Classical Hodgkin Lymphoma: Real-World Observations from Physicians, Patients, and Caregivers on the Disease and Its Treatment (CONNECT): Physician Frontline Treatment Preferences for Stage III or IV Classical Hodgkin Lymphoma

Andrew M. Evens,[1] Kristina S. Yu,[2] Nicholas Liu,[2] Andy Surinach,[3] Katie Holmes,[4] Carlos Flores,[3] Supriya Kumar,[4] Michelle Fanale,[2] Darcy R. Flora,[5] Susan K. Parsons[6]

[1]Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, USA; [2]Seagen Inc., Bothell, WA, USA; [3]Genesis Research, Hoboken, NJ, USA; [4]Ipsos Healthcare, New York, NY, USA; [5]GRYT Health, Rochester, NY, USA; [6]Tufts Medical Center, Boston, MA, USA

Background

- Mainstay therapies for patients with stage III or IV classical Hodgkin lymphoma (cHL) include several multiagent chemotherapy regimens[1]
- A combination of doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) is commonly administered in the frontline (1L) setting[2-4]
  - Approximately 30% of patients with stage III or IV cHL will be refractory to or relapse following 1L ABVD treatment[5-7]
- Brentuximab vedotin in combination with doxorubicin, vinblastine, and dacarbazine (A+AVD) is an option for 1L treatment of stage III or IV cHL and combines a novel targeted therapy with a standard chemotherapy regimen[3]
  - In the 5-year update of the ECHELON-1 trial, patients with stage III or IV cHL randomized to 1L A+AVD compared with ABVD continued to demonstrate a robust and durable improvement in progression-free survival (PFS: 82.2% [95% CI 79.0–85.0] vs 75.3% [71.7–78.5]) with a 32% reduction in the risk of disease progression or death (hazard ratio: 0.68 [0.53–0.87]; nominal *P*=0·002)[8]

Objective

- To understand the decision-making process behind the selection of a cHL treatment regimen for patients with stage III or IV cHL, we surveyed physicians about their preferred regimens and factors influencing treatment choices as part of the CONNECT survey, the first real-world observational survey in cHL that includes physicians, patients, and caregivers

Methods

Study Design

- The CONNECT physician survey was an anonymous double-blind, online survey administered from October 19, 2020, to November 16, 2020
  - Participating physicians were blinded to the study sponsor, and participant identities were blinded to the sponsor and researchers
  - The survey was reviewed and approved by the New England Institutional Review Board

Participants

- Physicians were recruited using a large online panel of healthcare providers in the United States that leverages multiple sources of physician recruitment
- Eligible physicians
  - Included medical oncologists, hematologist/oncologists, and hematologists with ≥2 years medical practice experience
  - Treated ≥1 adult (aged ≥18 years) with stage III or IV cHL and ≥1 adult with cHL in the 1L setting within the past 12 months
- Recruited physicians were invited to take part in the survey via email

Statistical Analysis

- Quantitative data were summarized as mean and standard deviation or median and range
- Categorical data were reported as individual totals or percentages
- Non–mutually exclusive data were reported as a number and percentage of total sample size

Results

- In total, 301 physicians participated in the survey (**Figure 1**)

Overall 1L cHL Treatment Considerations

- Physicians reported clinical trial, efficacy, and safety data and official guideline recommendations as the most important considerations (ranked 1 or 2) when selecting 1L cHL treatments; patient personal goals, treatment costs, and patient financial support programs were ranked 1 or 2 by <10% of physicians (**Figure 2A**)
  - Within clinical data considerations, efficacy attributes were the dominant drivers of 1L stage III or IV cHL treatment decisions, including overall survival (OS; 91%), long-term PFS (86%), curative potential (85%), and complete response rate (81%), which physicians rated as having had the greatest or most essential impact on their decision-making when they considered cHL treatments
  - When asked about acceptable long-term toxicity trade-offs for increased efficacy in patients with stage III or IV cHL, physicians stated an additional median of 8 months of OS and 6 months of PFS were worth the potential for downstream toxicity

