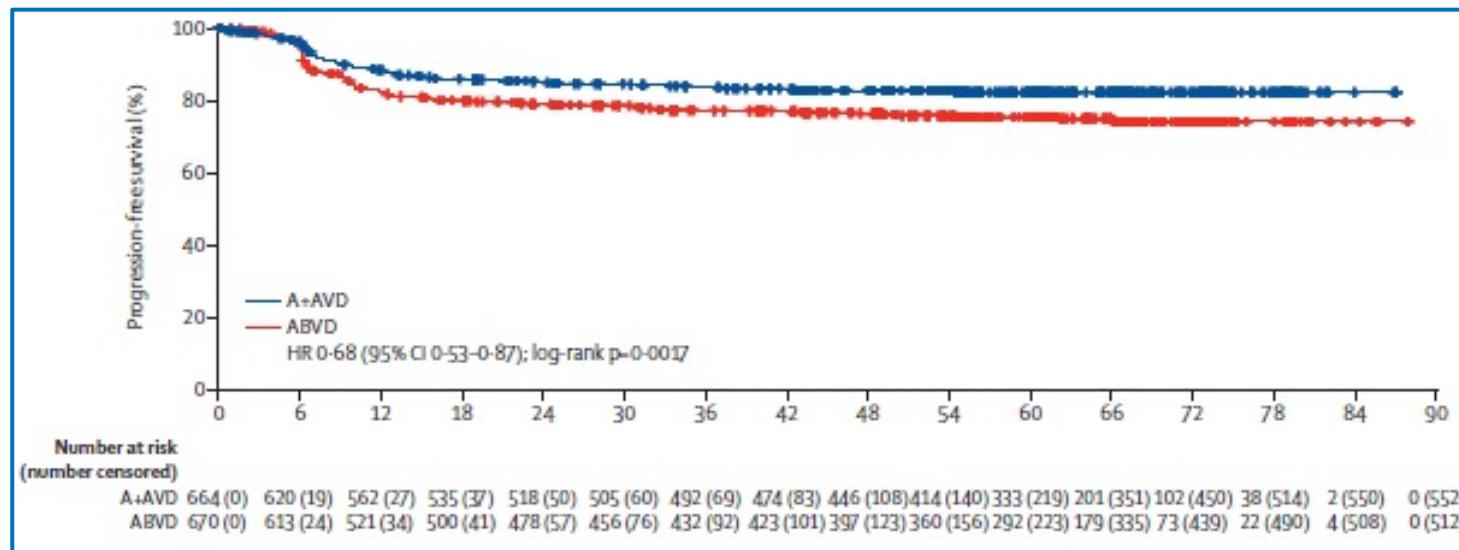


# Hodgkin Lymphoma (HL)

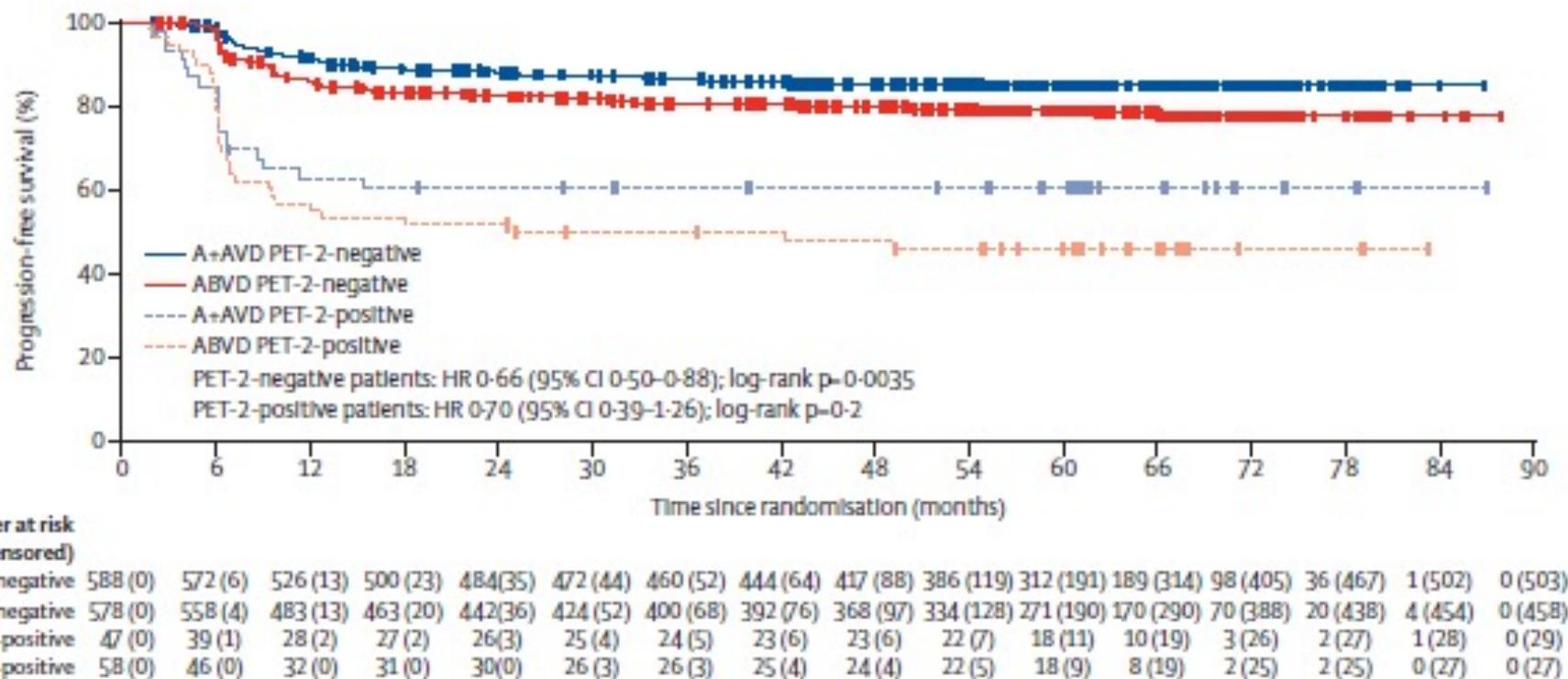
Dr LaCasce

# 5 year follow-up of Echelon-1: BV-AVD with improved PFS, particularly in younger patients



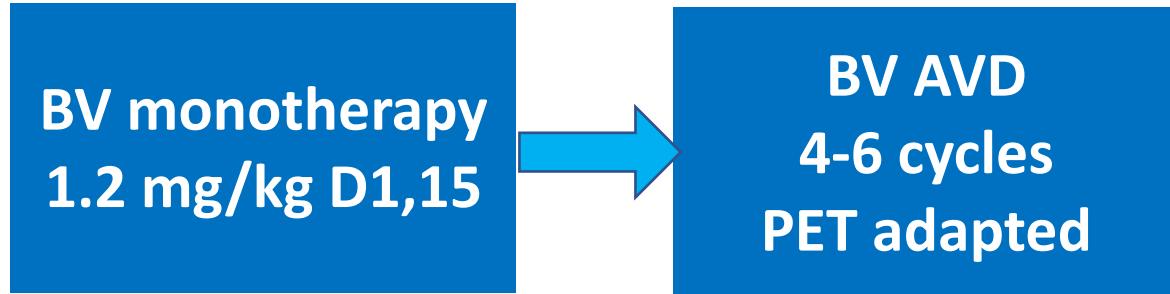
	n	BVAVD PFS	n	ABVD PFS	p-value
All	664	82%	670	75%	0.002
< 60	580	84%	568	78%	0.034
≥ 60	84	67%	102	62%	0.44

