STATO DELL'ARTE E NUOVI ORIZZONTI TERAPEUTICI NEL TRATTAMENTO DEI LINFOMI

Milano, 21 Gennaio 2020

Il concetto del consolidamento nel linfoma di Hodgkin

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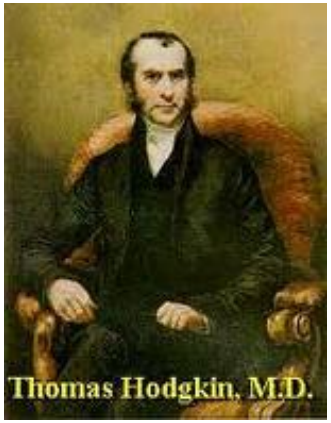


CONFLITTO DI INTERESSI

Relatore: Alessandro Re

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Consulenza ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazione ad Advisory Board **(MSD, Takeda, Italfarmaco, Janssen Cilag)**
- Titolarietà di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**

Consolidation in pts with HL

***Aim*: eliminating minimal residual disease and preventing subsequent relapse**

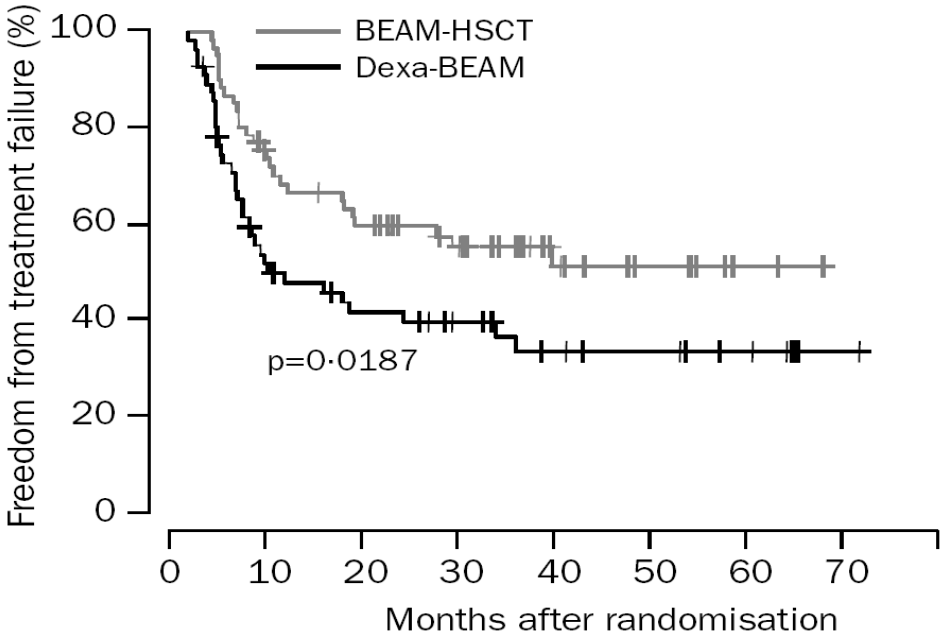
- **When?**
- **How?**
- **Which patients?**

…different challenge for different conditions…

HL	Standard tx	PFS %	aim
Early	ABVD 2-4 + RT	90%	- tox
Advanced	ABVD 6-8	75 %	+ efficacy - tox
Ref/Rec	HDT ASCT	50%	++ efficacy

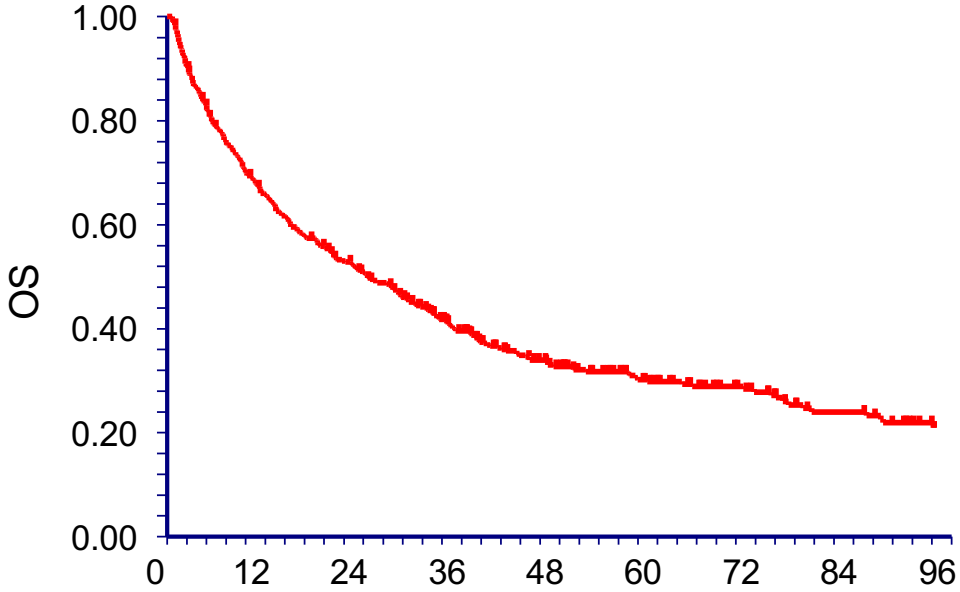
Salvage with ASCT in Hodgkin Lymphoma

FFTF after ASCT



Schmitz N, Lancet 2002

OS from relapse after ASCT



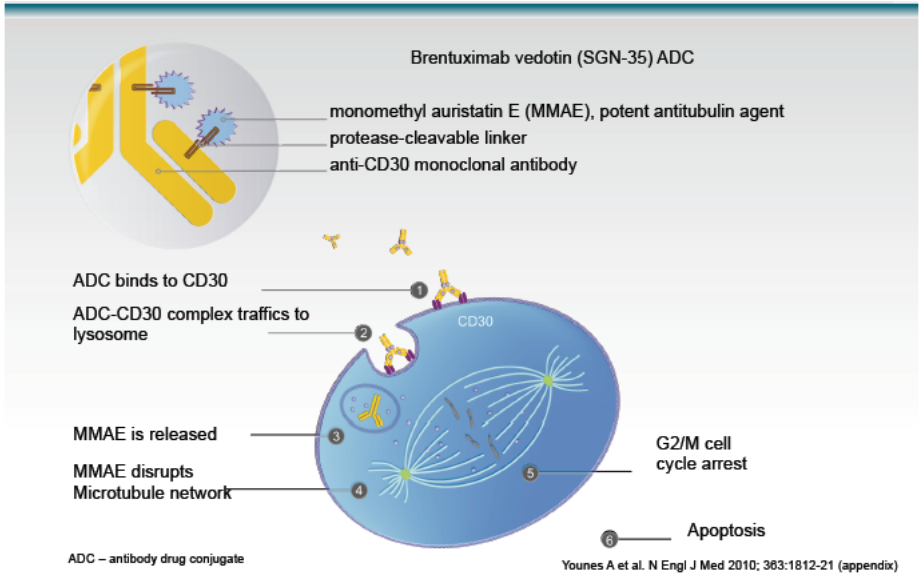
LWP EBMT/GITMO, Martinez,Ann Oncol 2013

How to improve outcome after ASCT?

- **Various treatment strategies have been investigated (for high risk pts, variably defined)**
  - **Intensification of the conditioning regimen (Josting A, J Clin Oncol 2010)**
  - **Tandem transplantation Auto-Auto or Auto-Allo (Fung HC, BBMT 2007; Morshhauser F, JCO 2008, Castagna L, BMT 2015)**
  - **Radiation before or after transplantation (Moskowitz AJ, Br J Haematol 2009)**
  - **PET-adapted approaches (Moskowitz AJ, Blood 2012)**
  - **Consolidation with chemotherapy after ASCT (Rapoport AP, BMT 2004)**
  - **Consolidation with Panobinostat after ASCT (von Tresckow B, Blood 2013 abx)**
- **Challenge: difficult of delivery effective and well-tolerated therapy early after ASCT, where there might be the greatest therapeutic effect**

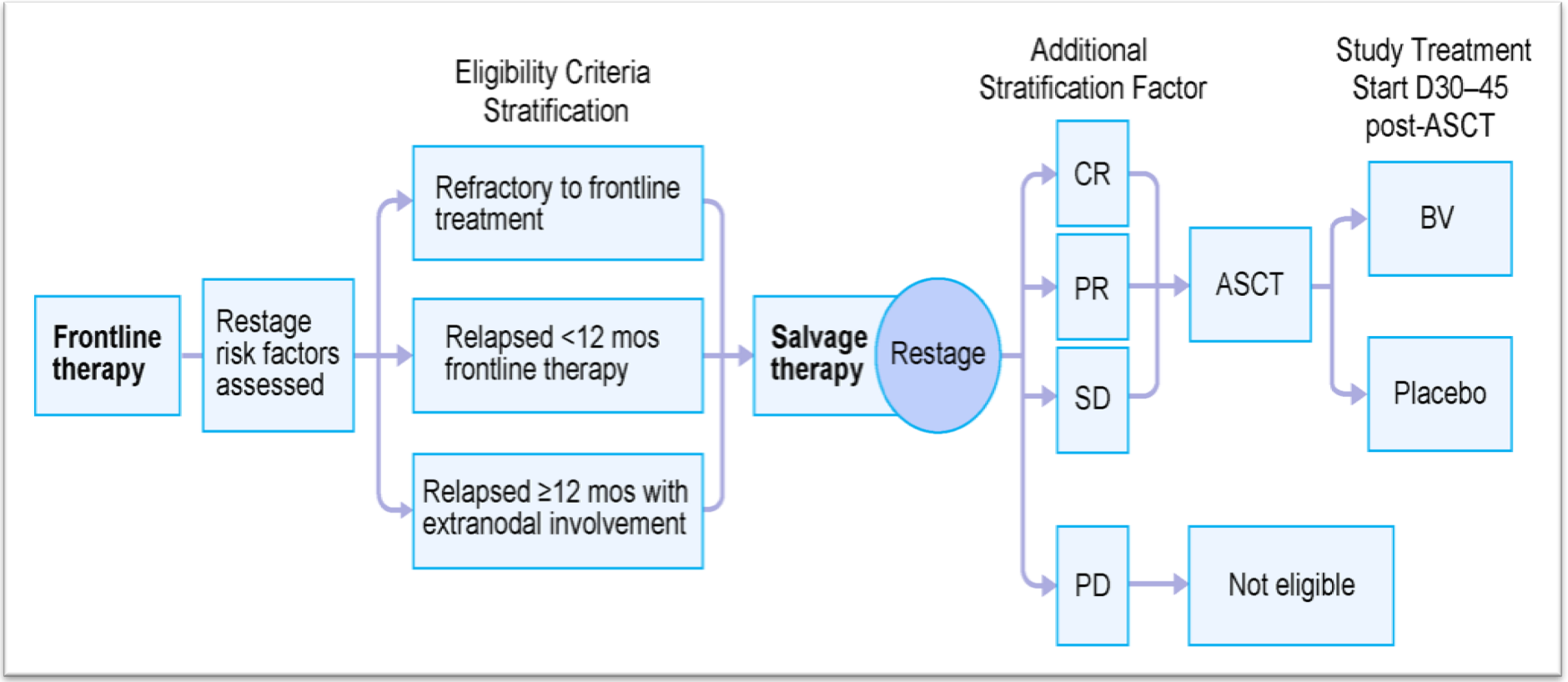
BRENTUXIMAB VEDOTIN

- **Delivery of cytotoxic agent specifically to malignant cells (CD30 is usually not tipically expressed in most human tissue under normal physiologic conditions)**