Patient-Specific Treatment Considerations

- Fifty percent of physicians reported that disease stage was the most important patient characteristic to consider when deciding on a 1L treatment for stage III or IV cHL followed by fitness/frailty (Eastern Cooperative Oncology Group performance score; 35%), and comorbidities (28%; **Figure 2B**)

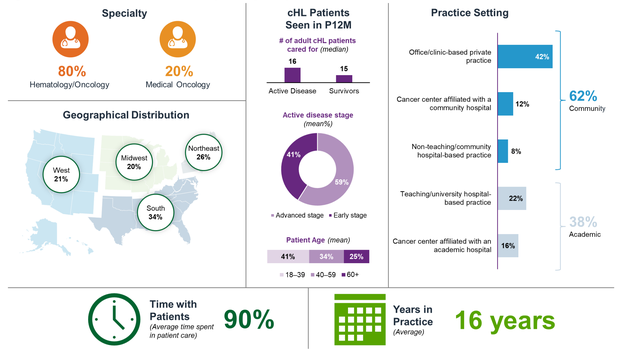
Stage III or IV cHL 1L Treatment Preferences

- When physicians were asked to choose their first-choice treatment among A+AVD, ABVD, or PET-adapted ABVD for various patient types with stage III or IV cHL (**Figure 3**)
  - A+AVD was generally selected by more physicians than ABVD or PET-adapted ABVD with 37%-50% of physicians selecting A+AVD as their first-choice regimen
  - Significantly more physicians selected A+AVD than ABVD as their first-choice treatment for all patient types
  - Numerically more physicians selected A+AVD than PET-adapted ABVD for all patient types except for younger, more fit, patients; these differences were significant for those with stage III disease, those with stage IV disease, and those with a perceived high-risk of relapse
- No significant differences in treatment preferences were noted between physicians practicing in community compared with academic settings

Stage III or IV cHL 1L Treatment Preferences by Patient Profile

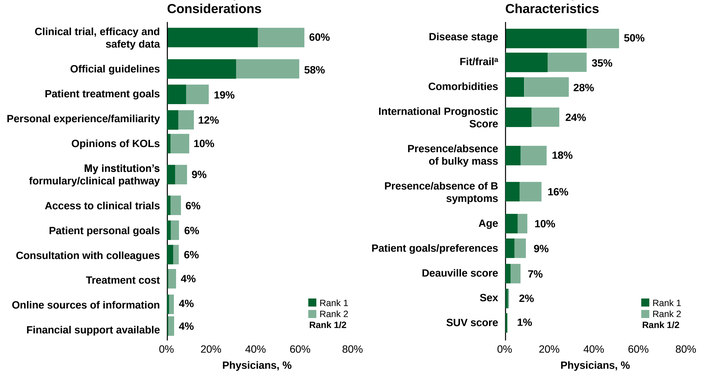
- When presented with several patient profiles and various treatment options that may be given with or without radiotherapy
  - 51% of participating physicians preferred a brentuximab vedotin-based therapy for older, unfit patients with stage III or IV cHL as demonstrated by Patient 4 (**Figure 4A**); brentuximab vedotin monotherapy was a less dominant choice in the other patient profiles
  - OS and PFS were selected by physicians as the top reasons for choosing the treatment regimen selected in Figure 4A (**Figure 4B**)
  - Patient age, comorbidities, and quality of life were selected as top reasons for choosing a less intensive treatment regimen (e.g., brentuximab vedotin monotherapy, AVD)

Figure 1. Overview of Participating Physicians



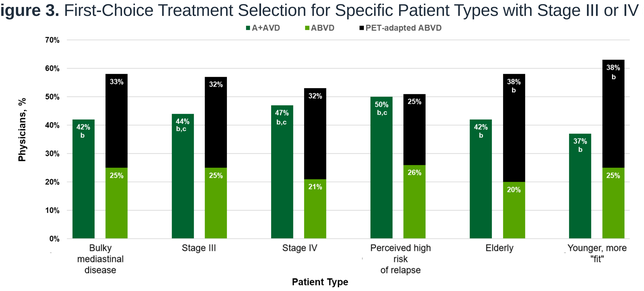
Abbreviations: cHL, classical Hodgkin lymphoma; P12M, past 12 months

