22nd INTERNATIONAL ULTMANN CHICAGO LYMPHOMA SYMPOSIUM

Optimal Approach to Treating Newly Diagnosed Hodgkin Lymphoma? – Bv-AVD

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Disclosures and COI

- Educational Speaking: BioAscend, CME Concepts
- Advisory: Aptitude Health, Sago Marketing

No relevant conflicts of interest regarding the content of this conference

Advanced Stage Hodgkin Lymphoma

- Good outcomes with combination chemotherapy
- Local combinations roughly all equivalent but most common used: ABVD
- Developed in 1975 and no real change to this standard of care

. . . Until . . .

ECHELON-1

- 1:1 Randomization between ABVD and Bv-AVD (A-AVD) given every 28 days for 6 cycles

- Eligibility Criteria:
  - 18 and older
  - Stage III of IV
  - ECOG of 2 or less

- Primary outcome of modified progression-free survival (PFS)

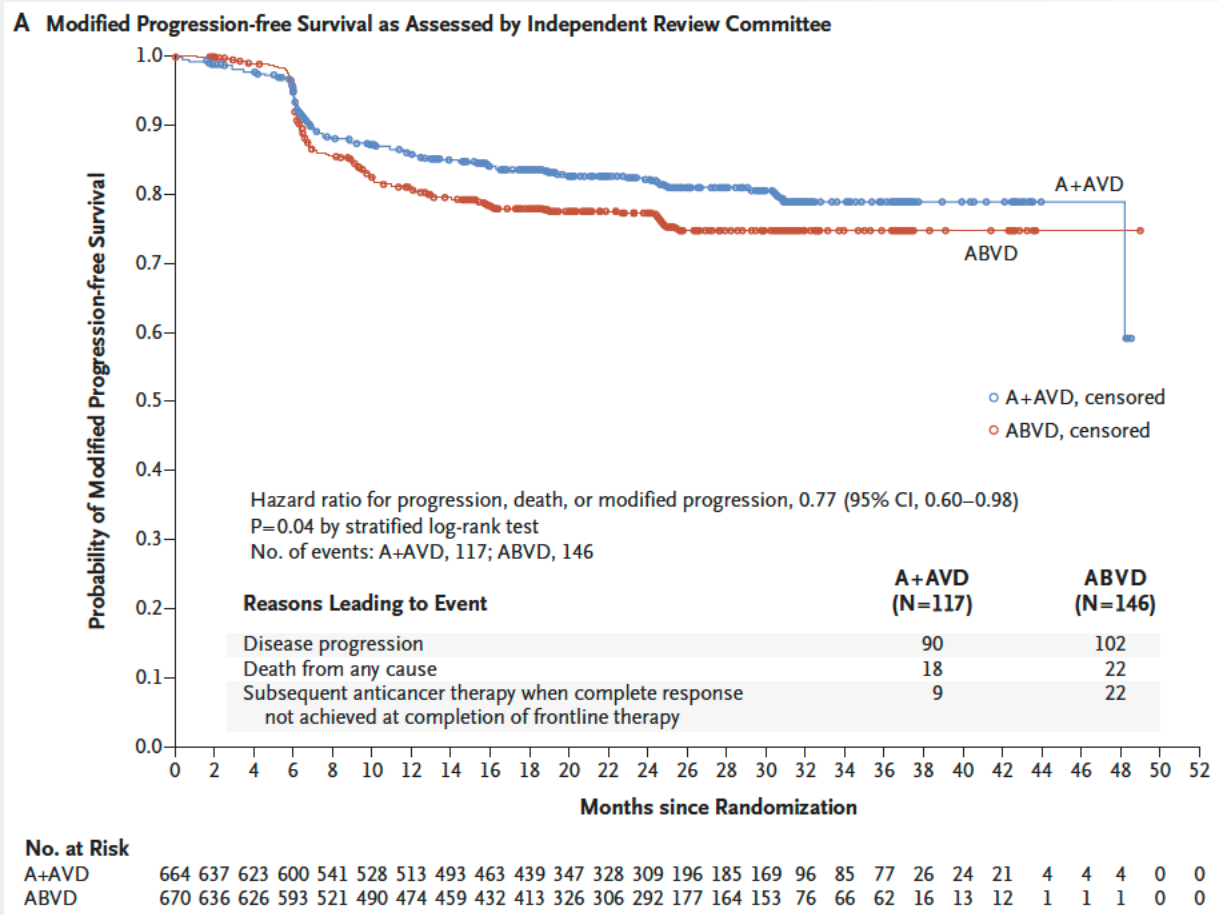
Connors JM et al. NEJM 2018.
Ansell SM et al. NEJM 2022.
Crosswell HE et al. Haematologica 2023.