- **Active in Hodgkin Lymphoma in different settings**
- **Acceptable toxicity**

Brentuximab-Vedotin as consolidation post ASCT: AETHERA trial



329 pts

Median age: 33 (18-76)

Primary objectives: PFS by IRF

Mosckowitz CH et al, Lancet 2015

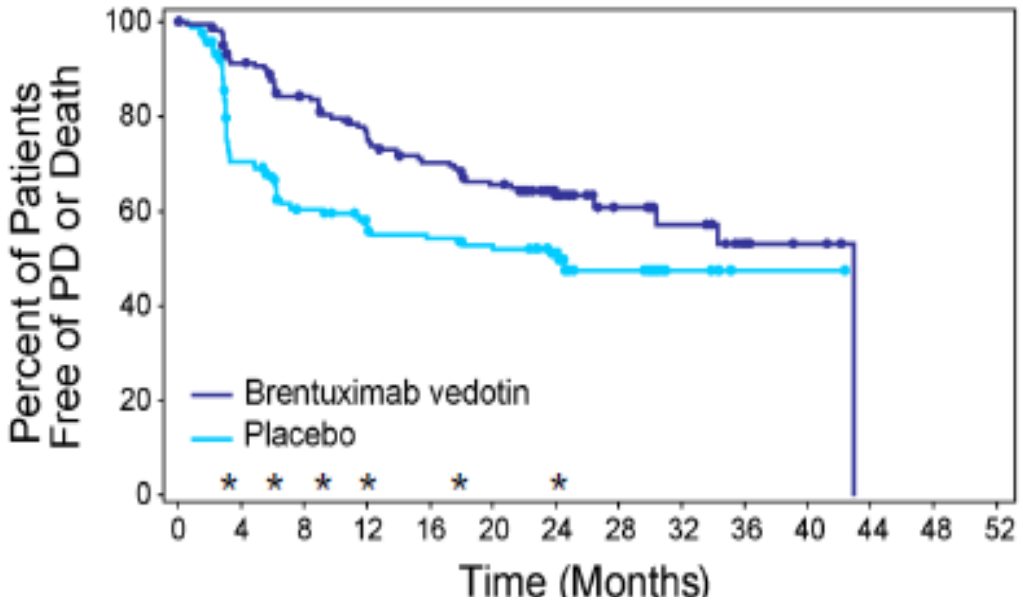
AETHERA trial: Baseline characteristics

Characteristic	Brentuximab vedotin (n=165)	Placebo (n=164)
Median age, yrs (range)	33 (18–71)	32 (18–76)
No. of prior systemic salvage therapies		
1	57%	52%
≥2	43%	48%
HL status after frontline therapy		
Refractory	60%	59%
Relapse <12 mos	32%	33%
Relapse ≥12 mos	8%	8%
Response to salvage therapy pre-ASCT		
CR	37%	38%
PR	35%	34%
SD	28%	28%
Extranodal involvement at pre-ASCT relapse	33%	32%
B symptoms after frontline therapy	28%	24%
Pre-ASCT PET status		
FDG avid	39%	31%
FDG negative	34%	35%
Not available	27%	34%

Mosckowitz CH et al, Lancet 2015

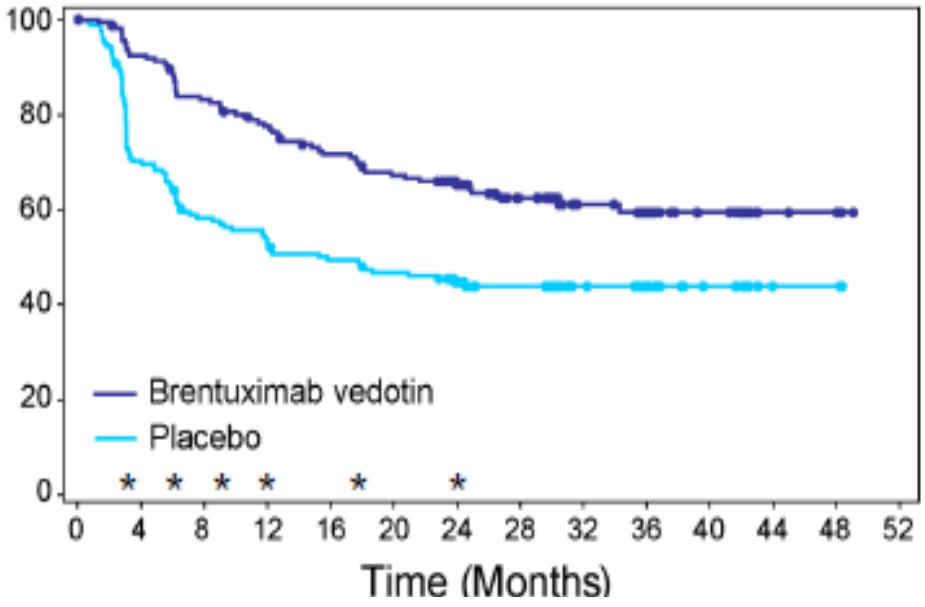
AETHERA trial: Progression free-Survival

PFS per IRF



PFS outcome	Brentuximab vedotin (n=165)	Placebo (n=164)
Median PFS	43 mos	24 mos
HR (95% CI)	0.57 (0.40, 0.81) *p*=0.001	
2-year PFS	63%	51%

PFS per investigator†

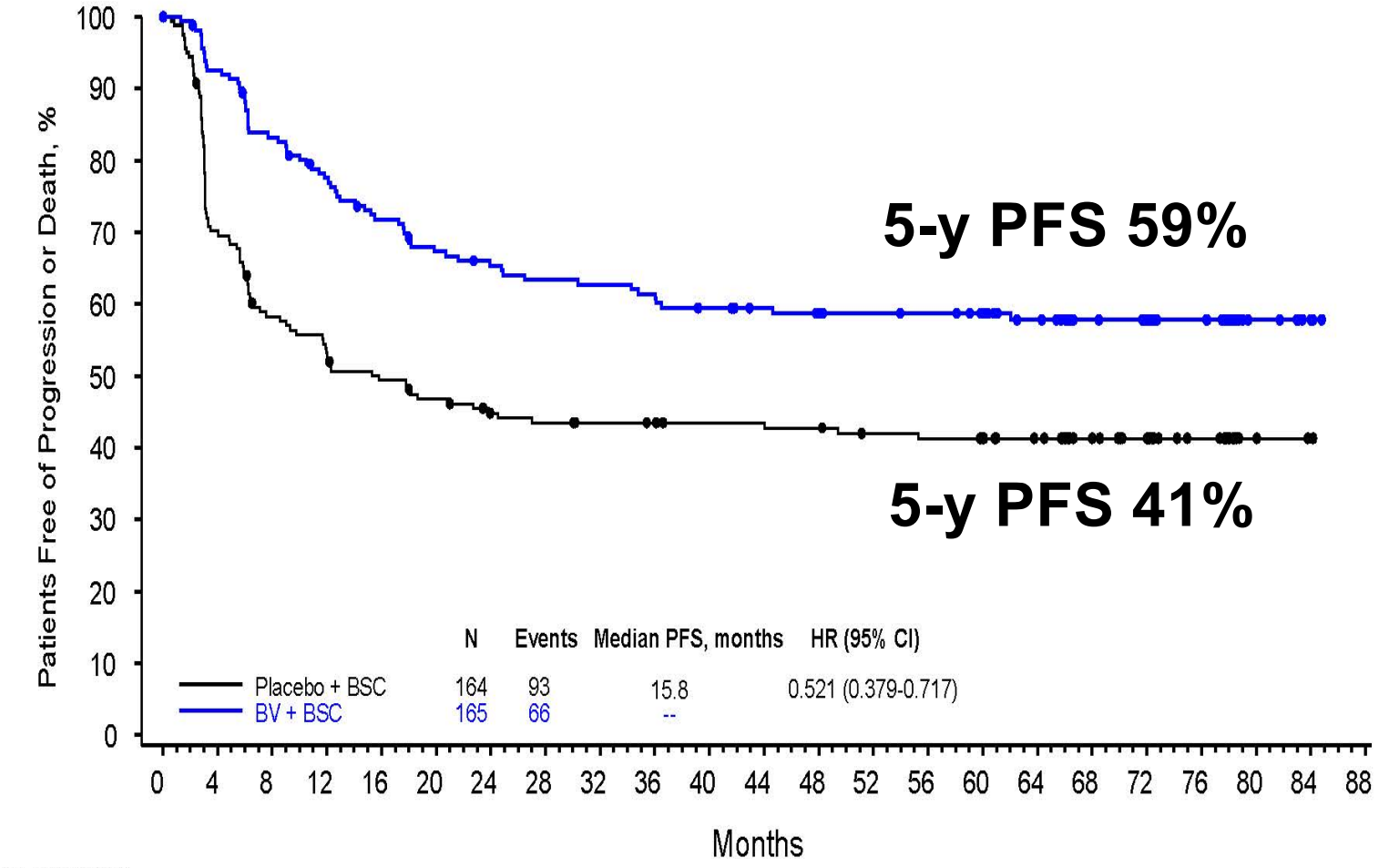


PFS outcome	Brentuximab vedotin (n=165)	Placebo (n=164)
Median PFS	NR	16 mos
HR (95% CI)	0.50 (0.36, 0.70) *p*-value NR	
2-year PFS	65%	45%

* Scheduled CT scans

† Includes information from both radiographic assessments and clinical lymphoma assessments

AETHERA trial: 5-Year PFS per investigator: All patients

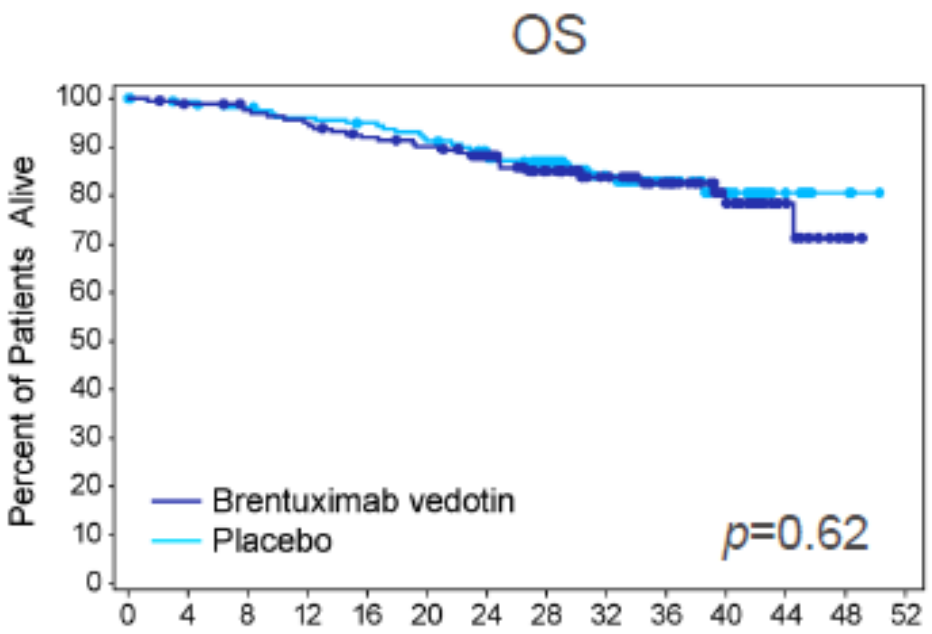


No. at risk (events)