# PFS according to PET status



PET 2 negative:  
 89% BV-AVD  
 86% ABVD

# Phase 2 study of BV + chemotherapy in stage I/II non-bulky patients

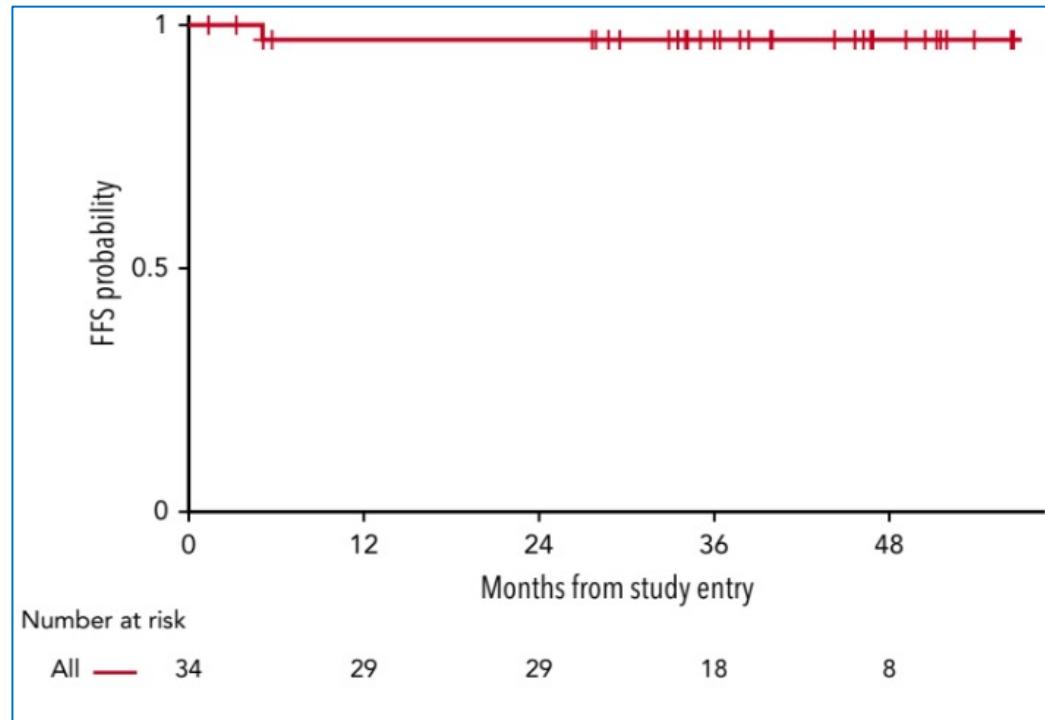


**Table 1. Patient characteristics (N = 34)**

Characteristic	n
Age, median (range), y	36 (20-75)
Female/male	17/17
<b>Stage</b>	
IA	6 (18%)
IIA	24 (71%)
IIB	4 (12%)
Size of largest lesion, median (range), cm	3.34 (1.51-8.33)
<b>Risk</b>	
Early favorable	21 (62%)
Early unfavorable	13 (38%)
<b>Histology</b>	
Nodular sclerosis	18 (53%)
Mixed cellularity	4 (12%)
Lymphocyte-rich	4 (12%)
Classical not otherwise specified	8 (24%)

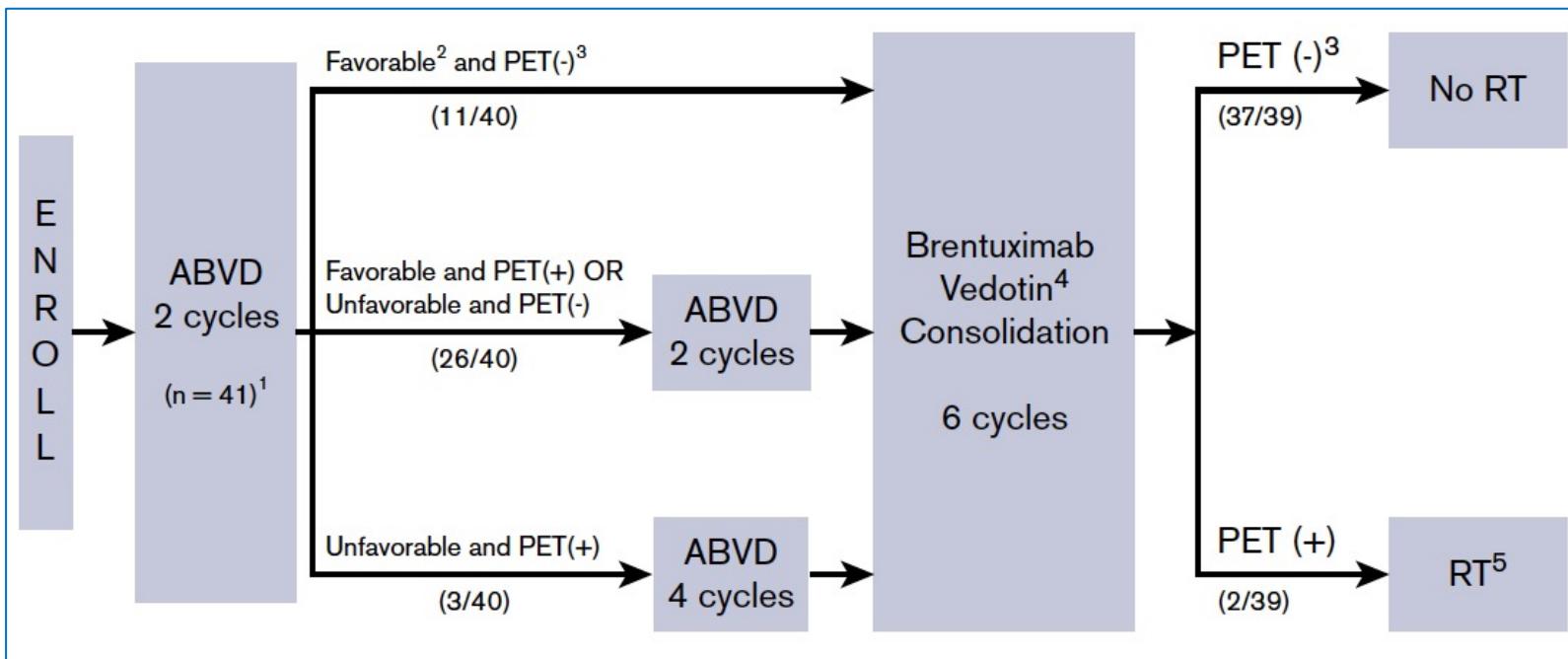
# BV + AVD in early stage patients: outcome and toxicity

Time point	Overall response	CR	Partial response
Monotherapy lead-in	34 (100; 89.7-100)	18 (52.9; 35.1-70.2)	16 (47.1; 29.8-64.9)
Cycle 2	33 (97.1; 84.7-99.9)	33 (97.1; 84.7-99.9)	0 (0; 0-10.3)
End of treatment	31 (91.2; 76.3-98.1)	31 (91.2; 76.3-98.1)	0 (0; 0-10.3)