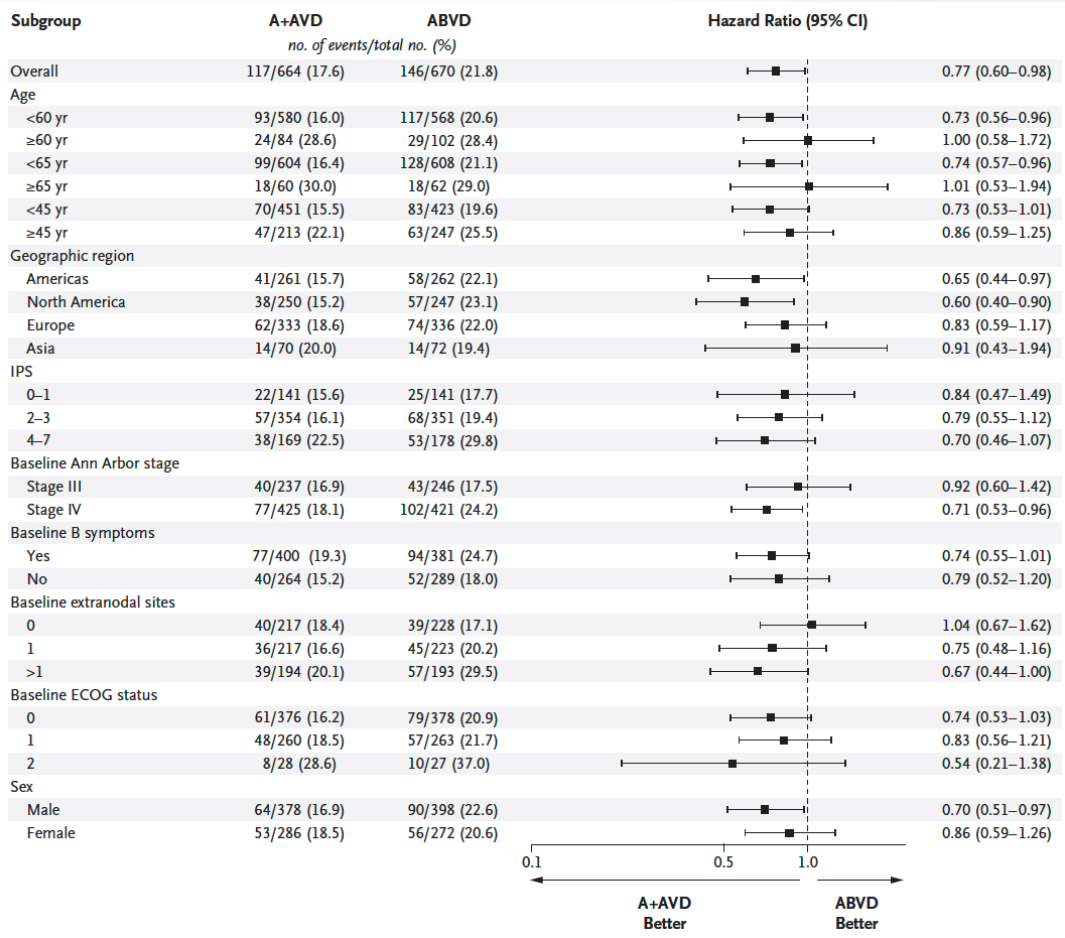
ECHELON-1

Characteristic	A+AVD (N=664)	ABVD (N=670)	Total (N=1334)
Male sex — no. (%)	378 (57)	398 (59)	776 (58)
Age — yr			
Median	35	37	36
Range	18–82	18–83	18–83
Age categories — no. (%)			
<45 yr	451 (68)	423 (63)	874 (66)
45–59 yr	129 (19)	145 (22)	274 (21)
60–64 yr	24 (4)	40 (6)	64 (5)
≥65 yr	60 (9)	62 (9)	122 (9)
Regions — no. (%)			
Americas	261 (39)	262 (39)	523 (39)
Europe	333 (50)	336 (50)	669 (50)
Asia	70 (11)	72 (11)	142 (11)
Ann Arbor stage at initial diagnosis — no. (%)†			
Stage II‡	1 (<1)	0	1 (<1)
Stage III	237 (36)	246 (37)	483 (36)
Stage IV	425 (64)	421 (63)	846 (64)
Not applicable, unknown, or missing	1 (<1)	3 (<1)	4 (<1)
International Prognostic Score — no. (%)§			
0 or 1	141 (21)	141 (21)	282 (21)
2 or 3	354 (53)	351 (52)	705 (53)
4 to 7	169 (25)	178 (27)	347 (26)

Connors JM et al. NEJM 2018.

