Mi experiencia em recaída post transplante autologo o no elegible

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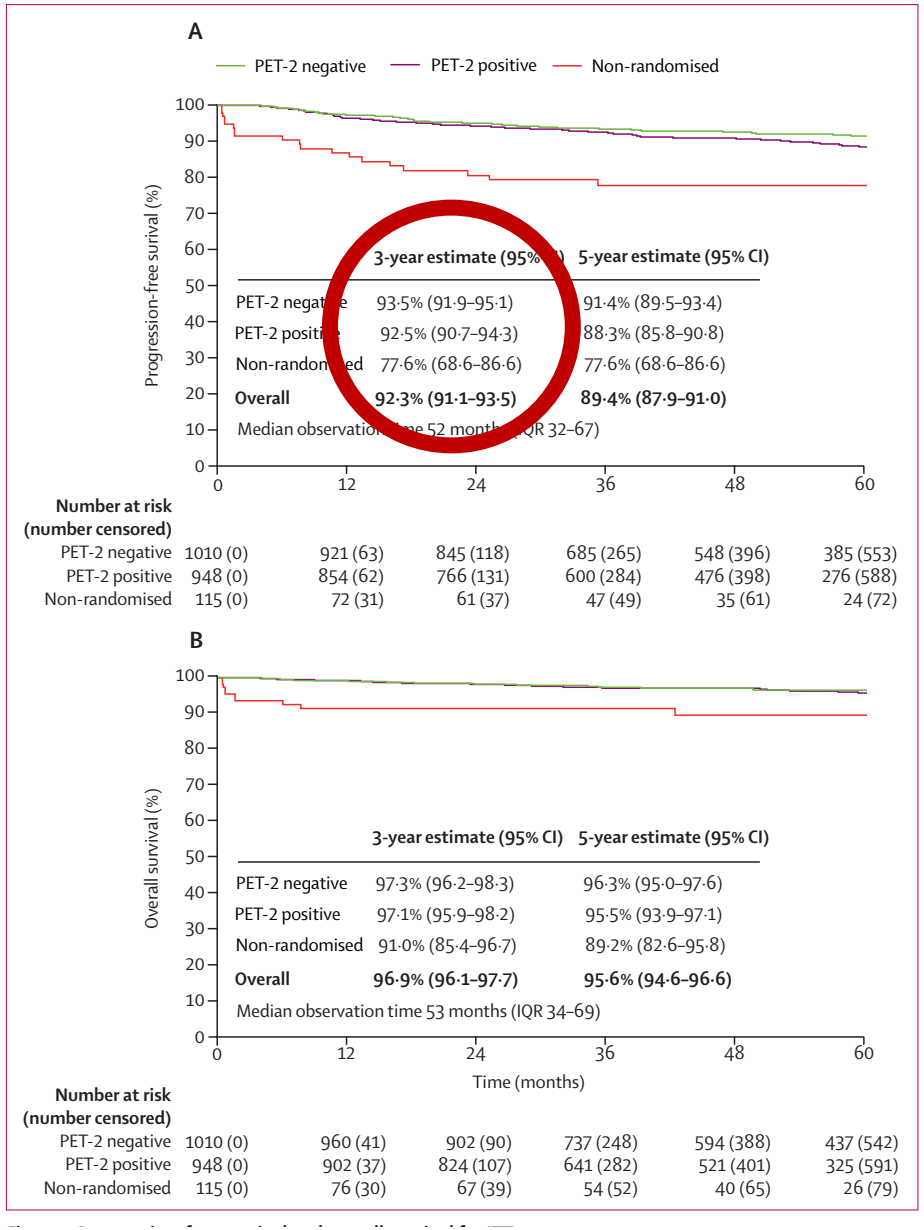
- Ac Camargo Cancer Center

Disclosure

No disclosure for this presentation

First line

HD18



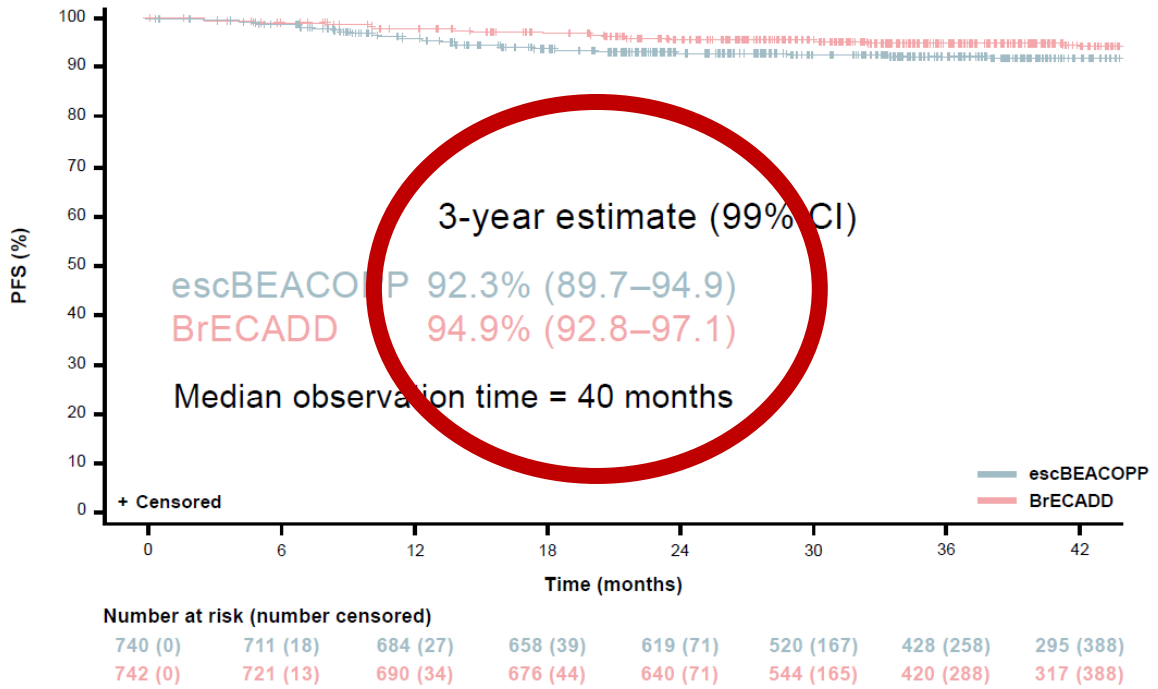
Borchmann P. *Lancet*. 2017

PFS in the ITT population

PFS events at a median follow-up of 40 months

	escBEACOPP (N=740)		BrECADD (N=742)	
	n	%	n	%
Progression/relapse	55	7.4	32	4.3
Progression	14	1.9	5	0.7
Early relapse, follow-up ≤1 year	23	3.1	11	1.5
Late relapse, follow-up >1 year	18	2.4	16	2.2
Death without previous progression or relapse	6	0.9	7	0.9
Total PFS events	**61**	**8.4**	**39**	**5.3**

3-year PFS in the ITT population

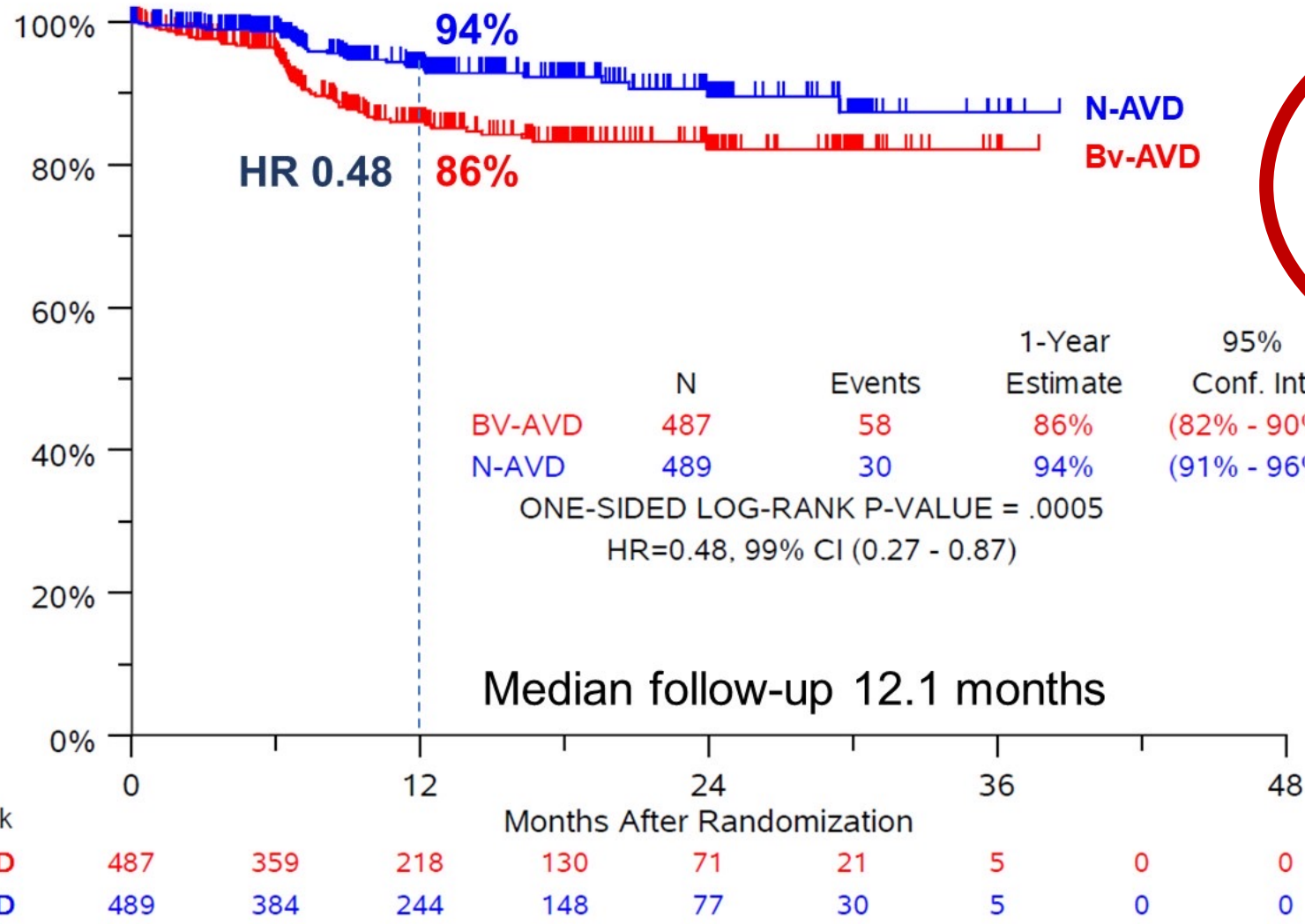


With an HR of 0.63 for PFS (in favor of BrECADD), the HR bound of 1.02 is excluded and non-inferiority of BrECADD established vs escBEACOPP. The 99% CI for the HR (1.07–0.37) indicates a trend towards superiority (to be determined at final analysis with 95% CI)

BrECADD, brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone; CI, confidence interval; escBEACOPP, escalated bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone; HR, hazard ratio; ITT, intention-to-treat; PFS, progression-free survival.

Borchmann P et al. Oral presentation LBA4. Presented at the 17th International Conference on Malignant Lymphoma, June 13–17, 2023.

N-AVD improves PFS compared to Bv-AVD



	N	Events	1-Year Estimate	95% Conf. Int.
BV-AVD	487	58	86%	(82% - 90%)
N-AVD	489	30	94%	(91% - 96%)

ONE-SIDED LOG-RANK P-VALUE = .0005

HR=0.48, 99% CI (0.27 - 0.87)

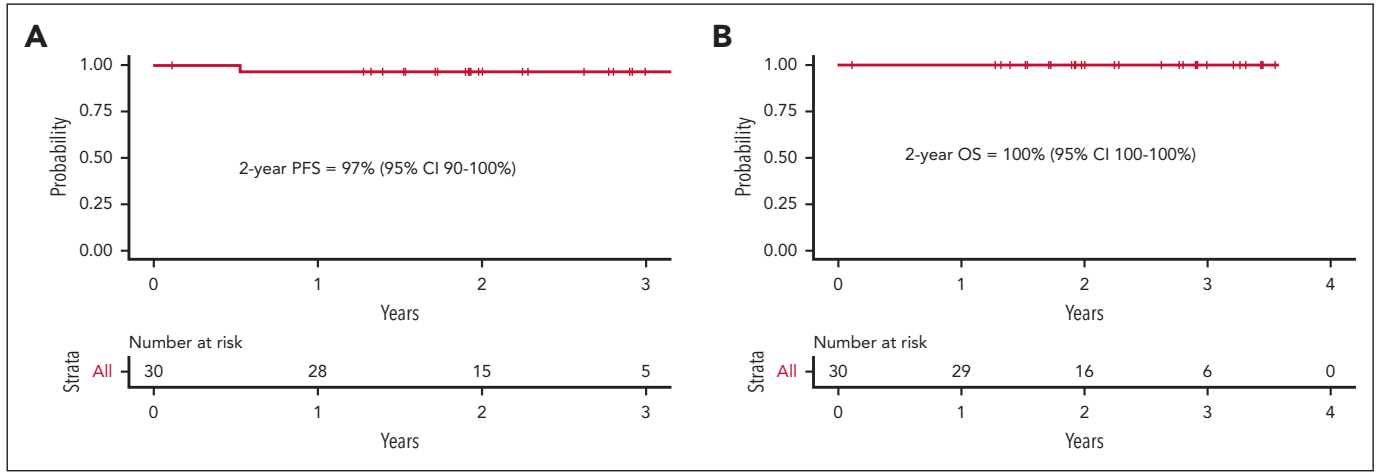
# at Risk									
BV-AVD	487	359	218	130	71	21	5	0	0
N-AVD	489	384	244	148	77	30	5	0	0

