Real-World Treatment Patterns and Clinical Outcomes With Brentuximab Vedotin or Other Standard Therapies in Patients With Previously Treated Cutaneous T-Cell Lymphoma (CTCL): A Retrospective Chart Review Study in the United States

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Background

- Cutaneous T-cell lymphomas (CTCL) are a rare group of non-Hodgkin lymphomas that present primarily in the skin[1]
- CD30 is expressed uniformly in primary cutaneous anaplastic large-cell lymphoma (pcALCL) and heterogeneously in mycosis fungoides (MF)[2]
- CTCL treatment varies depending on the extent of skin involvement and disease stage[3,4]
- Brentuximab vedotin (BV) was FDA-approved in 2017 for adult patients with relapsed pcALCL or CD30-positive MF who have received prior systemic treatment[5,6]
- In the ALCANZA trial that enrolled previously treated patients with pcALCL or CD30-positive MF, patients randomized to BV compared with physician's choice of methotrexate or bexarotene with a median follow-up of 45.9 months had[7]
  - Significantly higher objective response rate (ORR) lasting ≥4 months (ORR4; 54.7% vs 12.5%; *P*<0.001)
  - Significantly longer progression-free survival (PFS; 16.7 vs 3.5 months; HR, 0.38; [95% CI, 0.25-0.58]; *P*<0.001)
  - Significantly longer time to next treatment (TTNT; 14.2 vs 5.6 months; HR, 0.27 [95% CI, 0.17-0.42]; *P*<0.001)
  - Estimated 3-year overall survival (OS) rates of 64.4% vs 61.9% (*P*=0.310)
- While the ALCANZA trial has demonstrated the relative efficacy of BV, there is limited information on its effectiveness among patients with CTCL in real-world clinical practice

Objective

- This study describes real-world patient characteristics, treatment patterns, clinical outcomes, and healthcare resource use (HRU) in patients with CTCL previously treated with ≥1 systemic therapy and subsequently treated with BV or other standard therapy (OST)

Methods

- A retrospective, physician panel-based chart review was conducted from October 2021-January 2022 (approved by the WCG IRB)
  - Participating physicians were hematologists-oncologists with access to complete medical records for ≥1 eligible patient
  - Eligible patients were adults with pcALCL or MF, previously treated with ≥1 systemic therapy, treated with BV or OST from November 2017-March 2021, with ≥6 months of follow-up after initiating second-line (2L) systemic therapy except in the event of death
  - Approximately equal numbers of eligible patients who received BV and OST were targeted via weekly monitoring of recruitment
- The index date was the initiation of 2L systemic therapy for CTCL; the observation period was from the index date to the earliest of death, loss to follow-up, or chart abstraction
  - Treatment patterns were assessed from CTCL diagnosis to the end of the observation period
  - Clinical outcomes for 2L systemic therapy and HRU were assessed during the observation period; treatment response was calculated via the Global Response Score[8]
    - Real-world PFS (rwPFS) was determined from the index date to the earliest of progression, treatment discontinuation due to progression, or death before start of next line of therapy
    - Real-world TTNT (rwTTNT) was determined from the index date to the earlier of initiation of a new line of therapy or death
    - Real-world OS (rwOS) was determined from the index date to death
- Median times-to-event were computed using Kaplan-Meier (KM) methods
- Since median times-to-event were not reached (NR) in both cohorts for multiple outcomes, restricted mean survival time (RMST), a measure of the average event-free survival time during a specific period estimated by the area under the KM curve, at 1 and 2 years was estimated

Results

Physician Characteristics

- 125 physicians participated in the study and abstracted data for a median of 2 eligible patients with CTCL; among participating physicians
  - 83.2% had a primary specialty of hematology-oncology and 16.8% had a primary specialty of medical oncology
  - 75.2% had been in practice for >10 years
  - 68.0% practiced in a community-based setting; practice sites were across the continental United States (Midwest, 31.2%; South, 29.6%; Northeast, 20.8%; West, 18.4%)
  - 65.6% worked in practices with >10 physicians
  - Each participating physician treated on average 70 (SD: 102.5; median 25) patients with CTCL annually
  - 80.0% of physicians attested to following National Comprehensive Cancer Network guidelines for CTCL treatment