ECHELON-1



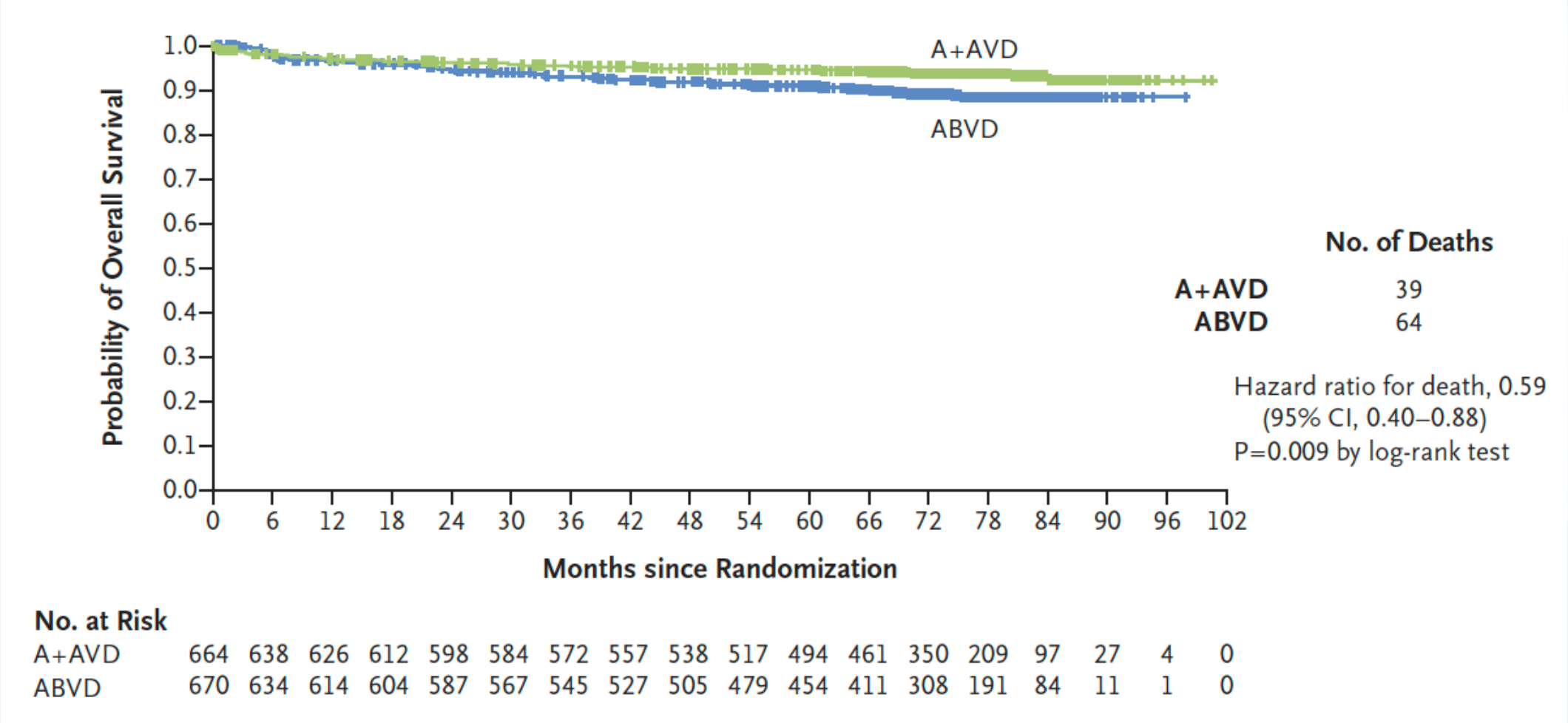


Connors JM et al. NEJM 2018.

But do patients care about PFS?

When asked patients prioritize overall survival (living longer) and minimizing short and long term toxicity (living better)

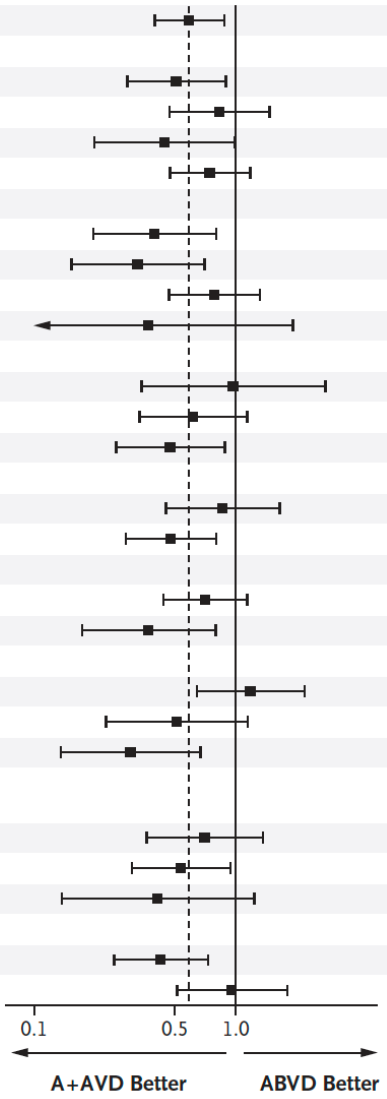
ECHELON-1 Long Term Survival Follow Up



Ansell SM et al. NEJM 2022.

