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Title:

Updated efficacy and safety data from the AETHERA trial of consolidation with brentuximab vedotin after autologous stem cell transplant (ASCT) in Hodgkin lymphoma patients at high risk of relapse

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Updated Efficacy and Safety Data from the AETHERA Trial of Consolidation with Brentuximab Vedotin after Autologous Stem Cell Transplant (ASCT) in Hodgkin Lymphoma Patients at High Risk of Relapse

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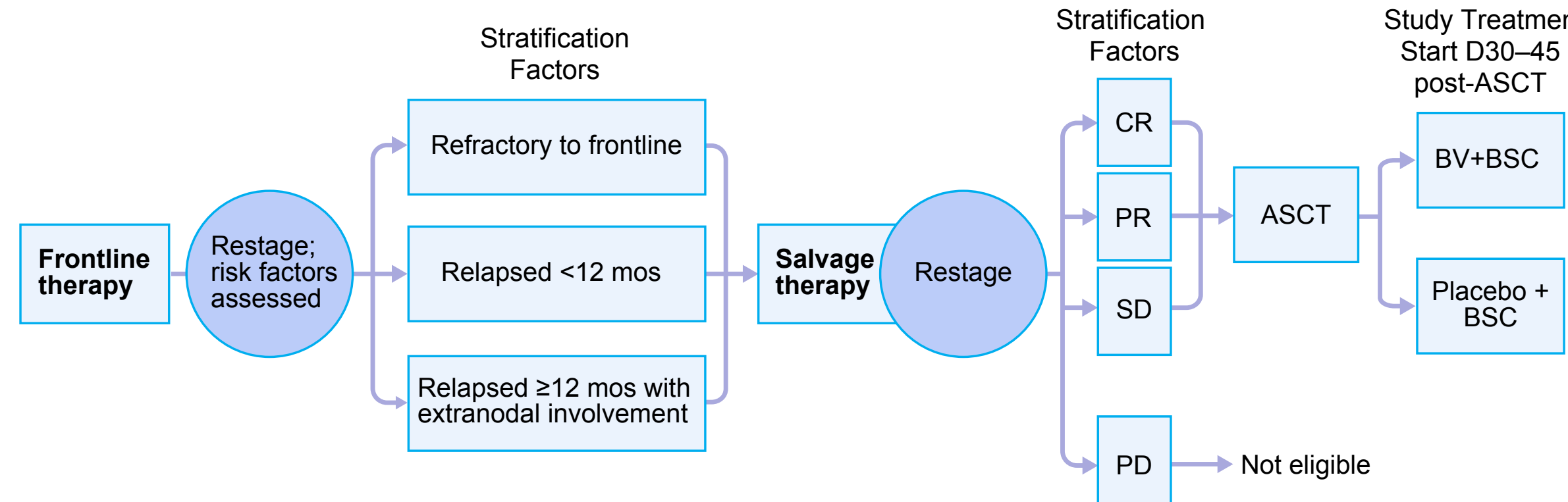
Background

- The AETHERA trial is a phase 3, randomized, placebo-controlled trial that evaluated post-ASCT consolidation treatment with brentuximab vedotin (BV) in patients with Hodgkin lymphoma (HL) at high risk for relapse or progression
- The AETHERA study met its primary endpoint: significant improvement in progression-free survival (PFS) per independent review with BV versus placebo (hazard ratio [HR]=0.57, P=0.001)^a
- The most common adverse events (AEs) in the BV-treatment group were peripheral sensory neuropathy (56%) and neutropenia (35%)
- Updated efficacy and safety data after approximately 3 years of follow-up since the last patient enrolled are reported here

^a Moskowitz et al. Lancet 2015, 385: 1853.

