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ORAL ABSTRACTS

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

Brentuximab Vedotin, Nivolumab, Doxorubicin, and Dacarbazine for Advanced Stage Classical Hodgkin Lymphoma: Efficacy and Safety Results from the Single Arm Phase 2 Study

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Introduction:
Brentuximab vedotin (BV) is an antibody-drug conjugate approved for multiple cancer types, including previously untreated stage III or IV classical Hodgkin lymphoma (cHL), in combination with doxorubicin, vinblastine, and dacarbazine (AVD) in adults. The combination of BV and nivolumab are both individually active and well tolerated in patients with cHL and have distinct and complementary mechanisms of action. BV and nivolumab have been previously studied in combination and with multiagent chemotherapy as BV+AD (omitting vinblastine) and N+AVD. It was hypothesized that the combination of BV and nivolumab with doxorubicin and dacarbazine (AN+AD) would result in high response rates and a well-tolerated safety profile with potentially less toxicity than vinblastine-containing regimens. SGN35-027 (NCT03646123; EudraCT Number 2020-004027-17; Part B) is an open-label, multiple-part, multicenter, phase 2 clinical trial. Preliminary results of this study showed promising efficacy (objective response rate [ORR] 93%; complete response [CR] rate 88% at end of therapy [EOT]) with no cases of febrile neutropenia or grade 5 adverse events (AEs) (Lee ASCO 2022). Of the patients with stage III or IV cHL who relapse, most will relapse within 18 to 24 months of treatment initiation.

Methods:
Part B enrolled patients with stage II bulky mediastinal disease (≥10 cm), stage III, or stage IV cHL. Patients received up to 6 cycles of AN+AD (BV 1.2 mg/kg [A], nivolumab 240 mg [N], doxorubicin 25 mg/m ^{2} [A], and dacarbazine 375 mg/m ^{2} [D]). The primary efficacy endpoint was CR rate at EOT. Key secondary endpoints included safety and tolerability, ORR, duration of response (DOR), duration of complete response (DOCR), and progression-free survival (PFS). Disease response and progression were assessed by investigator using Lugano Classification Revised Staging System for malignant lymphoma, incorporating Lymphoma Response to Immunomodulatory Therapy Criteria for nodal non-Hodgkin and Hodgkin lymphomas.

Results:
Fifty-eight patients were enrolled; all but 1 patient received ≥1 dose of study drug (data cutoff 22 May 2023). Median age was 35 years (range, 19-78 years). Among efficacy evaluable patients (n = 56), ORR (CR+ PR) at EOT was 95% (95% CI: 85.1, 98.9); CR rate was 89% (95% CI: 78.1, 96.0) (Table 1). A total of 88.3% (95% CI: 75.7, 94.6) of responders had a DOR of at least 24 months, and 88.4% (95% CI: 76.0, 95.0) of responders had a DOCR of at least 24 months. Seven patients (12%) had a PFS event: 6 with disease progression and 1 who died (sepsis, outside safety reporting period). The estimated PFS rate at 24 months was 88.3% (95% CI: 75.7, 94.6) (Figure 1). Median follow-up was 24.2 months (95% CI: 23.4, 26.9).
The most common treatment-related AEs of any grade were nausea (37 patients [65%]), fatigue (28 patients [49%]), and peripheral sensory neuropathy (25 patients [44%]). Of the patients with treatment-related peripheral sensory neuropathy, most (23 of 25 patients [92%]) were grade 1 or 2; the remaining 2 patients had grade 3 peripheral sensory neuropathy. Dose modifications due to peripheral sensory neuropathy occurred in 9 patients (16%). Grade ≥3 treatment-related AEs occurred in 19 patients (33%) (most common: alanine aminotransferase increased in 6 [11%] and neutropenia in 5 [9%]). No febrile neutropenia or Grade 5 AEs occurred. Treatment-related serious AEs (SAEs) occurred in 8 patients (14%). Seven patients (12%) had a treatment-emergent AE that led to discontinuation of BV. Treatment-emergent immune-mediated AEs (IMAEs) occurred in 19 patients (33%); treatment-emergent IMAEs that occurred in ≥5% of patients were hypothyroidism (5 patients [9%]) and pneumonitis and rash maculopapular (3 patients [5%] each). All cases of pneumonitis resolved.
Conclusions:
The use of 2 active, targeted agents with distinct and complementary mechanisms of action for the frontline treatment of advanced stage cHL resulted in promising efficacy, safety, and tolerability. These results demonstrate continued tolerability of AN+AD with no new safety signals observed. AN+AD may provide a future first-line treatment option for patients with advanced stage cHL; long-term follow-up is ongoing.