Patient Characteristics

- Medical charts for 303 eligible patients with CTCL were abstracted (**Table 1**)
  - 187 (61.7%) patients were diagnosed with MF (BV, 56.8%; OST, 65.9%) and 116 (38.3%) patients were diagnosed with pcALCL (BV, 43.2%; OST, 34.1%)
  - Of patients with an available CD30 expression test result at index (BV, 72.7%; OST, 47.6%), 86.1% of patients treated with BV and 57.7% of patients treated with OST were CD30-positive
  - 86.3% of patients treated with BV and 67.1% of patients treated with OST had an Eastern Cooperative Oncology Group performance status of 0-1

Table 1. Demographic and Disease Characteristics for Patients With CTCL[a]

	BV, n=139[b]	OST, n=164[c]
Age at index, median y (IQR)	60.3 (52.6-67.2)	62.6 (55.8-68.2)
Male, n (%)	93 (66.9)	111 (67.7)
Race, n (%)		
White	100 (71.9)	122 (74.4)
Black or African American	20 (14.4)	30 (18.3)
Asian	9 (6.5)	8 (4.9)
Hispanic or Latino	9 (6.5)	7 (4.3)
Native Hawaiian or other Pacific Islander	1 (0.7)	0
Disease stage at diagnosis, n (%)		
MF	79 (56.8)	108 (65.9)
Stage IA-IIA	26 (32.9)	35 (32.4)
Stage IIB	15 (19.0)	21 (19.4)
Stage IIIA-IIIB	13 (16.5)	22 (20.4)
Stage IVA1	14 (17.7)	18 (16.7)
Stage IVA2	8 (10.1)	4 (3.7)
Stage IVB	3 (3.8)	7 (6.5)
Stage unknown	0	1 (0.9)
pcALCL	60 (43.2)	56 (34.1)
Skin		
T1	17 (28.3)	11 (19.6)
T2	13 (21.7)	31 (55.4)
T3	26 (43.3)	11 (19.6)
Unknown	4 (6.7)	3 (5.4)
Node		
N0	16 (26.7)	8 (14.3)
N1	13 (21.7)	23 (41.1)
N2	20 (33.3)	15 (26.8)
N3	7 (11.7)	7 (12.5)
Unknown	4 (6.7)	3 (5.4)
Visceral		
M0	44 (73.3)	25 (44.6)
M1	10 (16.7)	26 (46.4)
Unknown	6 (10.0)	5 (8.9)
CD30 expression at index, n (%)		
Test result available	101 (72.7)	78 (47.6)
Positive[d]	87 (86.1)	45 (57.7)
ECOG performance status, n (%)[e]		
0	32 (23.0)	17 (10.4)
1	88 (63.3)	93 (56.7)
2	14 (10.1)	44 (26.8)
3	5 (3.6)	8 (4.9)
4	0	2 (1.2)
Disease involvement, n (%)[e]		
Skin-only	67 (48.2)	59 (36.0)
Extracutaneous disease	63 (45.3)	100 (61.0)
Unknown	9 (6.5)	5 (3.0)
Charlson Comorbidity Index (CCI)[e]		
Median (IQR)	0 (0.0-1.0)	0 (0.0-1.0)

[a]The baseline period was defined as the period up to 12 months prior to the index date; the index date was defined as the initiation of second-line systemic therapy for CTCL. [b]The BV cohort consisted of patients treated with BV as a second or later line of systemic therapy. [c]The OST cohort consisted of patients who did not receive BV as a second or later line of systemic therapy. Systemic therapies included alemtuzumab, bendamustine, bexarotene, bortezomib, chlorambucil, cisplatin, cyclophosphamide, cytarabine, doxorubicin, etoposide, fludarabine, gemcitabine, interferon alpha, interferon gamma, lenalidomide, methotrexate, mogamulizumab, pembrolizumab, pentostatin, extracorporeal photopheresis, pralatrexate, prednisone, romidepsin, vinblastine, vincristine, vorinostat, and 8-methoxypsoralen. Systemic therapies with or without skin-directed therapies were included. Skin-directed therapies included topical carmustine, topical corticosteroids, topical imiquimod, topical mechlorethamine, topical retinoids (eg, bexarotene, tazarotene), phototherapy (UVB or PUVA), and radiation therapy. [d]CD30 positivity was physician-defined with no pre-specified CD30-expression threshold. [e]The most recent assessment during the 12 months prior to or at the index date was reported.
Abbreviations: BV, brentuximab vedotin; CTCL, cutaneous T-cell lymphoma; ECOG, Eastern Cooperative Oncology Group; IQR, interquartile range; MF, mycosis fungoides; OST, other standard therapies; pcALCL, primary cutaneous anaplastic large-cell lymphoma