1-year PFS
N-AVD 94%
Bv-AVD 86%

First line-Pembro-AVD

Table 1. Patient characteristics

Characteristic	n = 30
Male sex, n (%)	12 (40)
Age, median (range), y	33 (18-69)
Stage, n (%)	
I	1 (3)
II	11 (37)
III	7 (23)
IV	11 (37)
B symptoms, n (%)	13 (43)
Mediastinal bulk, >10 cm, n (%)	6 (20)
Elevated erythrocyte sedimentation rate, >50, n (%)	11 (37)
Extranodal involvement, n (%)	11 (37)
Spleen involvement, n (%)	7 (23)
Early-stage unfavorable, National Comprehensive Cancer Network (n = 12), n (%)	6 (50)
International Prognostic Score (advanced stage, n = 18), n (%)	
0-1	6 (33)
2 and 3	7 (39)
4, 5, 6, and 7	5 (28)



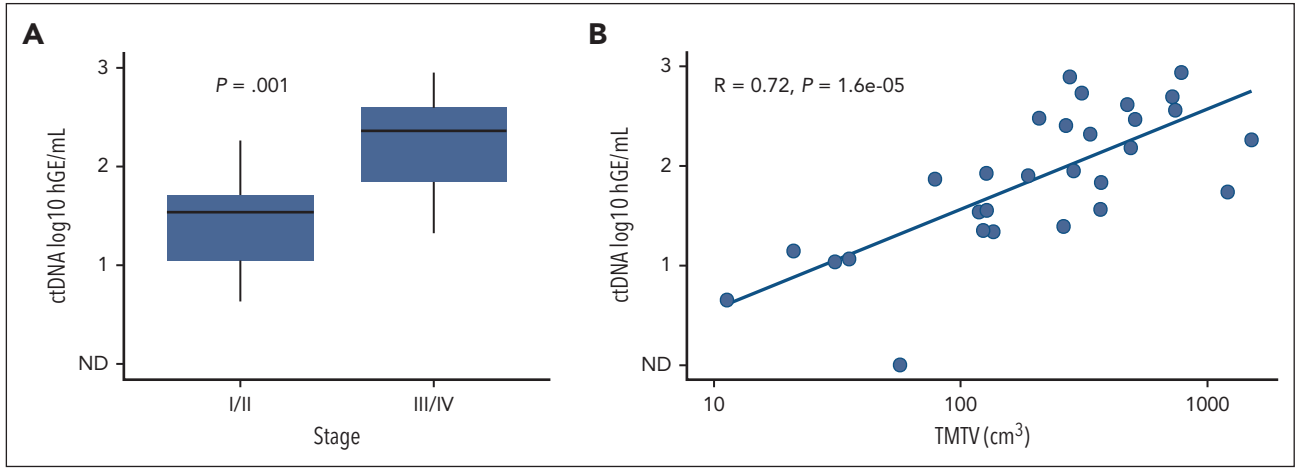
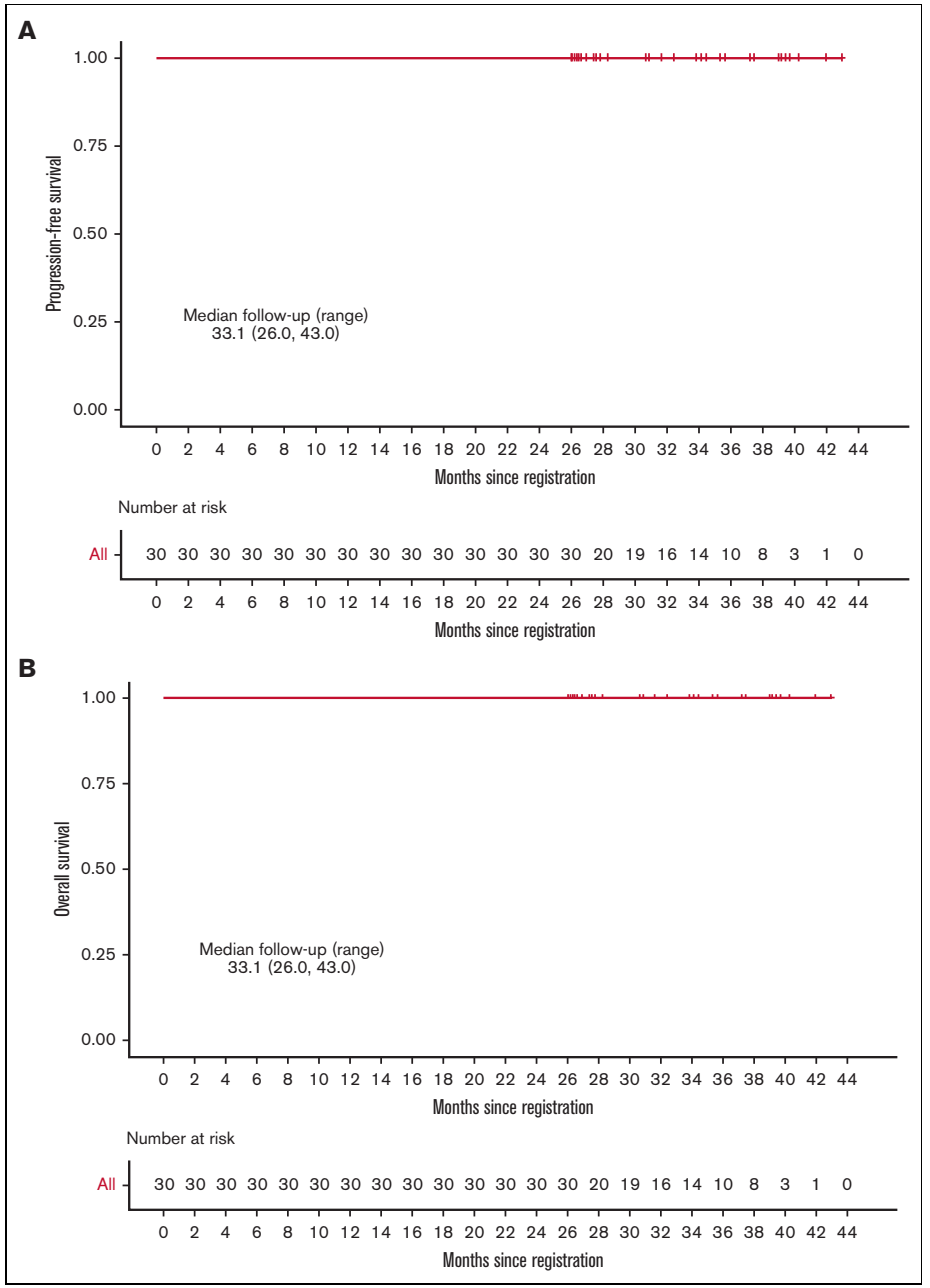


Figure 3. Total metabolic tumor volume and ctDNA analyses. (A) Comparison of baseline ctDNA levels in patients at early-stage I or II compared with in those at stage III or IV. (B) Scatterplot comparing baseline ctDNA levels to TMTV. hGE, haploid genome equivalents.

Lynch R. *Blood*. 2023

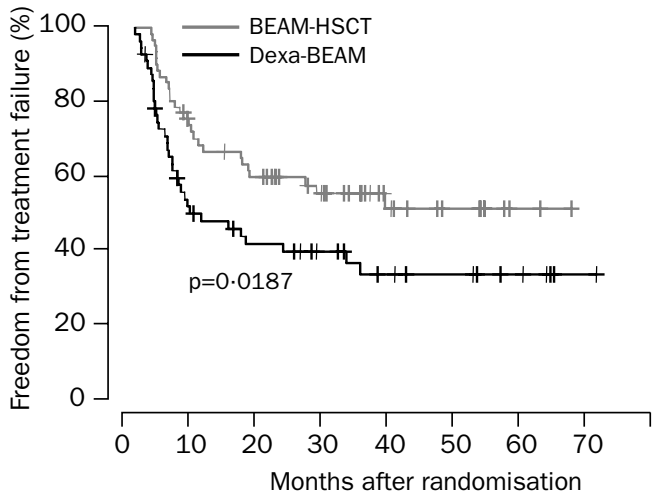
Introdution- PembroAVD sequencial



Allen P. *Blood Adv*. 2023

Refractory and recidive disease

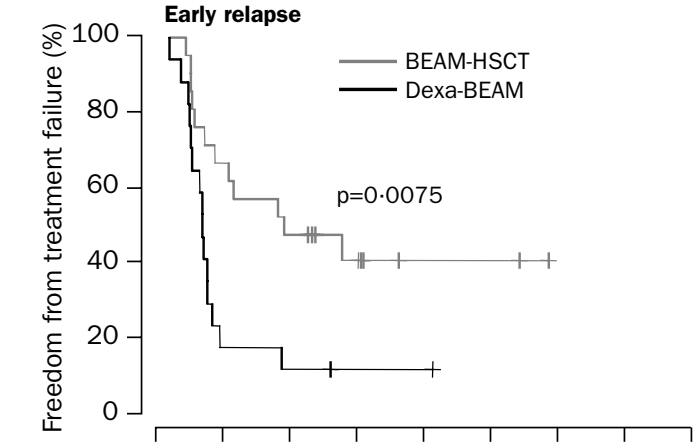
Recidive AutoPBSCT



Number of patients

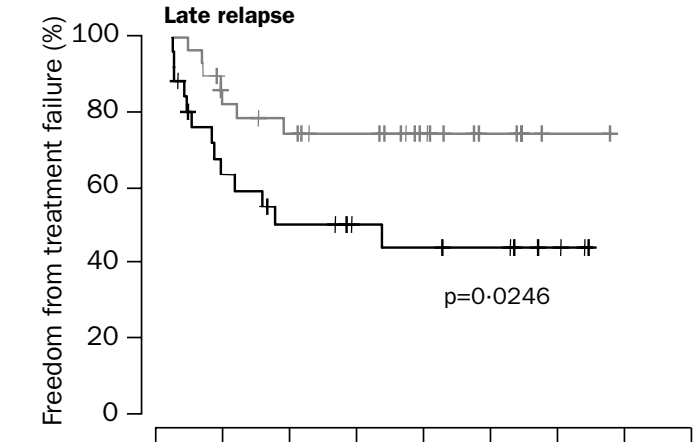
BEAM-HSCT	61	43	34	25	13	8	7	0
Dexa-BEAM	56	27	20	15	10	8	5	1

Figure 3: **Freedom from treatment failure for patients with relapsed chemosensitive Hodgkin's disease**



Number of patients

BEAM-HSCT	21	14	10	6	2	2	0	0	0
Dexa-BEAM	17	3	2	1	1	0	0	0	0



Number of patients

BEAM-HSCT	29	22	19	16	10	5	1	0	0
Dexa-BEAM	26	15	11	8	7	6	3	0	0

Schmitz N. *Lancet*. 2002

Pre PBSCT

Early recidive: PFS 44% 4 years
Late recidive: PFS 72% 4 years

Table III

Univariate and multivariate analysis of factors for EFS after ASCT (N= 161).

	Univariate		Multivariate	
Covariates	**HR (95% CI)**	***P*-value†**	**HR (95% CI)**	***P*-value†**
Age >45 years	1·36 (0·67–2·77)	0·39	–	
Female gender	0·89 (0·54–1·49)	0·67	–	
B symptoms	2·05 (1·21–3·46)	**0·007**	1·46 (0·85–2·50)	0·17
Extranodal disease	2·82 (1·65–4·84)	**<0·001**	_★	★
Tumour bulk >5 cm	2·11 (1·26–3·52)	**0·004**	1·41 (0·82–2·43)	0·22
Stage IV	3·51 (2·04–6·02)	**<0·001**	2·55 (1·43–4·57)	**0·002**
Positive FI Pre-ASCT	2·79 (1·67–4·66)	**<0·001**	2·00 (1·16–3·44)	**0·013**
Chemo + RT conditioning	0·54 (0·31–0·94)	**0·029**	0·78 (0·44–1·36)	0·38

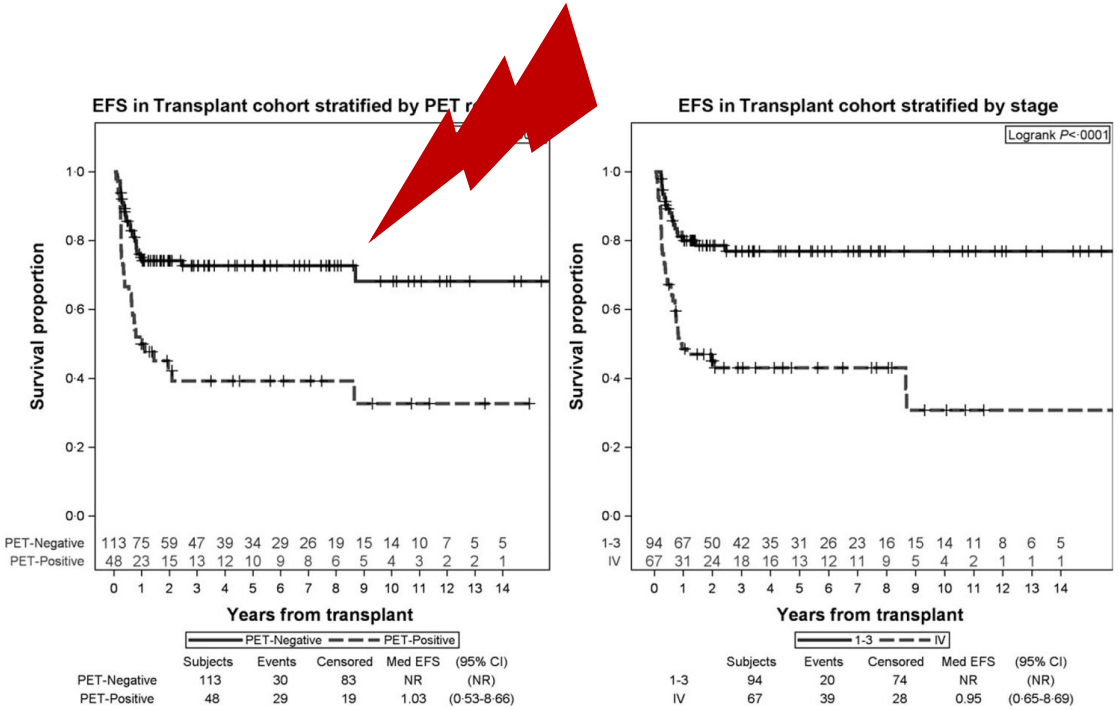


Fig 3.
EFS by Significant Covariates. (a) by functional imaging prior to autologous stem cell transplantation (b) by Stage. EFS, event-free survival; PET, positron emission tomography; 95% CI, 95% confidence interval; NR, not reached.