Study Design

Key Eligibility Criteria and Stratification



- Randomization stratified by risk factors after frontline therapy and best clinical response to salvage therapy before ASCT
- Patients with progressive disease after salvage therapy were not eligible

Treatment and Assessment Schedule

- 329 patients were randomized at 78 sites in Europe and North America to receive BV 1.8 mg/kg and best supportive care (BSC) or placebo and BSC for 16 X 21-day cycles, starting 30–45 days after ASCT
- Clinical lymphoma evaluations were performed every 21 days at time of treatment during year 1, quarterly during year 2, then every 6 months thereafter
- CT imaging was performed quarterly for first 12 months, then at 6-month intervals through 24 months
- Patients on placebo arm with progressive disease had access to BV

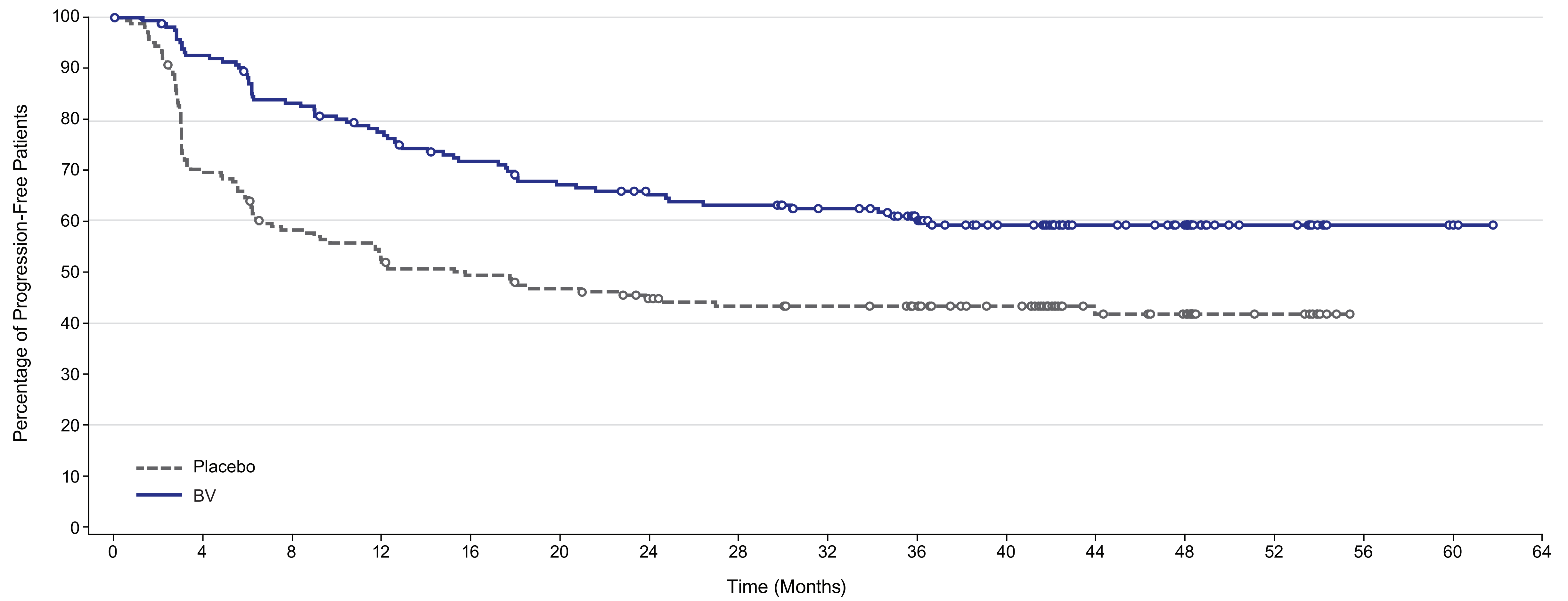
Patient Population

Demographics and Disease Characteristics

	BV+BSC (N=165)	Placebo+BSC (N=164)
Age, years; median (range)	33 (18–71)	32 (18–76)
Gender	46% M / 54% F	59% M / 41% F
No. prior cancer-related systemic salvage therapies		
1	94 (57%)	86 (52%)
≥2	71 (43%)	78 (48%)
HL status after frontline therapy		
Refractory	99 (60%)	97 (59%)
Relapse <12 months	53 (32%)	54 (33%)
Relapse ≥12 months	13 (8%)	13 (8%)
Response with salvage therapy pre-ASCT		
Complete remission	61 (37%)	62 (38%)
Partial remission	57 (35%)	56 (34%)
Stable disease	47 (28%)	46 (28%)
Extranodal involvement at pre-ASCT relapse	54 (33%)	53 (32%)
B symptoms after frontline therapy	47 (28%)	40 (24%)
Pre-ASCT PET status		
FDG avid	64 (39%)	51 (31%)
FDG negative	56 (34%)	57 (35%)
Not available	45 (27%)	56 (34%)