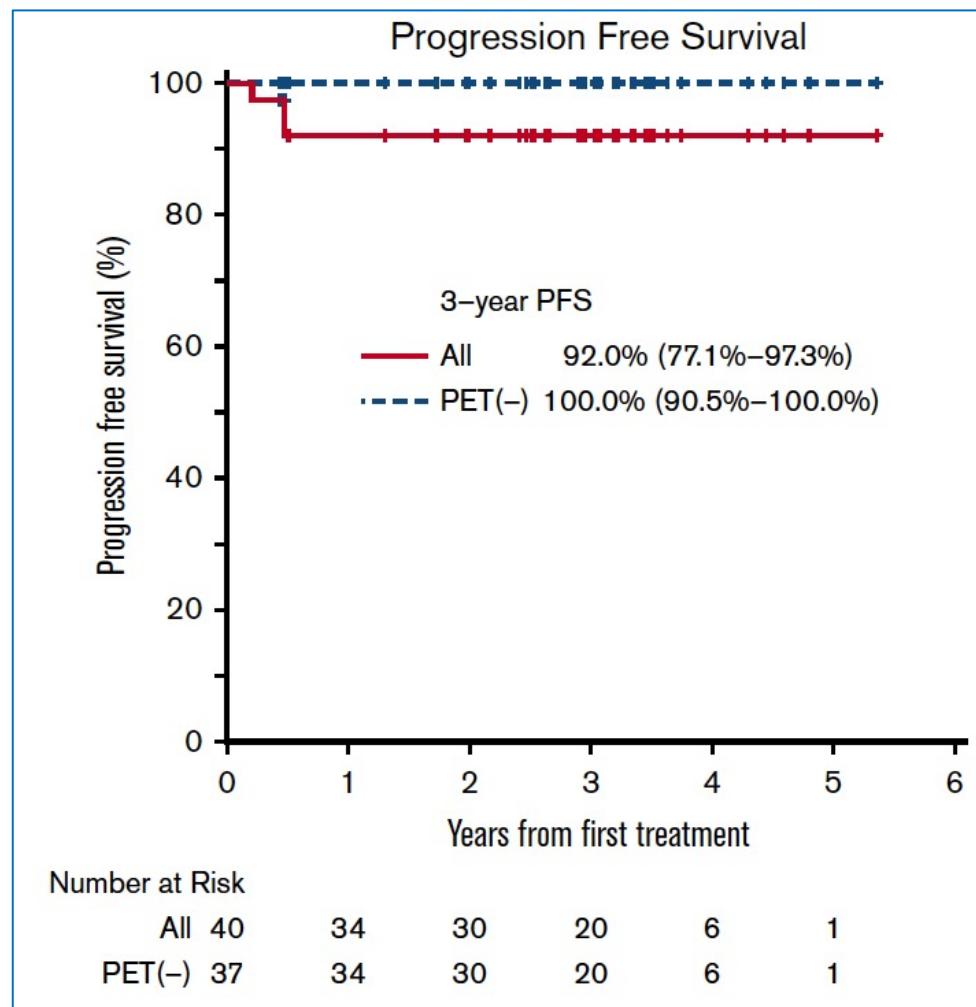
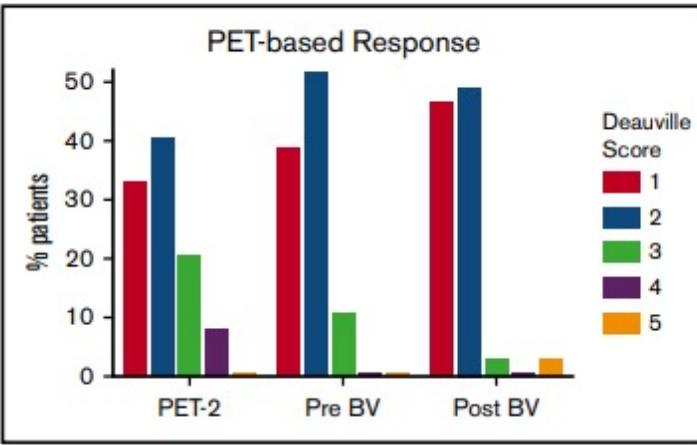
Toxicity	Any grade	Grade 1	Grade 2	Grade 3	Grade 4
PSN	27 (79)	16 (47)	3 (9)	8 (24)	0
Neutropenia	26 (76)	4 (12)	1 (3)	3 (9)	18 (53)
F+N	12 (35)	0	0	10 (29)	2 (6)*

# Risk adapted chemotherapy followed by BV in early stage patients



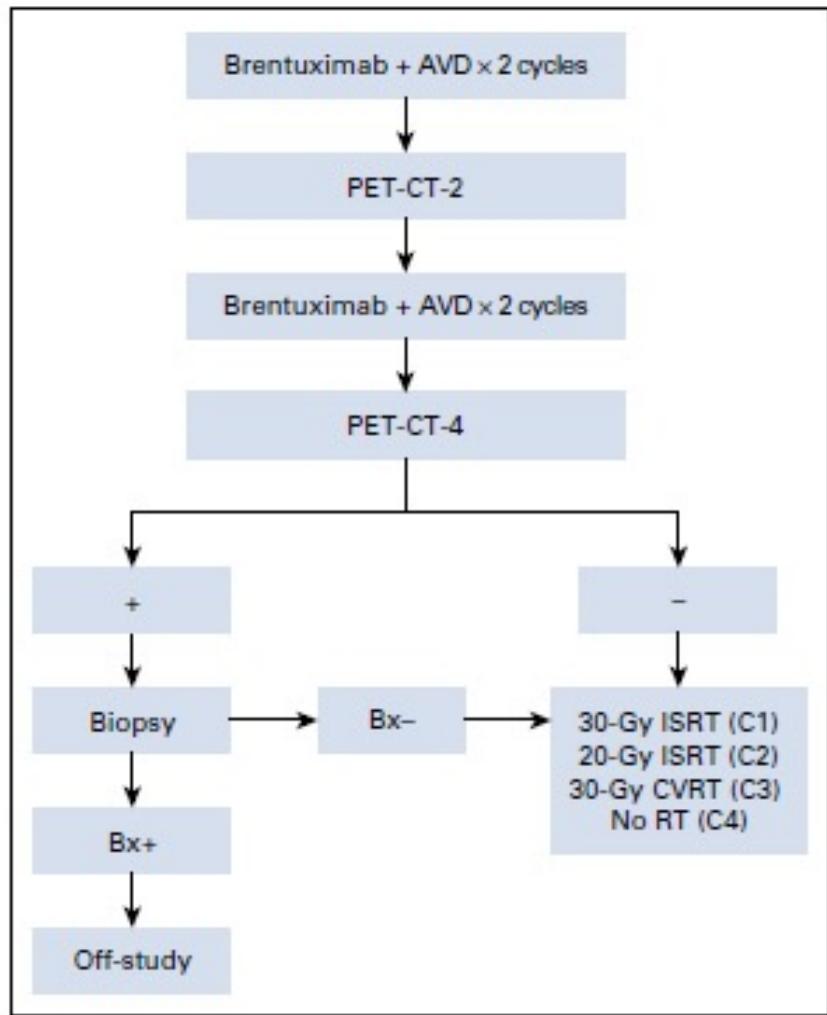
	n=40
<b>Median age</b>	<b>29 (19-67)</b>
<b>Stage</b>	
IA	<b>1 (2%)</b>
IB	<b>0 (0%)</b>
IIA	<b>29 (73%)</b>
IIB	<b>10 (25%)</b>
<b>Favorable</b>	<b>22 (55%)</b>
<b>Unfavorable</b>	<b>18 (45%)</b>