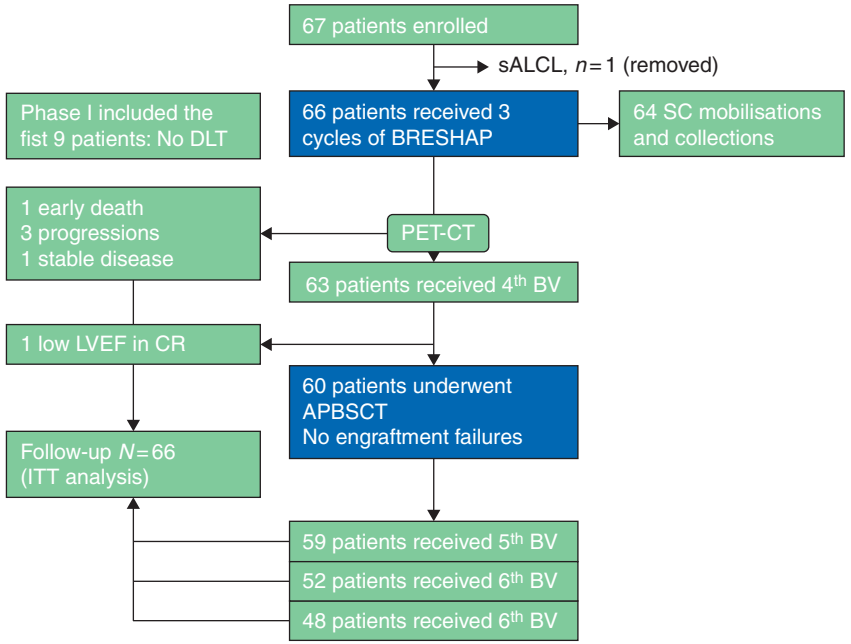
Shah GL. *Br J Haematol*.2016

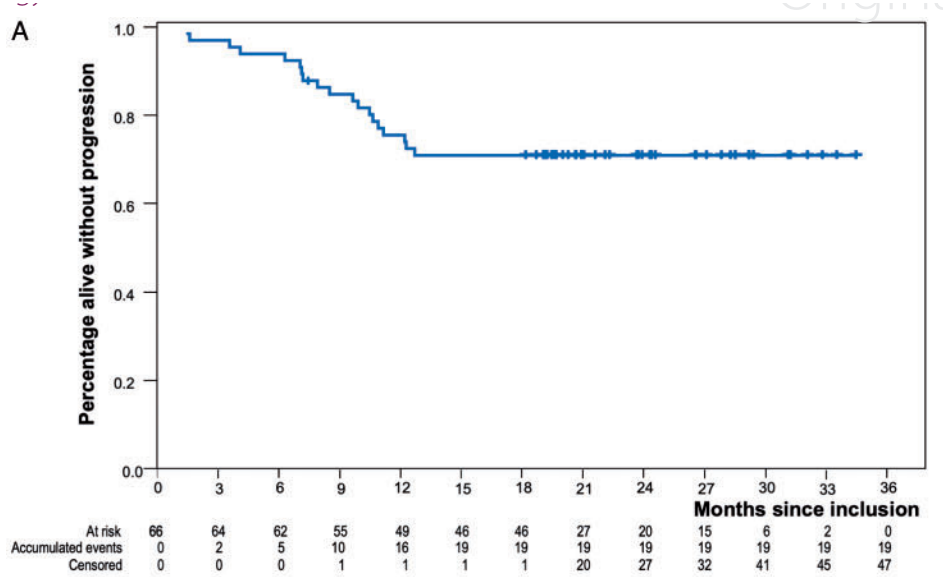
Table 1. Conventional Salvage Chemotherapy Regimens for Relapsed/Refractory cHL; Adapted from Vassilakopoulos et al. [22].

	Regimen	Trial	# Pts	ORR (%)	CR (%)
ESHAP	Etoposide, cytarabine, cisplatin, methylprednisolone	Aparicio [10]	22	73	41
ASHAP	Adriamycin, solumedrol, high-dose cytarabine, cisplatin	Rodriguez [11]	56	70	34
DHAP	Dexamethasone, cytarabine, cisplatin	Josting [12]	281	NR	72
ICE	Ifosfamide, carboplatin, etoposide	Moskowitz [13]	65	88	26
ICE	Ifosfamide, carboplatin, etoposide	Hertzberg [14]	6	100	67
IVOx	Ifosfamide, etoposide, oxaliplatin	Sibon [15]	34	76	32
GDP	Gemcitabine, dexamethasone, cisplatin	Baetz [16]	23	69	17
GEM-P	Gemcitabine, cisplatin, methylprednisolone	Chau [17]	21	80	24
IGEV	Ifosfamide, gemcitabine, vinorelbine, prednisone	Santoro [18]	91	81	54
BeGEV	Bendamustine, gemcitabine, vinorelbine	Santoro [19]	59		75

Takiar R. *Cancers.* 2022.

BV-ESHAP





71% CR

Garcia-Sanz. *Annals of Oncol.* 2019

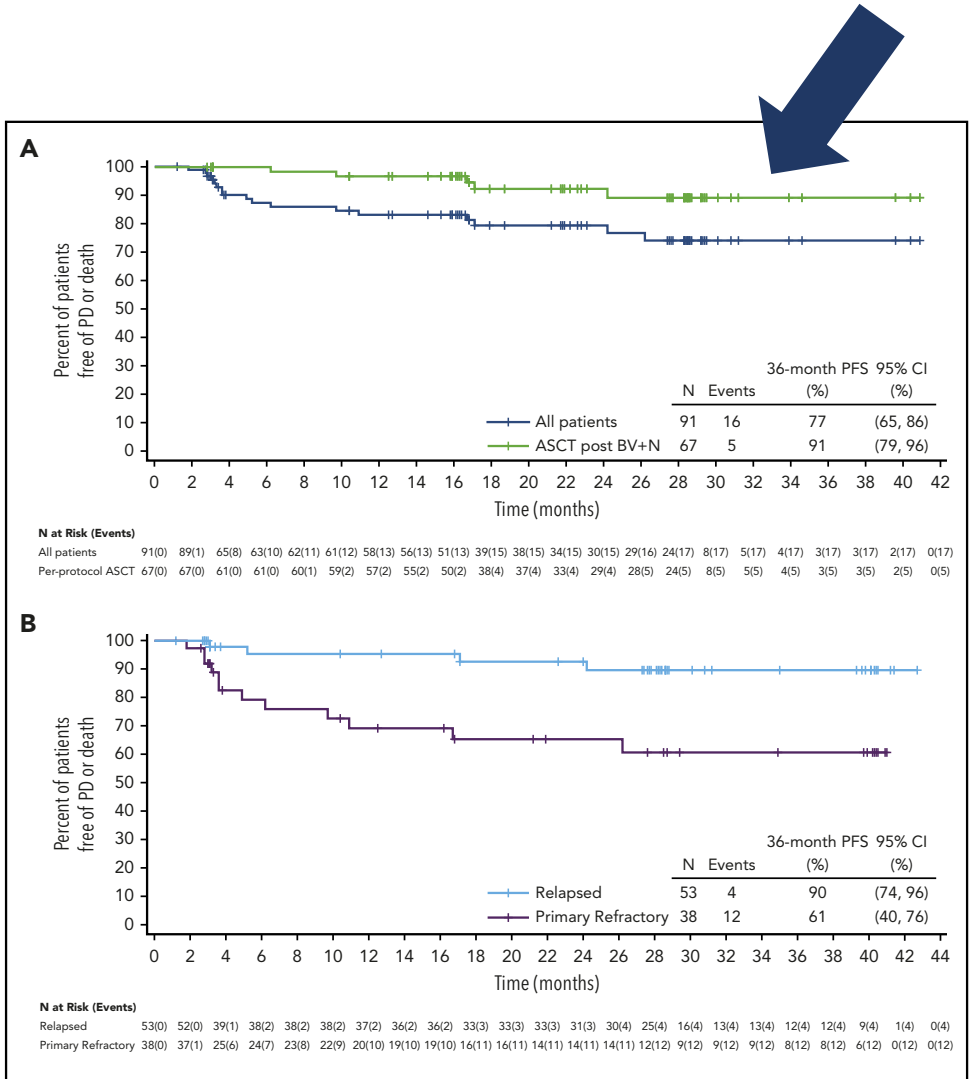
Brentuxi-Nivo

Table 1. *Continued*

	All treated patients, N = 91
PD to frontline therapy	24 (26)
Unknown response to frontline therapy	1 (1)
Relapsed, remission duration ≤1 y	27 (30)
Relapsed, remission duration >1 y	26 (29)
ECOG performance status, n (%)	
Grade 0	58 (64)
Grade 1	32 (35)
Bulky disease at baseline, n (%)	12 (13)
Extranodal disease at baseline, n (%)	24 (26)

Table 2. Best clinical response and Deauville 5-point scale

	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
Deauville score = 1	23 (25)	
Deauville score = 2	20 (22)	
Deauville score = 3	12 (13)	
Deauville score = 4*	2 (2)	
Deauville score = 5*	4 (4)	
PMR/PR	16 (18)	10.4, 27
Deauville score = 4	9 (10)	
Deauville score = 5	7 (8)	
NMR/SD	5 (5)	1.8, 12.4
Deauville score = 4	1 (1)	
Deauville score = 5	4 (4)	
PMD/PD	7 (8)	3.1, 15.2
Deauville score = 5	7 (8)	
Not evaluable	1 (1)	
Not applicable†	1 (1)	



Advani R. *Blood*. 2021

Brentuxi-Pembro

Table 1. Baseline characteristics of patients (n = 10).

Characteristics		Patients, *n*.
Median age, years (range)		30.7 (20.6–36.4)
Sex, male/female		8 (80%)/2 (20%)
Median time from diagnosis to pembro-BV, months (range)		27.7 (13.6–51)
First-line treatment	ABVD BEACOPP esc CHOEP	5 (50%) 4 (40%) 1 (10%)
Number of prior treatments before pembro-BV salvage	2 3 5	3 (30%) 6 (60%) 1 (10%)
First salvage therapy	DHAP BEGEV ICE	6 (60%) 3 (30%) 1 (10%)
Second salvage therapy	BEGEV Bendamustine ICE BEACOPP esc	2 (20%) 2 (20%) 1 (10%) 1 (10%)
Refractory disease		6 (60%)
Complete remission < 12 months		4 (40%)
Extranodal involvement at relapse		6 (60%)
Advanced stage at relapse		9 (90%)

ABVD, doxorubicin, bleomycin, vinblastine, dacarbazine; BEACOPP esc, doxorubicin, cyclophosphamide, etoposide, procarbazine, prednisolone, bleomycin, vincristine; CHOEP, cyclophosphamide, doxorubicin, vincristine, etoposide, prednisolone; BEGEV, bendamustine, gemcitabine, vinorelbine; DHAP, dexamethasone, cytarabine, cisplatin; ICE, ifosfamide, carboplatin, etoposide; BV, brentuximab vedotin.

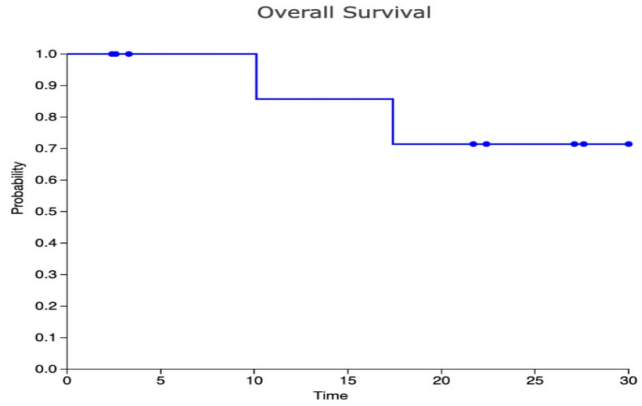


Figure 1. Kaplan–Meier curve for OS.

Table 2. Treatment details for each patient in study.

	Prior Lines of Treatment	Pembro + BV (Cycles)	PET2	ASCT	BV Post-ASCT (Cycles)	PD after ASCT	Allo SCT	Follow-Up (Months)	Last Disease Status	Patient Status
Pt1	3	2	DS3	Yes	14	No	No	29.9	CR	Alive
Pt2	2	4	DS3	Yes	5	Yes	Yes a	17.4	CR	Dead
Pt3	3	7	DS4	Yes	9	No	No	27.1	CR	Alive
Pt4	3	2	DS2	Yes	14	No	No	27.6	CR	Alive
Pt5	2	4	DS5	No b	No	Yes	Yes	10.1	PR	Dead
Pt6	2	6	DS1	Yes (+RT)	3	No	Yes c	22.4	CR	Alive
Pt7	3	6	DS2	Yes	1	No	No	21.7	CR	Alive
Pt8	3	4	DS1	Yes	Not yet	NA	No	3.3	CR	Alive
Pt9	5	4	DS1	Not yet	Not yet	NA	No	2.4	CR	Alive
Pt10	3	4	DS2	Not yet	Not yet	NA	No	2.6	CR	Alive

[a] After subsequent treatment line (nivolumab [illegible]) due to PD after ASCT. [b] ASCT after subsequent treatment line (nivolumab + gemcitabine and RT) due to PD. [c] Directly after ASCT (tandem strategy).