Results

PFS* per Investigator – 3 Years Since Last Patient Randomized

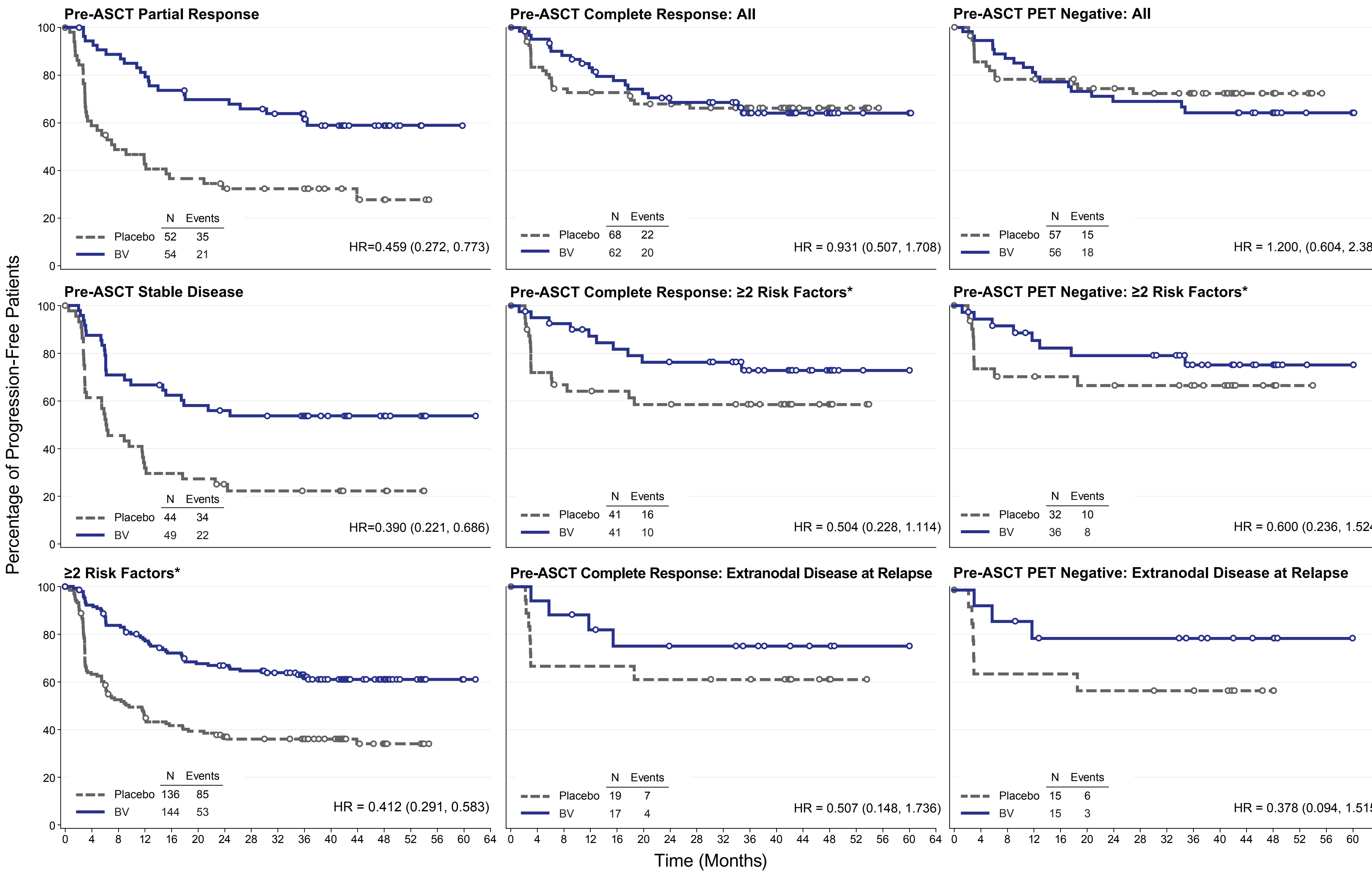


N at Risk (Events)	BV 165 (0)	149 (12)	133 (27)	122 (36)	111 (45)	103 (52)	97 (55)	94 (58)	87 (59)	74 (61)	56 (63)	39 (63)	32 (63)	13 (63)	4 (63)	3 (63)	0 (63)
Placebo	164 (0)	113 (48)	92 (67)	83 (76)	77 (81)	72 (85)	65 (88)	61 (90)	59 (90)	54 (90)	44 (90)	26 (91)	22 (91)	9 (91)	0 (91)	0 (91)	0 (91)

