Real-World Patient Characteristics, Treatment Patterns, and Outcomes in Patients With Stage III or IV Classic Hodgkin Lymphoma Treated With Frontline ABVD: A Retrospective Analysis Using a Real-World Database

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Background

- Approximately 30% of patients with newly diagnosed stage III or IV classic Hodgkin lymphoma (cHL) are refractory to or relapse following treatment with ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine)[1]
  - PET/CT imaging is important with frontline (1L) ABVD at initial staging and during follow-up, including after 2 cycles to adapt treatment based on response (RATHL 2016)[2]
- Based on the ECHELON-1 trial, 1L A+AVD (brentuximab vedotin in combination with doxorubicin, vinblastine, dacarbazine) is the first regimen to show an overall survival (OS) advantage compared with ABVD in patients with stage III or IV cHL in several decades and continues to show durable improvement in progression-free survival since FDA approval in 2018[3]
  - After approximately 6-years of follow-up, A+AVD had a 41% reduction in the risk of death (hazard ratio [HR]: 0.59; 95% CI: 0.40-0.88; *P*=0.009) and a 32% reduction in the risk of progression or death (HR 0.68 [95% CI: 0.53-0.86]) compared with ABVD
  - Patients treated with A+AVD also received fewer subsequent therapies (20.4% vs 23.8%), including autologous stem cell transplantations (SCTs; 6.6% vs 9.0%) and allogeneic SCTs (0.6% vs 1.8%)
- While randomized controlled trials are the gold standard for evaluating drug safety and efficacy, the external validity of these trials may be limited[4]

Objective

- This study assessed real-world characteristics, treatment patterns, interim PET scan use, and clinical outcomes for patients in the United States with stage III or IV cHL treated with 1L ABVD

Methods

- This is a retrospective observational study of structured/unstructured data from the nationwide de-identified electronic health record–derived Flatiron Health research database (FHRD; January 1, 2011-August 31, 2020)
  - The FHRD is a longitudinal database, comprising de-identified patient-level structured and unstructured data, curated via technology-enabled abstraction
  - During the study period, the de-identified data originated from approximately 280 United States cancer clinics (~800 sites of care)[5,6]
- Patients meeting the following criteria were selected into a broad cohort based on structured data analysis: diagnosed with cHL based on International Classification of Disease (ICD)-9/ICD-10 codes, ≥2 documented visits in the FHRD, and evidence of medication administration or non-cancelled order for an antineoplastic drug
- A random sample of patients were selected from the broad cohort for unstructured data analysis using the following criteria: pathology consistent with a cHL diagnosis and aged ≥18 years at cHL diagnosis
  - Patients with nodular lymphocyte–predominant HL were excluded
- This analysis includes data from a random sample of patients with stage III or IV cHL treated with 1L ABVD
- Outcomes evaluated included baseline disease and clinical characteristics, treatment patterns including granulocyte colony–stimulating factor (GCSF) use, PET scan use, subsequent therapy (systemic therapies, SCT, radiation therapy [RT]), and real-world OS (rwOS)

Statistical Analysis

- Descriptive statistics (median, interquartile range [IQR], number, percentage) were used to describe baseline demographic and clinical characteristics; treatment characteristics including GCSF use; PET scan use, including assigned Deauville score and standardized uptake values (SUV) when available; and subsequent therapies, including SCT and RT
- To evaluate rwOS for patients treated with 1L ABVD, survival curves were generated using Kaplan–Meier methods
- rwOS was evaluated from start of 1L treatment to date of death

Results

Patient Demographics and Characteristics

- Data from 167 patients with stage III or IV cHL treated with 1L ABVD were included in this analysis. At treatment initiation, median patient age was 45 years and most patients were white and were male (**Table 1**)
  - Patients were evenly split between stage III (49.7%) and stage IV (50.3%) disease
  - International Prognostic Score (IPS) at baseline ranged from 0-3 for 40.7% of patients and 4-7 for 6.6% of patients; 52.7% of patients did not have a documented baseline IPS
  - Eastern Cooperative Oncology Group performance status (ECOG PS) of 0-1 was reported for 37.8% of patients and ≥2 for <1% of patients at baseline; 61.7% of patients did not have an ECOG PS score documented at baseline
  - Among all patients, 49.1% had extranodal disease, 59.9% had B symptoms at diagnosis, and 33.5% had bulky disease

Table 1. Demographic and Clinical Characteristics at Treatment Initiation for Patients With Stage III or IV cHL Treated With 1L ABVD

