Where Science Becomes Hope

OPTIMAL MANAGEMENT OF ADVANCED STAGE HL: NIVO-AVD VS BV-AVD

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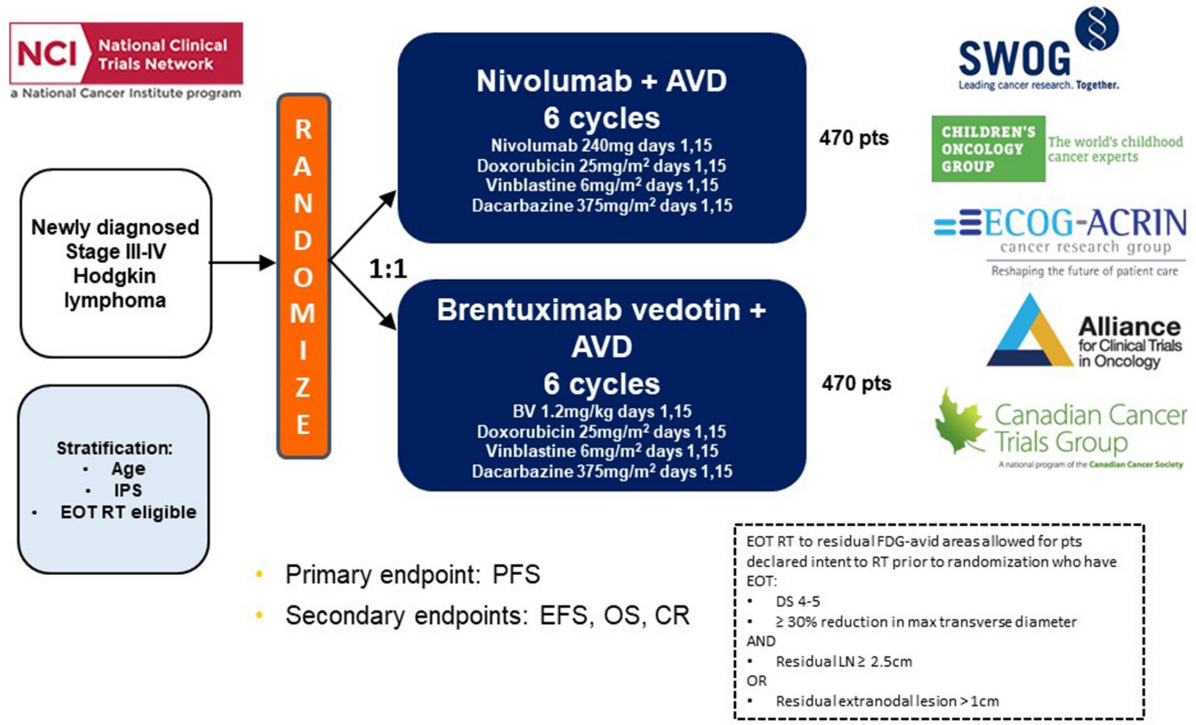
SWOG S1826

S1826: A Phase III Randomized Trial of Nivolumab (Opdivo) or Brentuximab Vedotin (Adcetris) Plus AVD in Patients (Age ≥ 12 Years) With Newly Diagnosed Advanced Stage Classical Hodgkin Lymphoma



Blood (2020) 136 (Supplement 1): 23–24.

BV-AVD demonstrated improved PFS compared to ABVD at the cost of higher rates of neutropenia, sepsis, peripheral neuropathy