	Treatment cycles (median)	Events	PFS Rate, % (95% CI)		Median PFS (mos)	Hazard ratio
			24 months	36 months		
BV (N=165)	15	63	65 (57, 72)	61 (53, 68)	—	0.52
Placebo (N=164)	15	91	45 (37, 52)	43 (36, 51)	15.8	

*Includes clinical assessments of lymphoma

PFS Per Investigator – Subgroup Analyses



* Risk factors include (1) relapsed <12 months or refractory to frontline therapy, (2) best response of PR or SD to most recent salvage therapy, (3) extranodal disease at pre-ASCT relapse, (4) B symptoms at pre-ASCT relapse, and (5) 2 or more prior salvage therapies

PFS Rate per Investigator by Treatment Duration: BV Arm

Months after first BV dose	Number of Treatment Cycles			
	1–4 (n=18)	5–8 (n=7)	9–12 (n=24)	13–16 (n=92)
12	58%	67%	91%	98%
24	58%	67%	69%	82%
36	58%	67%	63%	77%

Excluding patients who discontinued treatment due to PD
Not a randomized comparison

Peripheral Neuropathy (SMQ): BV Arm

- 112/167 (67%) patients reported PN; 22 of these patients reported a maximum Grade 3 event. No PN event was ≥ Grade 4

N = 112	Sep 2014 n (%)	Oct 2015 n (%)
Resolution or improvement	95 (85)	99 (88)
Complete resolution	66 (59)	74 (66)

- 38/112 patients had ongoing PN at last assessment
 - 15 are off study and can no longer be followed for resolution
 - 23 patients remaining on study have ongoing PN
- Of patients remaining on study with ongoing PN
 - 17 have maximum Grade 1
 - 5 have maximum Grade 2
 - 1 has maximum Grade 3 (patient has ongoing Grade 3 radiation myelitis confounding assessment of PN)

SMQ = standardized MedDRA query; includes peripheral sensory neuropathy, peripheral motor neuropathy, paresthesia, muscular weakness, hypoesthesia, gait disturbance, neuralgia, amyotrophy, decreased vibratory sense, hyporeflexia, peroneal nerve palsy, and sensory disturbance

Second Malignancies

	BV+BSC (N=165)	Placebo+BSC (N=164)
	n (%)	n (%)
Secondary malignancies	5 (3)	2 (1)
Myelodysplastic syndrome	2 (1)	1 (1)
Bladder cancer	1 (1)	0
Lung neoplasm malignant	1 (1)	0
Mantle cell lymphoma	0	1(1)
Pancreatic carcinoma	1 (1)	0

- Patients with secondary malignancies had increased age (median 57 years, range 46–71 years) compared with the study population overall (median 32 years)
- Of the 26 patients enrolled in the study with age ≥55 years, 13 were in BV arm and 8 were in the placebo arm
- Time to onset: BV (179–1427 days); Placebo (188–638 days)

