Real-World Treatment Patterns and Overall Survival Among Medicare Fee-For-Service Beneficiaries Newly Diagnosed With Peripheral T-Cell Lymphoma

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At the time of study conduct.

Background

- Peripheral T-cell lymphomas (PTCLs) are a rare heterogeneous group of lymphoid malignancies characterized by a clinically aggressive course with poor prognosis.[1,2]
- A majority of patients with PTCL are aged ≥60 years and typically present with advanced-stage disease and multiple comorbidities.[3,4]
- There remains no consensus on the standard of care for patients with most PTCL subtypes.
- In December 2018, NCCN Clinical Practice Guidelines In Oncology (NCCN Guidelines®) were updated to recommend brentuximab vedotin plus CHP (cyclophosphamide, doxorubicin, and prednisone) as a preferred regimen for anaplastic large cell lymphoma (ALCL; category 1) and other CD30-expressing PTCL histologies (category 2A), following US Food and Drug Administration (FDA) approval in this setting based on the ECHELON-2 trial (November 2018).[5-7]
  - Prior to ECHELON-2, treatment options for nodal subtypes were generally limited to participation in a clinical trial or multi-agent chemotherapies such as CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) or CHOEP (CHOP with etoposide).
  - ECHELON-2 demonstrated a statistically significant improvement in both progression-free survival (48.2 vs 20.8 months) and overall survival (OS; hazard ratio 0.66; 95% confidence interval [CI]: 0.46–0.95) with brentuximab vedotin plus CHP compared with CHOP.[6]
- Limited contemporary real-world data exist on the treatment patterns and OS of patients with PTCL treated with CHOP or non-CHOP regimens in the US prior to the FDA approval of brentuximab vedotin plus CHP in adults with previously untreated CD30-expressing PTCL.
- Such data would be of value to inform understanding of the PTCL landscape as well as provide a baseline for future studies evaluating changes in real-world outcomes.

Objective

- To evaluate treatment patterns and OS among Medicare Fee-for-Service (FFS) beneficiaries newly diagnosed with PTCL prior to the FDA approval of brentuximab vedotin plus CHP in this setting.
  - OS analysis focused on patients with PTCL who received CHOP vs non-CHOP treatment regimens.

Methods

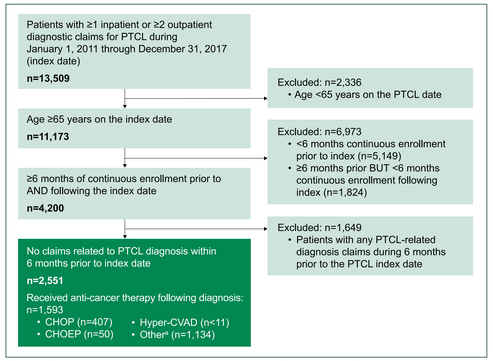
- The 100% sample of Medicare FFS claims (Parts A/B/D) was used to identify patients aged ≥65 years with ≥1 inpatient or ≥2 distinct outpatient diagnosis claims for PTCL (index event) from January 2011 to December 2017.
- Patients were required to have at least 6 months prior and 12 months post-index continuous Medicare enrollment, and were followed until disenrollment, death, or the end of the study period, whichever occurred first.
- Treatment patterns, including time to initiation of therapy, were identified using relevant Healthcare Common Procedure Coding System codes and National Drug Codes and evaluated against the guideline-recommended line of therapy following diagnosis.
- OS, defined as the time from initial episode or treatment start date to the validated date of death and analyzed according to CHOP vs non-CHOP regimen, was measured using the Kaplan-Meier method; patients without a death date were assumed to be alive at the time of analysis and were censored.

Results

Patient population

- A total of 2,551 Medicare FFS beneficiaries with a PTCL diagnosis met study criteria and were included for analysis (**Figure 1**).
- The majority of patients were white (86.9%), over half were male (52.9%), and mean age was 75 years (standard deviation [SD]: 6.94 years; median: 74 years) (**Table 1**).
- Patients had multiple comorbidities at diagnosis (mean Charlson Comorbidity Index [CCI] score 4.47), including hypertension (77.3%), diabetes (32.9%), and chronic obstructive pulmonary disease (28.1%).
- The median duration of follow-up post-index was approximately 2.4 years.

