ELSEVIER

Blood 142 (2023) 4435–4437

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

624.HODGKIN LYMPHOMAS AND T/NK CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Brentuximab Vedotin in Frontline Therapy of Hodgkin Lymphoma in Patients with Significant Comorbidities Ineligible for Standard Chemotherapy (SGN35-015 Part E)

Christopher Yasenchak, MD[1], Rodolfo Bordoni[2], Dipti Patel-Donnelly, MD[3], Timothy Larson, MD[4], Jerome Goldschmidt, MD[5], Ralph Boccia[6], Vivian J. M. Cline[7], Shweta Jain[8], Jingmin Liu[8], Joseph Thaddeus Beck, MD[9]

[1] Willamette Valley Cancer Institute and Research Center/US Oncology Research, Eugene, OR
[2] Georgia Cancer Specialists, Marietta, GA
[3] Virginia Cancer Specialists, Fairfax, VA
[4] Minnesota Oncology P.A, Minneapolis, MN
[5] Oncology and Hematology Associates of SW Virginia, Blacksburg, VA
[6] Center for Cancer and Blood Disorders, Johns Hopkins Medicine, Bethesda, MD
[7] US Oncology, Austin, TX
[8] Seagen Inc., Bothell, WA
[9] Highlands Oncology Group, P.A., Fayetteville, AR

Brentuximab vedotin (BV) is approved for the treatment of adults with treatment-naïve stage III or IV classical Hodgkin lymphoma (cHL) combined with doxorubicin, vinblastine, and dacarbazine (AVD) and targets CD30, a receptor expressed on the Reed Sternberg cells. Treatment with BV plus AVD has demonstrated improved overall survival (OS) (6-year OS estimate of 93.9% vs 89.4%; HR, 0.59; 95% CI, 0.40-0.88; P=0.009) compared with the standard chemotherapy combination of doxorubicin, bleomycin, vinblastine, and dacarbazine (Ansell 2022). For patients (pts) newly diagnosed with cHL, current treatment options have improved pt outcomes in recent years, but survival rates are still very low for those with significant comorbidities. Pts with comorbid conditions can have poor outcomes due to decreased ability to tolerate dose intensity, increased treatment-related toxicity, and cHL relapse. This study is evaluating the efficacy and safety of single-agent BV as frontline therapy in cHL pts who are ineligible for conventional combination chemotherapy because of comorbidities.

SGN35-015 Part E (NCT01716806) was a phase 2, open-label study of BV as frontline cHL therapy. Eligible pts (≥18 years) were unfit for initial conventional combination chemotherapy for cHL as documented by a modified Cumulative Illness Rating Scale score ≥10 or because they required or depended on others for instrumental activities of daily living. Pts received BV (1.8 mg/kg) on Day 1 of each 3-week cycle for up to 16 cycles. Granulocyte colony-stimulating factor prophylaxis was not required. The primary endpoint, objective response rate (ORR), was assessed by Blinded Independent Central Review (BICR) according to the Modified Lugano Criteria (Cheson 2014). Key secondary endpoints included safety, duration of response (DOR), complete response (CR) rate using the Lugano Criteria (Cheson 2014), duration of CR, progression-free survival (PFS), and OS.

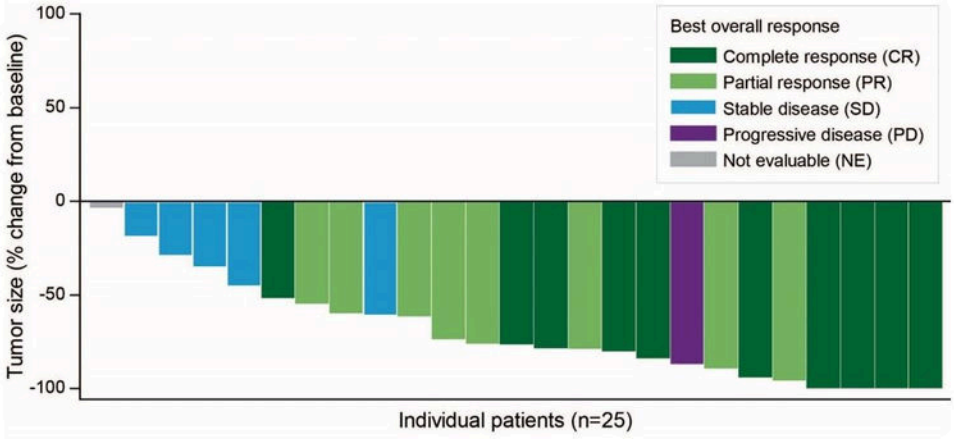
Thirty pts with cHL received BV and the median age was 76 years (range, 54 to 93 years). Most pts were female (53%) and had a disease stage of II (37%) or III (37%), an Eastern Cooperative Oncology Group (ECOG) performance status of ≥2 (50%; 10 pts [33%] and 5 pts [17%] had an ECOG performance status of 2 and 3, respectively). The median treatment duration was 18 weeks (range, 1 to 50 weeks). Per BICR, the ORR was 60% (18/30) (95% CI: 40.6%, 77.3%), including 33% (10/30) with a CR and 27% (8/30) with a partial response. Six pts (20%) did not respond to treatment: 1 (3%) with progressive disease and 5 (17%) with stable disease; one pt (3%) was not evaluable and the remaining 5 pts (17%) did not have postbaseline responses, either because of death before first scheduled response assessment or not yet reaching the first scheduled response assessment. Median DOR was 7.4 months (95% CI: 7.4 months, not estimable) and median PFS was 8.7 months (95% CI: 5.1 months, not estimable). Median duration of CR was not estimable (95% CI: 7.4 months, not estimable). With a median follow-up of 14.6 months (range, 0 to 44 months), the 2-year OS rate was 70% (95% CI: 48%, 84%).