# PET response and PFS with risk adapted BV strategy



One case of  
gr 3 PN  
One infectious  
death

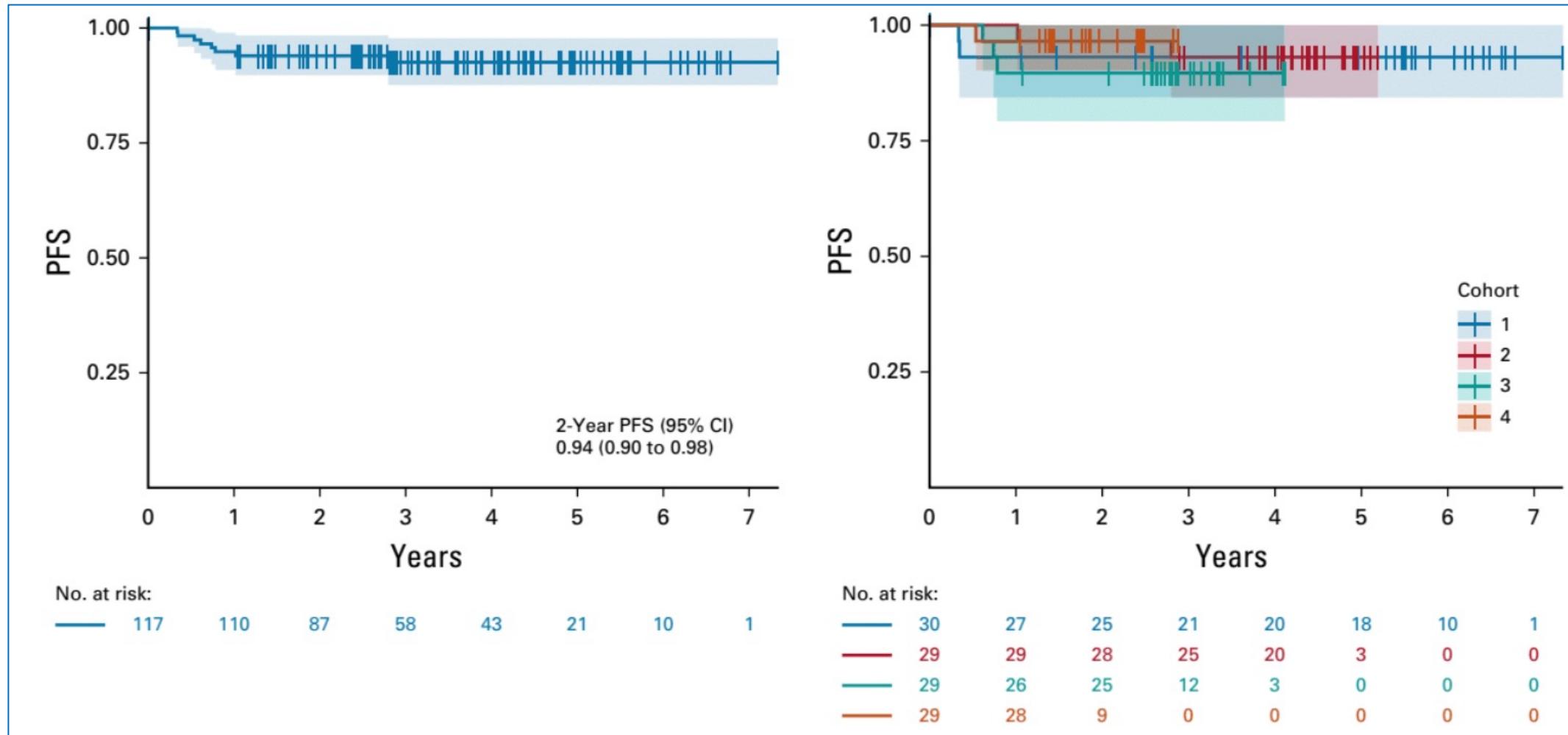
# BV-AVD in early unfavorable HL



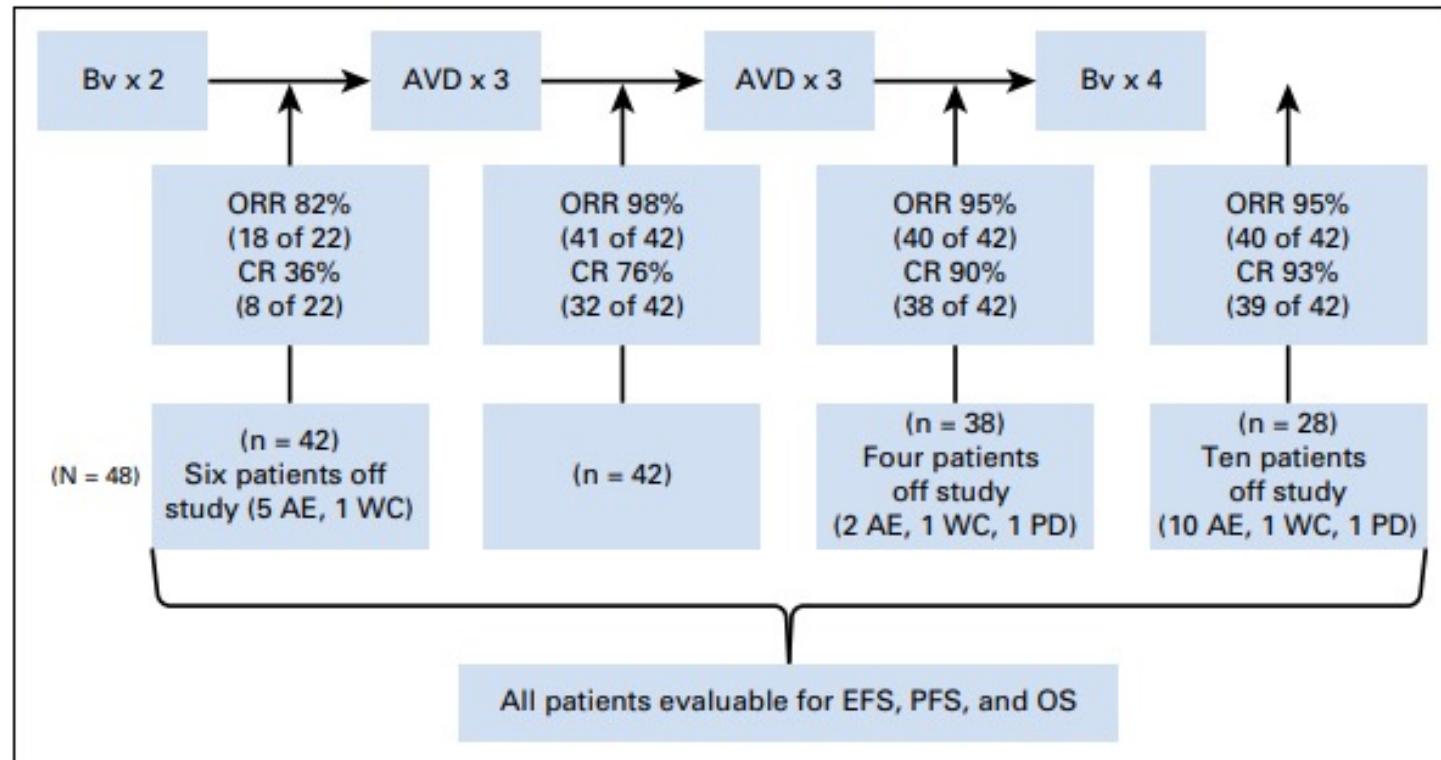
Cohort	1	2	3	4	all
n	30	29	29	29	117
Age, med range	31 18-59	33 19-55	31 20-58	30 20-58	32 18-59
Stage II	30 (100)	29 (100)	28 (97)	28 (97)	115 (98)
Stage IIBX	6 (20)	7 (24)	0 (0)	3 (10)	16 (14)
IIBE	4 (13)	0 (0)	0 (0)	1 (3)	5 (4)
IIBXE	2 (7)	2 (7)	1 (3)	1 (3)	6 (5)
Bulky disease	12(40)	9 (31)	6 (21)	7 (24)	32 (27)
MSK bulky*	23(77)	20(69)	29(100)	29(100)	101(86)