Massaro F. *Cancers*. 2022

23 Years old girl. LH IVB IPS 4. eBEACODD=CR. Early recidive/ IGEV-NR/DHAP- PR and progression- no PBSCT candidate.UCI and pulmonar failure

Brentu

Table 1. Baseline characteristics

Characteristics
Median age, years (range)
Sex, male/female
Median time from diagnosis pembro-BV, months (range)
First-line treatment
Number of prior treatments before pembro-BV salvage
First salvage therapy
Second salvage therapy
Refractory disease
Complete remission < 12 mon
Extranodal involvement at rela
Advanced stage at relapse

ABVD, doxorubicin, bleomycin, vinb side, procarbazine, prednisolone, bl etoposide, prednisolone; BEGEV, be cisplatin; ICE, ifosfamide, carboplati

Follow-Up (Months)	Last Disease Status	Patient Status
29.9	CR	Alive
17.4	CR	Dead
27.1	CR	Alive
27.6	CR	Alive
10.1	PR	Dead
22.4	CR	Alive
21.7	CR	Alive
3.3	CR	Alive
2.4	CR	Alive
2.6	CR	Alive

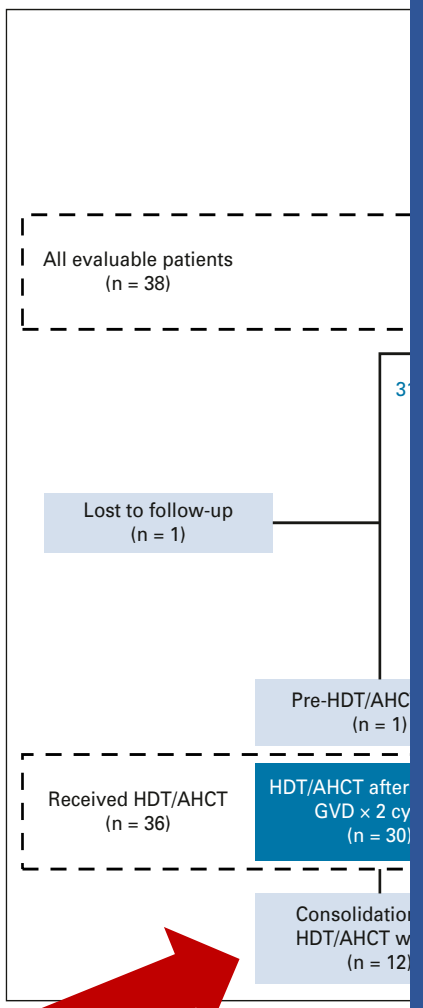
) after ASCT. [b] ASCT after subsequent fter ASCT (tandem strategy).

30

Massaro F. *Cancers*. 2022

Pembro-

My personal/institucional protocol for early recidive/refractory disease. We have been using in 6 patients last year with 5 CR and 1 PR. All in CR until now.



Armand P. *JCO*. 2018

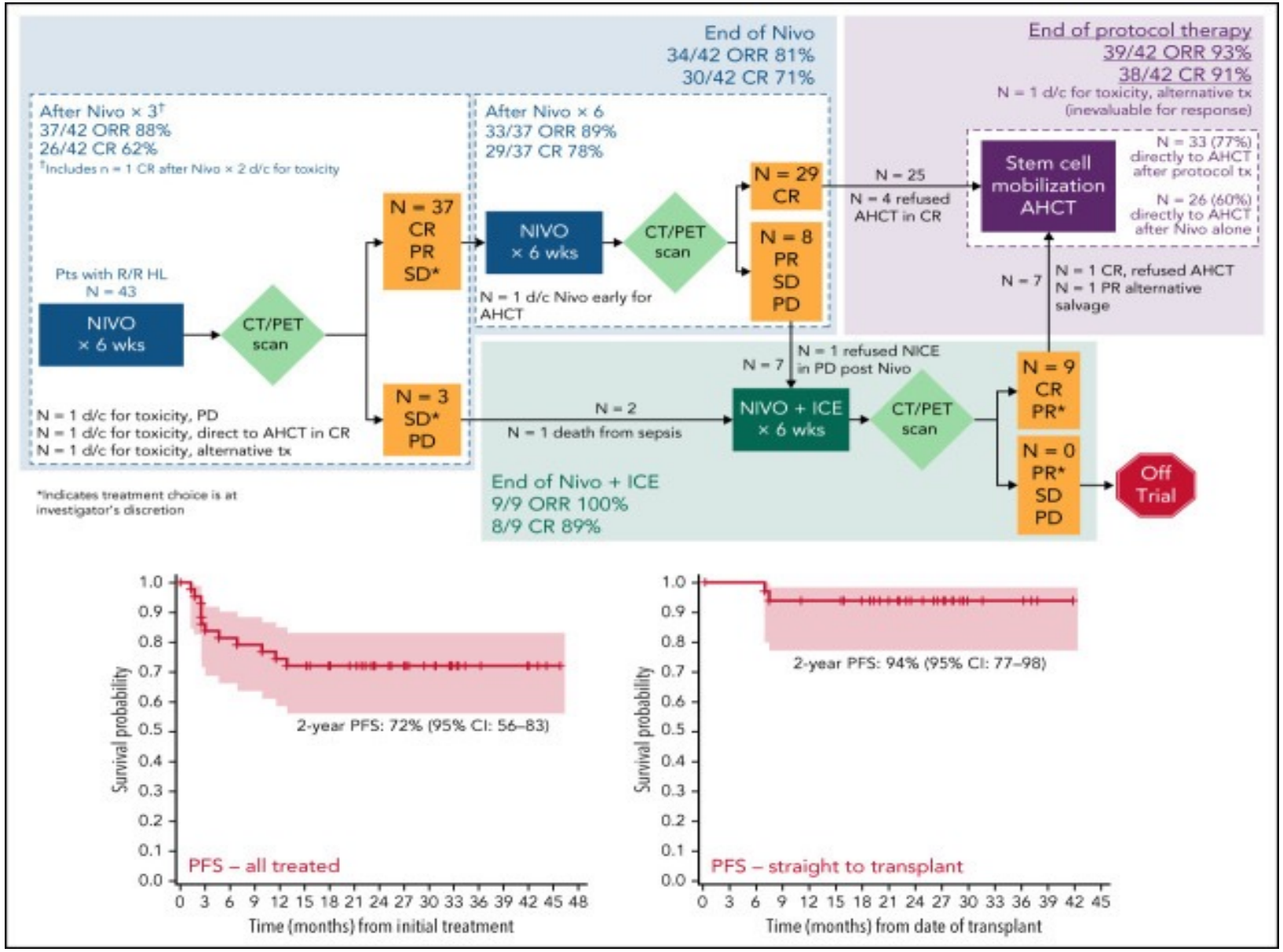
nbro-GVD Overall (n = 38)
100 (91 to 100)
95 (82 to 99)
5 (1 to 18)
36 (95)
2 (5.3)

se ou

A. *JCO*. 2021

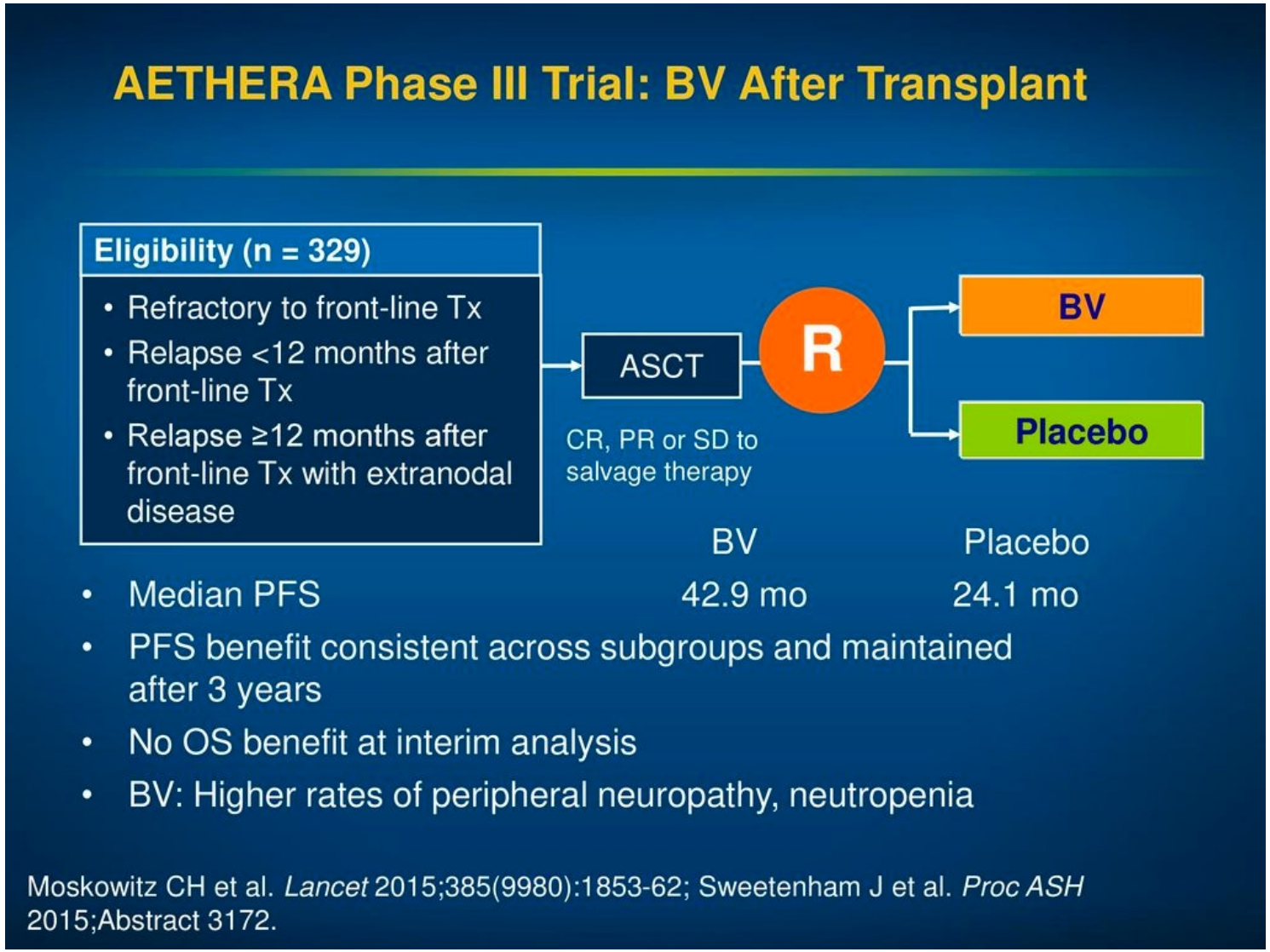
Nivo- ICE

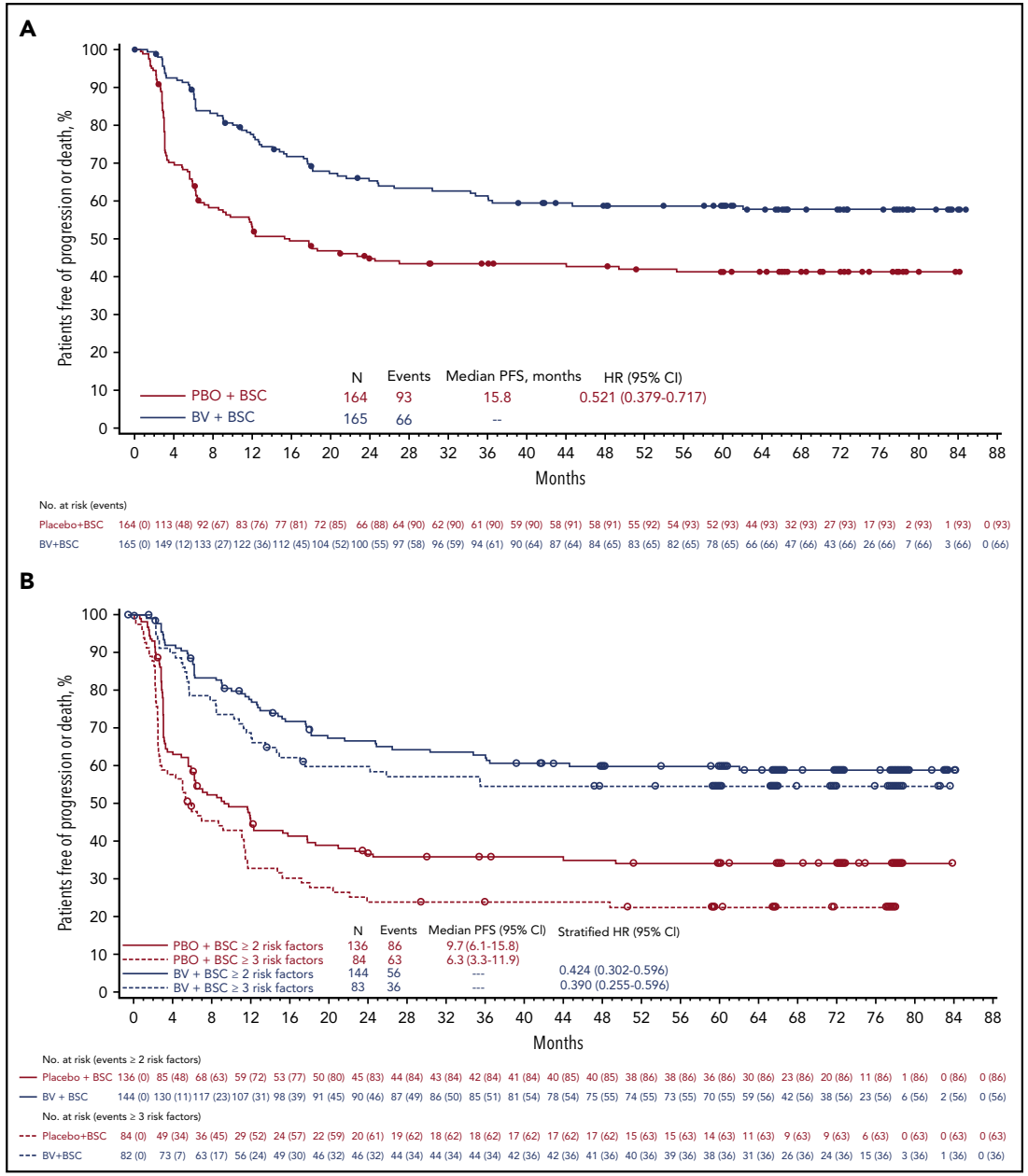
43 patients
44% primary refractory



Mei M. *Blood*. 2022

Aethera


AETHERA Phase III Trial: BV After Transplant
Eligibility (n = 329)
• Refractory to front-line Tx
• Relapse <12 months after front-line Tx
• Relapse ≥12 months after front-line Tx with extranodal disease
ASCT
R
CR, PR or SD to salvage therapy
BV
Placebo
BV
Placebo
• Median PFS
42.9 mo
24.1 mo
• PFS benefit consistent across subgroups and maintained after 3 years
• No OS benefit at interim analysis
• BV: Higher rates of peripheral neuropathy, neutropenia
Moskowitz CH et al. Lancet 2015;385(9980):1853-62; Sweetenham J et al. Proc ASH 2015;Abstract 3172.