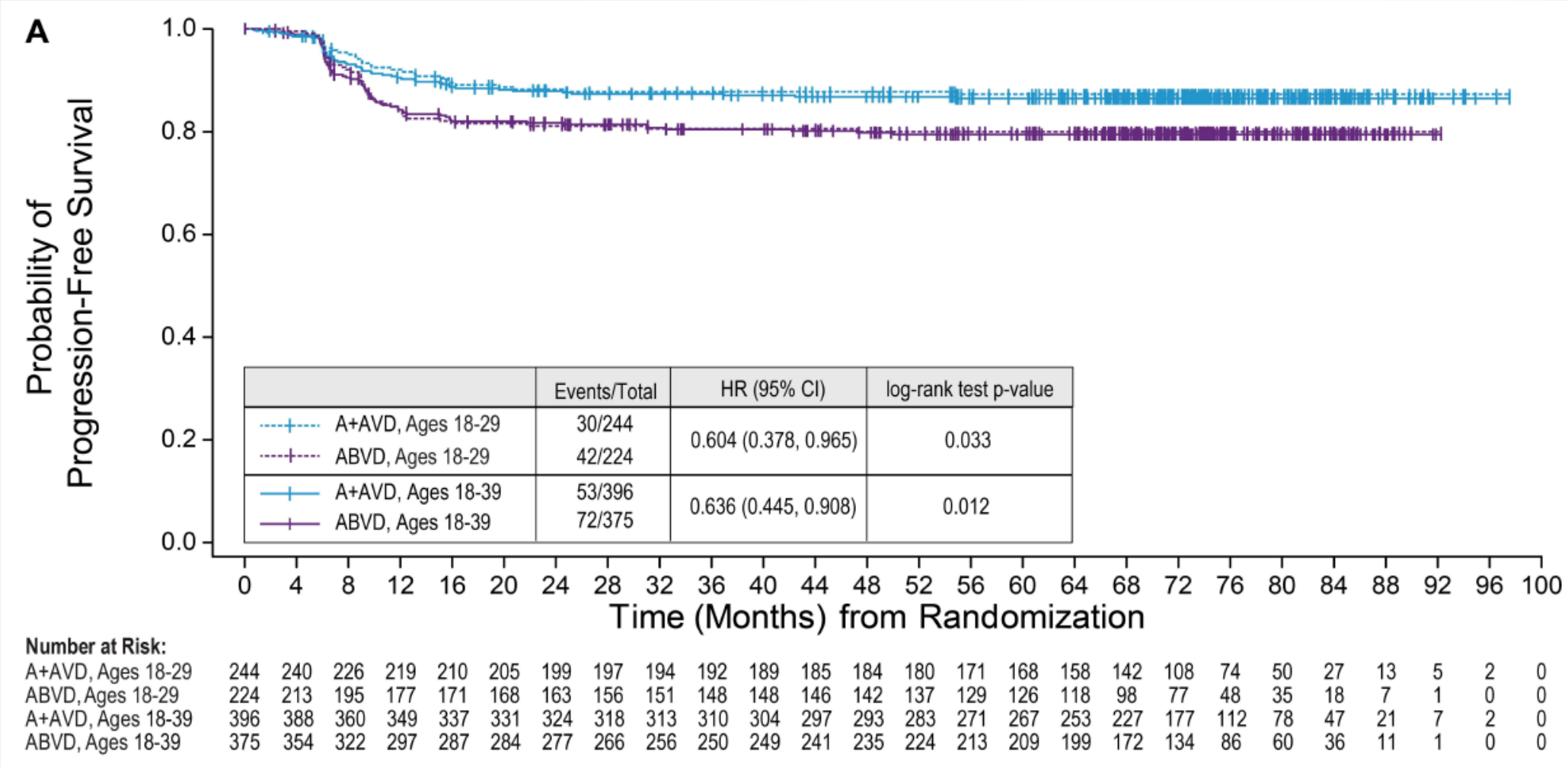
ECHELON-1 Long Term Survival Follow Up

Subgroup	A+AVD	ABVD	Hazard Ratio for Death (95% CI)
	no. of deaths/total no. of patients (%)		
Overall	39/664 (5.9)	64/670 (9.6)	0.59 (0.40–0.88)
Age			
<60 yr	19/580 (3.3)	35/568 (6.2)	0.51 (0.29–0.89)
≥60 yr	20/84 (24)	29/102 (28.4)	0.83 (0.47–1.47)
<45 yr	9/451 (2.0)	18/423 (4.3)	0.44 (0.20–0.99)
≥45 yr	30/213 (14.1)	46/247 (18.6)	0.75 (0.47–1.18)
Geographic region			
Americas	11/261 (4.2)	27/262 (10.3)	0.40 (0.20–0.80)
North America	9/250 (3.6)	26/247 (10.5)	0.33 (0.15–0.70)
Europe	26/333 (7.8)	32/336 (9.5)	0.78 (0.47–1.32)
Asia	2/70 (3)	5/72 (7)	0.37 (0.07–1.91)
No. of IPS risk factors			
0 or 1	7/142 (4.9)	7/141 (5.0)	0.97 (0.34–2.77)
2 or 3	17/355 (4.8)	26/357 (7.3)	0.62 (0.33–1.14)
4–7	15/167 (9.0)	31/172 (18.0)	0.48 (0.26–0.88)
Cancer stage at baseline			
III	17/237 (7.2)	20/246 (8.1)	0.86 (0.45–1.65)
IV	22/425 (5.2)	43/421 (10.2)	0.48 (0.29–0.80)
B symptoms at baseline			
Present	30/400 (7.5)	39/381 (10.2)	0.71 (0.44–1.14)
Absent	9/264 (3.4)	25/289 (8.7)	0.37 (0.17–0.80)
Extranodal site at baseline			
0	22/217 (10.1)	19/228 (8.3)	1.18 (0.64–2.19)
1	9/217 (4.1)	17/223 (7.6)	0.51 (0.23–1.14)
>1	8/194 (4.1)	25/193 (13.0)	0.30 (0.14–0.67)
ECOG performance-status score at baseline			
0	15/376 (4.0)	21/378 (5.6)	0.70 (0.36–1.37)
1	19/260 (7.3)	34/263 (12.9)	0.54 (0.31–0.94)
2	5/28 (18)	9/27 (33)	0.41 (0.14–1.23)
Sex			
Male	19/378 (5.0)	45/398 (11.3)	0.43 (0.25–0.73)
Female	20/286 (7.0)	19/272 (7.0)	0.96 (0.51–1.80)