\* > 7 cm transverse/coronal

# Favorable PFS without difference between cohorts



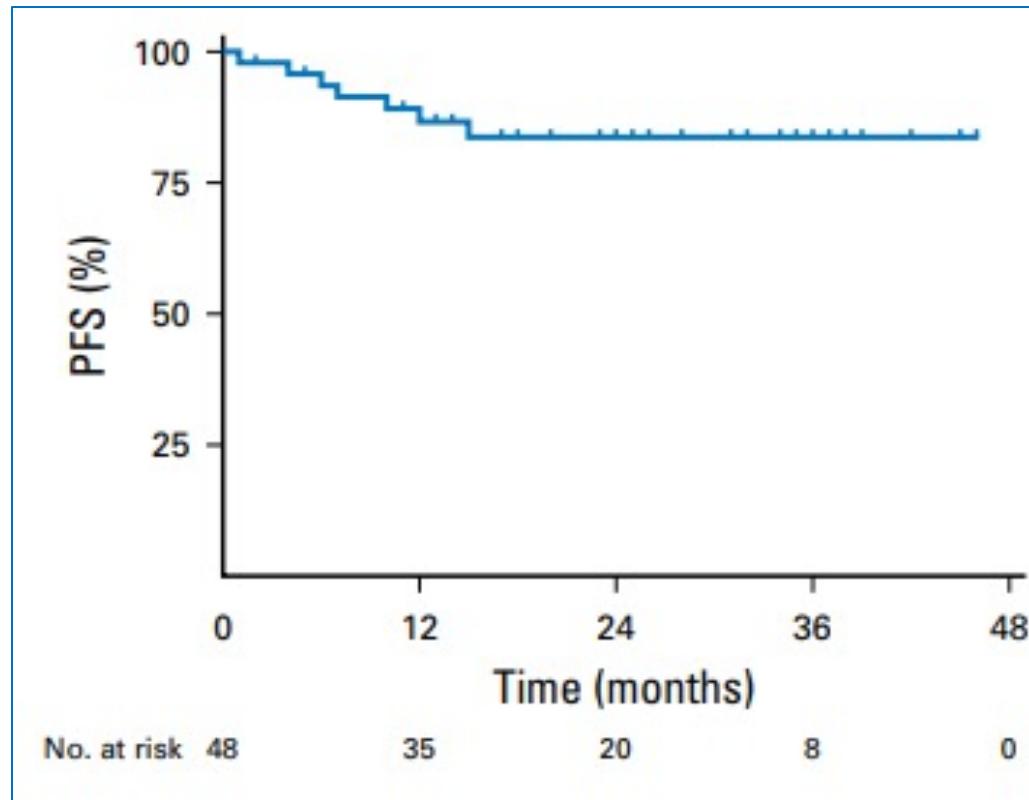
# Sequential BV-AVD in elderly patients



**Table 1.** Patient Characteristics

Characteristic	No. (N = 48)*	%
Age, years		
60-70	25	52
71-80	15	31
> 80	8	17
Sex		
Female	18	37
Male	30	63
Histology		
Nodular sclerosis	22	46
Mixed cellularity	12	25
Classic, not otherwise specified	12	25
Lymphocyte rich	2	4
ECOG PS		
0	19	40
1	20	41
2	9	19
B symptoms	18	37
Albumin		
Low (< 4.0 g/dL)	22	46
International Prognostic Score		
0-2	20	42
3-7	28	58
Bone marrow		
Involved	11	23
Bulky disease ( $\geq 10$ cm)	5	10
Stage		
I†	9	19
III	18	37
IV	21	44
Median CIRS-G score (range)	7 (0-20)	

# BV followed by AVD with favorable PFS and manageable toxicity



AE	Gr 3	Gr 4
Neutropenia	8(17%)	13(27%)
F+N	3(6%)	1(2%)
Pancreatitis	1(2%)	1(2%)*
PSN	2(4%)	0(0%)

\* Gr 5

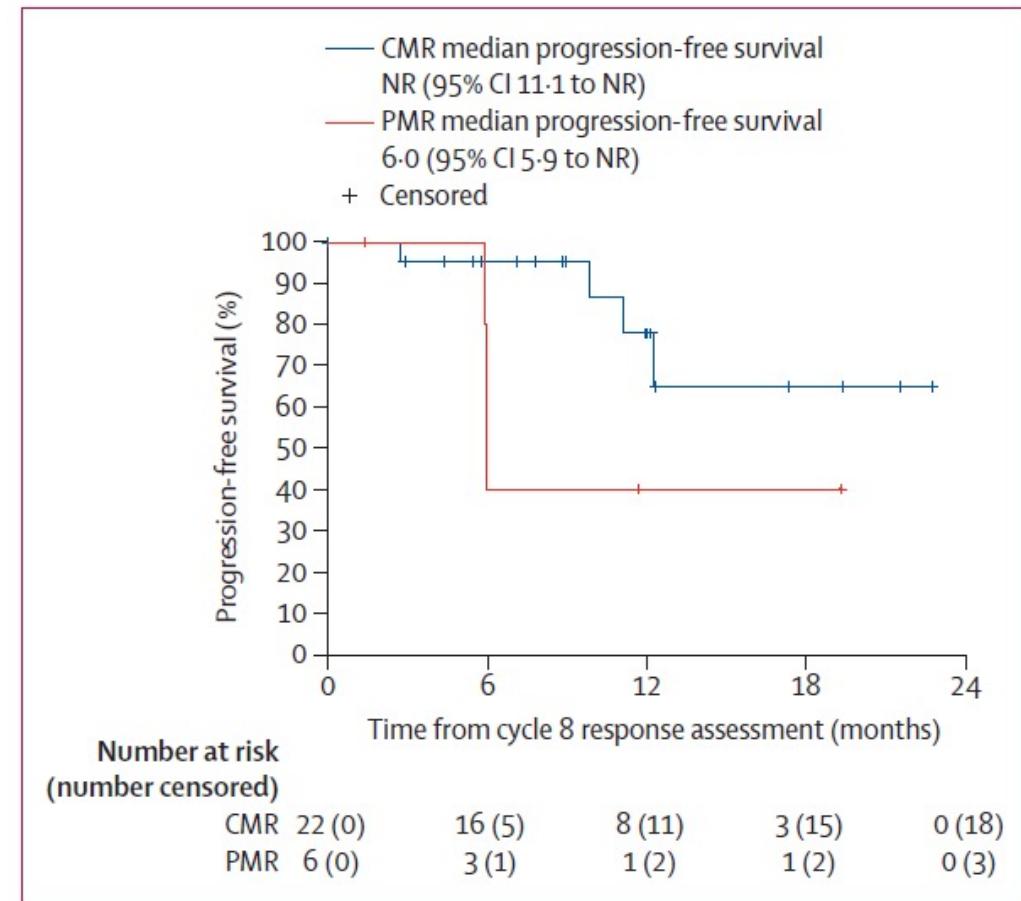
# BV-nivo in older/chemotherapy ineligible patients