Pla+BSC	164 (0)	113 (48)	92 (67)	83 (76)	77 (81)	72 (85)	66 (88)	64 (90)	62 (90)	61 (90)	59 (90)	58 (91)	58 (91)	55 (92)	54 (93)	52 (93)	44 (93)	32 (93)	27 (93)	17 (93)	2 (93)	1 (93)	0 (93)
BV+BSC	165 (0)	149 (12)	133 (27)	122 (36)	112 (45)	104 (52)	100 (55)	97 (58)	96 (59)	94 (61)	90 (64)	87 (64)	84 (65)	83 (65)	82 (65)	78 (65)	66 (66)	47 (66)	43 (66)	26 (66)	7 (66)	3 (66)	0 (66)

Mosckowitz CH et al, Blood 2018

AETHERA trial: No difference in overall survival



Subsequent antitumor therapies

Pts with subsequent antitumor therapy, n (%)	Brentuximab vedotin (n=51)	Placebo (n=85)
Single-agent BV	8 (16)	72 (85)
Multi-agent regimen including BV	1 (2)	1 (1)
SCT*	13 (25)	24 (28)
Multi-agent chemotherapy	35 (69)	34 (40)
Radiation	22 (43)	23 (27)
Single-agent chemotherapy	22 (43)	22 (26)
Donor lymphocyte infusion	2 (4)	1 (1)
Other treatment	1 (2)	2 (2)

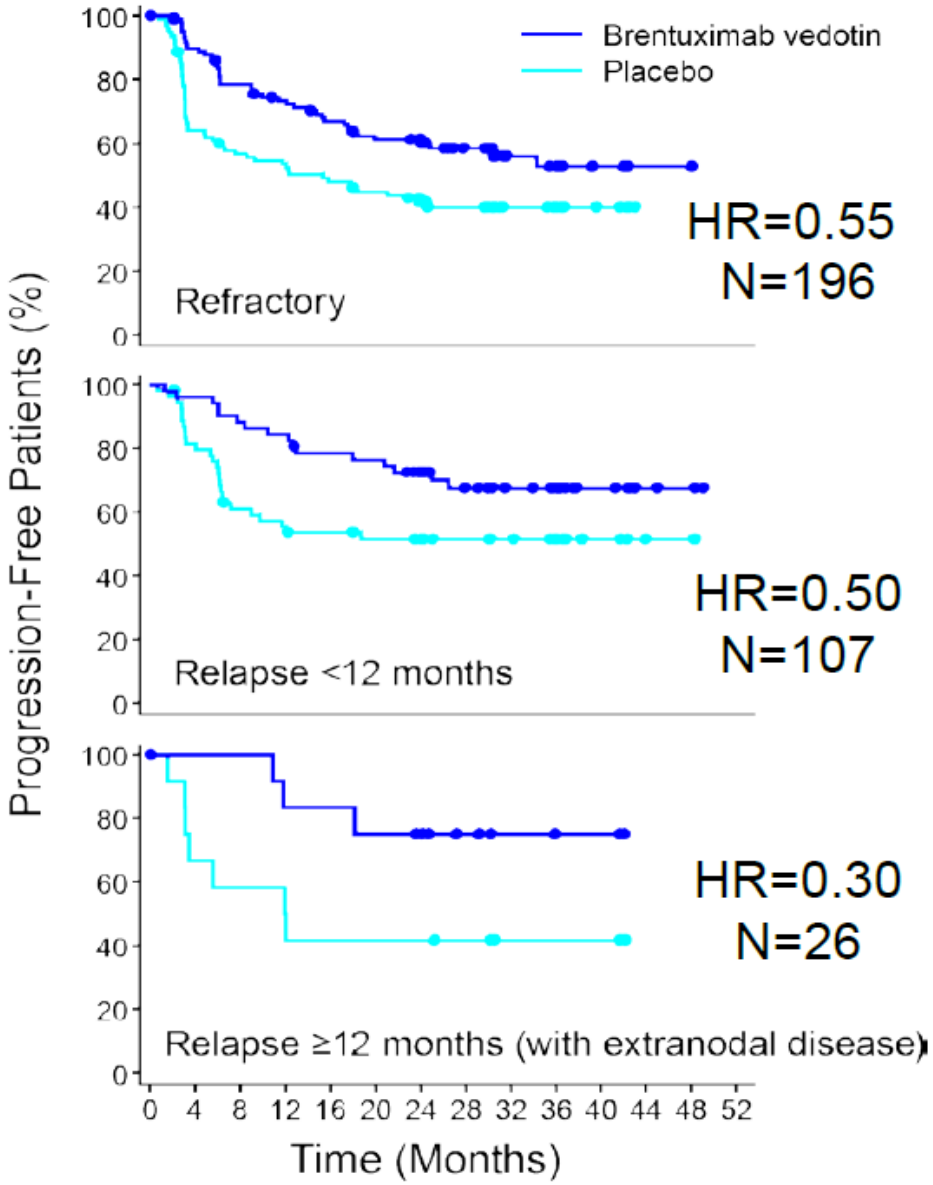
* Allo-SCT in 12 BV and 23 placebo pts

Response to Single-Agent BV as a Subsequent Therapy*

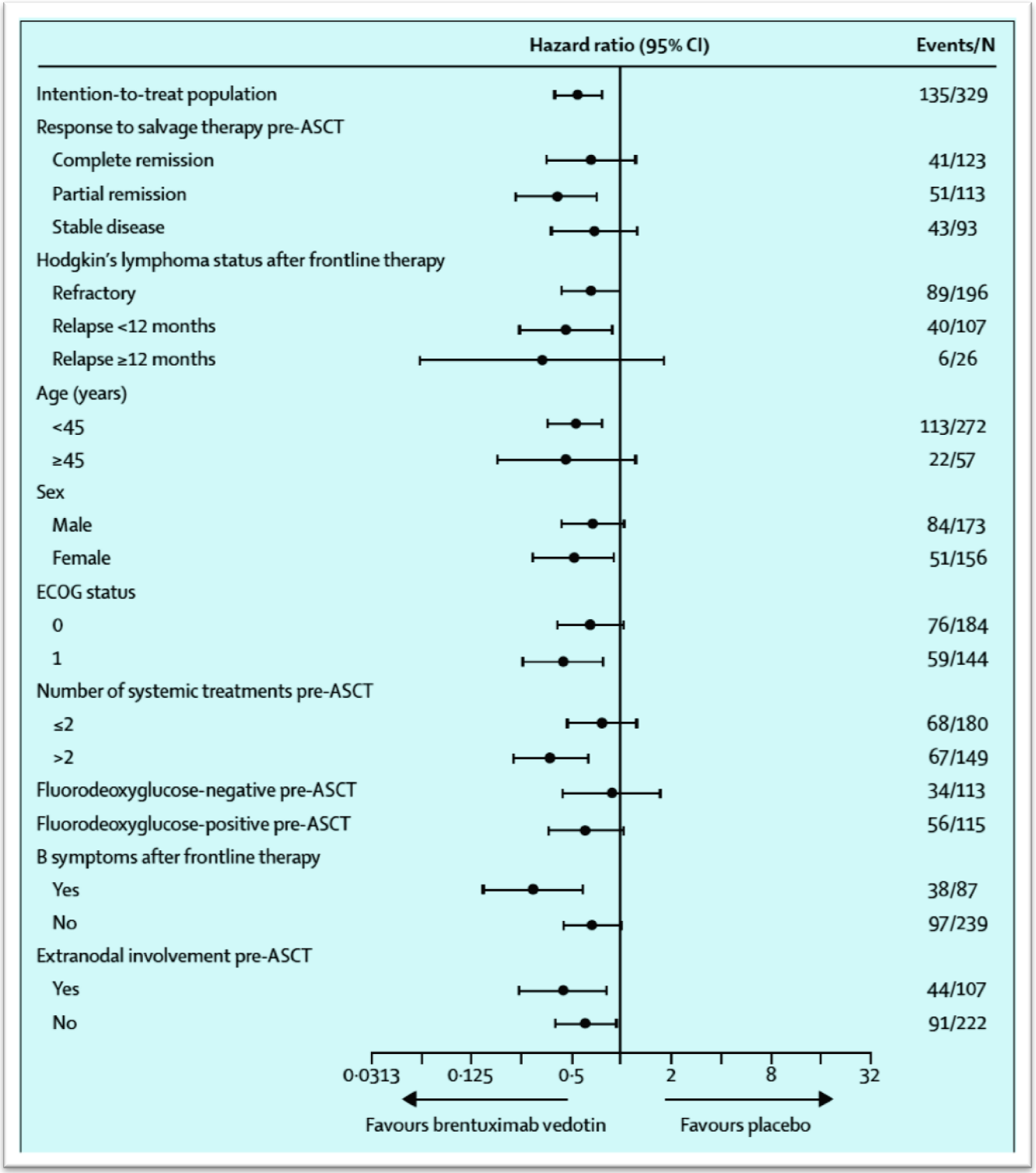
	BV arm (N=8)	Placebo arm (N=73)
Response known	7	61
ORR	6 (86%)	41 (67%)
CR	3 (43%)	21 (34%)
PR	3 (43%)	20 (33%)
SD	0	9 (15%)
PD	1 (14%)	10 (16%)
Other	0	1 (2%)
Response unknown	1	12

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

AETHERA trial: PFS by response to frontline therapy (eligibility criteria)



Mosckowitz CH et al, Lancet 2015



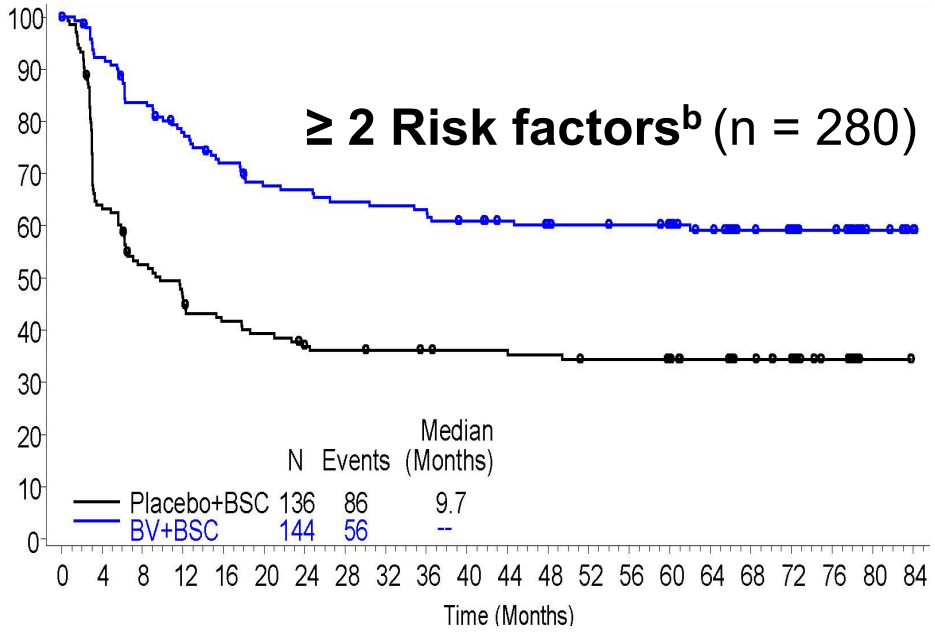
Subgroup analysis of PFS by indipendent review