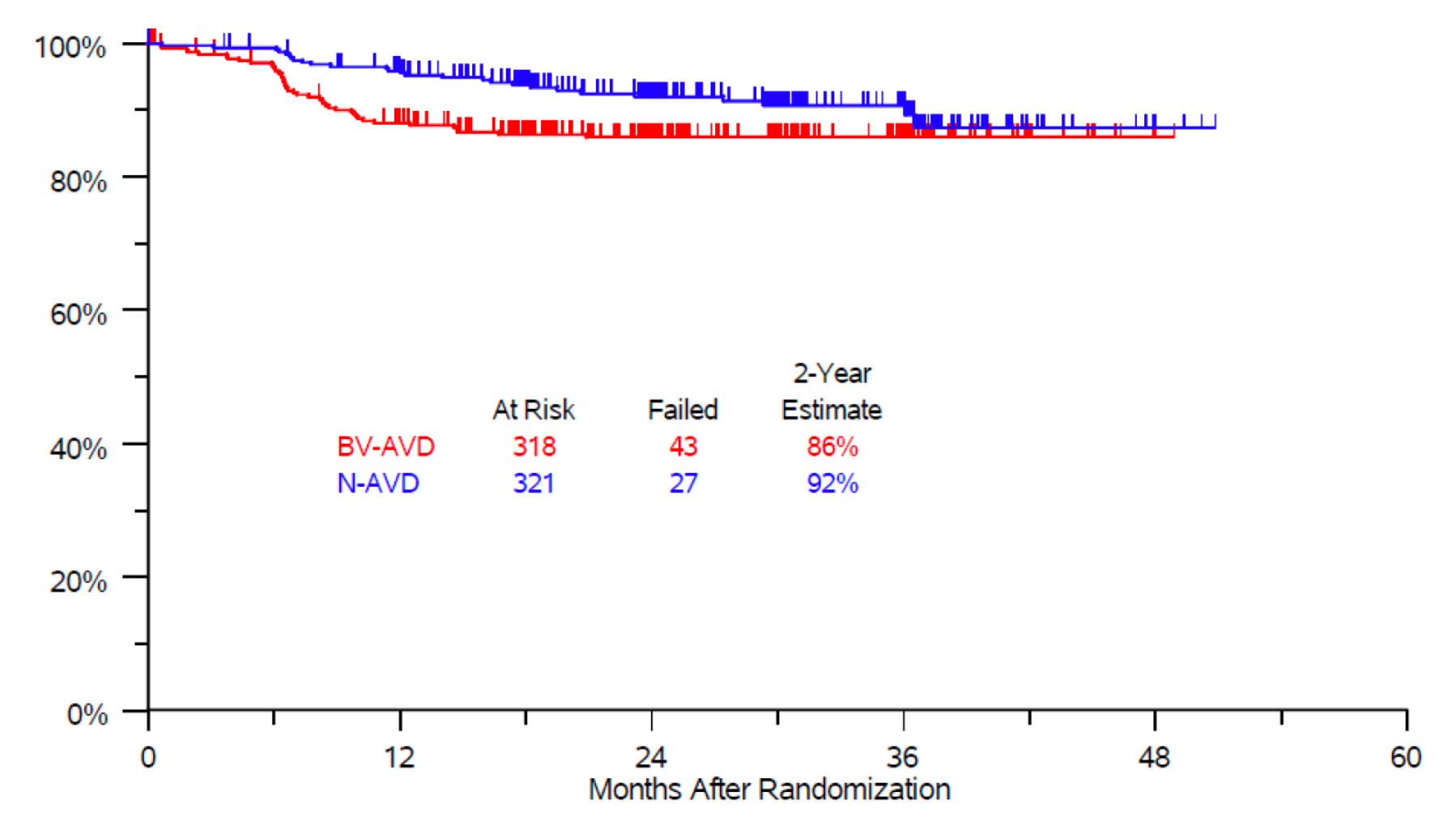
Ansell SM et al. NEJM 2022.