Characteristic	Patients (N=167)
Median age (IQR), years	45 (27-60)
Age, n (%)	
<45 years	83 (49.7)
45-59 years	42 (25.2)
≥60 years	42 (25.2)
Male sex, n (%)	96 (57.5)
Race, n (%)	
White	101 (60.5)
Black or African American	19 (11.4)
Other	34 (20.4)
Missing	13 (7.8)
Practice type, n (%)	
Community	151 (90.4)
Academic	16 (9.6)
Region, n (%)	
Midwest	16 (9.6)
Northeast	17 (10.2)
South	87 (52.1)
West	21 (12.6)
Missing	26 (15.6)
Median follow-up, months (IQR)	31.8 (15.6-61.1)
Disease stage, n (%)	
Stage III	83 (49.7)
Stage IV	84 (50.3)
IPS, n (%)	
0 to 1	21 (12.6)
2 to 3	47 (28.1)
4 to 7	11 (6.6)
Missing	88 (52.7)
ECOG, n (%)	
0	37 (22.2)
1	26 (15.6)
≥2	1 (0.6)
Missing	103 (61.7)
B-symptoms present at diagnosis, n (%)	100 (59.9)
Extranodal site involvement, n (%)	82 (49.1)
Bulky disease, n (%)	56 (33.5)

Abbreviations: 1L, frontline; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; cHL, classic Hodgkin lymphoma; ECOG, Eastern Cooperative Oncology Group; IPS, International Prognostic Score; IQR, interquartile range

Treatment Characteristics, 1L ABVD

- The median duration of follow-up from initiation of 1L ABVD therapy was 31.8 months
- Patients received a median of 6 cycles of ABVD, with a median duration of therapy of 22.3 weeks (**Table 2**)
  - 162 patients had a treatment discontinuation reason recorded; those reported by >5% of patients were completion of treatment (80.2%), toxic effect of therapy (6.2%), and progression (5.6%)
- GCSF was given to 49.7% of patients treated with 1L ABVD (primary prophylaxis: 34.9%; secondary prophylaxis: 65.1%), with a mean of 5.5 doses administered (**Table 2**)
  - 78.3% of patients treated with GCSF received pegfilgrastim

Table 2. Treatment Characteristics of Patients With Stage III or IV cHL Treated With 1L ABVD

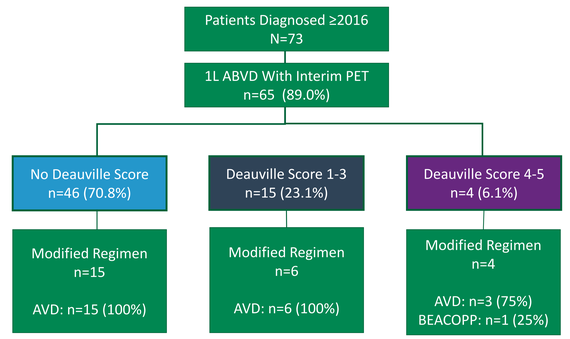
Characteristic	Patients (N=167)
Median ABVD treatment cycles, n (IQR)	6 (2-6)
Median duration of ABVD therapy, wks (IQR)	22.3 (22-24.4)
Documented reason for ABVD discontinuation, n (%)	**n=162**
Completed treatment	130 (80.2)
Toxic effect	10 (6.2)
Progression	9 (5.6)
Other	8 (4.9)
No evidence of disease	7 (4.3)
Patient request, financial reasons, stable disease/no change, unknown	<1
GCSF use during 1L ABVD therapy, n (%)	83 (49.7)
Primary prophylaxis[a]	29 (34.9)
Secondary prophylaxis[b]	54 (65.1)
Received a subsequent LOT, n (%)[c]	92 (55.1)
Median time to subsequent therapy, months (IQR)	11 (6.9-17.3)
SCT following 1L ABVD, n (%)	53 (31.7)
Median time to SCT, months (IQR)[d]	16 (11.7-24)
Type of SCT, n (%)	
Allogeneic	4 (7.5)
Autologous	48 (90.6)
Unknown/not documented	1 (1.9)
RT following 1L ABVD, n (%)	31 (18.6)
Median time to RT, months (IQR)[d]	9 (6.6-24.1)

