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ORAL ABSTRACTS

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

Nivolumab-AVD Is Better Tolerated and Improves Progression-Free Survival Compared to Bv-AVD in Older Patients (Aged ≥60 Years) with Advanced Stage Hodgkin Lymphoma Enrolled on SWOG S1826

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Background: Survival rates in patients (pts) with classic Hodgkin lymphoma (HL) aged ≥60 years (y) are lower than younger pts. The difference is due to comorbidities, impaired performance status, decreased chemotherapy tolerance, and increased treatment-related toxicity and mortality. The frontline regimen Bv-AVD can be challenging to administer in older patients due to toxicities, particularly infection and neuropathy. The PD-1 pathway is central to pathogenesis of HL; PD-1 blockade is effective in HL. The randomized, phase 3 trial, S1826, was conducted by the National Clinical Trials Network to evaluate N-AVD vs Bv-AVD in pts with newly diagnosed advanced stage (AS) HL and enrolled 994 pts; 97 were eligible and aged ≥60y.
Methods: In this subset analysis, eligible pts were ≥60y with stage 3-4 HL. Pts were randomized 1:1 to 6 cycles of N-AVD or Bv-AVD. G-CSF neutropenia prophylaxis was optional with N-AVD and required with Bv-AVD. Pre-specified pts could receive radiation therapy (RT) to residual lesions on end of treatment PET. Pts were stratified by age, international prognostic score (IPS), and intent to use RT. Response and progression were assessed by investigators using 2014 Lugano Classification. The primary endpoint was progression-free survival (PFS); secondary endpoints included overall survival (OS), event-free survival (EFS), and detailed toxicity and safety events. EFS events were death without progression, progression/relapse, receipt of non-protocol systemic anti-lymphoma therapy without progression, or receipt of RT in a pt not declared eligible for RT at registration or who did not meet protocol-specified criteria for RT.
Results: 97 pts aged ≥60y were enrolled from 7/9/19-10/5/22 and were randomized to N-AVD (n=48) or Bv-AVD (n=49). Median age was 66y (range, 60-83y), 62% were male, 86% were white, 3% were black, and 10% were Hispanic. 61% had stage IV disease and 47% had IPS 4-7. 69% of pts on N-AVD and 92% of pts on Bv-AVD received any G-CSF. No pts received RT per protocol.

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95 pts were evaluable for safety analysis. While grade (gr) ≥3 hematologic toxicity occurred in 52% of pts on N-AVD and 38% on Bv-AVD (gr 3 neutropenia 48% vs 30%), febrile neutropenia, sepsis, and infections were lower for pts who received N-AVD vs Bv-AVD. (Table) Peripheral neuropathy was much less frequent with N-AVD than Bv-AVD in overall incidence (sensory: 31% vs 66% and motor: 8% vs 15%, respectively) and severity (grades ≥2, sensory: 10% vs 49% and motor: 0% vs 8%, respectively). (Table) The following adverse events, AEs (mainly <gr 3) were less frequent on N-AVD vs Bv-AVD: nausea (38% vs 62%), diarrhea (25% vs 45%), anorexia (15% vs 38%) and weight loss (4% vs 36%). Hypothyroidism (15% vs 0%), and rash (16% vs 2%, no gr ≥3) were more frequent on N-AVD than Bv-AVD; rates of other immune-related toxicities were similar between arms.
In this subset analysis, median follow-up 12.1 months, PFS was superior in the N-AVD arm [HR 0.35 (95% CI 0.12-1.02) stratified one-sided logrank p=0.022]; 1-yr PFS was 93% (95% CI 79-98%) for N-AVD and 64% (95% CI 45-77%) for Bv-AVD. (Figure) 1-yr EFS was 93% (95% CI 79-98%) for N-AVD and 57% for Bv-AVD (95% CI 38-72%) [HR 0.19 (95% CI 0.06-0.61) stratified one-sided logrank p=0.0011]. 1-yr OS was 95% (95% CI 83-99%) for N-AVD and 83% (95% CI 67-92%) for Bv-AVD [HR 0.35 (95% CI 0.07-1.75) stratified one-sided logrank p=0.091]. On N-AVD, there were 2 deaths (due to infection/sepsis) and 3 progressions/relapses; on Bv-AVD, there were 7 deaths (5 due to infection/sepsis, 1 to pneumonitis, 1 unknown) and 8 progressions/relapses. Non-relapse mortality was 4% for N-AVD vs 14% for Bv-AVD. Treatment was discontinued early in 5 pts (10%) on N-AVD and 16 pts (33%) on Bv-AVD. N was discontinued early in 7 pts (15%) and Bv in 19 pts (39%). Reasons for discontinuation included (N vs Bv): AE (5 vs 14 pts), death (1 vs 3 pts), and disease progression (0 vs 1 pt).
Conclusions: N-AVD improved PFS and EFS, and was better tolerated than Bv-AVD in pts aged ≥60 with AS HL. Substantially more pts discontinued Bv-AVD than N-AVD, primarily due to toxicity. Fewer deaths occurred on N-AVD than Bv-AVD. N-AVD is poised to become a standard of care for older AS HL pts fit for anthracycline-based combination therapy.
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Table: Key Adverse Events by Treatment Arm (Any Grade and Grade ≥3).