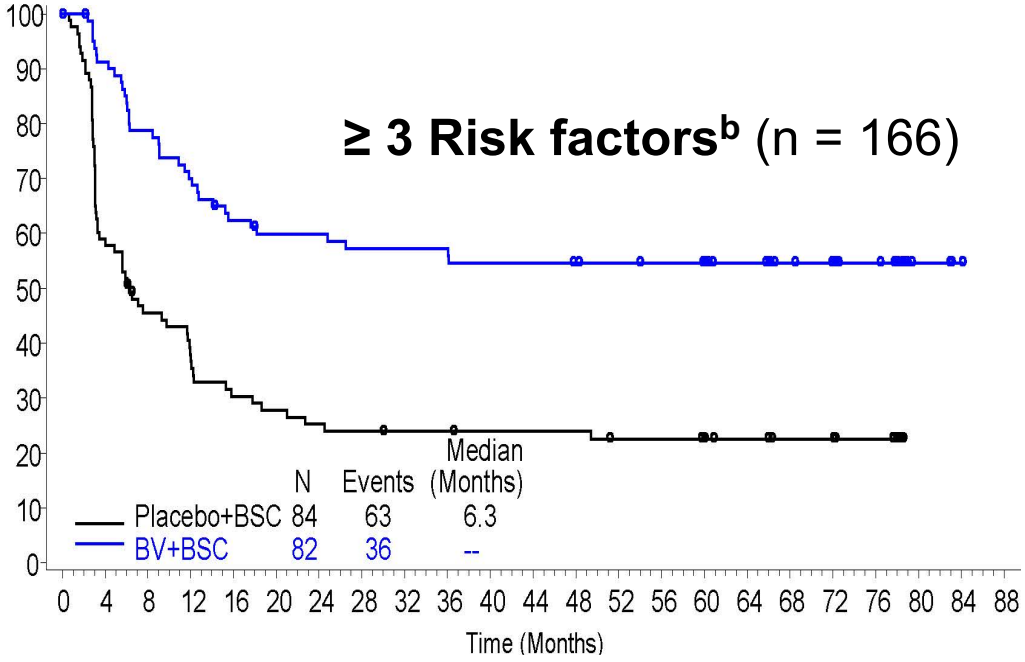
Mosckowitz CH et al, Lancet 2015

AETHERA trial: 5-Year PFS in pts according to risk factors

Risk factors:

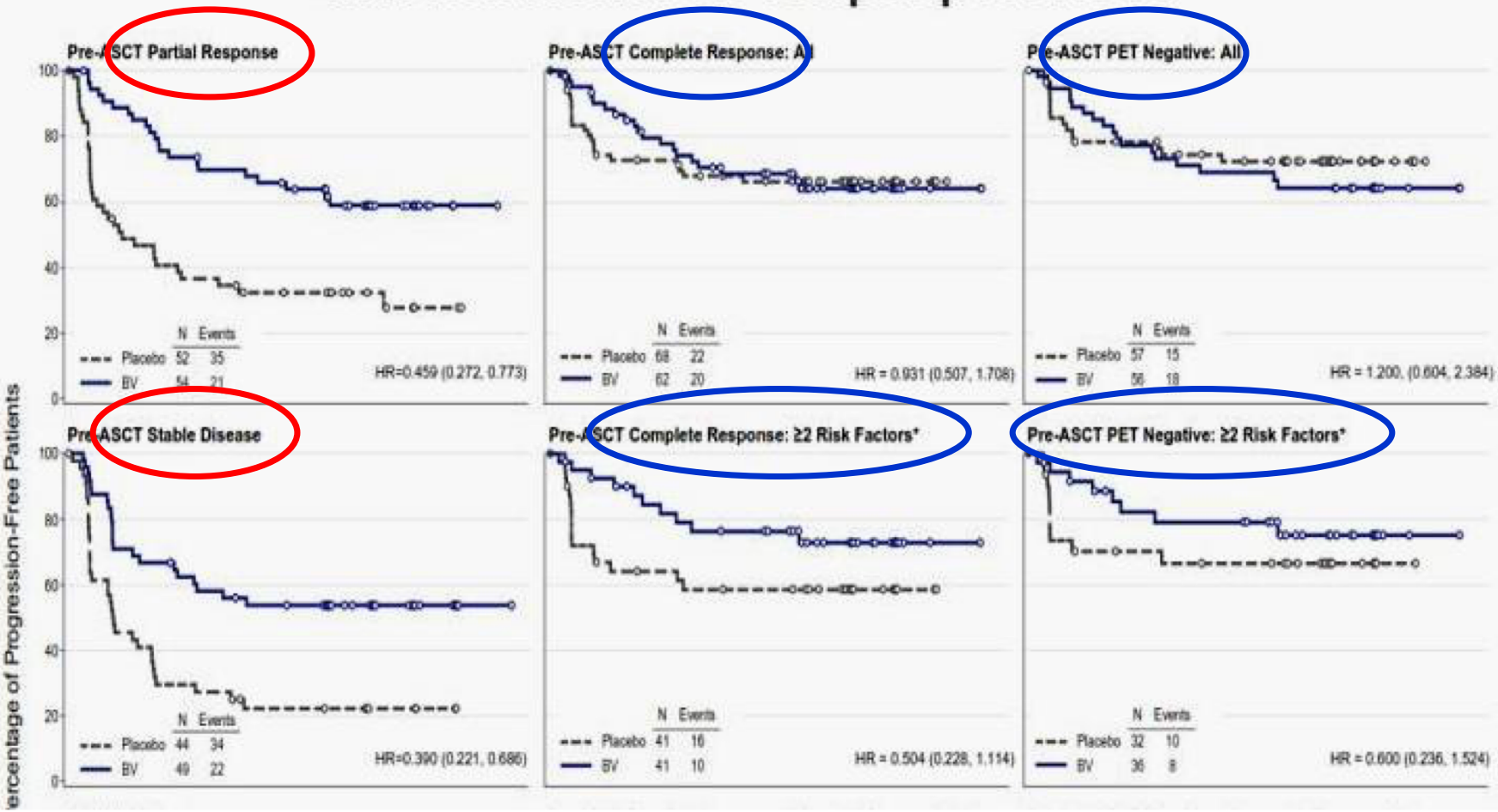
- **Primary refractory or relapse < 12 months from completion of front-line tx**
- **< CR achieved with salvage tx**
- **>1 previous salvage tx**
- **Extranodal disease at relapse or progression after frontline therapy**
- **B symptoms before starting salvage therapy**





No PFS difference in pts with 1 risk factor (<15% of pts)

Effect of brentuximab vedotin consolidation on PFS* in pts with risk factors for relapse post-ASCT



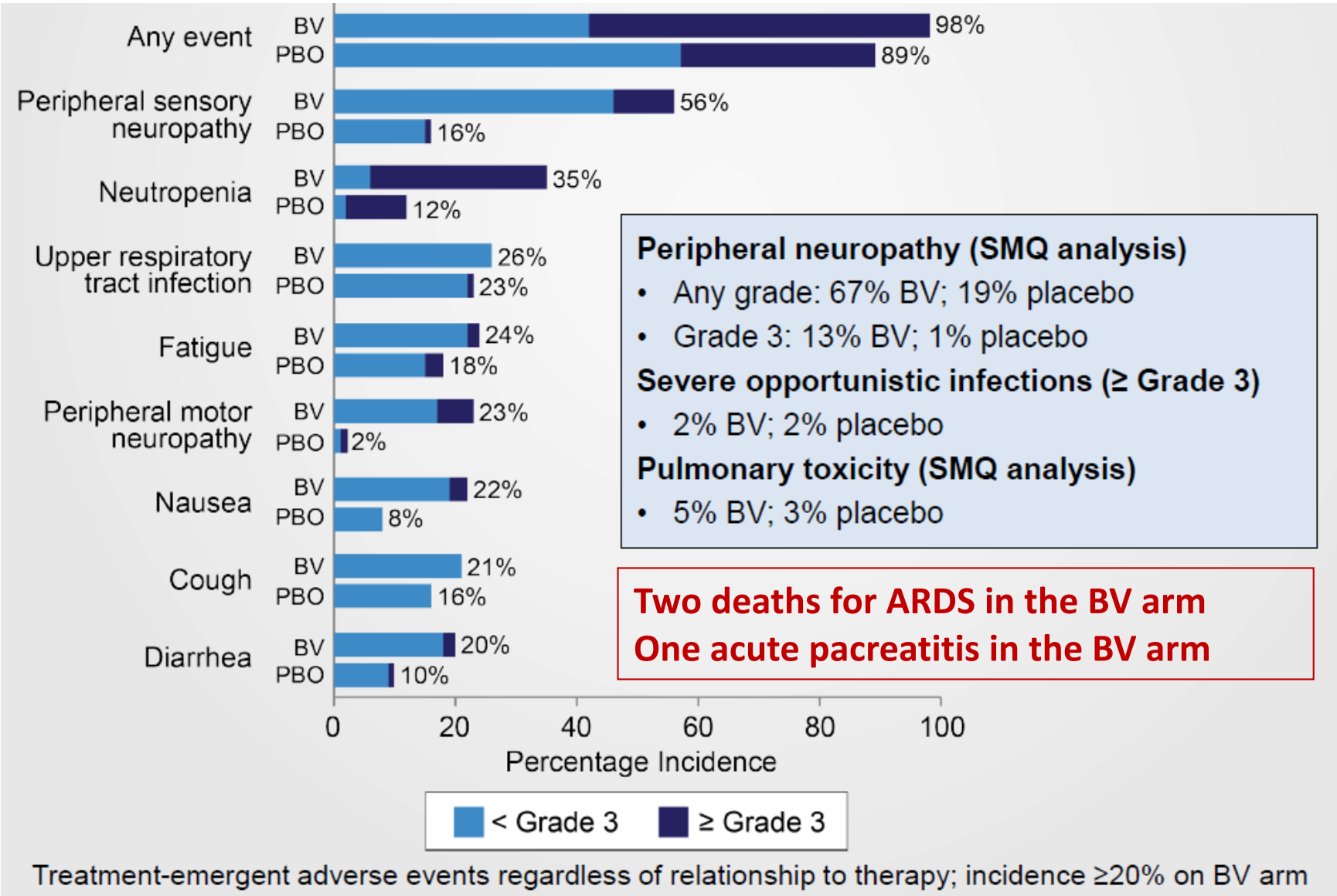
AETHERA trial: how many BV cycles do we need?