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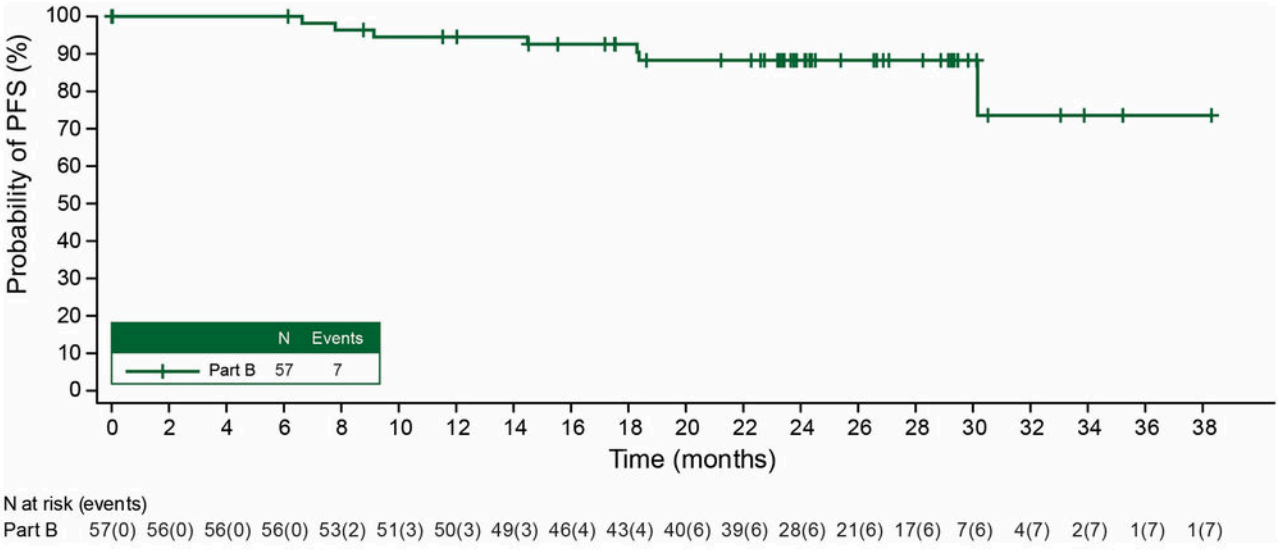
Table 1. Objective Response in Patients with Advanced-Stage Classical Hodgkin Lymphoma Treated with Brentuximab Vedotin and Nivolumab with Doxorubicin and Dacarbazine (SGN35-027 Part B)

Overall Response at EOT per Investigator, n (%)	Part B N = 56, Efficacy Evaluable
ORR at EOT (CR+PR)[a,b]	53 (95)
95% CI for ORR	(85.1, 98.9)[c]
CR	50 (89)
95% CI for CR	(78.1, 96.0)[c]
PR	3 (5)
95% CI for PR	(1.1, 14.9)[c]
SD	0
PD	2 (4)
IR[d]	1 (2)

CR: complete response; EOT: end of therapy; IR: indeterminate response; ORR: objective response rate; PD: progressive disease; PR: partial response; SD: stable disease
a. CR, PR, SD, and PD per Lugano per Investigator
b. CR, PR, SD, and PD are mutually exclusive.
c. Two-sided 95% exact confidence interval, computed with the Clopper-Pearson method (1934).
d. IR converted to CR in long-term follow-up.

Figure 1. Kaplan-Meier Plot of PFS in Patients with Advanced-Stage Classical Hodgkin Lymphoma Treated with Brentuximab Vedotin and Nivolumab with Doxorubicin and Dacarbazine (SGN35-027 Part B)



PFS: progression-free survival

Figure 1

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