	N-AVD (N=48)	Bv-AVD (N=47)		N-AVD (N=48)	Bv-AVD (N=47)	
Adverse Event	**Any Grade**	**Any Grade**	**p-value[3]**	**Grade ≥3**	**Grade ≥3**	**p-value[3]**
Febrile neutropenia	6 (13%)	9 (19%)	0.42	6 (13%)	9 (19%)	0.42
Sepsis	3 (6%)	10 (21%)	0.04	3 (6%)	10 (21%)	0.04
Infections and infestations	9 (19%)	16 (34%)	0.11	3 (6%)	10 (21%)	0.04
Peripheral sensory neuropathy[1]	15 (31%)	31 (66%)	0.001	1 (2%)	5 (11%)	0.11
Peripheral motor neuropathy[2]	4 (8%)	7 (15%)	0.36	0 (0%)	1 (2%)	0.49

[1]Peripheral sensory neuropathy by grade (gr): for N-AVD, gr 1: 21%, gr 2: 8%, and gr 3: 2%; for Bv-AVD, gr 1: 17%, gr 2: 38%, and gr 3: 11%.

[2]Peripheral motor neuropathy by gr: for N-AVD, gr 1: 8%; for Bv-AVD gr 1: 6%, gr 2: 6%, and gr 3: 2%.

[3]Two-sided Fisher's Exact Test

Figure: Progression-Free Survival for Patients Aged ≥60 years Enrolled on S1826.

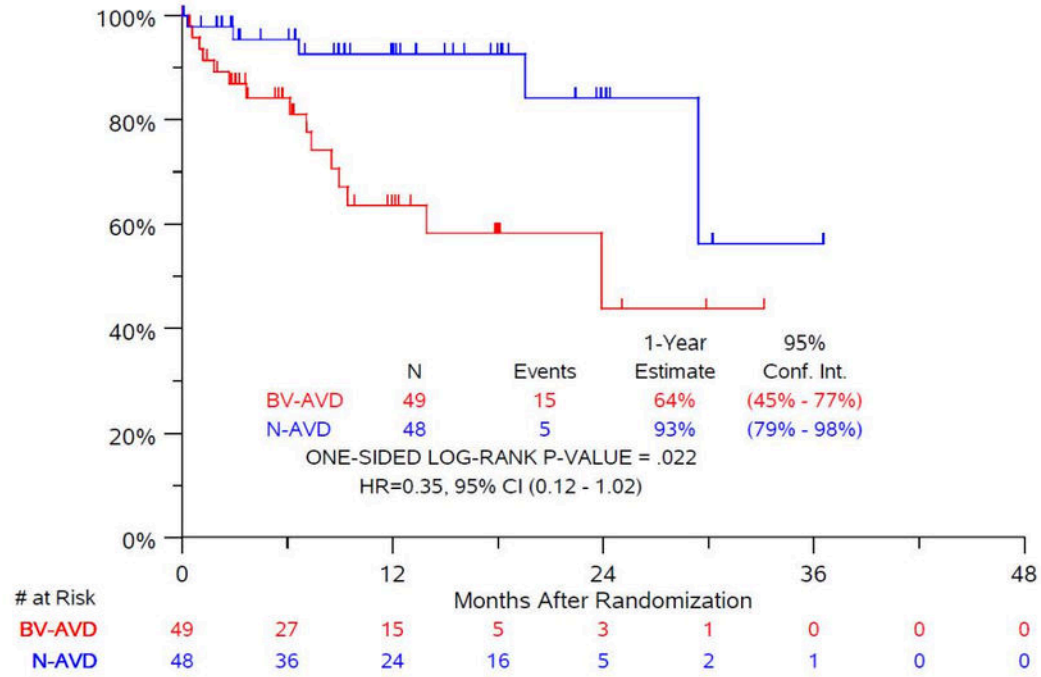

Figure 1

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