PFS Rate per Investigator by Treatment Duration: BV Arm

	Number of Treatment Cycles			
Months after first BV dose	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

AETHERA trial: Toxicity



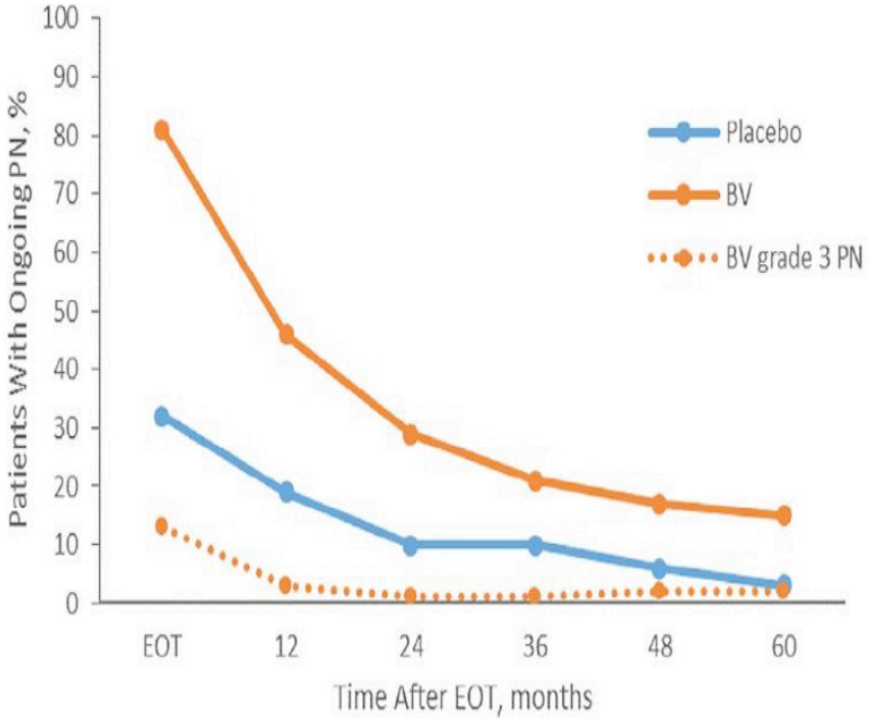
Mosckowitz CH et al, Lancet 2015

Safety Analysis of Brentuximab Vedotin from the Phase III AETHERA Trial in Hodgkin Lymphoma in the Post-Transplant Consolidation Setting

Nademanee A
BBMT 2018

Peripheral Neuropathy 67%

- 56% sensory and 23 motor PN
- Median time to PN onset 13.7wks (.1 to 47.4)
- **Most PN cases (57%) were managed with dose delays and reductions**
- **23% of pts discontinued treatment because of BV–associated PN** (no impact on PFS)
- After the end of treatment, **PN continued to resolve: 60 ms after treatment, 85% of pts had resolution**
- Median time to resolution or improvement was 37.6 weeks
- Of 95 pts (76 BV arm, 19 placebo arm) with treatment emergent PN who remained for > 5 ys without further treatment, 95% had resolution or improvement of PN



Infections and polmonary toxicity

Table 2
Infections and Pulmonary Toxicity* during the AETHERA Trial

	BV (n = 167)		Placebo (n = 160)	
	All	Grade ≥ 3†	All	Grade ≥ 3†
Any infections and infestations	100 (60)	15 (9)	80 (50)	15 (9)
Any opportunistic infections	20 (12)	4 (2)	6 (4)	3 (2)
→ Herpes zoster	12 (7)	2 (1)	4 (3)	2 (1)
→ Herpes simplex	7 (4)	0	1 (1)	0
Bronchopulmonary aspergillosis	0	0	2 (1)	1 (1)
Hepatic candidiasis	1 (1)	1 (1)	0	0
PCP‡	1 (1)	1 (1)	0	0
Any pulmonary toxicity event	8 (5)	8 (5)	5 (3)	4 (3)
→ Pneumonitis	4 (2)	4 (2)	1 (1)	0
→ Acute respiratory distress syndrome	2 (1)	4 (2)	1 (1)	2 (1)
Lung infiltration	1 (1)	0	2 (1)	0
Pulmonary toxicity	2 (1)	2 (1)	0	0
Idiopathic pneumonia syndrome	0	0	1 (1)	2 (1)
Radiation pneumonitis	1 (1)	0	0	0

Second Malignancies

	BV+BSC, (N=165) n	PBO+BSC, (N=164) n
Second malignancies (any)	6	2
AML	1	0
Myelodysplastic syndrome	2	1
Bladder cancer	1	0
Lung cancer	1	0
Mantle cell lymphoma	0	1
Pancreatic cancer	1	0

Nademanee A
BBMT 2018

BV consolidation: is feasible in other setting?

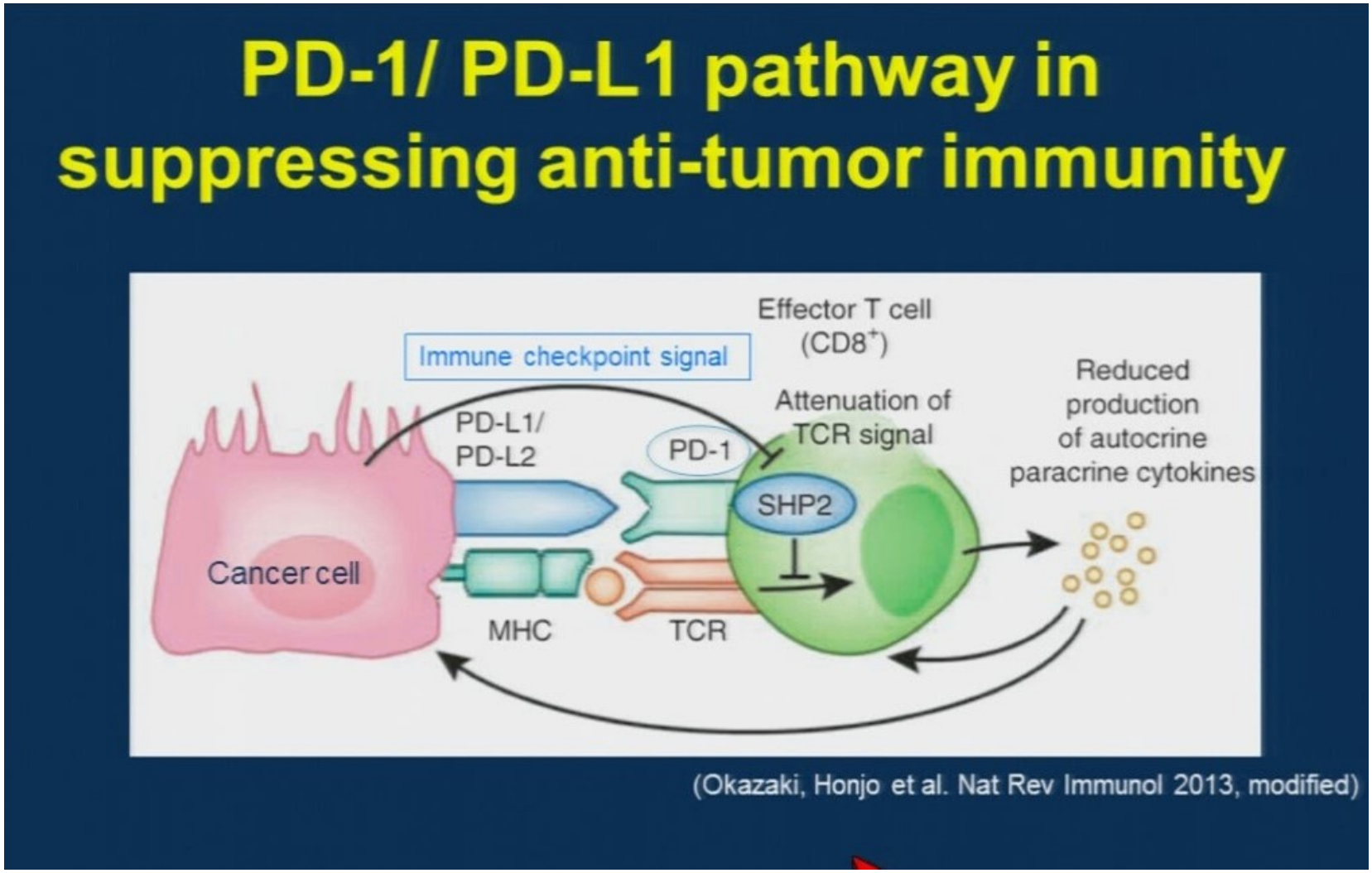
Brentuximab vedotin in combination with or without donor lymphocyte infusion for patients with Hodgkin lymphoma after allogeneic stem cell transplantation

- **13 patients with relapsed HL after allo-SCT received BV as treatment for active disease**
- **3 patients without progression of HL after allo-SCT received BV as consolidation (two in PR and one in CR at day +100)**
- **Ten out of 16 patients received BV in combination with DLI**

	OR rate	CR rate	PFS
13 pts relapsed after Allo	69%	54%	NR
3 pts without progression after Allo	100%	100%	NR

Tsirigotis P, et al. BMT 2016

Post-ASCT consolidation: other than BV?



PD-1 blockade with pembrolizumab for classical Hodgkin lymphoma after autologous stem cell transplantation

Table 1. Baseline patient characteristics

Variable	N (%*) or median (range)
Total	30 (100)
Age, y	33 (20-69)
Sex	
Male	16 (53)
Female	14 (47)
Frontline therapy	
A(B)VD†	24 (80)
BV-A(B)VD	1 (3)
ABVE-PC	1 (3)
BEACOPP‡	2 (7)
RCHOP/REPOCH	2 (7)
Prior brentuximab exposure	6 (20)
Prior nivolumab or pembrolizumab exposure	6 (20)
Prior radiotherapy	7 (23)
Conditioning regimen	
BEAM	30 (100)
Risk factors	
Primary refractory disease	17 (57)
Relapse within 12 mo	5 (17)
Extranodal disease at relapse	8 (27)
At least 1 of above 3 factors	26 (87)
Residual disease after salvage	3 (10)
B symptoms at relapse	2 (7)
>1 salvage therapy	5 (17)
At least 1 of above 6 factors	27 (90)
At least 2 of above 6 factors	12 (40)
Disease status at study entry (post-ASCT)	
Partial remission	2 (7)
Complete remission	28 (93)

Multicohort phase 2 study

Inclusion criteria:

- **Previous ASCT and chemosensitive disease (metabolic PR or CR)**
- **No more than 3 previous line of therapy**
- **Allow prior PD-1 blockade**

Pembrolizumab: 200 mg IV every 3 weeks for up to 8 cycles

Primary end point: to improve the progression-free survival (PFS) at 18 months after ASCT from 60% to 80%.

