REAL-WORLD CHARACTERISTICS OF PATIENTS WITH CLASSICAL HODGKIN LYMPHOMA RECEIVING FRONTLINE BRENTUXIMAB VEDOTIN WITH CHEMOTHERAPY: A RETROSPECTIVE ANALYSIS WITH PROPENSITY SCORE MATCHING

Tycel Phillips[1], Kristina Yu-Isenberg[2], Nicholas Liu[2], Andy Surinach[3], Carlos Flores[3], Julie Lisano[2], Michelle A. Fanale[2], John M. Burke[4]

[1]Department of Internal Medicine, Division of Hematology and Oncology, University of Michigan Medical School, Ann Arbor, MI; [2]Seagen Inc., Bothell, WA; [3]Genesis Research, Hoboken, NJ; [4]US Oncology Hematology Research Program, Rocky Mountain Cancer Centers, Aurora, CO

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Background

- Hodgkin lymphoma (HL) is an uncommon B-cell malignancy with an increased incidence in young adults aged 15–30 years, and among adults aged ≥55 years.[1]
  - HL represents ~10% of lymphomas in the United States (US), with an estimated 8,480 new cases in 2020; the 5-year survival rate is 87.4%.[1,2]
  - Classical HL (cHL) is a distinct, more common (~95%) form of HL characterized by the presence of malignant, multinucleated giant Reed-Sternberg cells.[1]
- In the phase 3 ECHELON-1 study (NCT01712490),[3] treatment with brentuximab vedotin (BV), doxorubicin, vinblastine, and dacarbazine (A+AVD) significantly improved modified progression-free survival in patients with newly diagnosed stage III or IV cHL compared with doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD).
  - These results supported the March 2018 US Food and Drug Administration approval of BV for the treatment of adult patients with previously untreated stage III or IV cHL, in combination with doxorubicin, vinblastine, and dacarbazine.[4]
- To optimize outcomes for patients with stage III or IV cHL receiving ABVD, the current National Comprehensive Cancer Network guidelines recommend an interim positron emission tomography/computed tomography (PET/CT) imaging at the end of cycle 2 (PET2) to inform escalation or de-escalation of therapy.[5]

Objective and Methods

This study described the real-world patient characteristics, supportive care use, and PET2 utilization in cHL patients newly treated with A+AVD or ABVD outside of the clinical trial setting in the US.

- **Study design**: Retrospective cohort study using medical and pharmacy claims data in the Symphony Health Solutions Patient-Level Claims database.
  - Patients are uniquely identified and can be tracked over 10 years across all settings.
  - Captures a significant portion of total medical and pharmacy activity in the US and is geographically representative, with all payment and payer types represented.
- **Study population:**
  - Patients ≥18 years with 1 inpatient or 2 outpatient ICD-9/10 cHL diagnosis codes.
  - Newly prescribed A+AVD or ABVD (index date) between March 2018 and January 2020; ≥6 months continuous enrollment before and ≥3 months after the index date.
- **Analysis:** 1:1 propensity score matching analysis was performed based on age, gender, baseline comorbidities, geographic region, and length of follow-up.

Results: Selected baseline characteristics of cHL patients initiating A+AVD vs ABVD before and after 1:1 propensity score matching

- 4,259 patients met inclusion criteria (1,002 A+AVD; 3,257 ABVD).
- In the unmatched cohorts, 59% and 51% of patients were male, and median age at index was 48 and 39 years for A+AVD and ABVD, respectively.
- Patients on A+AVD had higher comorbidity burden across all conditions included in the Charlson Comorbidity Index, with 41% vs 33% of ABVD patients reporting ≥1 comorbidity.

Baseline characteristics	Unmatched			Propensity score matched		
	A+AVD (n=1,002)	ABVD (n=3,257)	p-value	A+AVD (n=1,002)	ABVD (n=1,002)	p-value
Age, median (IQR)	48 (30, 65)	39 (28, 56)	<0.001	48 (30, 65)	48 (33, 62)	0.8
Male, %	59	51	<0.001	59	57	0.5
≥1 comorbidity, %	41	33	<0.001	41	41	>0.9
Common comorbidities, %						
Chronic pulmonary disease	18	14	0.006	18	17	>0.9
Diabetes, no complications	12	8.9	0.015	12	13	0.5
Diabetes, complications	3.3	2.1	0.032	3.3	3.8	0.6
Congestive heart failure	4.8	3.2	0.022	4.8	4.6	>0.9
Mild liver disease	8.1	6.1	0.030	8.1	7.9	>0.9
Peripheral vascular disease	6.8	4.6	0.007	6.8	5.4	0.2
Renal disease	4.5	2.9	0.019	4.5	4.8	0.8
Length of follow-up, median (IQR), months	14 (9, 20)	15 (9, 21)	0.2	14 (9, 20)	14 (9, 20)	0.5

A+AVD, brentuximab vedotin plus doxorubicin, vinblastine, and dacarbazine; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; cHL, classical Hodgkin lymphoma; IQR, interquartile range.