Treatment Patterns

- Most patients treated with BV or OST received 2 lines of therapy (87.8% vs 72.6%; **Table 2**)
  - Among patients treated with BV, the median duration of observation was 8.1 months
    - 96.4% (n=134) of patients received a BV-containing regimen as 2L systemic therapy (BV monotherapy, 95.5%; BV combination therapy, 4.5%)
  - Among patients treated with OST, the median duration of observation was 8.8 months
    - The most common 2L therapies were methotrexate (11.6%), mogamulizumab (9.1%), and bendamustine (9.1%) monotherapies
  - The median duration of 2L therapy for BV was 8.4 months and for OST was 5.2 months

Table 2. Treatment Characteristics of Patients With CTCL

	BV, n=139[a]	OST, n=164
Duration of observation period, median mo (IQR)[b]	8.1 (7.1-10.8)	8.8 (4.8-11.5)
Total lines of therapy, n (%)		
2	122 (87.8)	119 (72.6)
3	10 (7.2)	22 (13.4)
≥ 4	7 (5.0)	23 (14.0)
1L systemic therapy, median mo (IQR)		
Time from CTCL diagnosis to 1L	0.7 (0.2-1.9)	0.7 (0.2-1.9)
Duration of therapy	4.0 (1.8-6.2)	3.9 (1.2-6.2)
Time from 1L discontinuation to 2L initiation	0.7 (0.2-2.3)	1.0 (0.2-3.7)
Systemic lines of therapy with BV, n (%)		
2	134 (96.4)	-
3	5 (3.6)	-
≥ 4	1 (0.7)	-
2L systemic therapy, n (%)		
BV-containing therapy	134 (96.4)	-
BV monotherapy	128 (95.5)	-
BV combination therapy[c]	6 (4.5)	-
Methotrexate	0	19 (11.6)
Mogamulizumab	2 (1.4)	15 (9.1)
Bendamustine	0	15 (9.1)
Bexarotene	0	13 (7.9)
Alemtuzumab	0	12 (7.3)
Pralatrexate	0	12 (7.3)
Romidepsin	0	9 (5.5)
Bortezomib	1 (0.7)	6 (3.7)
Doxorubicin	0	7 (4.3)
Cisplatin	0	6 (3.7)
Vorinostat	0	6 (3.7)
Gemcitabine	1 (0.7)	4 (2.4)
Pembrolizumab	0	5 (3.0)
Other	1 (0.7)	35 (21.3)
Duration of 2L therapy, median mo (95% CI)[d]	8.4 (7.1-15.4)	5.2 (3.9-7.3)

[a]Patients may have been treated with BV across multiple systemic lines of therapy. [b]The observation period was defined as the time from the initiation of second-line systemic therapy for CTCL (index date) to the earliest of death, loss to follow-up, or date of chart abstraction. [c]BV + vorinostat, BV + cyclophosphamide + doxorubicin, BV + cyclophosphamide + vincristine, and BV + fludarabine. [d]Kaplan-Meier methods were used to estimate duration of therapy. If discontinuation was not reported during the observation period, patients was censored at the earliest of loss to follow-up or date of chart abstraction.
Abbreviations: 1L, frontline; 2L, second-line; BV, brentuximab vedotin; CTCL, cutaneous T-cell lymphoma; OST, other standard therapies