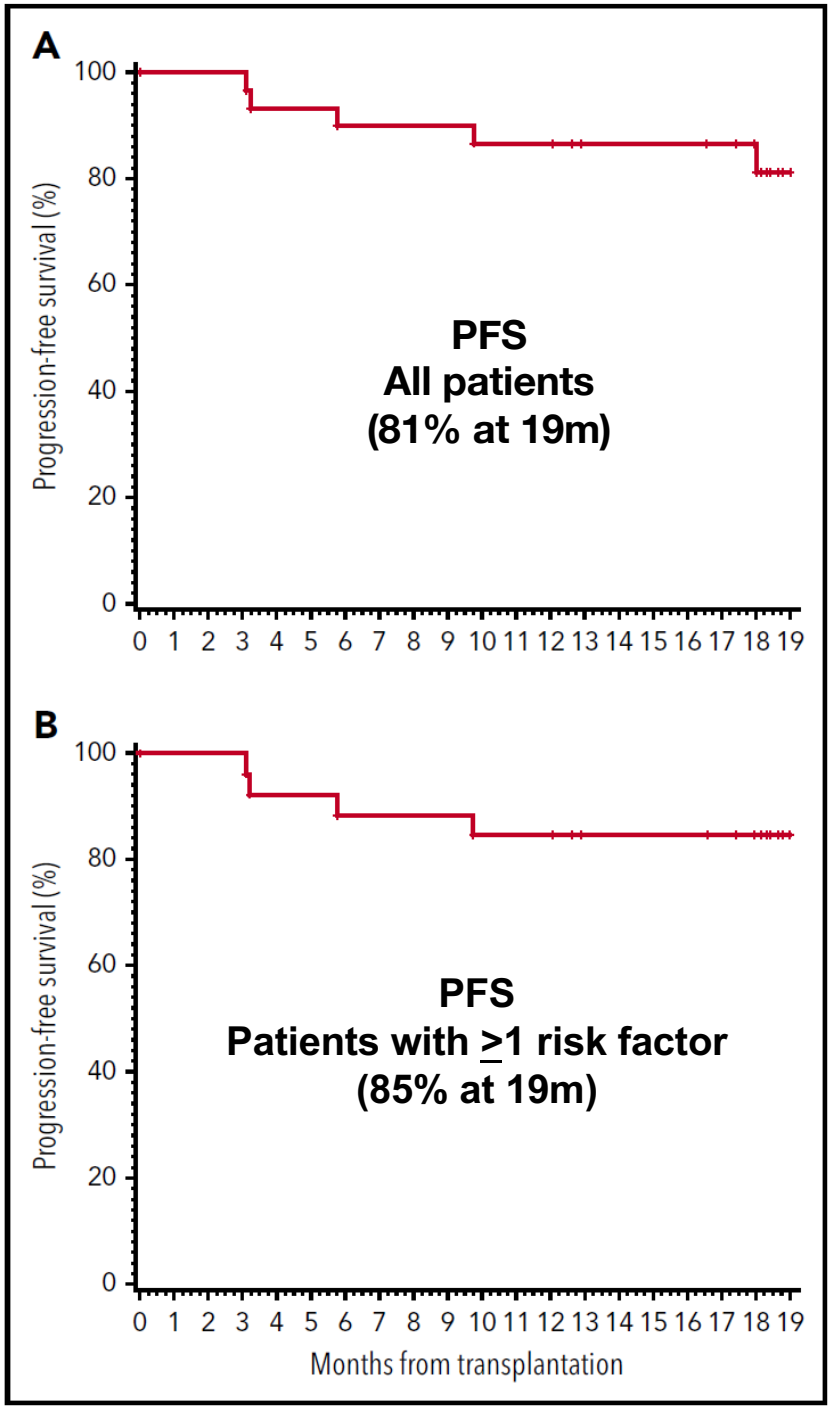
90% at least 1 risk factor (40% > 1):

- primary refractory or relapse within 1 year
- residual FDG-avid disease at ASCT
- >1 salvage regimen
- extranodal disease
- B symptoms at relapse

78% would have met eligibility criteria for the high-risk AETHERA study

Armand P, Blood 2019

Pembrolizumab as consolidation after ASCT in HL



Among patients who would have been eligible for the AETHERA study the 19-month PFS was 85% (95CI, 64% to 94%).

The 19-month PFS of 85% in this subgroup compares favorably to that of patients treated with placebo (45%) and that of patients treated with BV (70%) on AETHERA.

Armand P, Blood 2019

Table 2. Summary of toxicity

AE	Grade 1	Grade 2	Grade 3	Grade 4
Total no. of AEs	308 (93)	96 (77)	21 (30)	7 (10)
Grade 2-4 TRAE				
Leukopenia		4 (7)	5 (13)	1 (3)
Neutropenia		3 (7)		4 (10)
Transaminitis		3 (10)	3 (7)	
Diarrhea/colitis		1 (3)	3 (7)	
Pneumonitis/ dyspnea		3 (7)	1 (3)	
Hypothyroidism		4 (7)		
Rash		3 (7)		
Lymphopenia		1 (3)	1 (3)	
Thrombocytopenia		2 (7)		
Febrile neutropenia				1 (3)
Pulmonary hemorrhage*			1 (3)	
Hyperthyroidism		1 (3)		
Arthritis		1 (3)		
Fatigue		1 (3)		
Neck pain		1 (3)		
Creatinine increase		1 (3)		
Blurred vision		1 (3)		
Total no. of TRAEs	82 (67)	30 (47)	14 (27)	6 (10)
Grade 2-4 irAEs				
Transaminitis		2 (7)	3 (7)	
Pneumonitis/ dyspnea/cough		4 (10)	1 (3)	
Diarrhea/colitis		1 (3)	2 (7)	
Rash		3 (7)		
Hypothyroidism		3 (3)		
Pulmonary hemorrhage*			1 (3)	
Hyperthyroidism		1 (3)		
Arthritis		1 (3)		
Creatinine increase		1 (3)		
Total no. of irAEs	16 (33)	16 (33)	7 (20)	0 (0)

"Treatment-related" refers to AEs judged to be at least possibly related to study treatment. The number of patients, expressed as the percentage of total patients, is given in parenthesis for grade 2-4 TRAEs. Events are ordered by frequency.

*In a patient with prior cavitary tumor lesion.

Pembrolizumab as consolidation after ASCT in HL

77% completed all planned 8 cycles of therapy

- **Toxicity in this setting appeared similar to its use in other settings**
- **Pembro did not perturb the immune reconstitution of pts after ASCT**

KEY POINTS

- **PD-1 blockade using pembrolizumab administered after ASCT has an acceptable safety profile.**
- **This treatment results in a high PFS in patients with cHL, including in high-risk patients.**

Armand P, Blood 2019

Post-ASCT consolidation: perspectives?

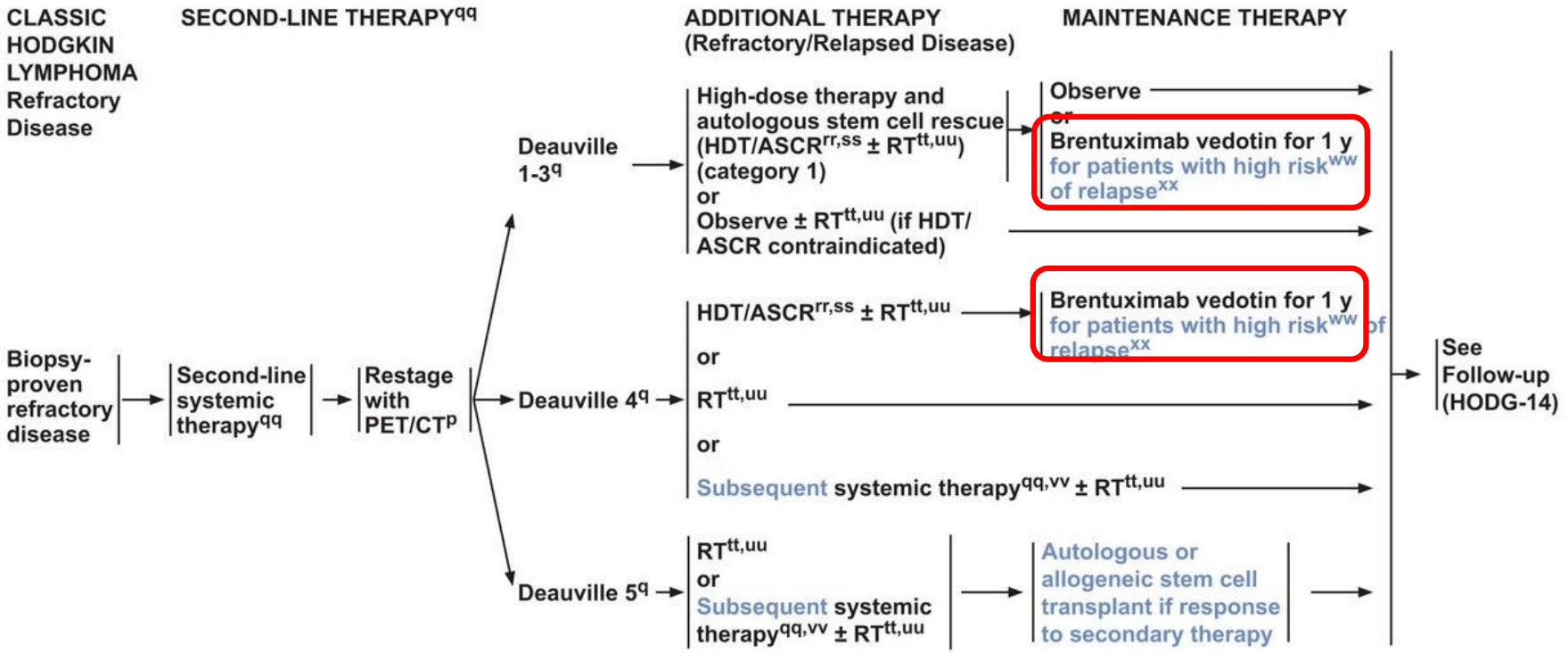
- Phase II Nivolumab as post-ASCT consolidation (NCT03436862). Nivo Maintenance Therapy After ASCT in Hodgkin Lymphoma Pts at Relapse/Progression Risk
- Brentuximab Vedotin + Nivolumab as post-ASCT consolidation (NVT03057795). A Phase 2 Study of Nivo and BV Consolidation After ASCT in Patients With High-Risk Classical Hodgkin Lymphoma
- Consolidation with BV after ABVD first-line, after AlloSCT, pre-post ASCT

Is it time to random BV vs anti PD-1 as consolidation after ASCT?

NCCN Guidelines® Insights

Hodgkin Lymphoma, Version 1.2018

Featured Updates to the NCCN Guidelines



[p]An integrated PET/CT or a PET with a diagnostic CT is recommended.
[q]See PET 5-Point Scale (Deauville Criteria) (HODG-D).
[qq]See Principles of Systemic Therapy for Relapsed or Refractory Disease (HODG-E).
[rr]Strongly consider radiation therapy for selected sites that have not been previously irradiated. In a radiation-naive patient, TLI may be an appropriate component of HDT.
[ss]Allotransplant is an option in select patients as a category 3 recommendation.
[tt]Conventional-dose chemotherapy may precede high-dose therapy. Timing of RT may vary.
[uu]See Principles of Radiation Therapy (HODG-C).
[vv]Subsequent systemic therapy options include second-line therapy options that were not previously used (See HODG-E).
[ww]Patients with 2 or more of the following risk factors are considered high risk: Remission duration less than 1 year, extranodal involvement, PET+ response at time of transplant, B symptoms, and/or >1 salvage/subsequent therapy regimen.
[xx]Moskowitz CH, Nademanee A, Masszi T, et al. Brentuximab vedotin as consolidation therapy after autologous stem-cell transplantation in patients with Hodgkin's lymphoma at risk of relapse or progression (AETHERA): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 2015;385:1853-1862.