	n=46
<b>Age</b>	<b>71.5 (64-77)</b>
<b>ECOG PS</b>	
0	<b>14 (30%)</b>
1	<b>26 (57%)</b>
2	<b>6 (13%)</b>
<b>Stage</b>	
I	<b>1 (2%)</b>
II	<b>15 (33%)</b>
III	<b>9 (20%)</b>
IV	<b>21 (46%)</b>

	<b>Best ORR</b>	
<b>CMR</b>	<b>30 (65%)</b>	
<b>PMR</b>	<b>12 (26%)</b>	
<b>Med PFS</b>	<b>18.3 m</b>	

<b>AE</b>	<b>Gr 3</b>	<b>Gr 4</b>
<b>PSN</b>	<b>2 (4%)</b>	0
<b>PMR</b>	<b>3 (7%)</b>	0
<b>Neutropenia</b>	<b>8 (17%)</b>	0

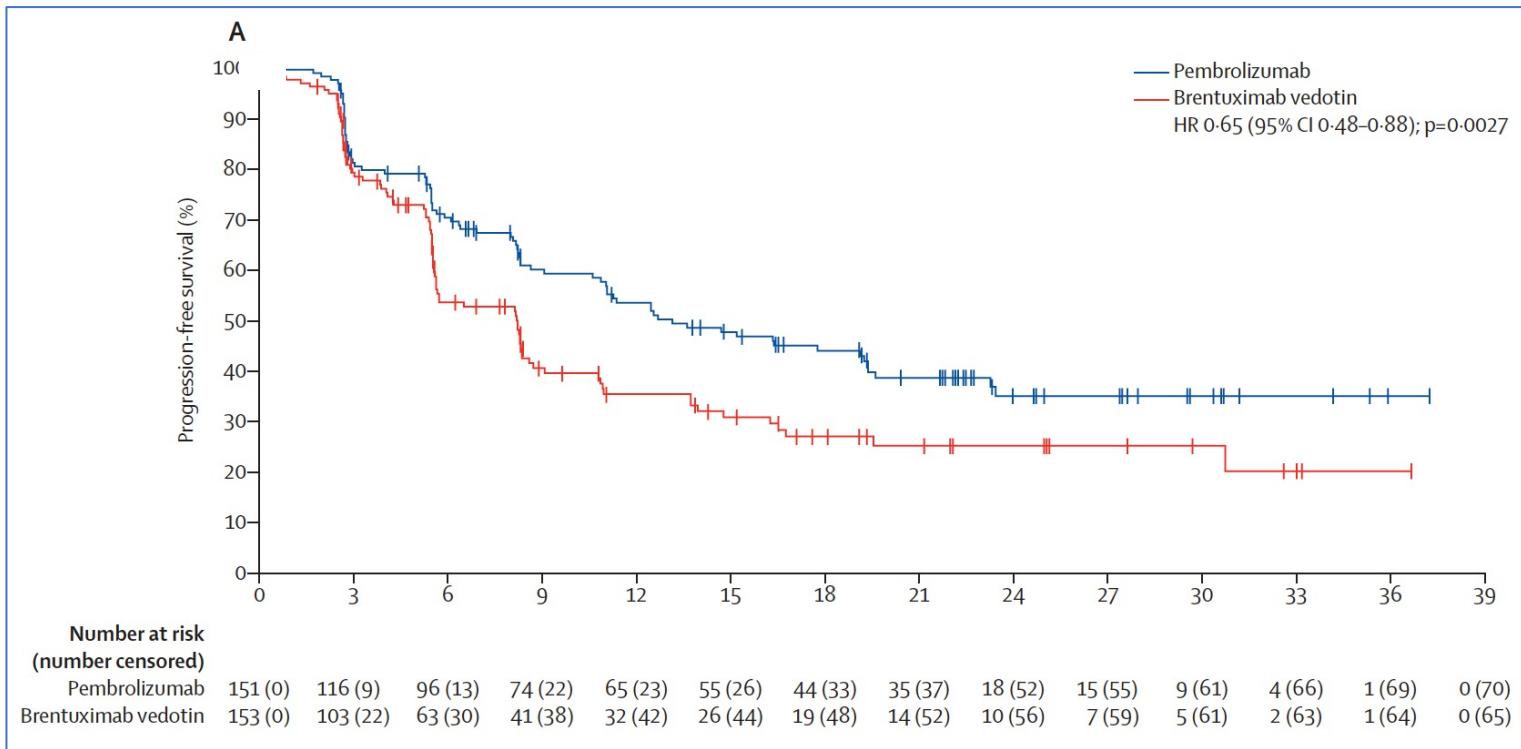


	Pembro n=151	BV N=153
<b>Age</b>	<b>36 (28-53)</b>	<b>35 (28-50)</b>
<65	<b>124 (82%)</b>	<b>131 (86%)</b>
≥65	<b>27 (18%)</b>	<b>22 (14%)</b>
<b>Male</b>	<b>84 (56%)</b>	<b>90 (59%)</b>
<b>Prior ASCT</b>	<b>56 (37%)</b>	<b>56 (37%)</b>
<b>Prim ref</b>	<b>61 (40%)</b>	<b>62 (41%)</b>
<b>Rel &lt; 12 m</b>	<b>42 (28%)</b>	<b>42 (27%)</b>
<b>Rel &gt; 12 m</b>	<b>48 (32%)</b>	<b>49 (32%)</b>
<b>Prior rx</b>	<b>2 (2-3)</b>	<b>3 (2-3)</b>
1	<b>27 (18%)</b>	<b>28 (18%)</b>
≥ 2	<b>124 (82%)</b>	<b>125 (82%)</b>
<b>Prior BV</b>	<b>5 (3%)</b>	<b>10 (7%)</b>

## Keynote 204: BV versus pembrolizumab

Response	Pembro n=151	BV n=153
<b>ORR</b>	<b>99(66%)</b>	<b>83(54%)</b>
<b>CR</b>	<b>37(25%)</b>	<b>37(24%)</b>
<b>PR</b>	<b>62(41%)</b>	<b>46(30%)</b>
<b>SD</b>	<b>2(14%)</b>	<b>36(24%)</b>
<b>PD</b>	<b>26(17%)</b>	<b>28(18%)</b>