Clinical Outcomes

- Real-world ORR (rwORR) for patients treated with 2L BV and OST were 82.1% and 66.5% and real-world ORR4 (rwORR4) for patients treated with 2L BV and OST were 42.5% and 25.0% (**Table 3**)

Table 3. Real-World Response Rates for 2L BV or OST in Patients With CTCL

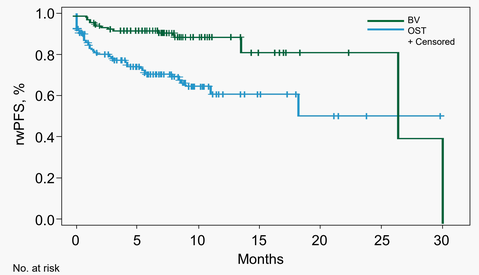
	Real-World Response Rates, % (95% CI)	
	BV, n=134[a]	OST, n=164[b]
rwORR	82.1 (74.5-88.2)	66.5 (58.7-73.6)
Complete response	38.8 (30.5-47.6)	27.4 (20.8-34.9)
Partial response	43.3 (34.8-52.1)	39.0 (31.5-46.9)
Stable disease	13.4 (8.2-20.4)	21.3 (15.3-28.4)
Progressive disease	4.5 (1.7-9.5)	12.2 (7.6-18.2)
rwORR4[c]	42.5 (34.0-51.4)	25.0 (18.6-32.3)

[a]5 patients were excluded from analysis of clinical outcomes due to being treated with BV as third line or later. [b]See Table 1 footnote c. [c]Defined as the proportion of patients achieving a global response (complete or partial response) lasting at least 4 months.
Abbreviations: 2L, second-line; BV, brentuximab vedotin; CTCL, cutaneous T-cell lymphoma; OST, other standard therapies; rwORR, real-world objective response rate; rwORR4, real-world objective response rate lasting at least 4 months

- The RMST (95% CI) for rwPFS was higher for patients treated with BV than OST at 1 year (11.1 vs 8.9 months, *P*<0.01) and 2 years (21.0 vs 15.7 months, *P*<0.01; **Figure 1A**)
- The RMST for rwTTNT was higher for patients treated with BV than OST at 1 year (11.2 vs 8.1 months, *P*<0.01) and 2 years (20.5 vs 13.7 months, *P*<0.01) (**Figure 1B**)
- The RMST for rwOS was higher for BV than OST at 1 year (11.3 vs 9.0 months, *P*<0.01) and 2 years (21.3 vs 15.8 months; *P*<0.01) (**Figure 1C**)

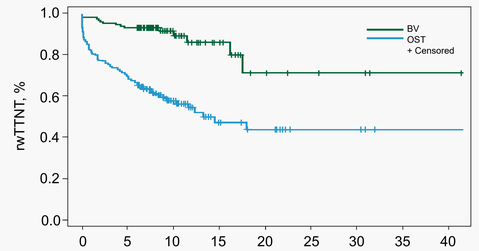
Figure 1. rwPFS, rwTTNT, and rwOS for 2L BV and OST in Patients With CTCL

A. rwPFS



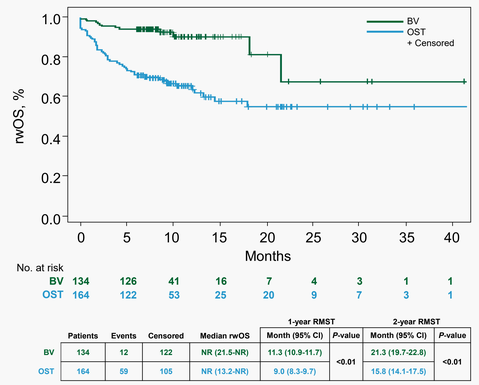
	Patients	Events	Censored	Median rwPFS	1-year RMST Month (95% CI)	1-year RMST *P*-value	2-year RMST Month (95% CI)	2-year RMST *P*-value
BV	134	15	119	26.5 (26.5-30.1)	11.1 (10.5-11.6)	<0.01	21.0 (19.1-22.9)	<0.01
OST	164	47	117	NR (18.2-NR)	8.9 (8.1-9.6)		15.7 (13.6-17.8)	