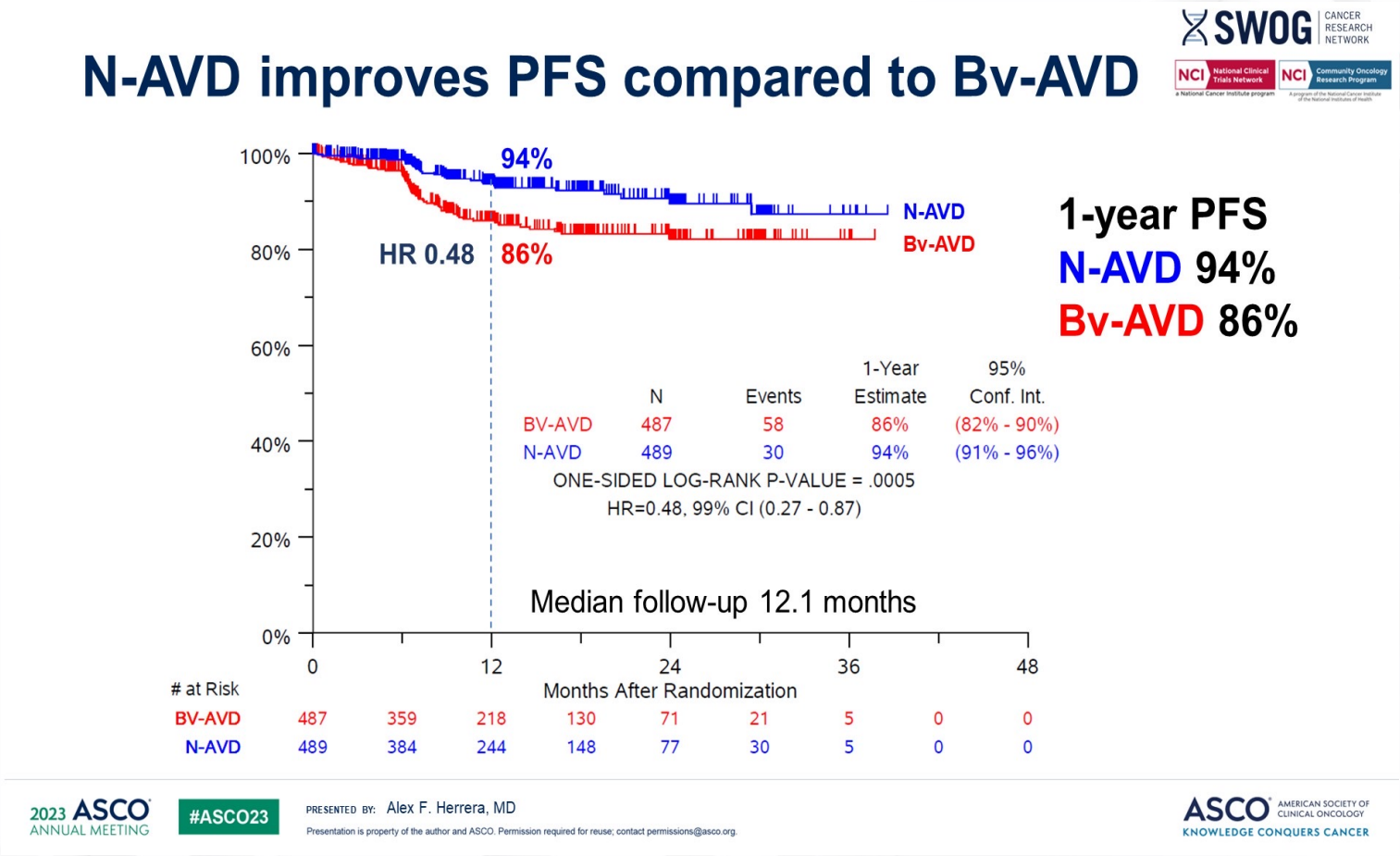
~7-20% failure rate with BV-AVD in Advanced Stage HL