Hodgkin lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

Relapsed disease

- For most patients with refractory or relapsed HL, the treatment of choice consists of HDCT followed by ASCT [I, A]
- ~~High-risk patients may benefit from tandem ASCT [III, B]~~
- Consolidating treatment with brentuximab vedotin following HDCT and ASCT is recommended in patients presenting with defined poor-risk factors [II, B]
- DHAP, IGEV or ICE can be given before HDCT and ASCT [II–III, A]
- In some patients, single-agent brentuximab vedotin may be sufficient as salvage therapy before HDCT and ASCT [III, B]
- Achieving a negative PET should be the goal of salvage therapy irrespective of the applied protocol [III, B]
- RT before HDCT and ASCT may be discussed in patients with single PET-positive lymph nodes after salvage therapy [IV, C]

Annals of Oncology 29 (Supplement 4): iv19–iv29, 2018

Consolidation in pts with HL

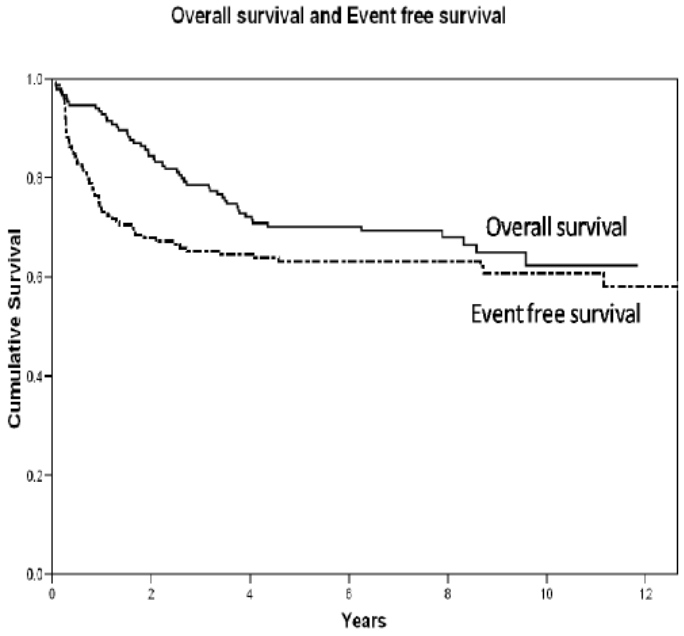
Which patients?

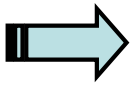
Risk factors from the AETHERA study (2 or more risk factors):

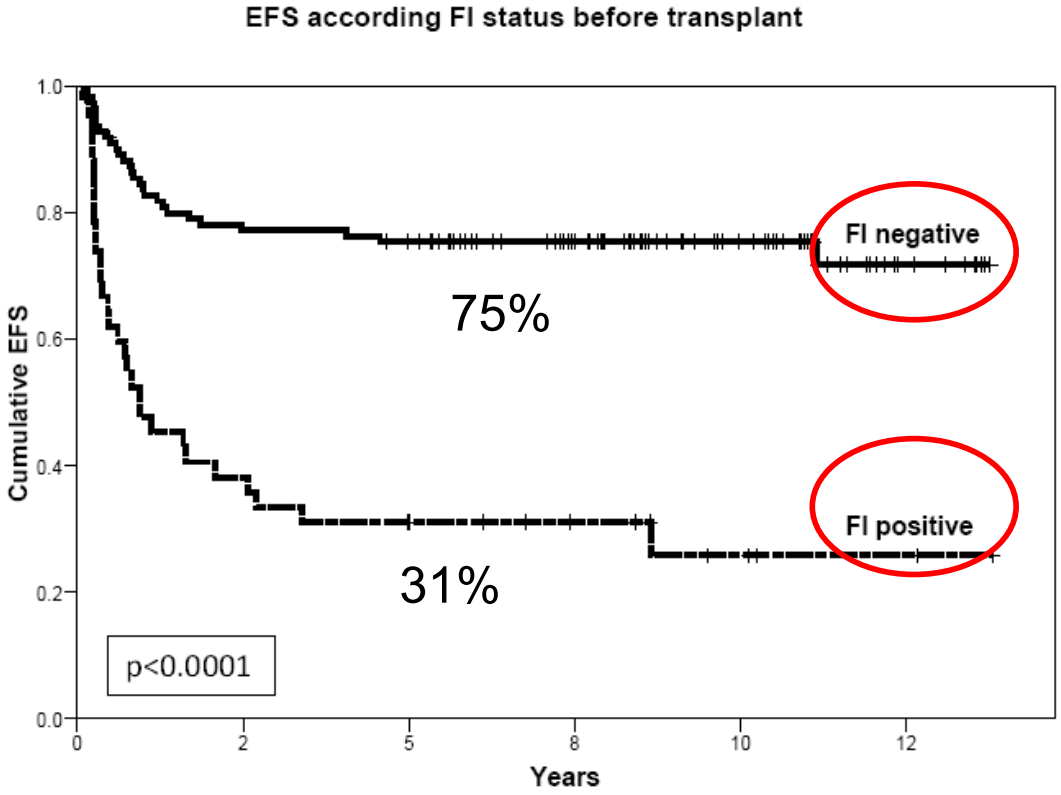
- **Primary refractory or relapse < 12 months from completion of front-line tx**
- **< CR achieved with salvage tx**
- **>1 previous salvage tx**
- **Extranodal disease at relapse or progression after frontline therapy**
- **B symptoms before starting salvage therapy**

- **Are there stronger risk factors?**
- **Other risk factors?**
- **If pt had already received BV?**

The role of pre-transplant PET in relapsed and refractory HL



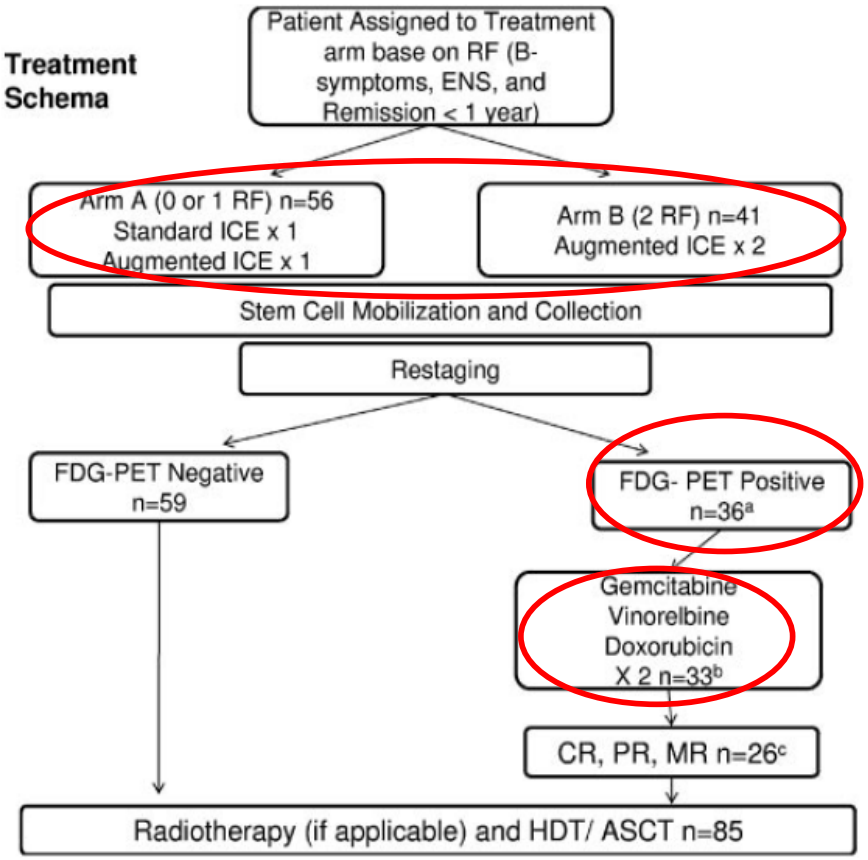




Spaepen, Blood 2003
Filmont, Cancer 2007
Jabbour, Cancer 2007
Gentzler, Br J Haematol 2014
Akthar, BMT 2013
Devillier, Haematologica 2012
Smeltzer, BBMT 2011
Mocikova, Leuk Lymphoma 2011

Moskowitz AJ; Blood 2010

Normalization of pre-ASCT, FDG-PET imaging with second-line, non–cross-resistant, chemotherapy programs improves event-free survival in patients with Hodgkin lymphoma



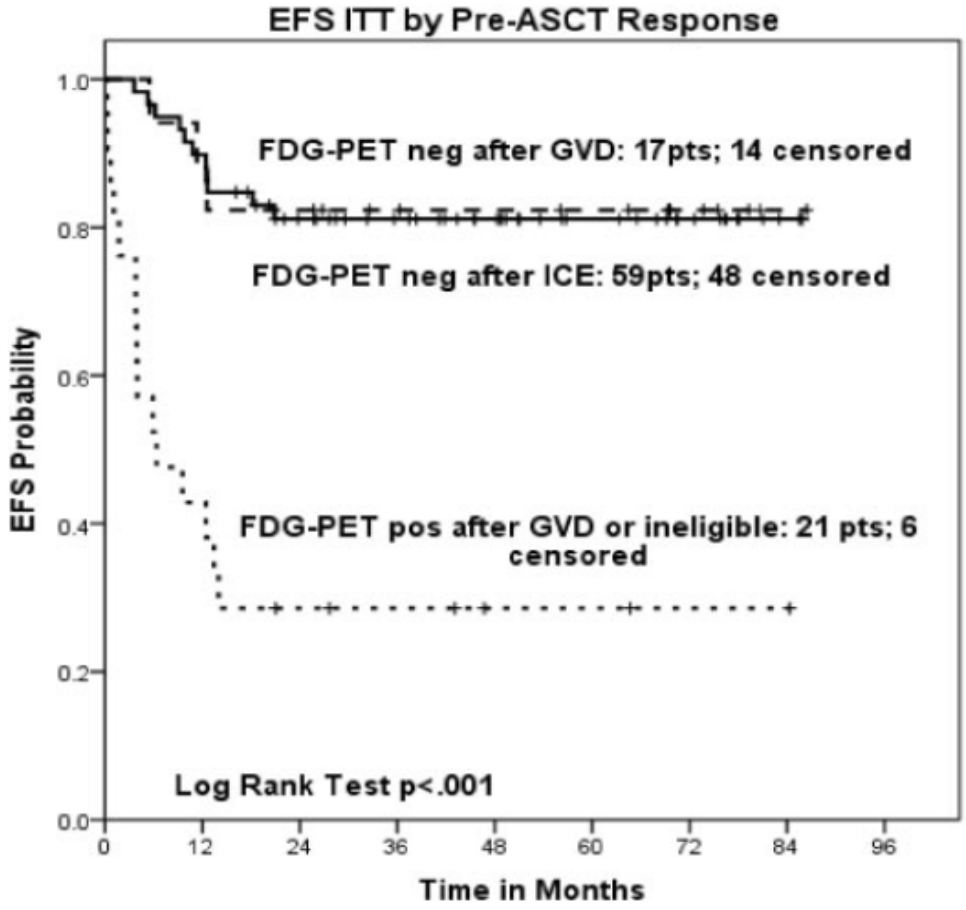


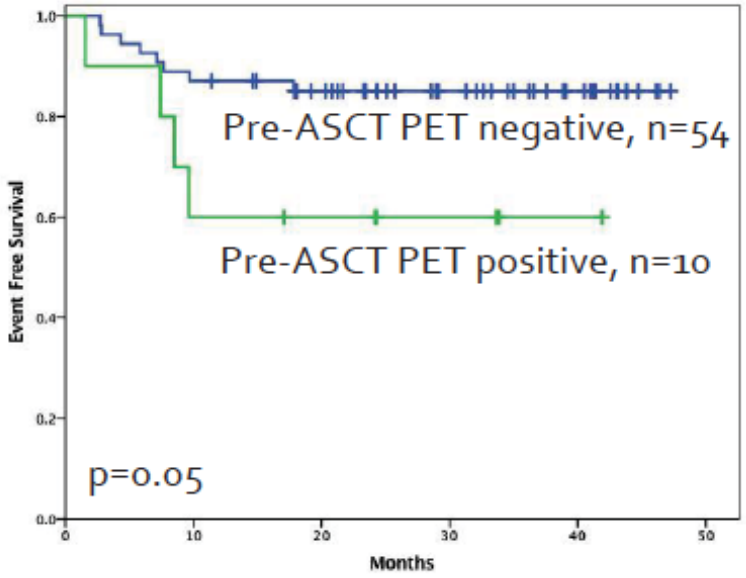
Figure 3. EFS intent to treat by pre-ASCT response.