Figure 1. Summary of cohort selection and identification of treatment



[a]Other includes other chemotherapy, immunotherapy, targeted therapy, or steroids.
CHOEP, cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisone; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; hyper-CVAD, cyclophosphamide, doxorubicin, vincristine, and dexamethasone; PTCL, peripheral T-cell lymphoma.

Pharmacological management of patients with PTCL

- Among the 2,551 patients in the study cohort, 62.4% (n=1,593 of 2,551) received at least 1 identifiable drug regimen; 25.5% of treated patients received CHOP (n=407), 3.1% CHOEP (n=50), and 71.2% (n=1,134) other regimens (**Figure 2**).
- Of patients treated with other regimens, 37.7% (n=427) received steroids only, 22.4% (n=254) steroids with unidentifiable chemotherapy, 6.9% (n=78) cyclophosphamide, 6.2% (n=70) methotrexate, 4.6% (n=52) brentuximab vedotin, 3.6% (n=41) bendamustine, 3.5% (n=40) romidepsin, and 15.2% (n=172) other therapy combinations.
- Almost all patients who received CHOP (n=398 of 407; 97.8%) discontinued the regimen during follow-up, of whom 16.6% (n=66) received an identifiable second line of therapy, 48.7% (n=194) an unidentifiable second line of therapy, and the remainder (34.7%; n=138) had no evidence of further anti-cancer treatment.
  - The median time from CHOP initiation to a subsequent line of therapy was 5.6 months, suggesting most patients completed the recommended 6 cycles of CHOP before receiving second-line therapy.[5]

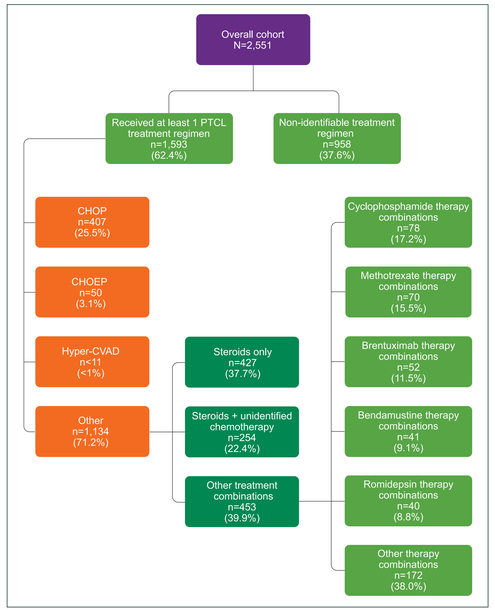
Table 1. Patient demographics and clinical characteristics during the 12 months prior to PTCL diagnosis

Demographics	PTCL cohort (n=2,551)	CHOP (n=407)	Non-CHOP (n=1,134)	p values: CHOP vs non-CHOP
Age at index, years				0.0034
Mean (SD)	75.15 (6.94)	73.94 (5.76)	74.97 (6.83)	
Median (IQR)	74 (11.00)	73 (9.00)	74 (11.00)	
Gender, %				0.3665
Female	47.08	45.45	48.06	
Male	52.92	54.55	51.94	
US region, %				0.0767
Midwest	25.56	24.82	26.46	
Northeast	23.64	19.90	23.81	
South	33.63	40.54	32.89	
West	17.05	14.74	16.75	
Other	NR	NR	NR	
Race, %				0.3615
White	86.95	86.73	86.95	
Black	6.90	8.11	6.79	
Asian	1.80	NR	1.76	
Hispanic	1.49	NR	1.23	
North American Native	NR	NR	NR	
Other/Unknown	2.59	NR	3.09	
Clinical characteristics				
Charlson Comorbidity Index, mean (SD)	4.47 (2.87)	4.33 (2.93)	4.76 (2.97)	0.0118
Comorbid conditions (>10%), %				
COPD	28.07	27.03	32.89	0.0287
Congestive heart failure	15.56	10.81	17.28	0.0020
Depression	15.76	14.50	18.34	0.0787
Diabetes	32.89	31.45	33.16	0.5288
Hypertension	77.26	83.05	77.69	0.0226
Other primary malignancies	67.44	68.40	70.80	0.3648
Concomitant medications, %				
Antibiotics	20.46	28.75	22.66	0.0141
Antidepressants	24.85	22.60	27.95	0.0360
Immunosuppressants	9.80	10.07	12.52	0.1903
Opioids	30.34	46.93	33.07	<0.0001

CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; COPD, chronic obstructive pulmonary disease; IQR, interquartile range; NR, not reported; PTCL, peripheral T-cell lymphoma; SD, standard deviation

- For most patients, anti-cancer treatment was initiated within the first 1–3 months following diagnosis (CHOP: 25.7 ± 33.9 days; CHOEP: 29.7 ± 25.1 days; hyper-CVAD [cyclophosphamide, doxorubicin, vincristine, and dexamethasone]: 6.0 ± 4.2 days; other therapy: 77.2 ± 91.8 days); stem cell transplant and radiotherapy were generally initiated in year 2 (618.6 ± 538.4 and 682.8 ± 517.6 days, respectively).
- The mean baseline CCI score for patients treated with CHOP was slightly lower (4.33 [SD: 2.93]) than for patients treated with non-CHOP regimens (4.76 [SD: 2.97]; p=0.0118).

Figure 2. Anti-cancer therapies received by patients newly diagnosed with PTCL

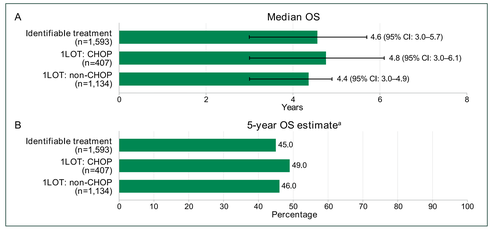


CHOEP, cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisone; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; hyper-CVAD, cyclophosphamide, doxorubicin, vincristine, and dexamethasone; PTCL, peripheral T-cell lymphoma.

Overall survival

- In patients receiving an identifiable first line of therapy, median OS among CHOP and non-CHOP recipients was 4.8 years (95% CI: 3.0–6.1) and 4.4 years (95% CI: 3.0–4.9), respectively (**Figure 3**).
- The 5-year OS estimate was 49% in patients receiving CHOP compared with 46% for non-CHOP recipients.

Figure 3. OS for Medicare beneficiaries newly diagnosed with PTCL, by anti-cancer therapy



[a]Estimates obtained using Kaplan-Meier (product limit) method.
CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; CI, confidence interval; LOT, line of therapy; OS, overall survival; PTCL, peripheral T-cell lymphoma.

Limitations

- There are limitations inherent in retrospective claims-based analyses, including:
  - Data collection lacks clinical specificity (eg, stage of cancer) and may be subject to misclassification due to coding limitations and potential for data entry error.
  - Possible selection bias for more fit PTCL patients receiving CHOP, as suggested by the lower CCI than non-CHOP recipients.
  - Treatments administered as part of a clinical trial or within the inpatient setting resulted in the specific drug regimen being unidentifiable for many study participants.
  - Lack of visibility into disease stage, PTCL subtype, and laboratory results.
  - OS was estimated using validated date of death from the Centers for Medicare and Medicaid Services.

Conclusions

- Fewer than 30% of Medicare beneficiaries newly diagnosed with PTCL were treated with intensive chemotherapy such as CHOP as first line of therapy.
- Patients with PTCL and receiving CHOP had similar or marginally higher OS compared with patients receiving non-CHOP therapy; however, the 5-year OS across all cohorts remained less than 50%.
- Further analyses will be of interest to determine changes in real-world prognosis and treatment patterns following the introduction of brentuximab vedotin in this setting, given the survival advantage,[6] as well as other therapeutic advances.

References

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