B. rwTTNT



	Patients	Events	Censored	Median rwTTNT	1-year RMST Month (95% CI)	1-year RMST *P*-value	2-year RMST Month (95% CI)	2-year RMST *P*-value
BV	134	14	120	NR (17.5-NR)	11.2 (10.8-11.7)	<0.01	20.5 (18.6-22.4)	<0.01
OST	164	73	91	13.17 (9.23-NR)	8.1 (7.4-8.9)		13.7 (11.9-15.5)	

C. rwOS



	Patients	Events	Censored	Median rwOS	1-year RMST Month (95% CI)	1-year RMST *P*-value	2-year RMST Month (95% CI)	2-year RMST *P*-value
BV	134	12	122	NR (21.5-NR)	11.3 (10.9-11.7)	<0.01	21.3 (19.7-22.8)	<0.01
OST	164	59	105	NR (13.2-NR)	9.0 (8.3-9.7)		15.8 (14.1-17.5)	

Abbreviations: 2L, second line; BV, brentuximab vedotin; CTCL, cutaneous T-cell lymphoma; NR, not reached; OST, other standard therapies; rwOS, real-world overall survival;; rwPFS, real-world progression-free survival; RMST, restricted mean survival time; rwTTNT, real-world time to next treatment

Healthcare Resource Utilization

- Overall, during the observation period, lower HRU was seen with BV than OST (**Table 4**)
  - A smaller percentage of patients were referred to palliative care with BV than OST (5.0% vs 11.0%)

Table 4. CTCL-Related Healthcare Resource Utilization During the Observation Period[a]

	BV, n=139[b]	OST, n=164[c]
≥1 CTCL-related visit, n (%)		
Outpatient	123 (88.5)	144 (87.8)
ED	42 (30.2)	64 (39.0)
Hospitalization	41 (29.5)	60 (36.6)
CTCL-related visits, per person-year, IR (95% CI)[d]		
Outpatient	10.5 (9.9-11.1)	10.7 (10.2-11.3)
ED	0.9 (0.7-1.0)	1.9 (1.7-2.1)
Hospitalization	1.3 (1.1-1.5)	1.9 (1.7-2.1)
Length of stay, median days (95% CI)[e]	13.7 (12.6-4.9)	21.1 (19.9-22.4)
Consultation/referral for palliative care, n (%)	**7 (5.0)**	**18 (11.0)**
Hospice – outpatient	5 (71.4)	13 (72.2)
Home care	2 (28.6)	2 (11.1)
Hospice – inpatient	0	2 (11.1)
Hospital – inpatient	0	1 (5.6)

[a]The observation period was defined as the time from the initiation of second-line systemic therapy for CTCL as reported by the physician to the earliest of death, loss to follow-up, or date of chart abstraction. [b]See Table 1 footnotes b and c. [c]Number of CTCL-related visits per person-year was calculated by dividing the total number of visits among all patients by the total duration of follow-up during the observation period. [d]The IR for length of stay was calculated among patients with hospitalizations; 15 records were removed due to implausible values
Abbreviations: BV, brentuximab vedotin; CTCL, cutaneous T-cell lymphoma; ED, emergency department; IR, incidence rate; OST, other standard therapies

Limitations

- Results should be interpreted with caution due to differences in patient clinical profiles across the treatment cohorts and the treatment heterogeneity of the OST cohort
- The study is limited by short duration of follow-up
- Participation in the study was subject to selection bias as panel members may differ from physicians who are not members or decline to participate; in addition, the majority of participating physicians represented community-based settings and results may not be generalizable to all patients and practice settings
- Physicians may select specific patients for inclusion; however, selection bias was mitigated by implementing a randomization scheme

Conclusions

- This retrospective, physician panel-based chart review study addresses the gap in the literature by assessing patient characteristics, treatment patterns, clinical outcomes, and HRU among patients with CTCL who received 2L BV or OST in real-world clinical practice
- Real-world outcomes with BV in patients with CTCL who received ≥1 prior systemic therapy were consistent with results from ALCANZA, demonstrating favorable clinical outcomes with BV

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