5 years

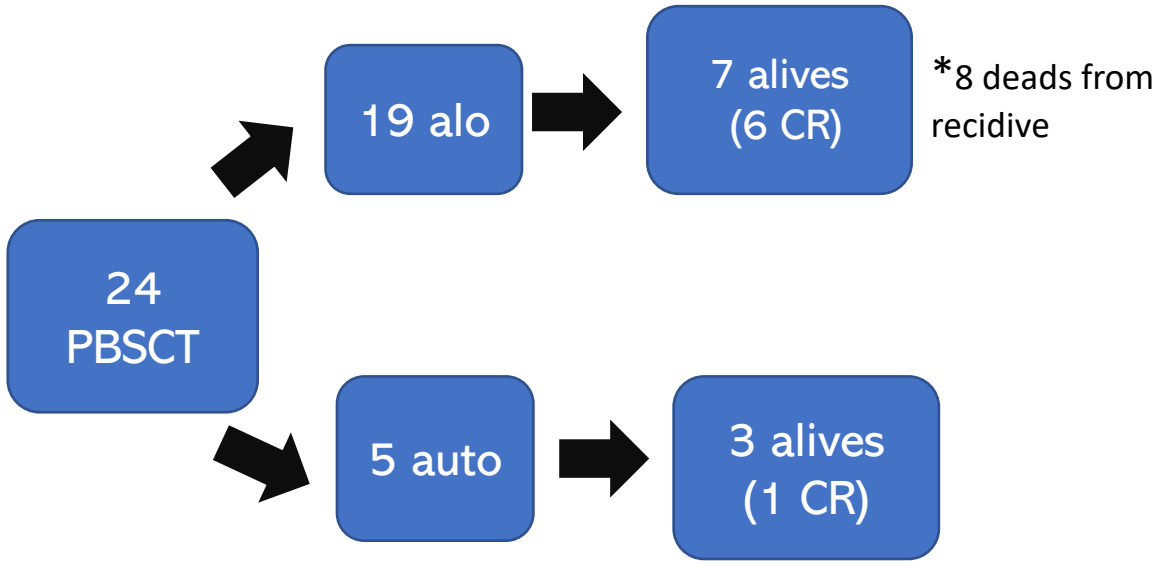
Moskowitz C. *Blood*. 2018

Nowadays as I use pembro-GVD before auto, I rarely use brentuxi after (despite it is included at Memorial protocol)

witz C. *Blood*. 2018

Recidive after auto PBSCT

- ✓196 patients
- ✓79% early recidive (1 year)
- ✓99,9% early recidive (2 Years)
- ✓24 second PBSCT
- ✓19 alo/ 5 auto



Moskowitz AJ. *Br J Haematol*.2009

Recidive after auto PBSCT

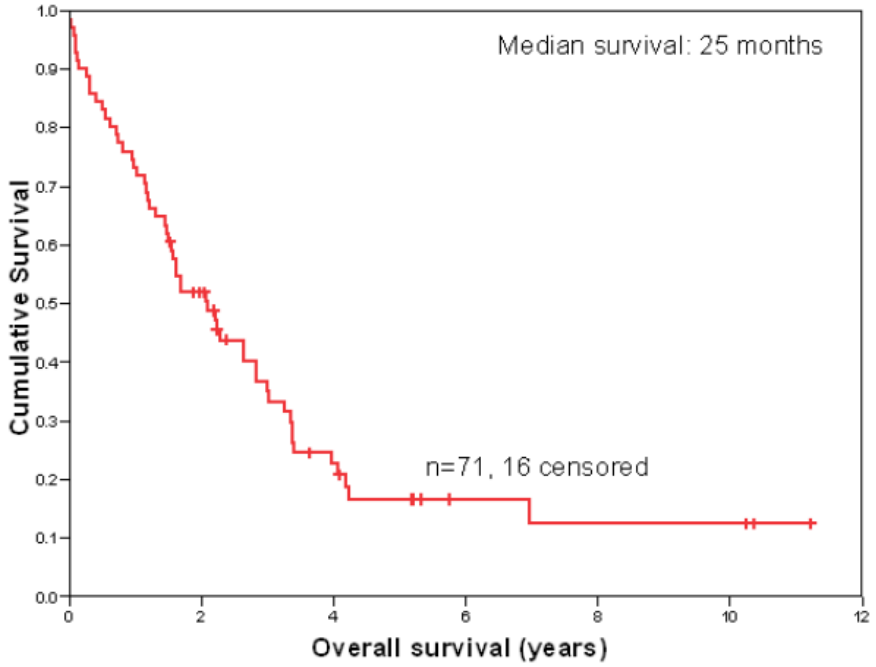


Fig 1.
Overall Survival Following HDT-ASCT Failure

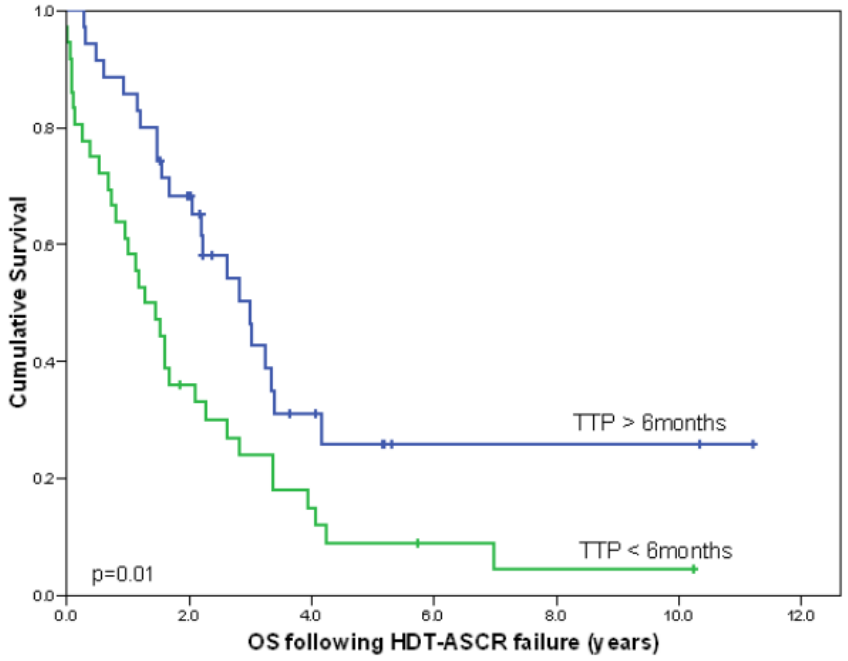
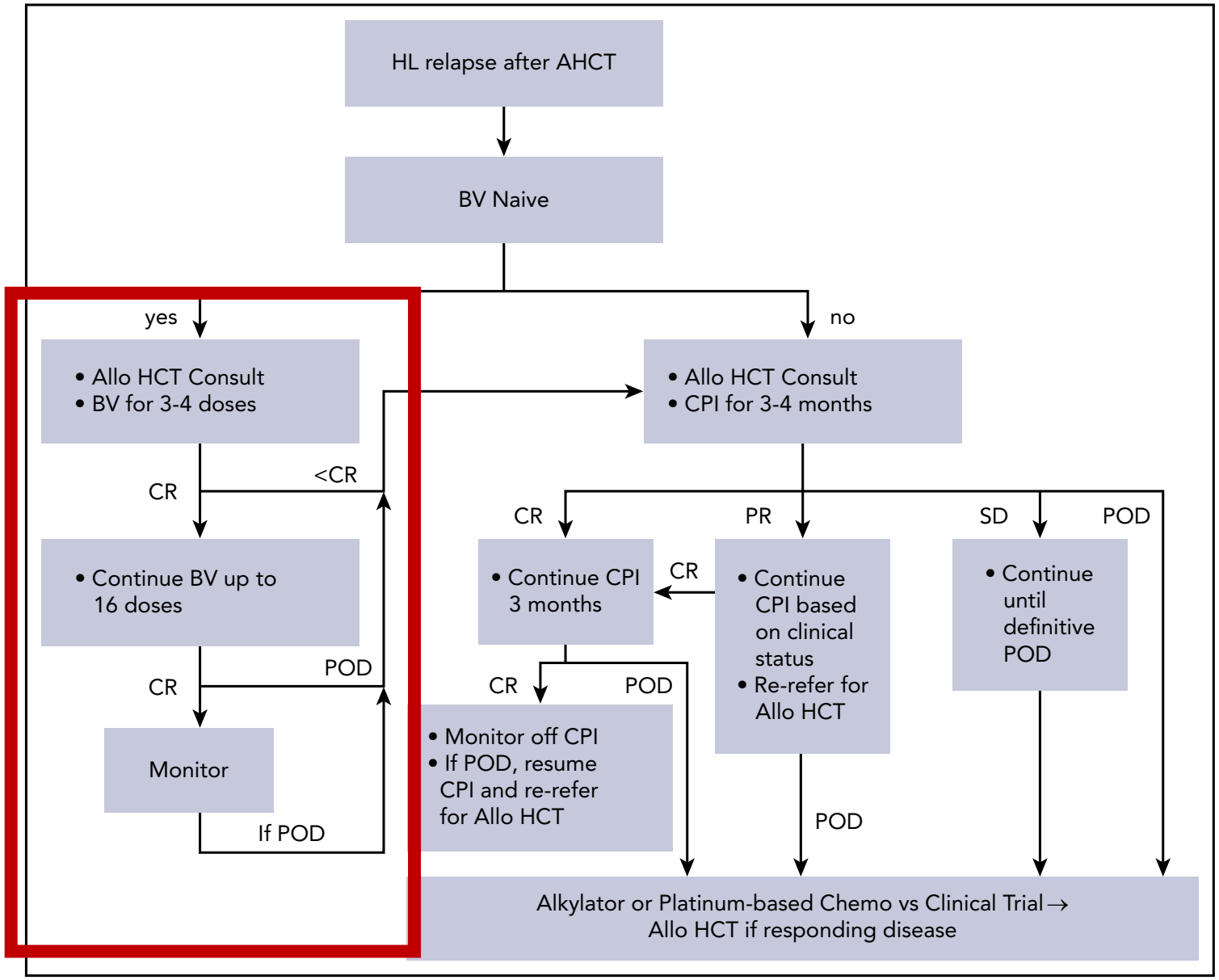


Fig 2.
Survival following relapse within 6 months and after 6 months from HDT-ASCT

Moskowitz AJ. *Br J Haematol*.2009

Allogenic in HL



Shah G. *Blood Review*. 2018

Brentuximab

Table 2. Key Response Results

Parameter	No. of Patients (N = 102)	%
Objective response	76	75
Complete remission	35	34
Partial remission	41	40
Stable disease	22	22
Progressive disease	3	3
Not evaluable	1	1
Duration of objective response, months		
Median	6.7	
95% CI	3.6 to 14.8	
Duration of response for patients with complete remission, months (n = 35)		
Median	20.5	
95% CI	10.8 to NE	
Progression-free survival, months		
Median	5.6	
95% CI	5.0 to 9.0	
Overall survival, months		
Median	22.4	
95% CI	21.7 to NE	

Abbreviation: NE, not estimable.