Targeting PD-1 pathway in HL seemed promising in heavily treated R/R HL

Phase II data of N-AVD showed promising efficacy and safety

S1826 largest advanced stage HL study in hx of North American cooperative groups

1. NIVO-AVD SHOWS SUPERIOR PFS TO BV-AVD



A. Herrera. SWOG S1826. 2023 ASCO Annual Meeting – Plenary Session, LBA4

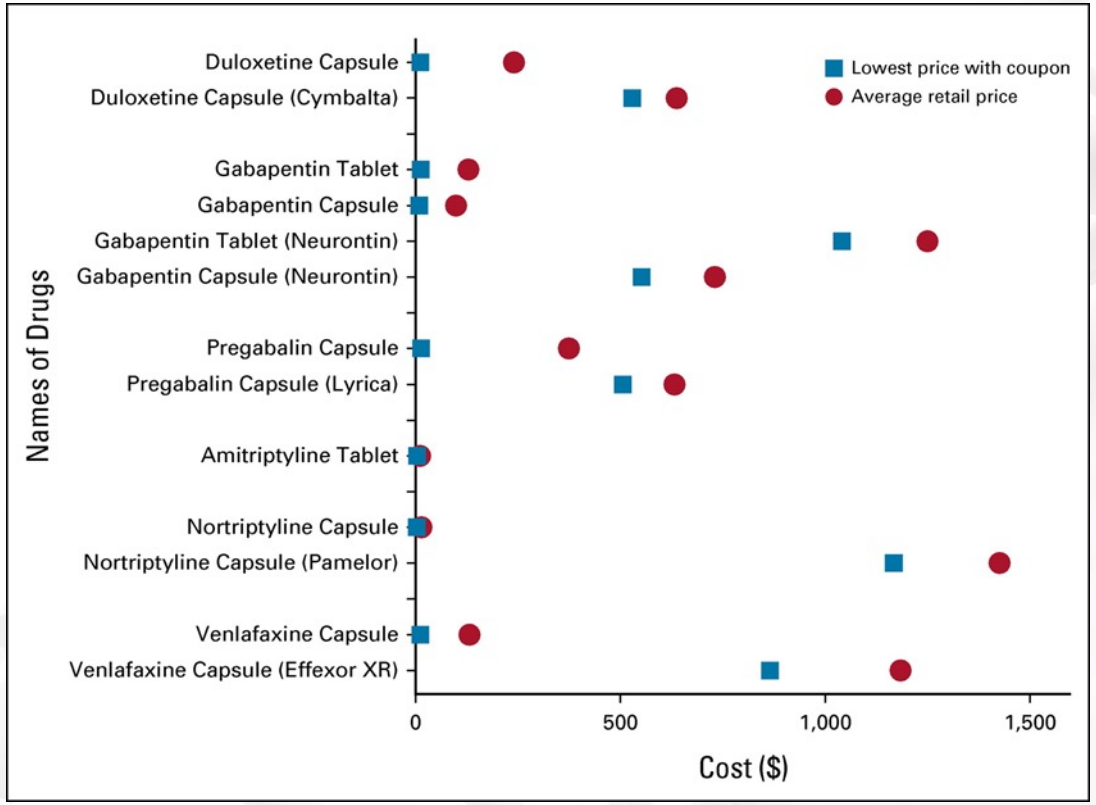
Addition of nivolumab to AVD associated with 52% reduction in risk of disease progression or death compared to BV-AVD

(HR 0.48, 99% CI 0.27-0.87, 1-sided P = 0.005)

At median 12.1 month follow up:

- PFS: 94% in N-AVD group vs 86% in BV-AVD group
- Deaths: 4 (3 due to AEs) in N-AVD group vs 11 (7 due to AEs) in BV-AVD group

2. BV-AVD RESULTS IN MORE NEUROTOXICITY



Range of costs of drugs used to manage chemotherapy-induced peripheral neuropathy for a typical fill (1 month). USD, US dollars

JCO Oncol Pract. 2022 Feb; 18(2): 140–147

Neurotoxicity higher in BV-AVD group

- Sensory: 28.1% in N-AVD vs 54.2% in BV-AVD
- Motor: 4% in N-AVD vs 6.8% in BV-AVD

Of particular concern to younger patients

Can have long-term implications for quality of life and ability to return to work or remain in disability

May require long-term palliation after achieving remission, lowering quality of life and contributing to healthcare expenditures

3. BV-AVD MORE MYELOSUPPRESSIVE

ECHELON-1: Increased rates of neutropenic fever with BV-AVD noted during interim → prophylactic G-CSF recommended, protocol amended

SWOG S1826: higher rates of neutropenia noted in Nivo-AVD arm since patients didn't require use of G-CSF, *but no increase in rate of infectious toxicity noted*

Toxicity	N-AVD (N = 483)	BV-AVD (N = 473)
Grade ≥3 neutropenia	47%	25%
Febrile Neutropenia	5.6%	6.4%
Sepsis	2%	3%
Infections / Infestations	5%	8%
Received G-CSF Support	54%	95%
Bone Pain	8%	20%