A total of 18 pts (60%) experienced grade ≥3 treatment-emergent adverse events (TEAEs). The most common grade ≥3 TEAEs were fatigue (n=3; 10%), acute kidney injury, anemia, atrial fibrillation, back pain, gait disturbance, hypoxia, neutrophil count decreased, pneumonia, sepsis, syncope, and vomiting (n=2 each; 7%). Nine pts (30%) discontinued treatment because of a

TEAE; 1 death due to a TEAE (failure to thrive) was considered treatment-related. Thirteen percent (n=4) of pts experienced grade ≥3 peripheral neuropathy.
In pts with cHL who are unfit for initial conventional chemotherapy due to comorbidities, BV monotherapy as frontline treatment appears effective, has an acceptable safety profile, and despite the small sample size could be considered as an option for pts with cHL who are unfit for conventional chemotherapy.

Disclosures Yasenchak: *Seagen Inc.:* Consultancy, Research Funding; *Beigene:* Speakers Bureau; *Takeda:* Research Funding. **Bordoni:** *Guardant Health:* Consultancy, Speakers Bureau; *Pfizer:* Membership on an entity's Board of Directors or advisory committees; *Phillips Gilmore Oncology:* Consultancy; *NeoGenomics Labs:* Speakers Bureau; *Chairman Annual Precision Oncology Symposium:* Other; *Oncocyte:* Membership on an entity's Board of Directors or advisory committees, Other: Travel Expenses; *AstraZeneca:* Consultancy, Speakers Bureau; *Sanofi US:* Membership on an entity's Board of Directors or advisory committees; *Janssen Biotech:* Speakers Bureau; *Northside Hospital Cancer Institute:* Other: Travel Expenses; *OneLive Clinical Congress Consultants:* Speakers Bureau. **Patel-Donnelly:** *American Board of Internal Medicine (ABIM):* Other: American Board of Internal Medicine (ABIM); *Roche:* Research Funding; *LAM Therapeutics:* Research Funding; *Boston Biomed:* Research Funding; *Gilead:* Research Funding. **Goldschmidt:** *Ontada:* Current Employment; *Bristol-Meyers Squibb:* Speakers Bureau; *Blue Ridge Cancer Care:* Current Employment; *AstraZeneca:* Consultancy; *G1 Therapeutics:* Consultancy, Speakers Bureau; *TG Therapuetics:* Consultancy; *Amgen:* Consultancy. **Boccia:** *Center for Cancer and Blood Disorders:* Current Employment; *Bristol Myers Squibb:* Consultancy, Honoraria, Research Funding, Speakers Bureau; *AbbVie:* Consultancy, Honoraria, Research Funding, Speakers Bureau; *Genmab:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Amgen:* Consultancy, Honoraria, Research Funding, Speakers Bureau; *Seagen:* Research Funding; *AstraZeneca:* Research Funding; *Janssen:* Honoraria, Research Funding, Speakers Bureau; *Daiichi Sankyo Inc:* Honoraria, Speakers Bureau; *Pharmacosmos:* Honoraria, Speakers Bureau. **Cline:** *Reflexion Medical:* Consultancy, Other: Travel Expenses; *Texas Oncology:* Current Employment; *Pfizer:* Honoraria. **Jain:** *Seagen:* Current Employment, Current equity holder in publicly-traded company. **Liu:** *Seagen Inc.:* Current Employment, Current equity holder in publicly-traded company. **Beck:** *Highlands Oncology Group:* Research Funding.

Figure 1 **Maximum SPD Percentage Reduction from Baseline by BICR**



Response assessments based on modified Lugano Criteria per BICR with integration of CT, PET, and clinical information. May include cases of CR with <100% reduction in SPD from baseline due to PET (+) at baseline becoming PET (-); cases of PR with 50-100% reduction in SPD from baseline due to post-baseline PET (+) target or non-target lesions; and a case of PD with >50% reduction in SPD from baseline due to presence of new lymphomatous lesions post-baseline.
BICR, Blinded Independent Central Review; CT, computed tomography; PET, positron emission tomography; SPD, sum of the product of the diameters.

Table 1 **Summary of Best Clinical Response in SGN35-015 Part E**

Category/Variable	Per BICR (n=30)	Per Investigator (n=30)
Best Clinical Response [a], n (%)		
Complete Response (CR)	10 (33)	9 (30)
Partial Response (PR)	8 (27)	14 (47)
Stable Disease (SD)	5 (17)	0
Progressive Disease (PD)	1 (3)	1 (3)
Not Evaluable (NE)	1 (3)	0
No Postbaseline Response Assessment [b]	5 (17)	6 (20)
95% CI [c] for Complete Response Rate	17.3, 52.8	14.7, 49.4
Objective Response Rate (CR + PR), n (%)	18 (60)	23 (77)
95% CI [c]	40.6, 77.3	57.7, 90.1
Disease Control Rate (CR + PR + SD), n (%)	23 (77)	23 (77)
95% CI [c]	57.7, 90.1	57.7, 90.1

[a] Response assessments were according to modified Lugano criteria (Cheson 2014) per BICR with integration of CT, PET and clinical information, and according to Lugano criteria per investigator using combination of CT and PET. Time point response was mainly PET-based response; CT results are used when PET was not performed. Best clinical response is derived for each subject from all the time point responses following this order: CR>PR>SD>PD>NE.
[b] Included subjects missing postbaseline response assessment because of withdrawal, loss to follow-up or death before first scheduled response assessment.
[c] Two-sided 95% exact confidence interval, computed with the Clopper-Pearson method (1934).
BICR, Blinded Independent Central Review; CT, computed tomography; PET, positron emission tomography.

Figure 1

https://doi.org/10.1182/blood-2023-190260