Results: Treatment characteristics after 1:1 propensity score matching

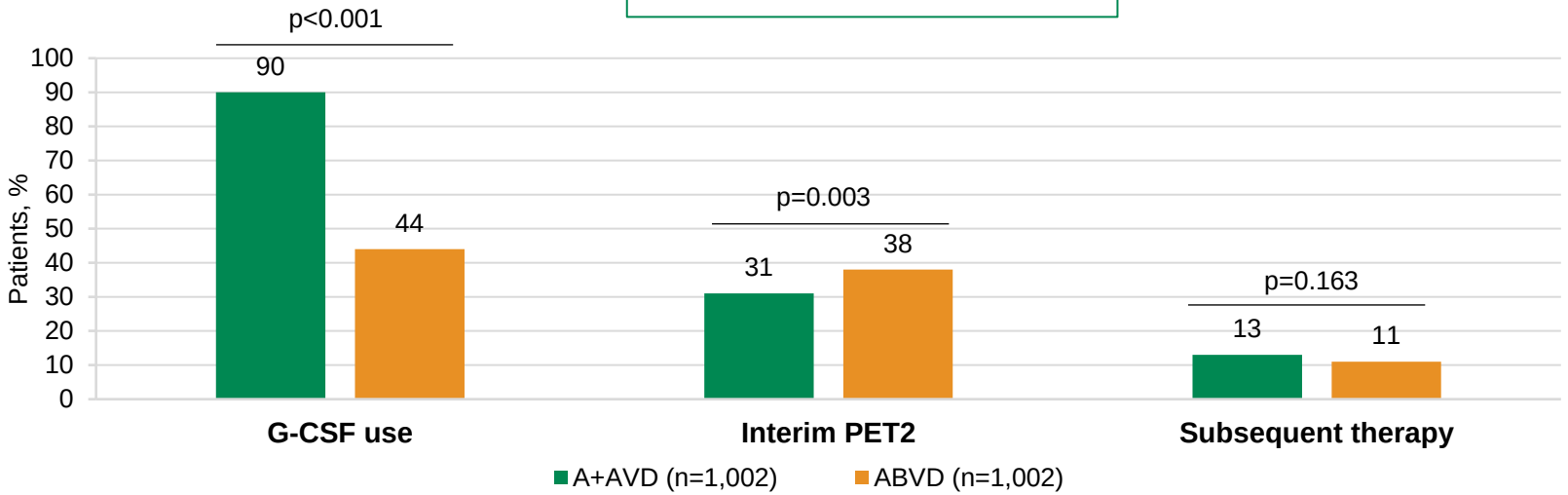
Significantly more A+AVD patients (90%) received granulocyte-colony stimulating factor (G-CSF) vs ABVD patients (44%), with 80% and 20%, respectively, receiving it as primary prophylaxis.

In the A+AVD and ABVD cohorts, only 31% and 38% of patients underwent interim PET2 restaging, respectively.

- In ABVD patients, 44% who received an interim PET2 and 33% who did not de-escalated treatment to AVD

Of the patients with subsequent therapy, a BV-containing regimen was received by:

- 43% of ABVD patients
- 19% of A+AVD patients



A+AVD, brentuximab vedotin plus doxorubicin, vinblastine, and dacarbazine; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; G-CSF, granulocyte-colony stimulating factor; PET, positron emission tomography; PET2, PET imaging at the end of cycle 2.

Limitations

- Claims data have inherent limitations, such as selection bias and reliance on complete and accurate coding.
- Confounding by unmeasured characteristics (eg, disease stage, PET/CT results, and response outcomes) is a limitation of this and any retrospective study based on claims data.
- Although the data represent ~40% of the US market and provide important information into real-world treatment use and patient characteristics, results may not be generalizable to all patients with cHL or to all practice settings.

Conclusions

- In this first real-world evaluation, patients with cHL receiving frontline A+AVD were older, had higher comorbidity burden, and utilized recommended G-CSF as primary prophylaxis compared with ECHELON-1 clinical trial patients.
- Only about one third of all patients underwent interim PET2 restaging, and less than half of the patients who started on ABVD were de-escalated to AVD.
    - Among ABVD patients, there was a discordance between the percentage of patients who underwent PET2 and the percentage of patients who de-escalated treatment to AVD, which suggests other factors may influence therapy decisions.
- This hypothesis-generating analysis suggests the need to:

    1. Control for patient characteristics (eg, age, comorbidities) in comparative real-world analyses;
    2. Understand reasons for the lack of PET/CT use given treatment guidelines; and
    3. Evaluate actual use of the interim PET2 results to escalate or de-escalate treatment in patients with cHL.

- Optimizing treatment outcomes while maximizing short- and long-term treatment efficacy and safety is paramount in managing cHL patients.
- Differences in the characteristics and management of this real-world cHL population as compared with the ECHELON-1 trial population demonstrate the importance of retrospective studies in assessing the impact of new regimens on clinical practice and in identifying areas for further education of practitioners.

References and Disclosures

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Corresponding author: Tycel Philips (tycelp@med.umich.edu).

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