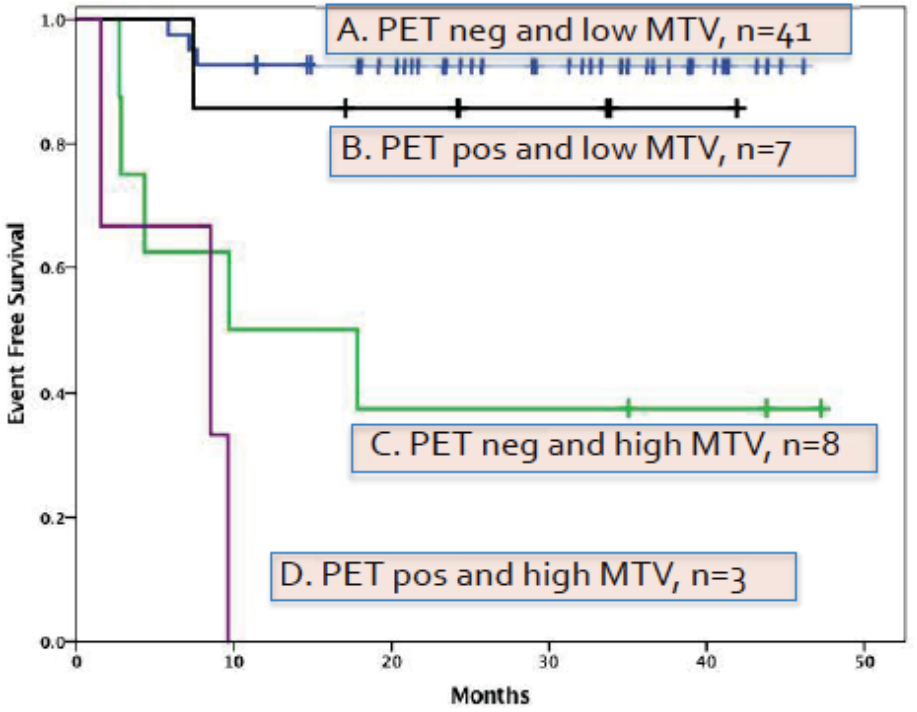
Craig H. Moskowitz BLOOD, 16 FEBRUARY 2012

Other risk factors?

Prognostic significance of baseline metabolic tumor volume in relapsed and refractory Hodgkin lymphoma

Rel/ref pts with HL enrolled in sequential BV > ICE protocol, receiving subsequent ASCT





- **MTV improved the predictive power of pre-ASCT PET**
- **MTV may be used to stratify pts for more or less aggressive therapy**

p-values

A->C, p<0.001 B->D, p=0.012

Moskowitz AJ et al. Blood 2017

If pts had already received BV?

Relapsed and Refractory Classical Hodgkin Lymphoma: Keeping Pace With Novel Agents and New Options for Salvage Therapy

Alison J. Moskowitz, MD[1]; Alex F. Herrera, MD[2]; and Anne W. Beaven, MD[3]

TABLE 1. Newer Salvage Regimens for Relapsed or Refractory Hodgkin Lymphoma

Regimen	n	% PET Negative	ASCT, n (%)	PFS/EFS (ITT)	PFS/EFS (Transplanted Patients)
BV-augICE (PET-adapted, sequential)[17,18]	65	83; 27 (BV alone)	64 (98)	82% at 3 years	NR
BV-ICE and others (PET-adapted, sequential)[19]	56	66; 43 (BV alone)	50 (89)	NR	67% at 2 years
BV plus bendamustine[20]	55	74	40 (72)	62.6% at 2 years	69.8% at 2 years
BeGEV[21]	59	73	43 (73)	62.2% at 2 years	80.8% at 2 years
BV plus gemcitabine[25]	42	67	34 (76)	NR	NR
BV plus ICE[23]	24	87	19 (79)	NR	NR
BV plus DHAP[22]	61	79	53 (87)	76% at 2 years	NR
BV plus ESHAP[24]	66	70	60 (91)	71% at 30 months	NR
BV-nivolumab[27]	62	61	42 (68) after only BV-nivolumab; 14 (23) after additional salvage	82% at 21 months	97% at 21 months for patients transplanted after only BV-nivolumab

2019 ASCO EDUCATIONAL BOOK

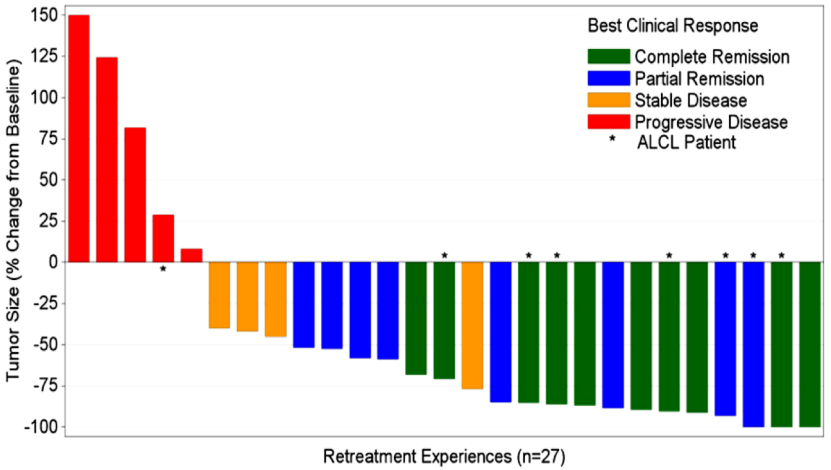
Retreatment with brentuximab vedotin in patients with CD30-positive hematologic malignancies

Nancy L Bartlett[1*], Robert Chen[2], Michelle A Fanale[3], Pauline Brice[4], Ajay Gopal[5], Scott E Smith[6], Ranjana Advani[7], Jeffrey V Matous[8], Radhakrishnan Ramchandren[9], Joseph D Rosenblatt[10], Dirk Huebner[11], Pamela Levine[12], Laurie Grove[12] and Andres Forero-Torres[13]

retreatment...

Table 2 Key response results

Parameter	HL patients (N = 20)	ALCL patients (N = 8)
Objective response rate (CR + PR)	12 (60)	7 (88)
Best clinical response[a]		
Complete remission	6 (30)	5 (63)
Partial remission	6 (30)	2 (25)
Stable disease	4 (20)	0
Progressive disease	4 (20)	1 (13)
95% CI for ORR[b]	36.1, 80.9	47.3, 99.7
95% CI for CR rate[b]	11.9, 54.3	24.5, 91.5
Duration of objective response for patients with OR, months[c]	12 (60)	7 (88)
Median (95% CI)[d]	9.2 (2.1, –)	12.3 (6.6, –)
Duration of response for patients with CR, months[c]	6 (30)	5 (63)
Median (95% CI)[d]	9.4 (1.7, 14.2)	12.9 (7.4, –)
Progression-free survival, months[e]		
Median (95% CI)[d]	9.9 (3.4, 13.4)	12.9 (1.4, 18.5)
Overall survival, months[e]		
Median (95% CI)[d]	- (11.4, –)	- (3.3, –)



Journal of Hematology & Oncology 2014, **7**:24

Post ASCT consolidation

JAMA Oncology | Special Communication

Maintenance Therapies for Hodgkin and Non-Hodgkin Lymphomas After Autologous Transplantation

A Consensus Project of ASBMT, CIBMTR, and the Lymphoma Working Party of EBMT

Abraham S. Kanate, MBBS; Ambuj Kumar, MD, MPH; Peter Dreger, MD; Martin Dreyling, MD; Steven Le Gouill, MD; Paolo Corradini, MD; Chris Bredeson, MD, MSc, FRCPC; Timothy S. Fenske, MD; Sonali M. Smith, MD; Anna Sureda, MD; Alison Moskowitz, MD; Jonathan W. Friedberg, MD; David J. Inwards, MD; Alex F. Herrera, MD; Mohamed A. Kharfan-Dabaja, MD; Nishitha Reddy, MBBS; Silvia Montoto, MD; Stephen P. Robinson, MD; Syed A. Abutalib, MBBS; Christian Gisselbrecht, MD; Julie Vose, MD; Ajay Gopal, MD; Mazyar Shadman, MD; Miguel-Angel Perales, MD; Paul Carpenter, MD; Bipin N. Savani, MD; Mehdi Hamadani, MD

JAMA Oncol. 2019;5(5):715-722.

Table 1. Final Clinical Practice Guidelines Consensus Statements on Maintenance Therapy After High Dose Therapy and Autologous Hematopoietic Cell Transplantation for Hodgkin Lymphoma

Consensus Statements: Hodgkin Lymphoma	Grading of Recommendations[a]	Panelists in Agreement, % (n=26)
1. The panel recommends post-autologous HCT consolidation/ maintenance with BV for 16 cycles in BV-naïve classic Hodgkin lymphoma (HL) with at least 1 or more high-risk features as defined by the AETHERA study[b]	A	92
2. The panel does not recommend postautologous HCT consolidation/ maintenance with BV for HL with prior evidence of disease refractory to BV	C	96
3. The recommended duration of post-auto-HCT BV consolidation/ maintenance therapy is for a maximum of 16 cycles every 3 weeks as described in AETHERA trial, or until unacceptable toxicity or disease relapse/progression (whichever occurs first)[b]	A	100
4. The panel recommends post-autologous HCT consolidation/ maintenance with BV in HL with one or more high-risk features as defined by the AETHERA trial and limited prior exposure to BV (approximately 4-6 cycles) preceding the autologous HCT, but without any evidence of BV refractory disease	C	100
5. Sufficient data do not exist to use the preautologous-HCT PET (or PET/CT) scan status to guide the use of post-autologous HCT consolidation/ maintenance therapy with BV for HL with one or more high-risk features as defined by AETHERA Trial	C	84

Comments (I)

- **Post ASCT BV consolidation:**
  - **Prevents a relevant proportion of relapses occurring early after ASCT**
  - **The sustained PFS advantage is stable over time. An updated OS estimation is programmed in 2020**
  - **Is effective in patients with risk factors**
  - **Is recommended by NCCN, ESMO, ASBMT, CIBMTR, EBMT-LWP**
  - **Also recommended if previous BV exposure (if responsive)**
- **Post ASCT CPI consolidation: promising (in pts coming from BV in first line?)**

Comments (II)

- **Which patients?**
  - **One or more risk factor? (PET)**
  - **Other risk factors (bMTV, biomarkers after ASCT?)**
- **How long is it useful to treat patients?**
- **Next studies should enroll pts previously treated with BV and/or CPI**

Guardiamo le stelle: guai a chi non le vede!

Grazie