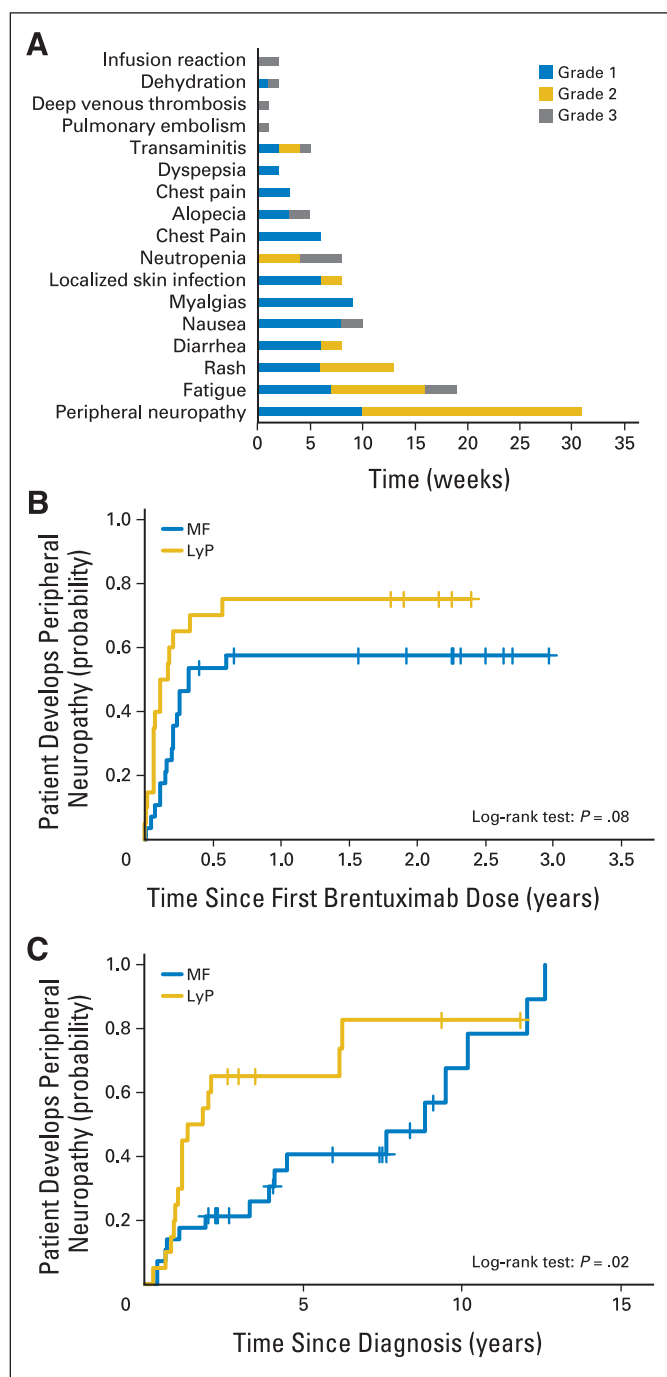


Fig 3. Adverse events occurring during the trial. (A) Bar graph plot of the incidence and the severity of the adverse events. Reverse Kaplan-Meier plots of time to onset of peripheral neuropathy comparing mycosis fungoides (MF) with lymphomatoid papulosis (LyP) dating from (B) first treatment and (C) date of diagnosis.

myalgias (17%), localized skin infection (15%), neutropenia (15%), and alopecia (11%). Grade 3 to 4 adverse events included neutropenia ($n = 3$), nausea ($n = 2$), unstable angina or myocardial infarction ($n = 2$), infection ($n = 2$), fatigue ($n = 1$), deep venous thrombosis ($n = 1$), pulmonary embolism ($n = 1$), aminotransferase elevation ($n = 1$), dehydration ($n = 1$), and arthralgia ($n = 2$).

There were six withdrawals, including two deaths from untreated sepsis (ulceration of a pc-ALCL tumor and untreated urosepsis). One

patient with LyP withdrew consent after two doses as a result of infusion reaction. One patient with MF with the highest (80%) CD30 expression withdrew as a result of severe fatigue and pruritus after four doses. One patient withdrew at dose 7 as a result of unrelated unstable angina and myocardial infarction. One patient with transformed MF received one dose before having a positron emission tomography/computed tomography scan showing leptomeningeal involvement at baseline. No patients with LyP developed new lymphomas, and only one patient with MF/LyP/pc-ALCL had progressive disease while on the study.