ECHELON-1 AYA Outcomes



Crosswell HE et al. Haematologica 2023.

S1826 Youngish Adult Outcomes



Herrera AF et al. NEJM 2024.

ECHELON-1 Long Term Toxicity Follow Up

Table 1. Summary of Causes of Death (Safety Population).*

Cause of Death	A+AVD (N=662)	ABVD (N=659)
Any cause — no. (%)	39 (5.9)	64 (9.7)
Hodgkin's lymphoma or complications — no.	32	45
Second cancer — no.	1	11
Other cause — no.	6	8
Unknown cause	1	5†
Accident or suicide	3	0
Covid-19	0	1
Heart failure	1	1
Intracranial hemorrhage	1	0
Lower respiratory tract infection	0	1

Treatment arm	Second Malignancy Category (Number of Patients)
A+AVD	Solid tumors (n=14)
	Gastrointestinal (n=3)
	Prostate (n=3)
	Lung (n=2)
	Urogenital (n=2)
	Dermatological (n=2)
	Breast (n=1)
	Thyroid (n=1)
	Hematological malignancies (n=10)
	Acute myeloid leukemia (n=2)
	Diffuse large B-cell lymphoma NOS (n=1)
	Double-hit lymphoma (n=1)
	Follicular lymphoma (n=1)
	Primary cutaneous marginal zone lymphoma (n=1)
	Angioimmunoblastic T-cell lymphoma (n=1)
	Peripheral T-cell lymphoma, not otherwise specified (n=1)
	Mycosis fungoides (n=1)
	Non-Hodgkin's Lymphoma, unspecified subtype (n=1)
ABVD	Solid tumors (n=14)*
	Gastrointestinal (n=5)
	Dermatological (n=4)
	Prostate (n=2)
	Lung (n=1)
	Thyroid (n=1)
	Gynecological (n=1)
	Gallbladder (n=1)
	Other (n=1)
	Hematological malignancies (n=17)
	Follicular lymphoma (n=4)
	Diffuse large B-cell lymphoma NOS (n=4)
	Primary mediastinal (thymic) large B-cell lymphoma (n=1)
	Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (n=1)
	Precursor B-acute lymphoblastic leukemia/lymphoblastic lymphoma (n=1)
	Acute promyelocytic leukemia (n=1)
	Acute myeloid leukemia or related precursor neoplasm (n=1)
	Myelodysplastic syndrome (n=1)
	Angioimmunoblastic T-cell lymphoma (n=1)
	Peripheral T-cell lymphoma, not otherwise specified (n=1)
	Other (n=1)
	Unknown malignancy (n=1)

*Numbers are reported by patient. Three solid tumors (basal cell carcinoma, colon tumor, melanoma) were reported for one patient.

Ansell SM et al. NEJM 2022.

ECHELON-1 Long Term Toxicity Follow Up

	A+AVD (n=662)	ABVD (n=659)
All female patients or partners of male patients pregnant — n*	82	61
Total pregnancies – n*	114	81
Live birth	96	59
Pregnancy ongoing	7	9
Early termination	11	13
Stillbirth	0	0
Female patients pregnant — n*	49	28
Total pregnancies – n*	70	35
Live birth†	56	23
Pregnancy ongoing	6	3
Early termination	8	9
Stillbirth	0	0
Partners of male patients pregnant — n*	33	33
Total pregnancies – n*	44	46
Live birth‡	40	36
Pregnancy ongoing	1	6
Early termination	3	4
Stillbirth	0	0

Treatment arm	Second Malignancy Category (Number of Patients)
A+AVD	Solid tumors (n=14) Gastrointestinal (n=3) Prostate (n=3) Lung (n=2) Urogenital (n=2) Dermatological (n=2) Breast (n=1) Thyroid (n=1) Hematological malignancies (n=10) Acute myeloid leukemia (n=2) Diffuse large B-cell lymphoma NOS (n=1) Double-hit lymphoma (n=1) Follicular lymphoma (n=1) Primary cutaneous marginal zone lymphoma (n=1) Angioimmunoblastic T-cell lymphoma (n=1) Peripheral T-cell lymphoma, not otherwise specified (n=1) Mycosis fungoides (n=1) Non-Hodgkin's Lymphoma, unspecified subtype (n=1)
ABVD	Solid tumors (n=14)* Gastrointestinal (n=5) Dermatological (n=4) Prostate (n=2) Lung (n=1) Thyroid (n=1) Gynecological (n=1) Gallbladder (n=1) Other (n=1) Hematological malignancies (n=17) Follicular lymphoma (n=4) Diffuse large B-cell lymphoma NOS (n=4) Primary mediastinal (thymic) large B-cell lymphoma (n=1) Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (n=1) Precursor B-acute lymphoblastic leukemia/lymphoblastic lymphoma (n=1) Acute promyelocytic leukemia (n=1) Acute myeloid leukemia or related precursor neoplasm (n=1) Myelodysplastic syndrome (n=1) Angioimmunoblastic T-cell lymphoma (n=1) Peripheral T-cell lymphoma, not otherwise specified (n=1) Other (n=1) Unknown malignancy (n=1)

*Numbers are reported by patient. Three solid tumors (basal cell carcinoma, colon tumor, melanoma) were reported for one patient.