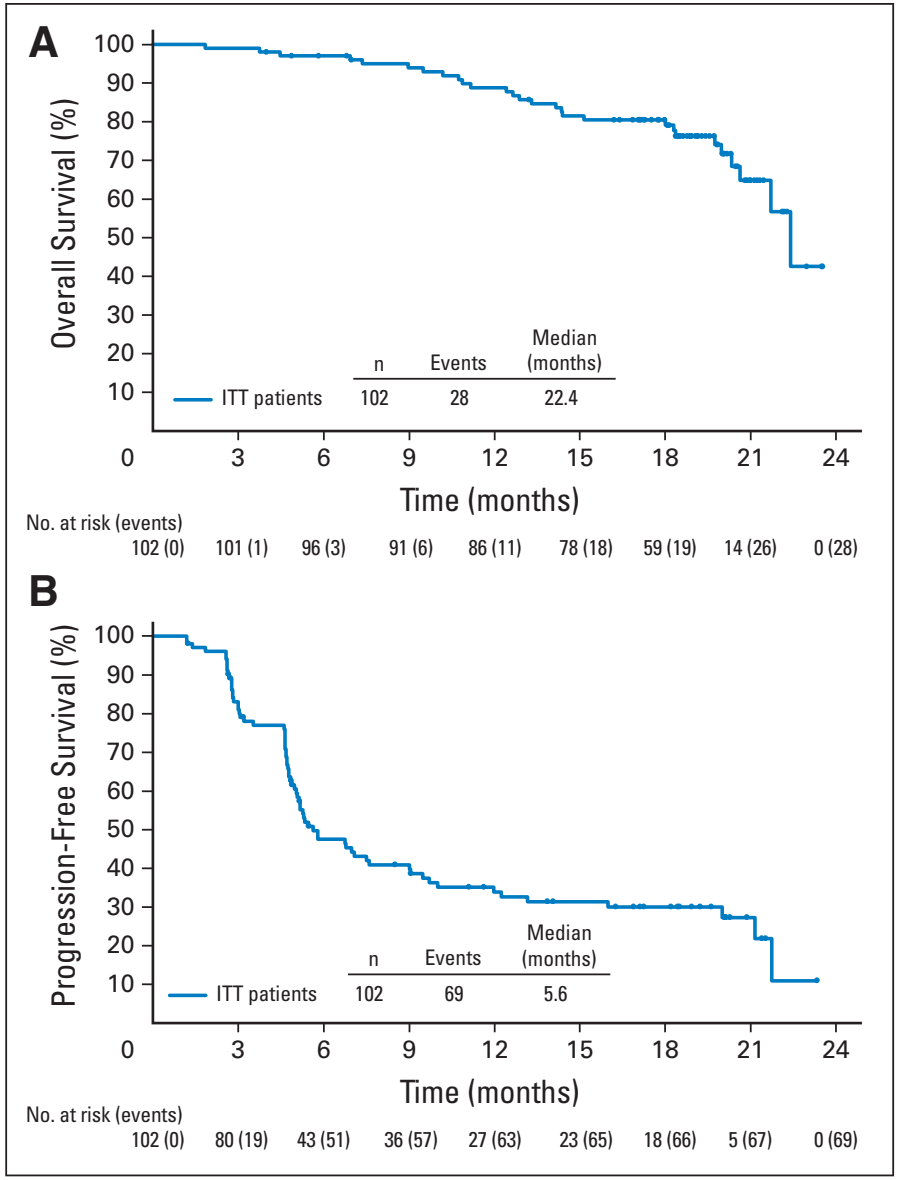


Fig 2. Secondary end points of overall survival (A) and progression-free survival (B). ITT, intent to treat.

Younes A. *JCO*. 2012

Allo pos iPD-1

Table 1: Baseline Characteristics of Patients

Patient Characteristics	N=39 (100%)[a]
Gender	
Male	20 (51%)
Female	19 (49%)
Age at transplant, years (median, range)	34 (21-67)
Institution [b]	
DFCI/BWH	19 (49%)
Mayo Clinic	3 (8%)
MSKCC	3 (8%)
University of Bologna	4 (10%)
Humanitas Clinical & Research Center	9 (23%)
Chaim Sheba	1 (3%)
Disease [c]	
Classical HL	31 (79%)
DLBCL	2 (5%)
FL	2 (5%)
PMBCL	2 (5%)
EATL	1 (3%)
MCL	1 (3%)
Total number of systemic treatments (median, range)	4 (2-8)
Radiation therapy	25 (64%)
Prior autologous transplant	32 (82%)
Number of cycles of PD-1 inhibitor (median, range)	8 (3-27)
PD-1 inhibitor received	
Nivolumab[d]	28 (72%)
Pembrolizumab	11 (28%)
Best response to PD-1 inhibitor	
Complete response	14 (36%)
Partial response	10 (26%)
Stable disease	7 (18%)
Progressive disease	8 (21%)
Number of patients with immune-related adverse events while on PD-1 inhibitor (prior to transplant):	4 (11%)
Colitis	2 (6%)
Pneumonitis	2 (6%)
Hepatitis	1 (3%)
Uveitis	1 (3%)
Interval between last PD-1 treatment and HSCT (days)	62 (7-260)
Patients with intervening salvage therapy between PD-1 and HSCT	19 (49%)
Graft source	
Peripheral blood (PB)	28 (72%)
Bone marrow (BM)	11 (28%)
Donor type	
Matched-related donor (MRD)	9 (23%)
Matched-unrelated donor (MUD)	12 (31%)
Haplo-identical transplant	14 (36%)
Mismatched-unrelated donor (MMUD) [e]	4 (10%)
Disease status at allogeneic transplant	
Complete response	25 (64%)
Partial response	11 (28%)
Stable disease	2 (5%)
Progressive disease	1 (3%)
Conditioning regimen [f]	
Reduced intensity conditioning (RIC)	38 (97%)
Cy, Flu, TBI	13 (33%)
Bu, Flu	11 (28%)
Flu, Mel	5 (13%)
TT, CY, Flu, ATG	4 (10%)
TT, CY, Flu, TBI	2 (5%)
TT, Flu, Mel	2 (5%)
TT, Flu	1 (3%)
Myeloablative conditioning (MAC)	1 (3%)
Bu, Flu	1 (3%)
GVHD prophylaxis [g]	
PCY	7 (18%)
PCY, Tacrolimus, MMF	7 (18%)
Tacrolimus, Sirolimus, MTX	6 (15%)
Tacrolimus and MTX	6 (15%)
CSA, MTX	5 (13%)
Other [h]	8 (21%)

[a] Percentages may not add to 100 because of rounding

Merryman R. *Blood*. 2017

Table 2: Toxicity, Outcomes, and Deaths

Toxicity and Outcomes (1 year cumulative incidence)		
	All patients (N = 39)	**HL subset (N = 31)**
Acute GVHD	**% (95% CI)**	**% (95% CI)**
Grade II-IV	44% (28-59)	45% (27-62)
Grade III-IV	23% (11-37)	26% (13-55)
Grade IV	13% (5-25)	13%(4-27)
Chronic GVHD	41% (22-60)	33% (13-55)
Hepatic SOS	8% (2-19)	6% (1-19)
OS	89% (74-96)	90% (71-97)
PFS	76% (56-87)	74% (50-88)
CIR	14% (4-29)	16% (3-36)
NRM	11% (3-23)	10% (3-25)
Deaths		

Pt #	**Histology**	**Donor Source** [a]	**Graft Source** [b]	**Interval between PD-1 and HSCT**	**Day of death**	**Complications**
3	Mixed cellularity HL	MMUD [c]	PB	17 days	Day 100	Febrile syndrome, hyperacute grade IV acute GVHD, bacteremia, acute kidney injury, hypoxic respiratory failure
8	Nodular sclerosing HL	MUD	PB	100 days	Day 123	Febrile syndrome, hyperacute grade IV acute GVHD, bacteremia, diffuse alveolar hemorrhage, posterior reversible encephalopathy syndrome
14	Nodular sclerosing HL	Haplo-identical	BM	156 days	Day 51	Severe SOS and renal failure requiring central veno-venous hemofiltration (CVVH)
18	Enteropathy-associated T cell lymphoma	MUD	PB	49 days [d]	Day 35	Grade IV acute GVHD, hepatic encephalopathy, and hypotension

Merryman R. *Blood*. 2017

Allo in H

Table 3

Study	
Robinson et al	
Sureda et al. [	
Sarina et al. [3	
Thompson et a	
Peggs et al. [3	
Alvarez et al.	elapse)
Anderlini et al	
Majhail et al.	
Devetten et al	

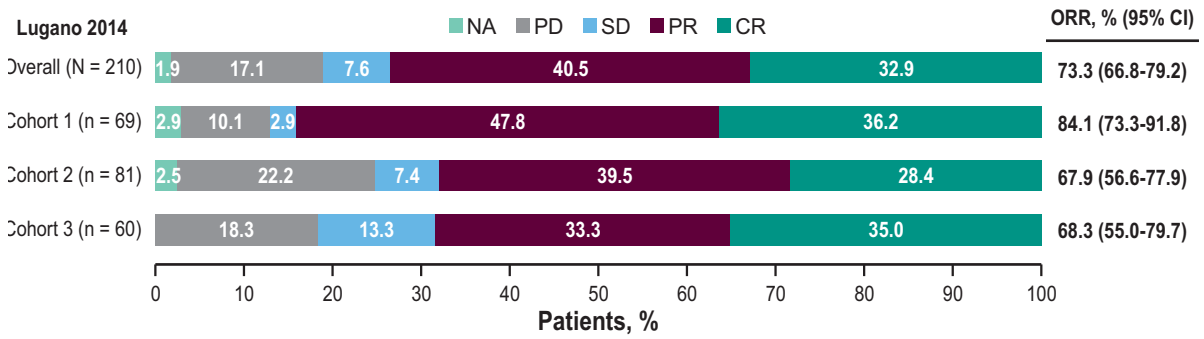
Note. BM = ched
related do ival;
RIC = reduc

10 alo in HL. 8 alives/6 without HL. 4 after iPD-1. (3 CR and 1 PR- 1 recidive). 1 death with hyperacute GVHD. +2 patients in PR with PD- now waiting.

Jehava Y. *Hematol Oncol Stem Cell Ther*. 2017

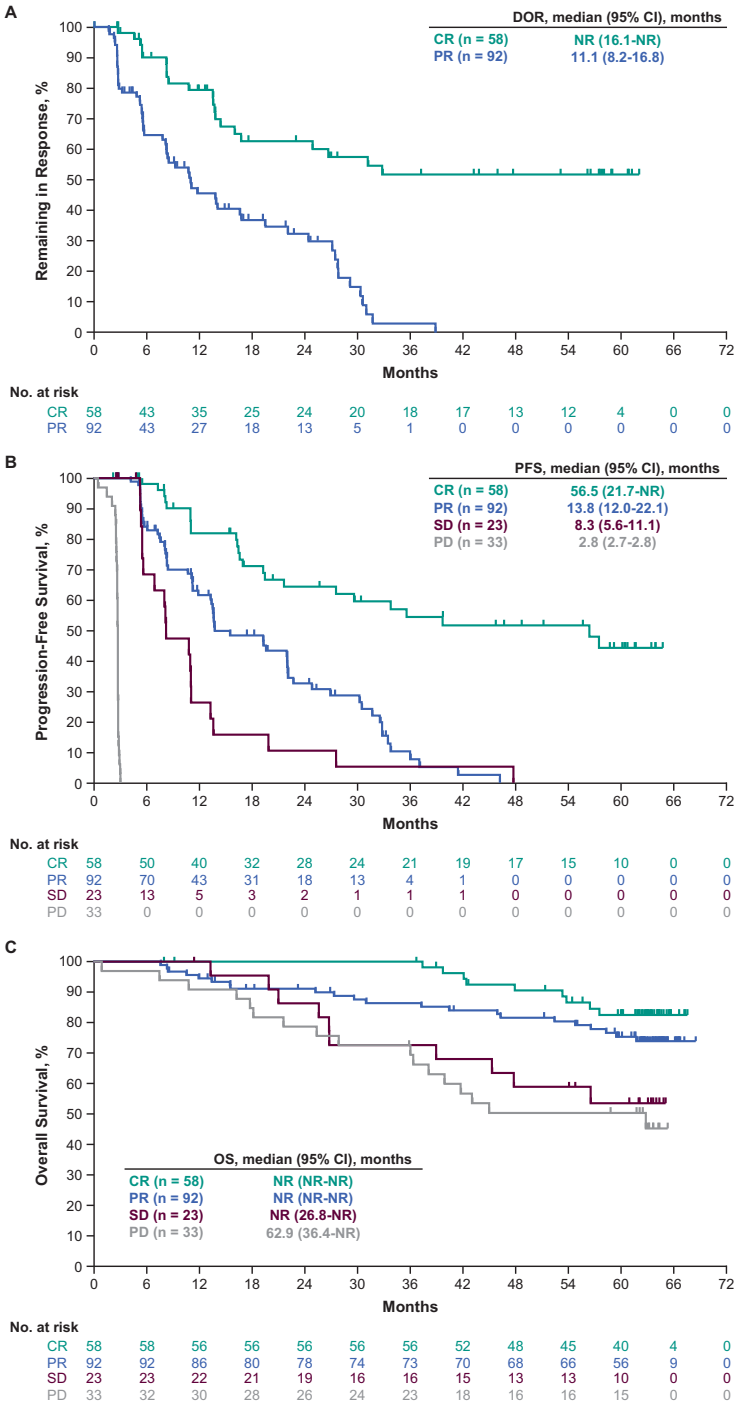
Pembro mono- 5 years keynote-087

Cohort 1: progression after AUTO and BV
Cohort 2: no answer AUTO
Cohort 3: progression after TMO without BV