Peripheral neuropathy was reported in 31 (67%; 95% CI, 54% to 80%) of 48 patients. Grade 1 neuropathy occurred in 30 patients with progression to grade 2 neuropathy in 21 patients. Patients with LyP had more neuropathy events than patients with MF when calculated from first dose (hazard ratio, 1.9; 95% CI, 0.9 to 3.8; $P = .08$; Fig 3B) and from date of diagnosis (hazard ratio, 2.3; 95% CI, 1.2 to 4.9; $P = .02$; Fig 3C). There was no significant difference in CD30 expression at baseline and neuropathy grade. In the event of grade 2 neuropathy, treatment was held or a dose reduction to 1.2 mg/kg was made. Neuropathy resolved in 14 of 31 patients with a median time to resolution of 41.5 weeks (range, 2 to 66 weeks).

DISCUSSION

Brentuximab vedotin is a safe and effective therapy for CD30⁺ cutaneous T-cell lymphomas (MF and pc-ALCL) and LyP.⁶ The dose schedule and response rate (73%) are similar to those in refractory/relapsed Hodgkin lymphoma (75%) and systemic anaplastic large T-cell lymphoma (86%) trials.³ The 73% overall response rate and 35% complete response rate are similar to the overall and complete response rates of 77% and 44%, respectively, in the phase II trial of naked antibody (cAC10)^{22,26} and support the design of an ongoing phase III randomized trial (NCT01578499) comparing brentuximab vedotin to bexarotene or methotrexate.

We addressed whether CD30⁺ expression is associated with stage or response. Baseline MF lesions with more than 20% CD30 expression were more common in advanced disease (T3 or T4; $P = .002$) but did not correlate with large-cell transformation.⁹ Patients with LyP and pc-ALCL had an overall response rate of 100%; 15 (75%) of 20 patients had complete responses, and median time to response was 12 weeks (three doses), suggesting that high expression gives faster, complete responses. The overall response rate in patients with MF was 54%, with two complete responses and a median time to response of 26 weeks. CD30⁺ expression, whether low, medium, or high, did not seem to correlate with response. Yet tumors responded faster than patch/plaques, and a significant difference between CD30 expression and duration of response was borderline ($P = .0463$). Relapsed MF lesions generally showed lower CD30 expression, suggesting a loss of the receptor or heterogeneity. Response in MF to brentuximab vedotin was comparable to the 30% to 50% response rates previously published, although comparison across studies is problematic.^{12,27}

The toxicity was similar to that seen in other trials with exceptions.³ Brentuximab vedotin was occasionally associated with a tumor flare, brisk inflammation in lesions and surrounding skin that resolved as treatment continued. Patients with high CD30 expression could experience itching and burning of their skin lesions. A pruritic hypersensitivity drug rash with epidermal spongiosis and eosinophilia occurred in 24% of patients at dose 2 to 3 that was managed with topical corticosteroids. The most common dose-limiting toxicities

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at www.jco.org.

AUTHOR CONTRIBUTIONS

Conception and design: Madeleine Duvic

Financial support: Madeleine Duvic

Provision of study materials or patients: Madeleine Duvic

Collection and assembly of data: Madeleine Duvic, Michael T. Tetzlaff, Pamela Gangar, Audra L. Clos, Rakhshandra Talpur

Data analysis and interpretation: Madeleine Duvic, Michael T. Tetzlaff, Dawen Sui, Rakhshandra Talpur

Manuscript writing: All authors

Final approval of manuscript: All authors

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Results of a Phase II Trial of Brentuximab Vedotin for CD30⁺ Cutaneous T-Cell Lymphoma and Lymphomatoid Papulosis

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Pamela Gangar

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Appendix



Fig A1. Examples of clinical responses in patients on the trial. (A) Patient with lymphomatoid papulosis (LyP), primary cutaneous anaplastic large-cell lymphoma (pc-ALCL), and mycosis fungoides (MF; stage IB) achieved a complete response of his LyP and pc-ALCL lesions at cycle 5. (B) Patient with stage IVA MF (lymph node positive) had rapid response in a tumor by cycle 6 but slower improvement in MF patches and plaques by cycle 11. (C) Patient with stage IIB folliculotropic MF experienced a tumor flare at cycle 2 followed by a partial response and almost complete resolution at follow-up at week 66. (D, E) Clearing of skin lesions occurred more slowly than clearing of the CD4⁺CD26⁻ Sézary cells in the blood of a 71-year-old woman with stage IVB Sézary syndrome who also developed a drug rash treated with topical corticosteroid cream. mSWAT, Modified Severity-Weighted Assessment Tool.