Ansell SM et al. NEJM 2022.

ECHELON-1 Long Term Toxicity Follow Up

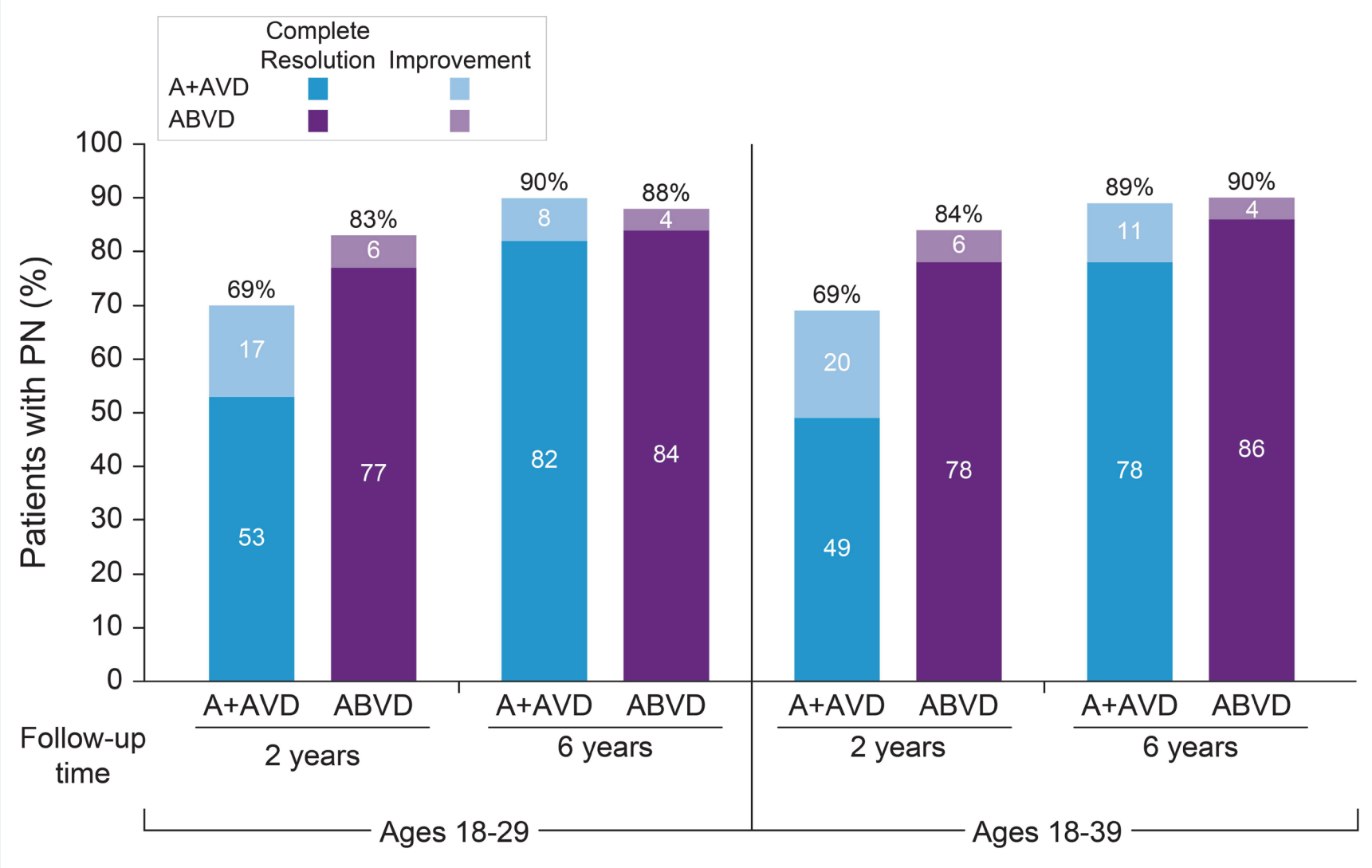
Table S11. Summary of Outcomes in Patients with Treatment-Emergent Peripheral Neuropathy (Safety Population)

Patients with treatment-emergent PN	**A+AVD (n=443)**	**ABVD (n=286)**
Patients with resolution/improvement of PN events at last follow-up — n (%)	379 (85.6)	249 (87.1)
Resolution*	318 (71.8)	227 (79.4)
Improvement†	61 (13.8)	22 (7.7)
Median time to resolution of PN events (range) — weeks	16.0 (0 to 283)	10.0 (0 to 343)
Median time to improvement of PN events (range) — weeks	42.0 (2 to 182)	72.5 (15 to 142)
Safety population	**A+AVD (n=662)**	**ABVD (n=659)**
Patients with ongoing PN events at last follow-up — n (%)	125 (18.9)	59 (9.0)
Grade 1	71 (10.7)	39 (5.9)
Grade 2	38 (5.7)	16 (2.4)
Grade 3‡	15 (2.3)	4 (0.6)
Grade 4‡	1 (0.2)	0

*Resolution was defined as resolved/recovered with or without sequelae; or return to baseline or lower severity as of the latest assessment for pre-existing events.