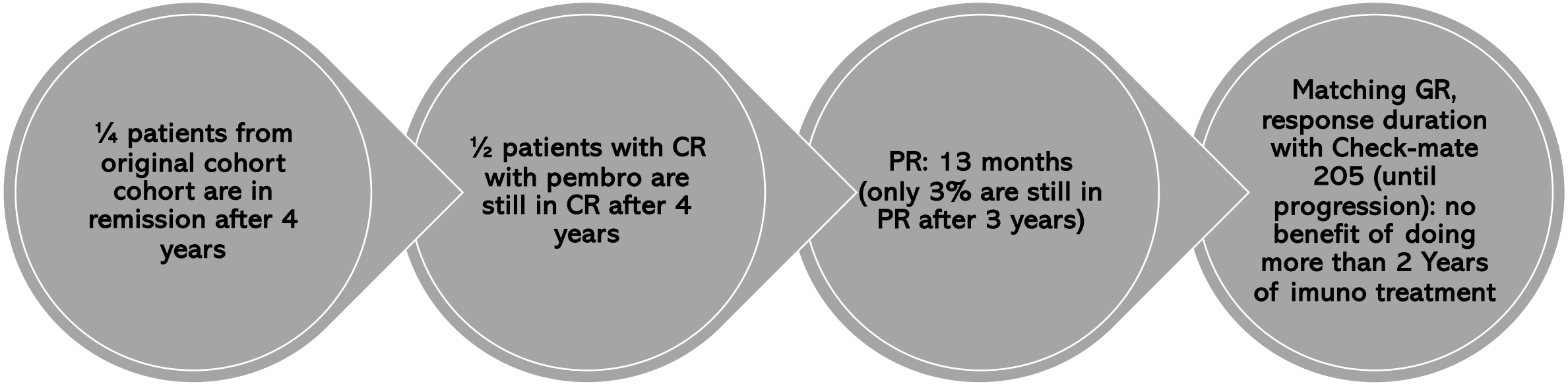


Armand P. *Blood* .Jun 2023

Figure 3



Pembro mono- 5 years keynote-087



Armand P. *Blood* .Jun 2023

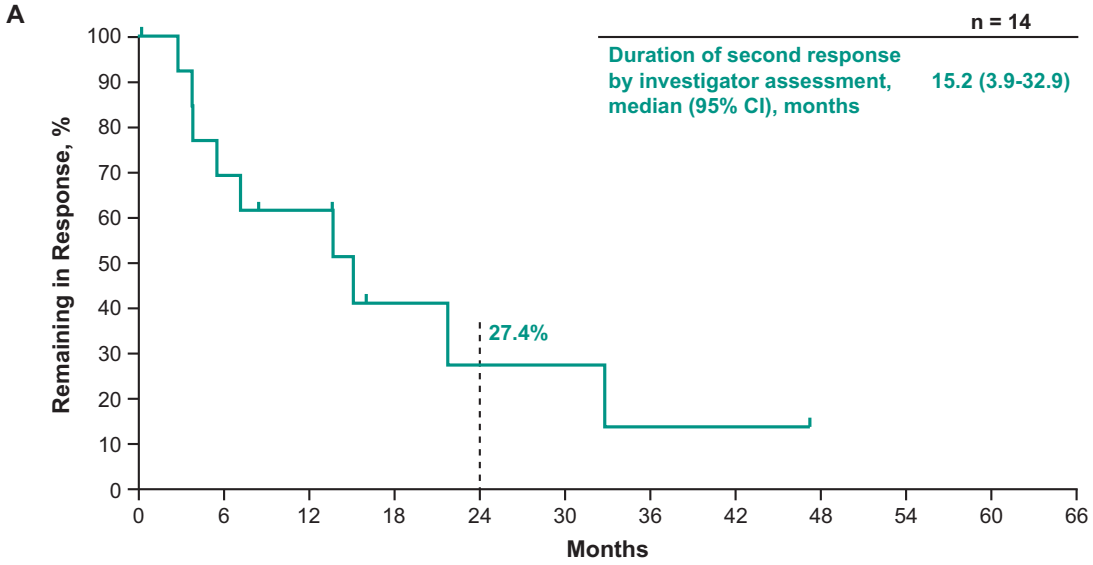
Pembro re-exposition

Table 1. Summary of overall response per the IWG 2007 criteria by investigator assessment in patients who received second-course treatment and had response data at data cutoff[a]

	Cohort 1 n = 9	Cohort 2 n = 7	Cohort 3 n = 3	Total n = 19
ORR, % (95% CI)	77.8 (40.0-97.2)	85.7 (42.1-99.6)	33 (0.8-90.6)	73.7 (48.8-90.8)
BOR, n (%)				
CR	1 (11.1)	6 (85.7)	0 (0)	7 (36.8)
PR	6 (66.7)	0 (0)	1 (33.3)	7 (36.8)
SD	1 (11.1)	0 (0)	2 (66.7)	3 (15.8)
PD	1 (11.1)	1 (14.3)	0 (0)	2 (10.5)

[a]One patient was not included because response data were not available at the time of data cutoff.

Figure 4

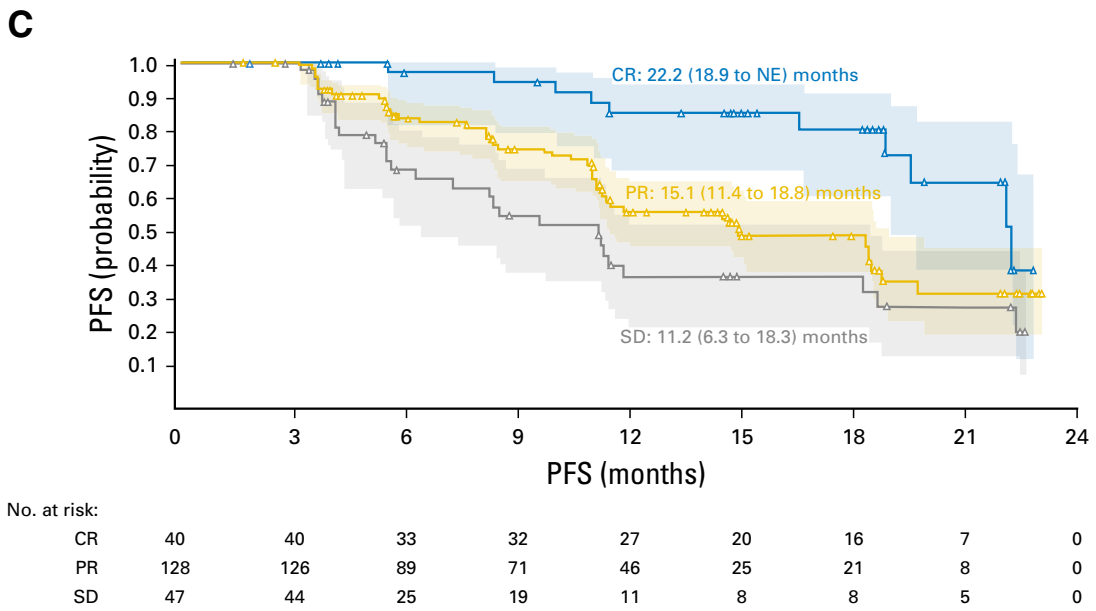


Armand P. *Blood* .Jun 2023

Nivolumab

Table 2. Objective and Best Overall Response per IRC

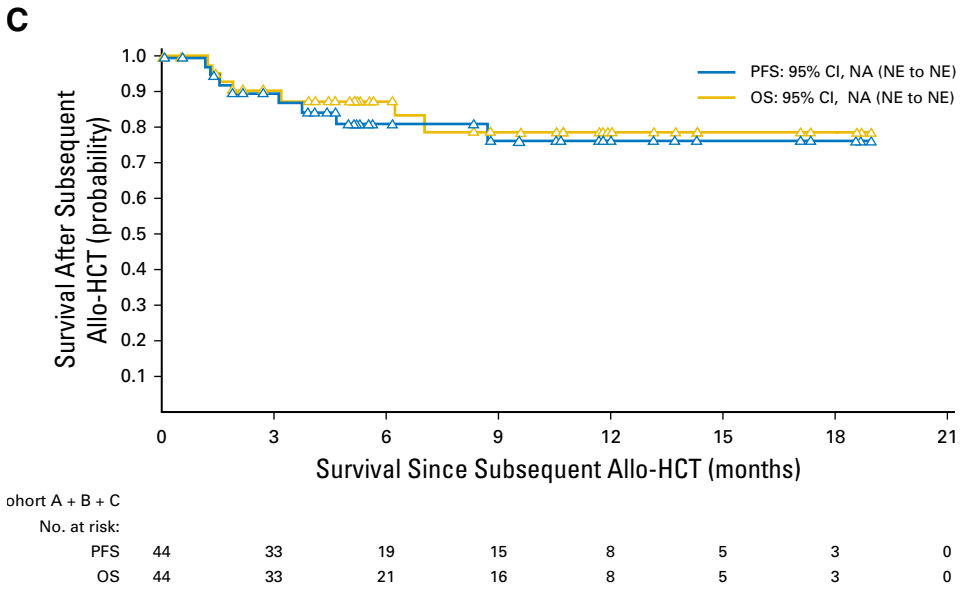
Response	Protocol-Specified Analysis by Cohort			All patients (N = 243)
	BV Naïve: Cohort A (n = 63)	BV After Auto-HCT: Cohort B (n = 80)	BV Before and/or After Auto-HCT: Cohort C (n = 100)	
ORR, % (95% CI)	65 (52-77)	68 (56-78)	73 (63-81)	69 (63-75)
Best overall response				
Complete remission	18 (29)	10 (13)	12 (12)	40 (16)
Partial remission	23 (37)	44 (55)	61 (61)	128 (53)
Stable disease	15 (24)	17 (21)	15 (15)	47 (19)
Progressive disease	7 (11)	6 (8)	10 (10)	23 (9)
Unable to determine	0	3 (4)	2 (2)	5 (2)