G-CSF: infusion room burden for patients and centers, cost for payers

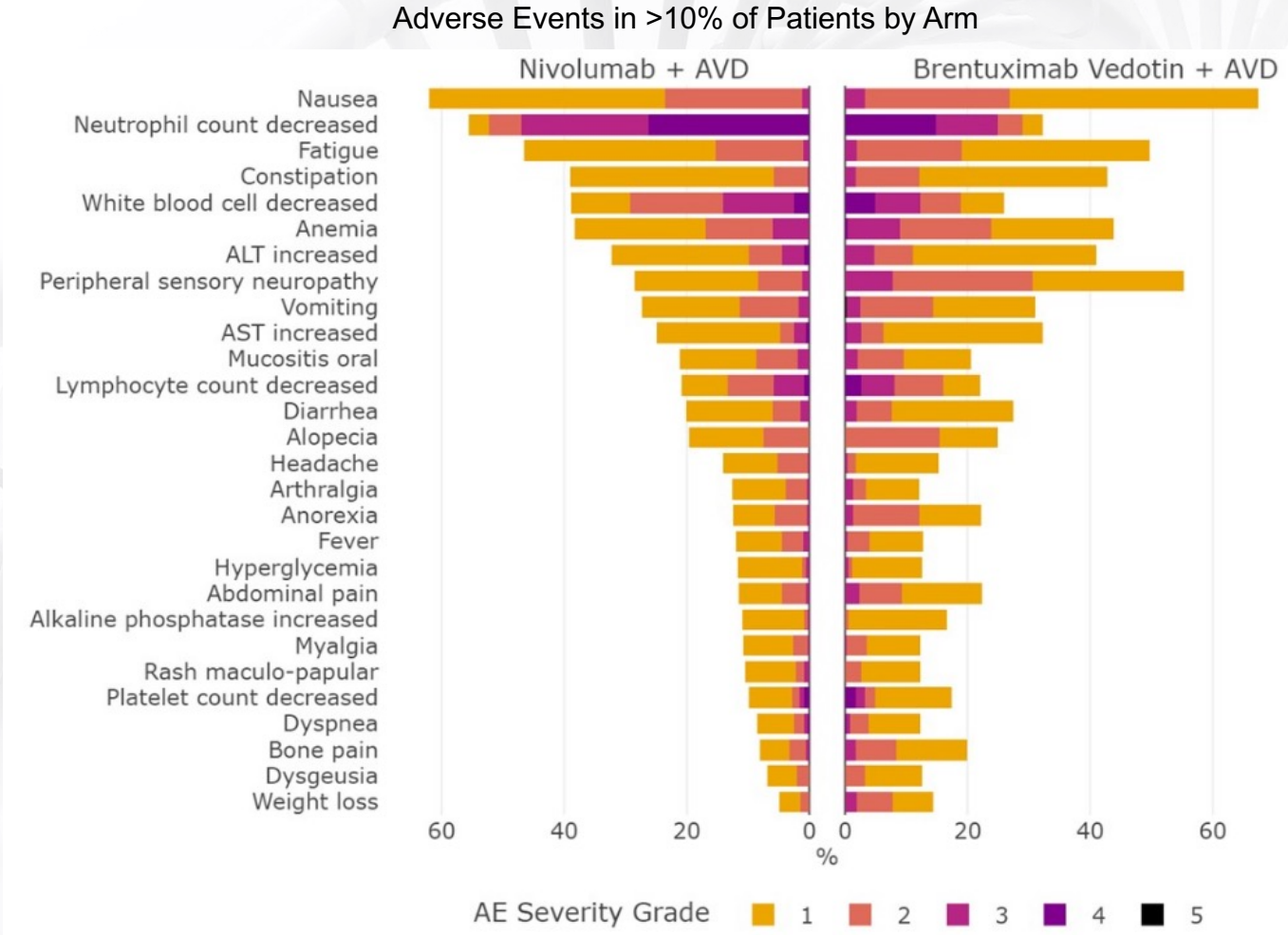
G-CSF support is precluded in some populations (e.g. pts with sickle cell disease)

4. NIVO-AVD NOT MORE TOXIC THAN BV-AVD

Immune-related toxicities similar (or lower) with Nivo-AVD vs BV-AVD:

- LFT abnormalities: 30.7% vs 39.8%
- Pneumonitis: 2.0% vs 3.2% in BV-AVD
- Colitis: 1% in Nivo-AVD vs 1.3% in BV-AVD

Twice as many treatment discontinuations with BV-AVD than with Nivo-AVD (22% vs 11%)