# Pembrolizumab with superior PFS



Toxicity	Pembro n=148	BV n=152
Any gr 3	16%	21%
Any gr 4-5	3%/1%*	4%/0%
SAE	16%	11%

\* gr5 pneumonia

Median PFS  
BV: 8.3 m  
Pembro: 13.2 m

# Brentuximab containing salvage regimens with high CR rates

PET CR rate associated with improved PFS

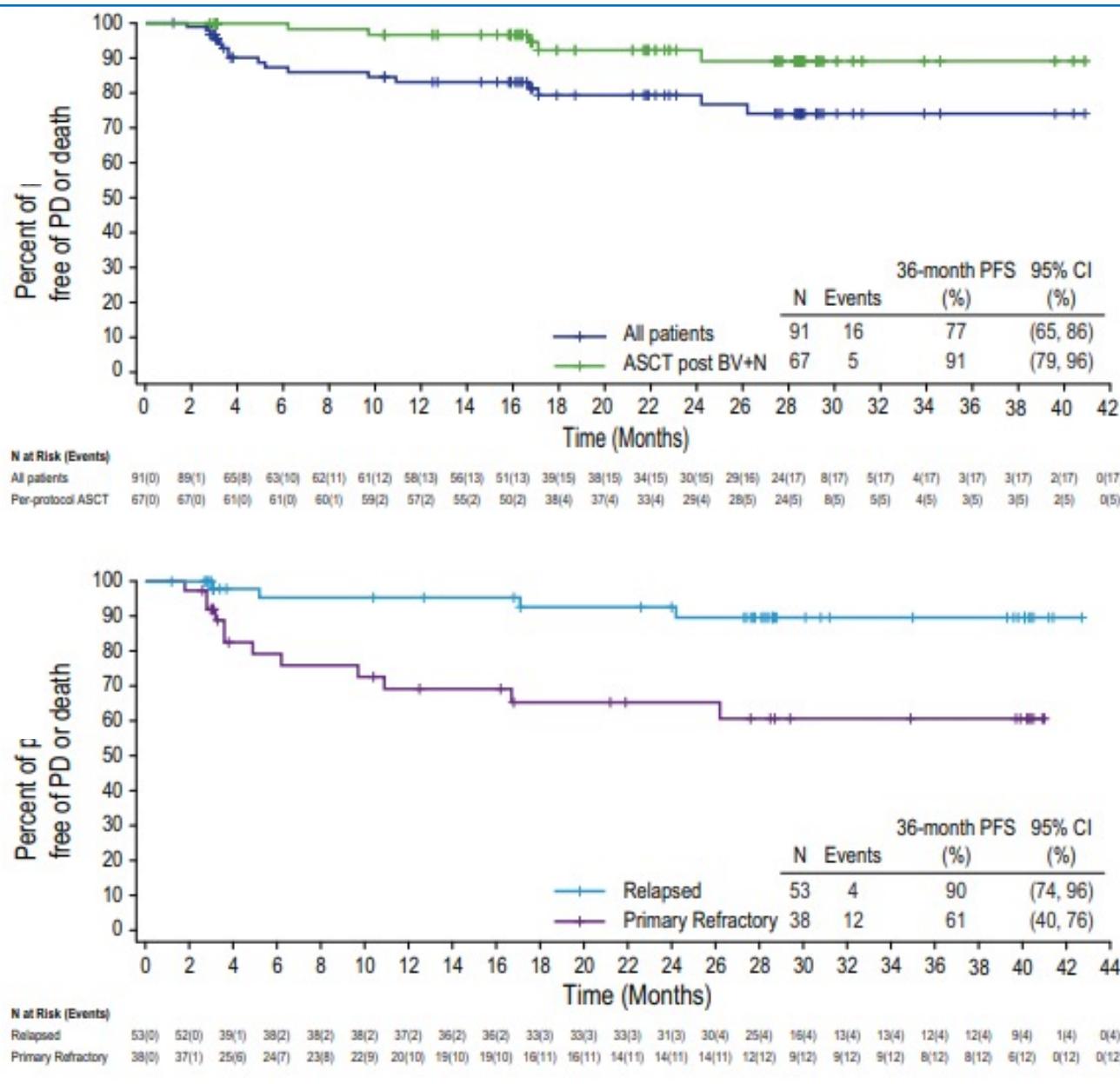
Standard salvage regimens with CR rates: 50-60%

Regimen	n	CR	2-year PFS	ref
BV augmented ICE	45	27% BV 76% total	80% (EFS)	Moskowitz Lancet Onc 2015
BV bendamustine	82	73%	70%/63%	LaCasce Blood 2018
BV ESHAP	66	70%	71%	Garcia-Sanz Ann Onc 2019

	All treated patients, N = 91
Median age (range), y	34 (18, 69)
<b>Sex, n (%)</b>	
Male	40 (44)
Female	51 (56)
<b>Prior systemic therapy regimens,* n (%)</b>	
ABVD	82 (90)
BEACOPP	2 (2)
Radiation	18 (20)
Stanford V	3 (3)
Other	8 (9)
<b>Disease status relative to frontline treatment, n (%)</b>	
Primary refractory	38 (42)
PR or SD to frontline therapy	13 (14)
Relapsed, remission duration ≤1 y	27 (30)
Relapsed, remission duration >1 y	26 (29)

# BV-nivo second line therapy

	All treated patients, N = 91	
	n (%)	95% CI
Objective response rate (CR + PR)	77 (85)	75.5, 91.3
CMR/CR	61 (67)	56.4, 76.5