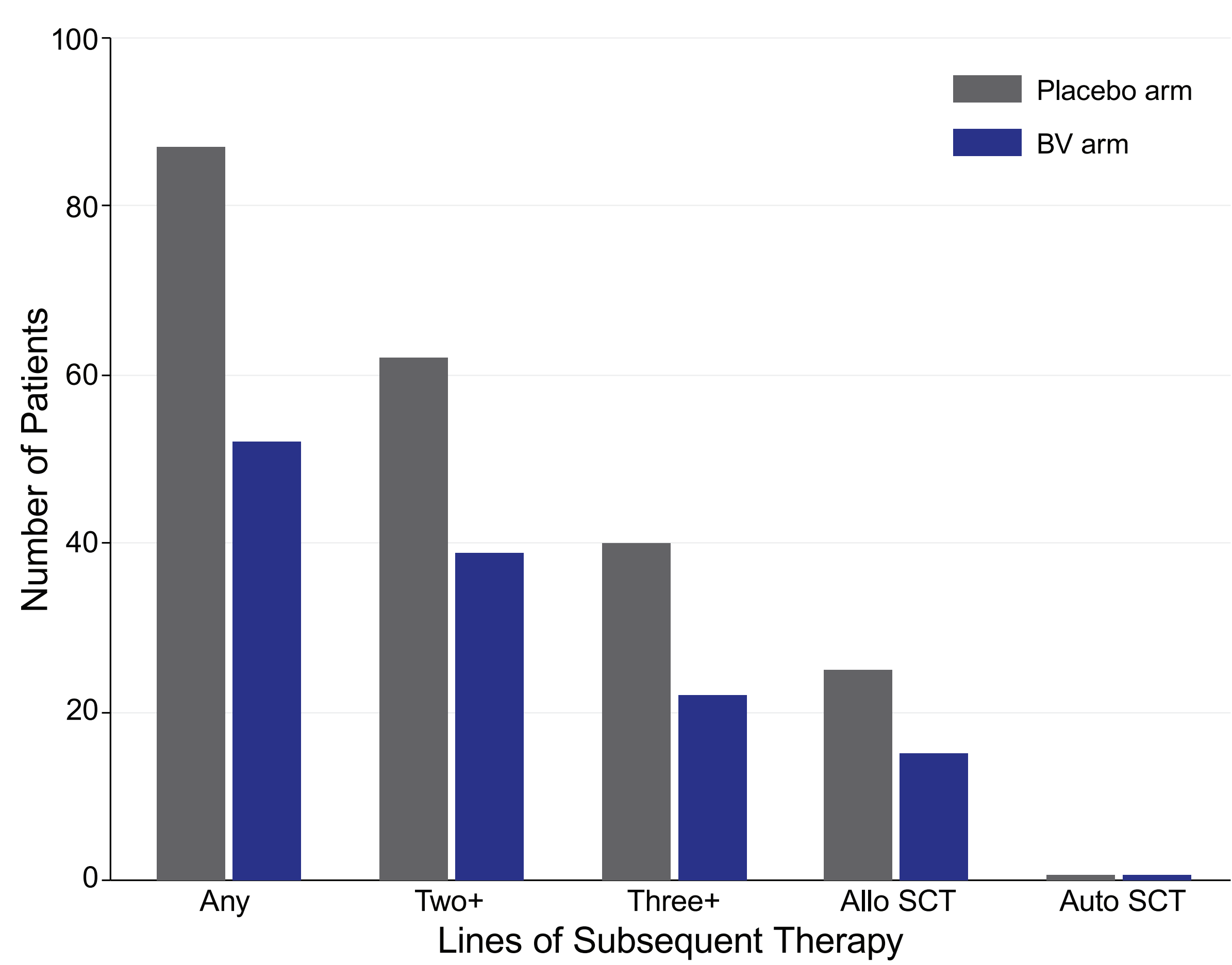
Conclusions

- Consolidation treatment with BV in HL patients at high risk of relapse or progression after ASCT showed sustained PFS benefit versus placebo approximately 3 years since the last patient was randomized
- Patients with more risk factors for relapse post-ASCT appeared to have the greatest benefit from consolidation therapy, including those who had a CR prior to ASCT. Physicians should consider each patient's complete risk factor profile when making treatment decisions
- Symptoms of peripheral neuropathy continued to improve or resolve during extended follow-up

Subsequent New Therapies

	BV (N=52) n (%)	Placebo (N=87) n (%)
Single-agent BV	8 (15)	73 (84)
Multi-agent regimen including BV	1 (2)	1 (1)
Stem cell transplant	16 (31)	26 (30)
Multi-agent chemotherapy	36 (69)	37 (43)
Radiation	24 (46)	26 (30)
Single-agent chemotherapy	23 (44)	24 (28)
Donor lymphocyte infusion	2 (4)	1 (1)

Number of Patients Receiving Subsequent Therapies



Response to Single-Agent BV as a Subsequent Therapy*

	BV arm (N=8)	Placebo arm (N=73)
Response known	7	61
ORR	6 (86%)	41 (67%)
CR	3 (43%)	21 (34%)
PR	3 (43%)	20 (33%)
SD	0	9 (15%)
PD	1 (14%)	10 (16%)
Other	0	1 (2%)
Response unknown	1	12

* For patients who received more than one course of BV, response to first course is reported