Figure 2. Physician Considerations When Selecting a 1L cHL Treatment



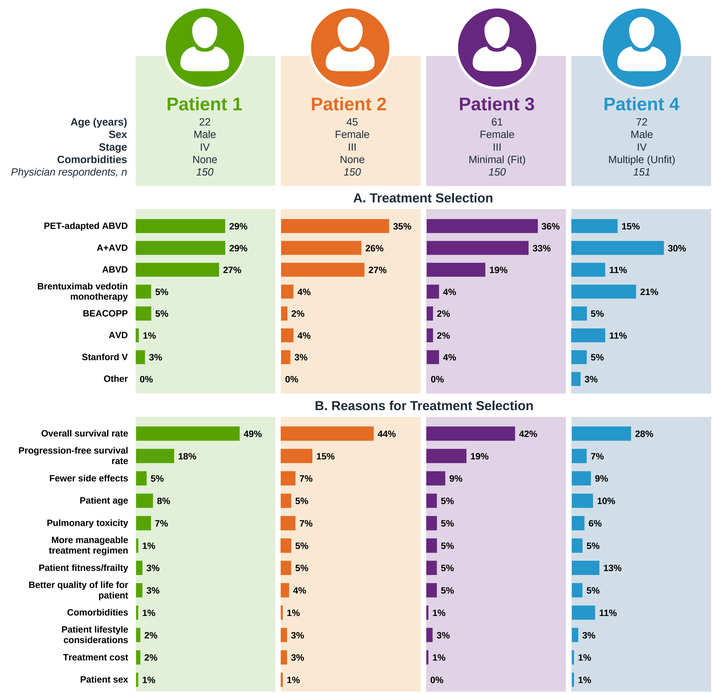
Note: Percentage of physicians (n=301) ranking consideration with a 1 or 2. [a] Fit/frail measured using ECOG (Eastern Cooperative Oncology Group) performance score. **Abbreviations:** 1L, frontline; cHL, classical Hodgkin lymphoma; KOL, key opinion leader; SUV, standardized uptake value.

Figure 3. First-Choice Treatment Selection for Specific Patient Types with Stage III or IV cHL[a]



[a] Physicians were provided a list of possible patient types and asked to assume that each patient type had stage III or IV cHL. For each patient type, physicians were asked to indicate which treatment regimen would be their first, second, and third choices, choosing between A+AVD, ABVD, and PET-adapted ABVD (from the RATHL et al. study). [b] Statistically significantly different than ABVD. [c] Statistically significantly different than PET-adapted ABVD. **Abbreviations:** A+AVD, brentuximab vedotin in combination with doxorubicin, vinblastine, and dacarbazine; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; cHL, classical Hodgkin lymphoma; PET, positron emission tomography; RATHL, risk-adapted treatment of advanced Hodgkin lymphoma

Figure 4. Treatment Selection and Reason for Selection by Patient Profile for Treatment-Naïve Stage III or IV cHL



Abbreviations: A+AVD, brentuximab vedotin in combination with doxorubicin, vinblastine, and dacarbazine; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; AVD, doxorubicin, vinblastine, and dacarbazine; BEACOPP, bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone; cHL, classical Hodgkin lymphoma; PET, positron emission tomography

Limitations

- As this was an opt-in group of survey participants already part of established research panels, results may not be applicable to all physicians who treat patients with cHL

Conclusions

- Treatment preferences for patients with stage III or IV cHL varied based on patient characteristics including presence of bulky mediastinal disease, disease stage, perceived risk of relapse, age, and comorbidities
- Efficacy attributes, including OS and PFS; quality of life; and patient age were top reasons cited by surveyed physicians for selecting a specific 1L treatment regimen in stage III or IV cHL

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Funding Statement

This study was funded by Seagen Inc. Medical writing support was provided by Sarah A Criddle, PharmD, and Beth A Lesher, PharmD, BCPS, and editorial support by Christina DuVernay, PhD, from Pharmerit International, LP, doing business as OPEN Health, and funded by the study sponsor.

For more information or questions, please contact Nicholas Liu, PharmD at nliu@seagen.com

Poster No. 2467
Presented at the American Society of Hematology (ASH) Annual Meeting; December 11–14, 2021; Atlanta, GA