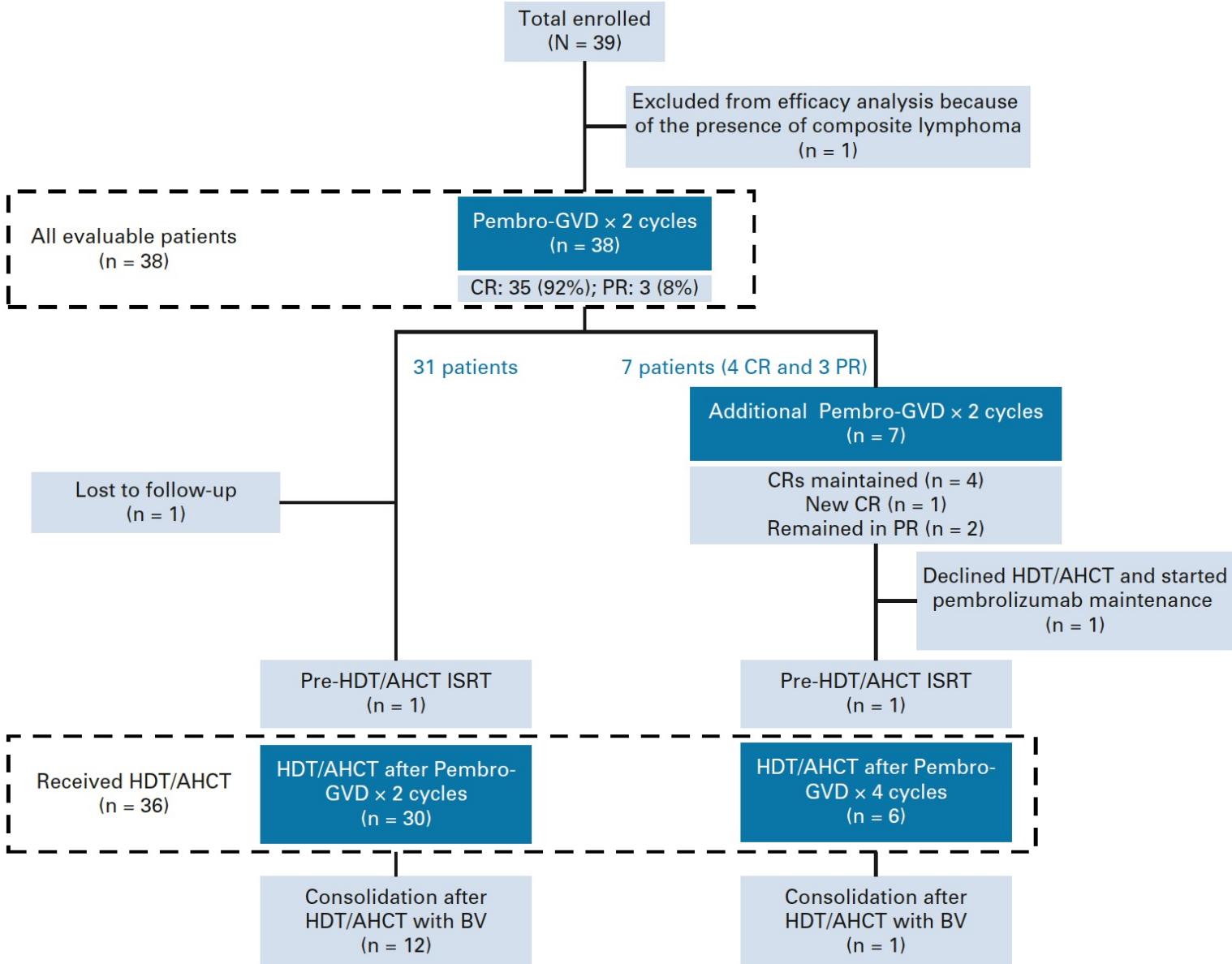
**BV plus nivolumab with favorable PFS in first relapse**



# Pembrolizumab + GVD is highly active in second line

Characteristic	No. (range or %), N = 39 <sup>a</sup>
Median age (range), years	38 (21-71)
Male	18 (46)
Disease characteristics at time of enrollment	
B-symptoms	6 (15)
Extranodal disease	12 (31)
EBV-positive	5 (13)
Disease status after frontline therapy	
Refractory (no CR to frontline and progression ≤ 1 year)	16 (41)
Relapse (CR to frontline and remission duration ≤ 1 year)	15 (38)
Relapse (CR to frontline and remission duration > 1 year)	8 (21)

Frontline therapy	
ABVD	14 (36)
ABVD and AVD	8 (21)
ABVD and escBEACOPP	3 (8)
ABVD and BV + AVD	2 (5)
ABVD and CMOPP	1 (3)
AVD	1 (3)
BV, AVD, and BV	1 (3)
BV + AVD	5 (13)
BV + AVD and escBEACOPP	1 (3)
Consolidation with radiation therapy <sup>b</sup>	3 (8)



Response	
ORR	100%
CR	95%
PR	5%

med f/u 13.5 m  
**All transplanted patients in remission**

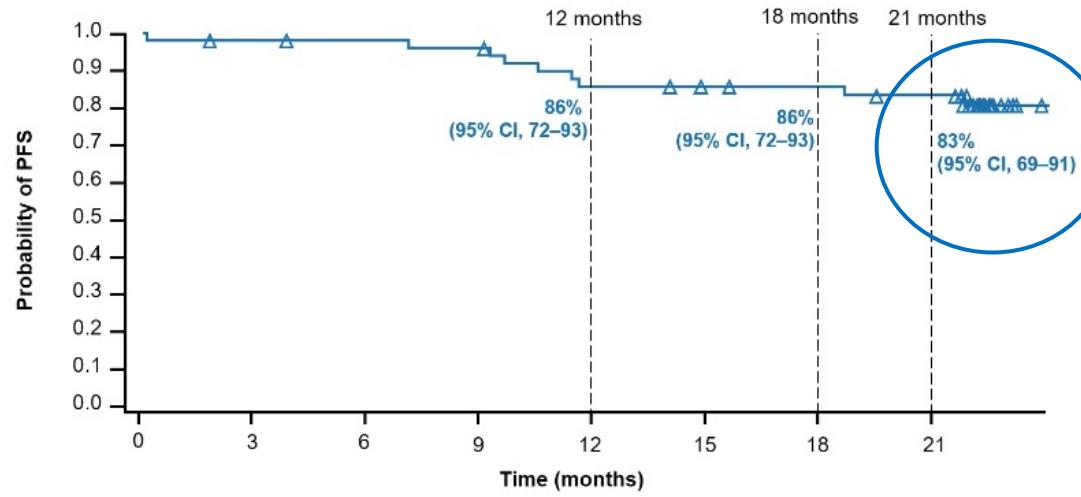


# PFS of nivolumab + AVD in untreated advanced stage HL

Nivo x 4  
n=51

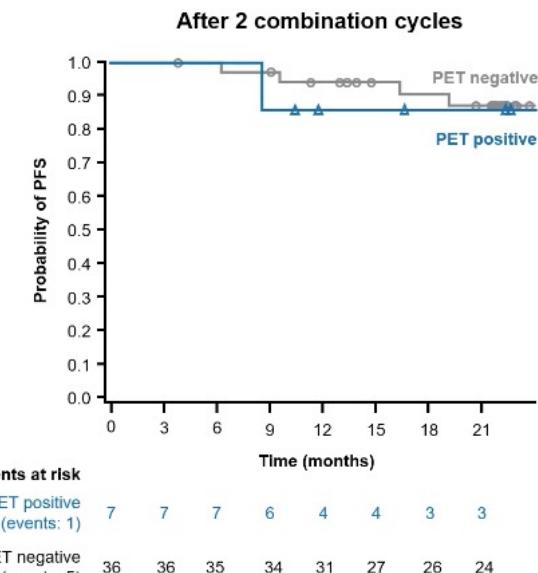
N-AVD x 6  
cycles

### PFS Per Investigator



Traditional PFS per IRC was not analyzed because tumor scans were not centrally collected in the study after patients receiving subsequent therapy.

### PFS by Deauville PET Status



Ansell et al. ICML 2019

# Pembrolizumab+AVD in early unfavorable and advanced stage HL

# Pembrolizumab x 3



Characteristic	Patients (N = 30)	
	n	%
Median age, y (range)	29 (21-77)	
Age 45-60	4	13.3
Age >60	4 (67-77)	13.3
<b>Sex</b>		
Male	11	36.7
Female	19	63.3
<b>Disease stage</b>		
IIA	6	20.0
IIB	6	20.0
IIB with >10 cm mass	5	16.7
IIIA	4	13.3
IIIB	1	3.3
IVA	6	20.0
IVB	7	23.3
<b>IPS Score*</b>		
0-1	4	13.3
2	6	20.0
3	6	20.0
≥4	2	6.7
ESR >50†	6	50
B symptoms	14	46.7
Extranodal disease	16	53.3
Bone‡	14	46.7
Lung‡	3	10.0
<b>Bulky</b>		
>7 cm†	11	91.7
>10 cm	10	33.3
MMR >1/3	9	30.0
>10 cm or MMR >1/3	12	40.0