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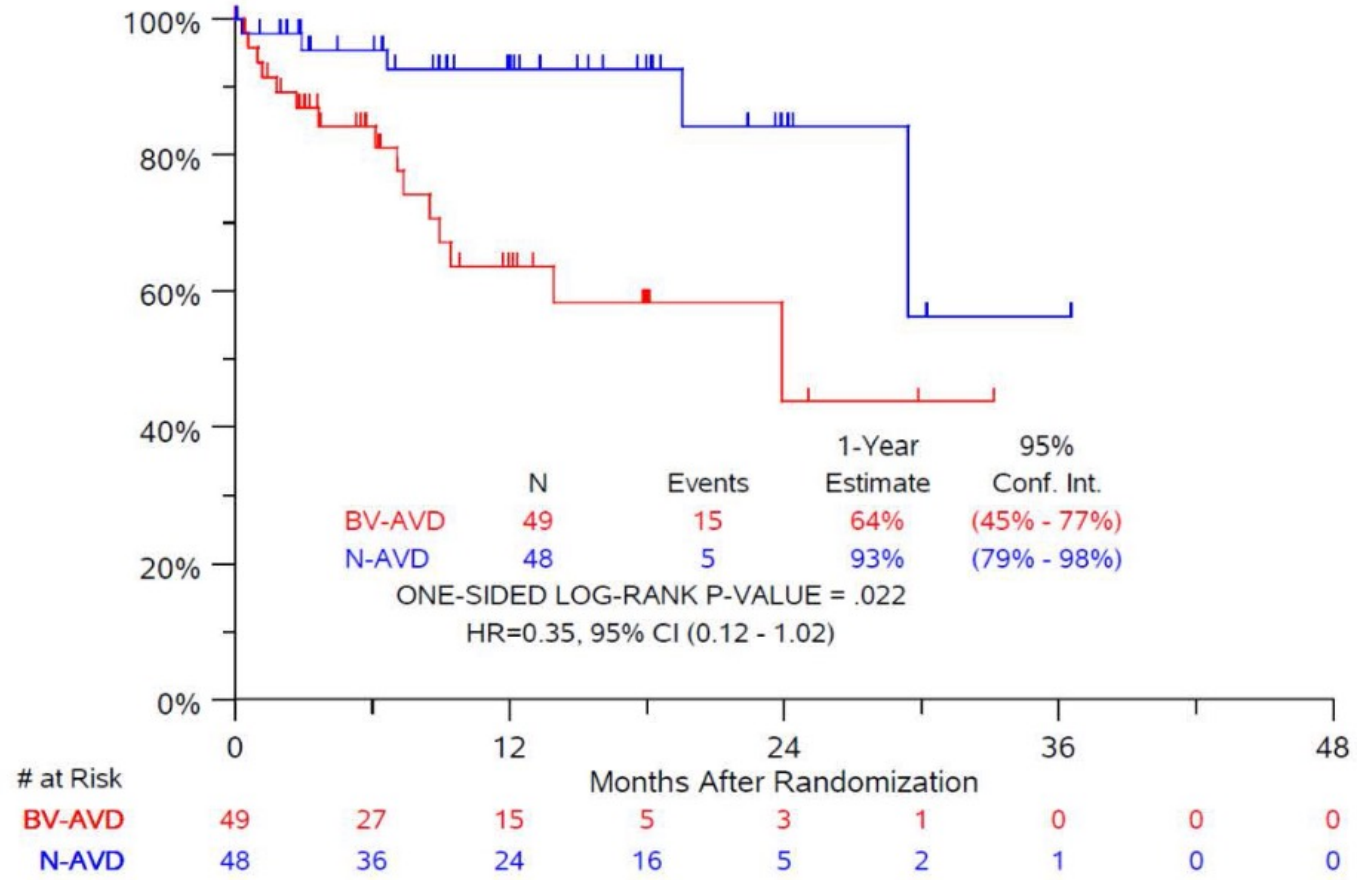
5. NIVO-AVD BETTER TOLERATED AND IMPROVES PFS IN OLDER PATIENTS

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



Blood (2023) 142 (Supplement 1): 181

5. NIVO-AVD BETTER TOLERATED AND IMPROVES PFS IN OLDER PATIENTS

	N-AVD (N=48)	BV-AVD (N=47)		N-AVD (N=48)	BV-AVD (N=47)	
Adverse Event	**Any Grade**	**Any Grade**	**P-value**	**Grade ≥3**	**Grade ≥3**	**P-value**
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	15 (31%)	31 (66%)	0.001	1 (2%)	5 (11%)	0.11
Peripheral Motor Neuropathy	4 (8%)	7 (15%)	0.36	0 (0%)	1 (2%)	0.49

Blood (2023) 142 (Supplement 1): 181

6. NIVO-AVD POTENTIALLY LESS EXPENSIVE

Nivolumab:

240 mg = 24 mL, given 2x per cycle = 480 mL
$374.25 / mL

= $17,964 per cycle

Brentuximab:

1.2 mg/kg every 2 weeks (max 120 mg)
For a 70 kg person = 168 mg for one cycle
$13,562.40 per 50 mg

= $45,568 per cycle

Source of pricing data estimates: Medi-Span Price Rx Online Pricing Tool

TAKE AWAYS

- S1826 provided high quality data that Nivo-AVD superior to BV-AVD
- PFS with Nivo-AVD is better than BV-AVD
- Nivo-AVD better tolerated than BV-AVD, particularly with regards to neuropathy and with lower discontinuation rates
- G-CSF not mandatory for Nivo-AVD, making administration easier
- Nivo-AVD better tolerated in older patients
- Nivo-AVD may be less costly to administer than BV-AVD per cycle