[a] Initiated on or within 5 days of 1L ABVD start; [b] Initiated more than 5 days after 1L ABVD start; [c] Subsequent LOT following 1L ABVD; [d] From start of 1L ABVD.
Abbreviations: 1L, frontline; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; cHL, classic Hodgkin lymphoma; GCSF, granulocyte colony–stimulating factor; IQR, interquartile range; LOT, line of therapy; RT, radiation therapy; SCT, stem–cell transplantation

PET Scan Utilization

- A baseline PET scan was obtained for 60.5% of patients and an interim PET scan for 89.8% of patients during treatment with 1L ABVD after a median (IQR) of 72 (53-109) days
- Of patients diagnosed in 2016 or later (43.7%, n=73), 64.4% received a baseline PET scan and 89.0% received an interim PET scan after a median (IQR) of 55 (50-68) days; Deauville scores were documented for 29% (score 1-3, 23.1%; score 4-5, 6.1%) and SUV scores for 63% of scans
  - Of patients who received an interim PET scan (n=65), 15 of 46 patients with no documented Deauville score, 6 of 15 patients with a score of 1-3, and 3 of 4 patients with a score of 4-5 de-escalated therapy to AVD (doxorubicin, vinblastine, dacarbazine); one patient with a score of 4-5 escalated therapy to BEACOPP (**Figure 1**)

Figure 1. Treatment Modification Based on Interim PET for Patients Diagnosed With Stage III or IV cHL in 2016 or Later and Treated With 1L ABVD



Abbreviations: 1L, frontline; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; AVD, doxorubicin, vinblastine, and dacarbazine; BEACOPP, bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone; cHL, classic Hodgkin lymphoma; PET, positron emission tomography

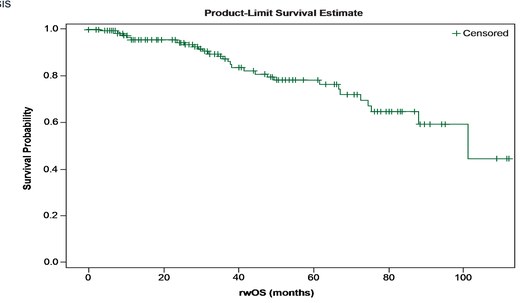
Treatment Outcomes

- Among all patients treated with 1L ABVD (**Table 2**)
  - 55.1% received subsequent therapy, 31.7% received an SCT (autologous: n=48, allogeneic: n=4), and 18.6% received RT, following 1L ABVD treatment
  - Median time from start of 1L ABVD to subsequent therapy, SCT, or RT was 11, 16, and 9 months, respectively

Treatment Outcomes Cont.

- At a median (IQR) follow-up of 31.8 (15.6-61.1) months, 82.0% of patients were alive, with a median rwOS of 101.2 months; estimated 2-year rwOS was 94.4% (**Figure 2**)

Figure 2. Estimated Real-World Overall Survival for Patients Treated With 1L ABVD, Kaplan–Meier Analysis



	Patients	Events, n (%)	Censored	Median rwOS, months (95% CI)	Median follow-up time, months (IQR)
ABVD	167	30 (18)	122	101.2 (87.9–NR)	31.8 (16–61)

Abbreviations: 1L, frontline; ABVD, doxorubicin, bleomycin, vinblastine, and dacarbazine; IQR, interquartile range; NR, not reported; rwOS, real-world overall survival

Limitations

- Most data in the FHRD are from community practices, and the majority of patients from this real-world cohort were from the Southern US; therefore, these results may not be representative of all patients with cHL treated with 1L ABVD in the United States
- FHRD data are generated from real-world clinical practice and may be subject to miscoding or errors in the oncology clinic
- As a reflection of real-world practice, several key patient prognostic variables were not available for most patients (e.g., IPS and ECOG PS); therefore, the results of this analysis may be confounded
- Monitoring procedures may not be uniform across hospital systems/platforms
- Response and progression variables were not assessed

Conclusions

- Patients with stage III or IV cHL treated with 1L ABVD in the real world were older and had higher rates of RT, subsequent therapy, and SCT than seen in clinical trials
- Approximately 50% of patients treated with 1L ABVD received GCSF prophylaxis
- For patients diagnosed in 2016 or later, interim PET scans and Deauville scores were not universally obtained after cycle 2 of ABVD. Despite this, de-escalation to AVD was observed; only 1 patient was escalated to BEACOPP
- Patients with stage III or IV cHL may benefit from 1L A+AVD, which has demonstrated improved OS with reduced burden of subsequent therapy, SCT, and RT compared with ABVD

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Disclosures

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