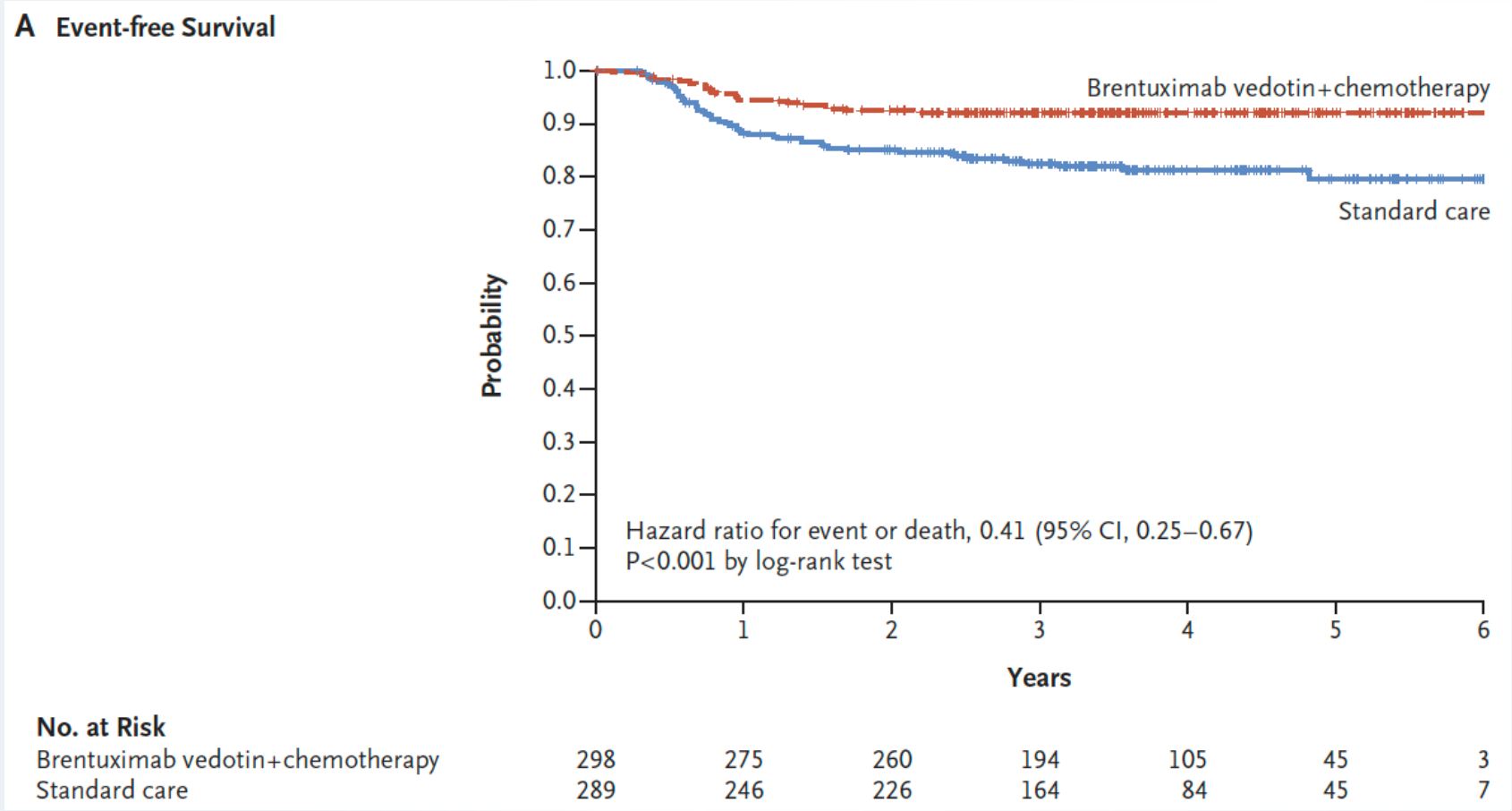
Ansell SM et al. NEJM 2022.

ECHELON-1 AYA Outcomes



Crosswell HE et al. Haematologica 2023.

Pediatric Approach – AHOD1331



Castellino SM et al. NEJM 2022.

Bv-AVD for Advanced Stage HL

- Only combination currently with overall survival benefit over standard chemotherapy
- Side effect of concern (neuropathy) almost completely resolves over time
  - Neutropenic infection risk mitigated by GCSF support
- Most available data for AYA population and consistent between adult and paediatric studies

Conclusion: Still a role for Bv-AVD in treatment algorithm