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

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Primary Objective

To evaluate the safety, efficacy, and tolerability of BV as frontline monotherapy in adults with cHL who are unsuitable or unfit for combination chemotherapy

Conclusions

In patients with cHL who are unfit for initial conventional chemotherapy because of comorbidities, BV monotherapy as frontline treatment appears effective and has an acceptable safety profile

As a result, BV monotherapy could be considered as an option for patients with cHL who are unfit for conventional chemotherapy

Abbreviations

AE, adverse event; AVD, doxorubicin, vinblastine, and dacarbazine; BICR, Blinded Independent Central Review; BV, brentuximab vedotin; cHL, classical Hodgkin lymphoma; CI, confidence interval; CR, complete response; CT, computed tomography; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; IV, intravenous; NE, not evaluable; ORR, objective response rate; OS, overall survival; PD, progressive disease; PET, positron emission tomography; PFS, progression-free survival; PR, partial response; PTCL, peripheral T-cell lymphoma; Q3W, once every 3 weeks; SD, stable disease; SPD, sum of the product of the diameters; TEAE, treatment-emergent adverse event.

References

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Background

- BV is a CD30-directed antibody-drug conjugate approved for use in combination with AVD for the treatment of adults with treatment-naive stage III or IV cHL, among other indications
- Treatment with BV plus AVD has demonstrated improved OS (6-year OS estimate of 93.9% vs 89.4%; HR, 0.59; 95% CI: 0.40 to 0.88; *P*=0.009) compared with the standard chemotherapy combination of doxorubicin, bleomycin, vinblastine, and dacarbazine[1]
- For patients newly diagnosed with cHL, current treatment options have improved patient outcomes in recent years, but survival rates are still very low for those with significant comorbidities
- Patients 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 patients who are ineligible for conventional combination chemotherapy because of comorbidities

Methods

SGN35-015 Part E (NCT01716806) was a phase 2, open-label study of BV as frontline cHL therapy (**Figure 1**)

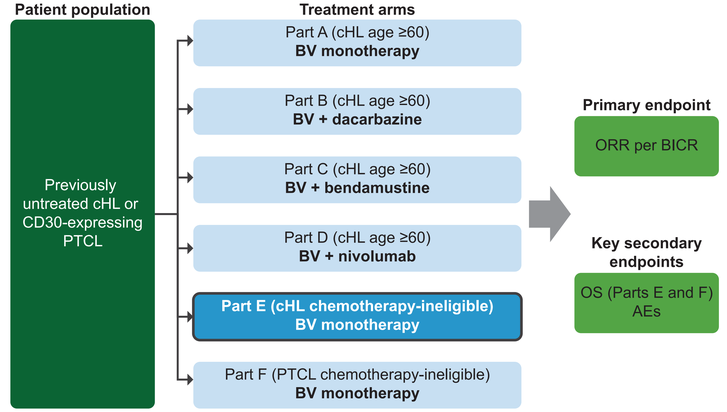
Eligibility Criteria

- Eligible patients (≥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

Treatment

- Patients 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, ORR, was assessed by BICR according to the Modified Lugano Criteria[2]
- Key secondary endpoints included safety, DOR, CR rate using the Lugano Criteria[2], duration of CR, PFS, and OS

Figure 1. SGN35-015 Study Design



Dose: BV 1.8 mg/kg IV Q3W

Results

Disposition

- Thirty patients with cHL received BV and the median age was 76 years (range, 54 to 93)
- Majority of patients were female (53%) and had a disease stage of II (37%) or III (37%)
- Half of patients had an ECOG performance status of ≥2 (50%; 10 patients [33%] and 5 patients [17%] had an ECOG performance status of 2 and 3, respectively)
- Median treatment duration was 18 weeks (range, 1 to 50)

Efficacy

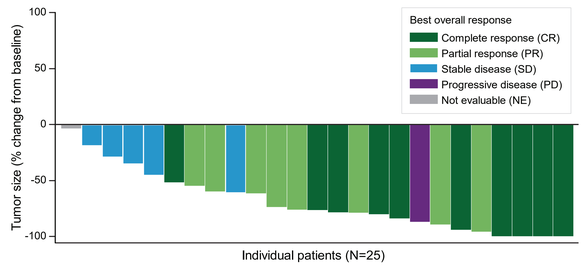
- Per BICR, the best overall response for ORR was 60% (95% CI: 40.6 to 77.3; n=18/30 patients), including 33% (10/30 patients) with a CR and 27% (8/30 patients) with a PR (**Table 1** and **Figure 2**)
- Median DOR was 7.4 months (95% CI: 7.4 to not estimable)
- Median duration of CR was not estimable (95% CI: 7.4 to not estimable)
- Median PFS was 8.7 months (95% CI: 5.1 to not estimable)
- With a median follow-up of 14.6 months (range, 0 to 44), the 2-year OS rate was 70% (95% CI: 48 to 84)

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)
95% CI[b]	17.3, 52.8	14.7, 49.4
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 post-baseline response assessment[c]	5 (17)	6 (20)
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 made according to modified Lugano criteria[2] per BICR with integration of CT, PET, and clinical information, and according to Lugano criteria per investigator using a combination of CT and PET. Time point response was mainly PET-based response; CT results were used when PET was not performed. Best clinical response was derived for each patient from all the time point responses following this order: CR>PR>SD>PD>NE.
b Two-sided 95% exact confidence interval, computed with the Clopper-Pearson method.[3]
c Included patients missing postbaseline response assessment because of withdrawal, loss to follow-up, or death before first scheduled response assessment.

Figure 2. 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. Included 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 postbaseline PET (+) target or nontarget lesions; and a case of PD with >50% reduction in SPD from baseline due to presence of new lymphomatous lesions after baseline.

Safety

- **Grade ≥3 TEAEs:** a total of 18 patients (60%) experienced grade ≥3 TEAEs
  - 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%) were the most common grade ≥3 TEAEs
- **Grade ≥3 peripheral neuropathy:** 4 patients (13%) experienced grade ≥3 peripheral neuropathy
- **Discontinuations:** 9 patients (30%) discontinued treatment because of an AE
- **Deaths:** 1 death due to a TEAE (failure to thrive) was considered treatment-related