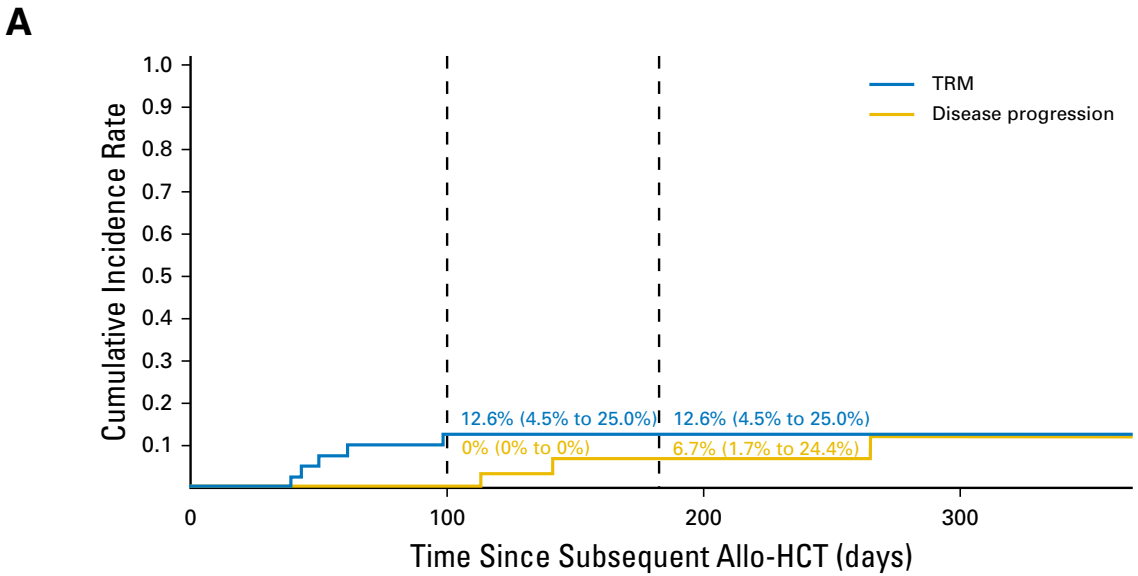


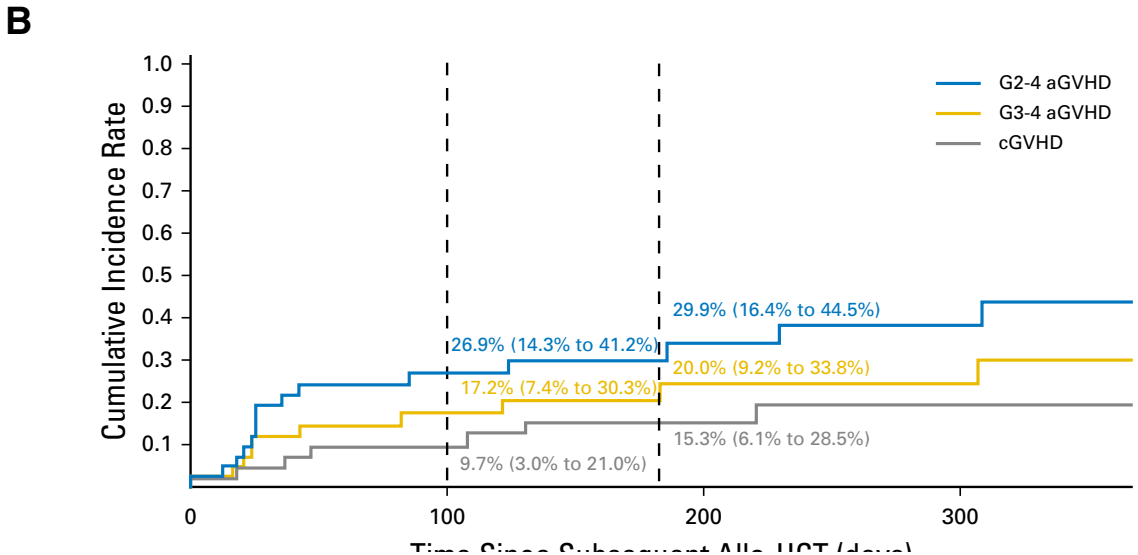
Armand P. *JCO*. 2018

Nivolumab

44 patients







Armand P. *JCO*. 2018

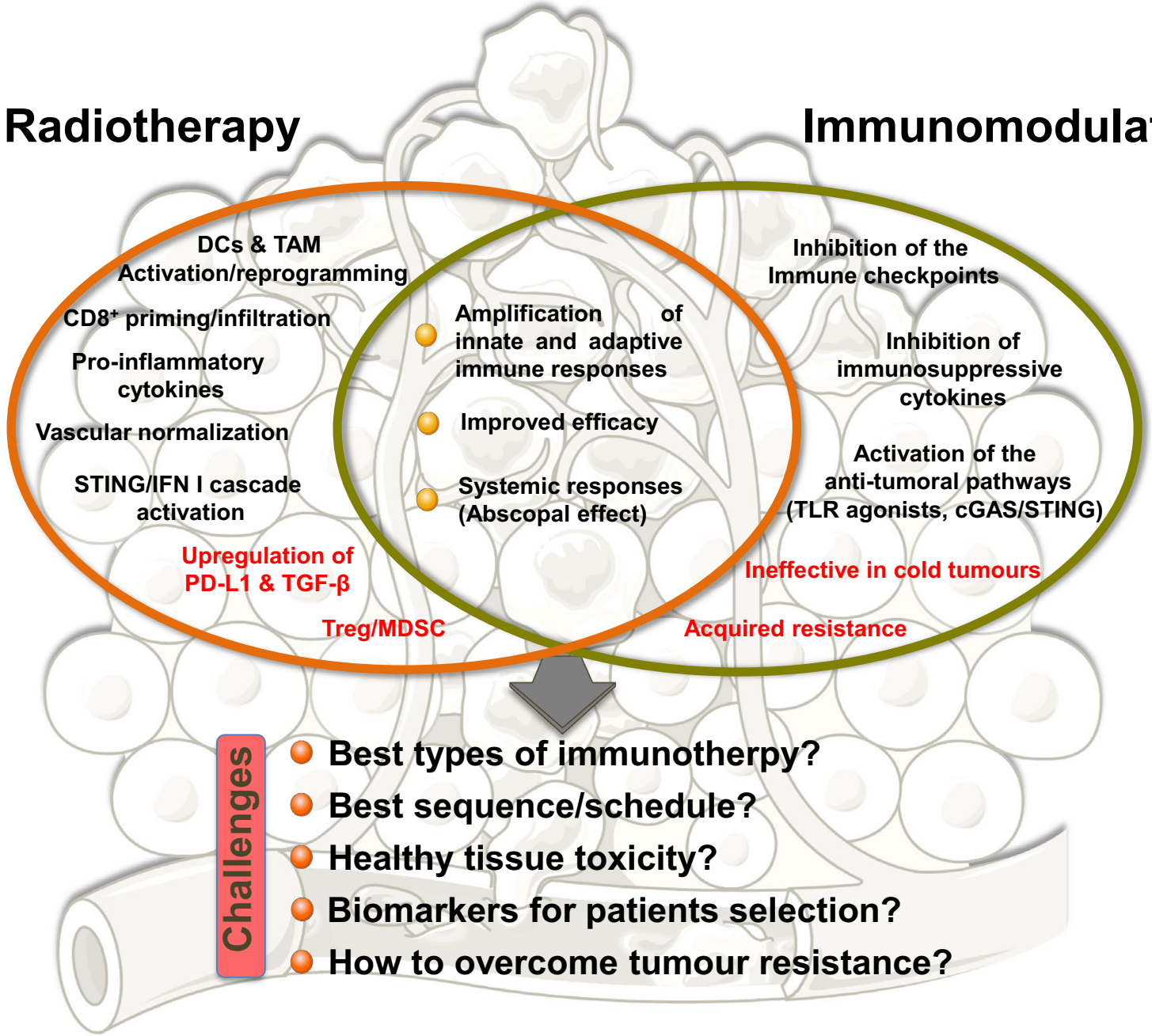


Fig. 2. Strengths, weaknesses and challenges of radiotherapy and immunotherapy combinations.

Mondini M. *Mol Oncology*. 2020

Keynote-204

	Pembrolizumab group (n=151)	Brentuximab group (n=153)
Proportion of patients with objective response	99 (65·6% [57·4–73·1])	83 (54·2% [46·0–62·3])
Best overall response		
Complete response	37 (25%)	37 (24%)
Partial response	62 (41%)	46 (30%)
Stable disease	21 (14%)	36 (24%)
Progressive disease	26 (17%)	28 (18%)
Not evaluable	1 (1%)	1 (1%)
No assessment	4 (3%)	5 (3%)

Data are n (% [95% CI]) or n (%).

Table 2: **Objective response as assessed by blinded independent central review by International Working Group 2007 criteria**

	Pembrolizumab group (n=151)	Brentuximab vedotin group (n=153)
Age, years	36 (28–53)	35 (28–50)
<65	124 (82%)	131 (86%)
≥65	27 (18%)	22 (14%)
Sex		
Male	84 (56%)	90 (59%)
Female	67 (44%)	63 (41%)
Geographical region		
North America	27 (18%)	30 (20%)
Europe	49 (32%)	46 (30%)
Japan	9 (6%)	7 (5%)
Other	66 (44%)	70 (46%)
ECOG performance status		
0	86 (57%)	100 (65%)
1	64 (42%)	53 (35%)
2*	1 (1%)	0
Previous autologous HSCT		
Yes	56 (37%)	56 (37%)
No (ie, ineligible for autologous HSCT)	95 (63%)	97 (63%)
Reason for ineligibility		
Chemorefractory	67 (44%)	66 (43%)
Age	14 (9%)	11 (7%)
Comorbidity	1 (1%)	5 (3%)
Other†	13 (9%)	15 (10%)
Disease status after front-line therapy		
Primary refractory	61 (40%)	62 (41%)
Relapsed <12 months	42 (28%)	42 (27%)
Relapsed ≥12 months	48 (32%)	49 (32%)
Number of previous lines of therapies	2 (2–3)	3 (2–3)
1	27 (18%)	28 (18%)
≥2	124 (82%)	125 (82%)
Previous brentuximab vedotin	5 (3%)	10 (7%)
Previous radiotherapy	58 (38%)	61 (40%)
Bulky disease	35 (23%)	25 (16%)
Baseline B-symptoms‡	43 (28%)	36 (24%)
Baseline bone marrow involvement	12 (8%)	5 (3%)

Data are median (IQR) or n (%). HSCT=haematopoietic stem-cell transplantation. ECOG=Eastern Cooperative Oncology Group. *One patient had an ECOG performance status of 1 at screening (meeting study criteria) which increased to 2 by the first dose of treatment. †Included physician decision, patient refusal, and social reasons. ‡Defined as fever, night sweats, or weight loss.

Table 1: **Baseline characteristics**

Kuruvila J. *Lancet Oncol*.2021

Keynote-2

	Pembrolizumab group (n=151)	Brentu (n=153
Proportion of patients with objective response	99 (65·6% [57·4–73·1])	83 (54
Best overall response		
Complete response	37 (25%)	37 (24
Partial response	62 (41%)	46 (30
Stable disease	21 (14%)	36 (24
Progressive disease	26 (17%)	28 (18
Not evaluable	1 (1%)	1 (1%
No assessment	4 (3%)	5 (3%

Data are n (% [95% CI]) or n (%).

Table 2: **Objective response as assessed by blinded independent central review by In Working Group 2007 criteria**

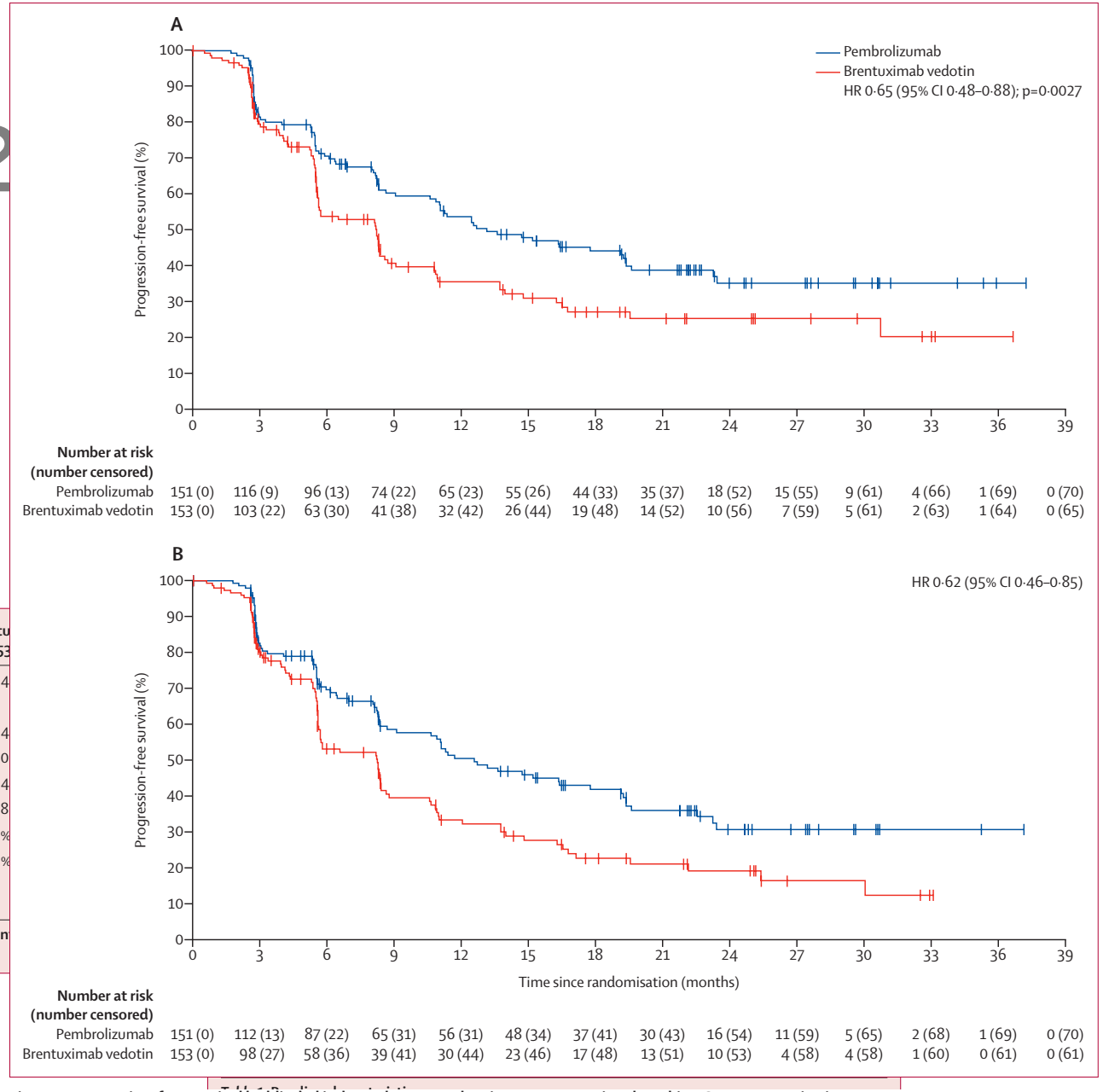
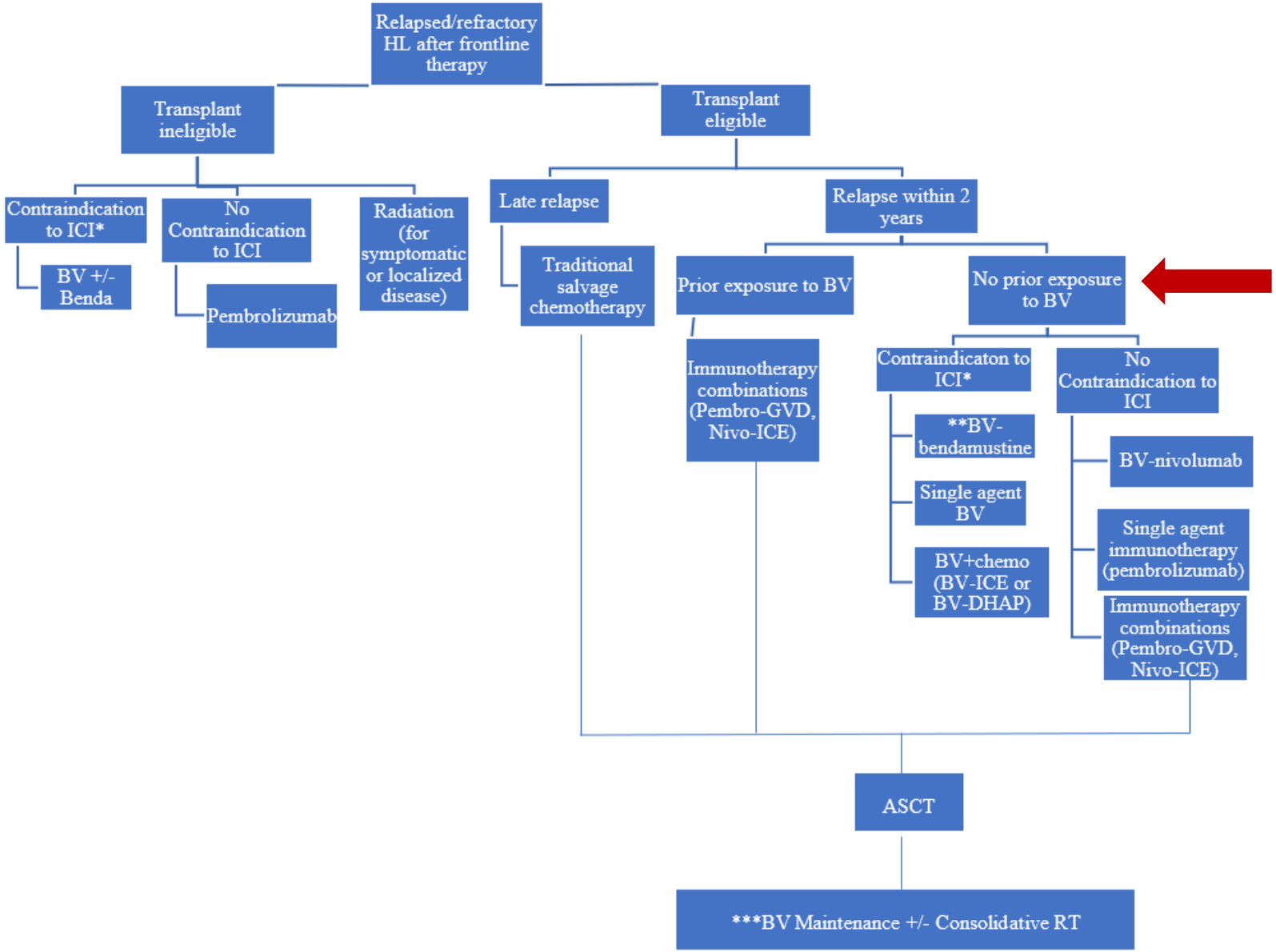


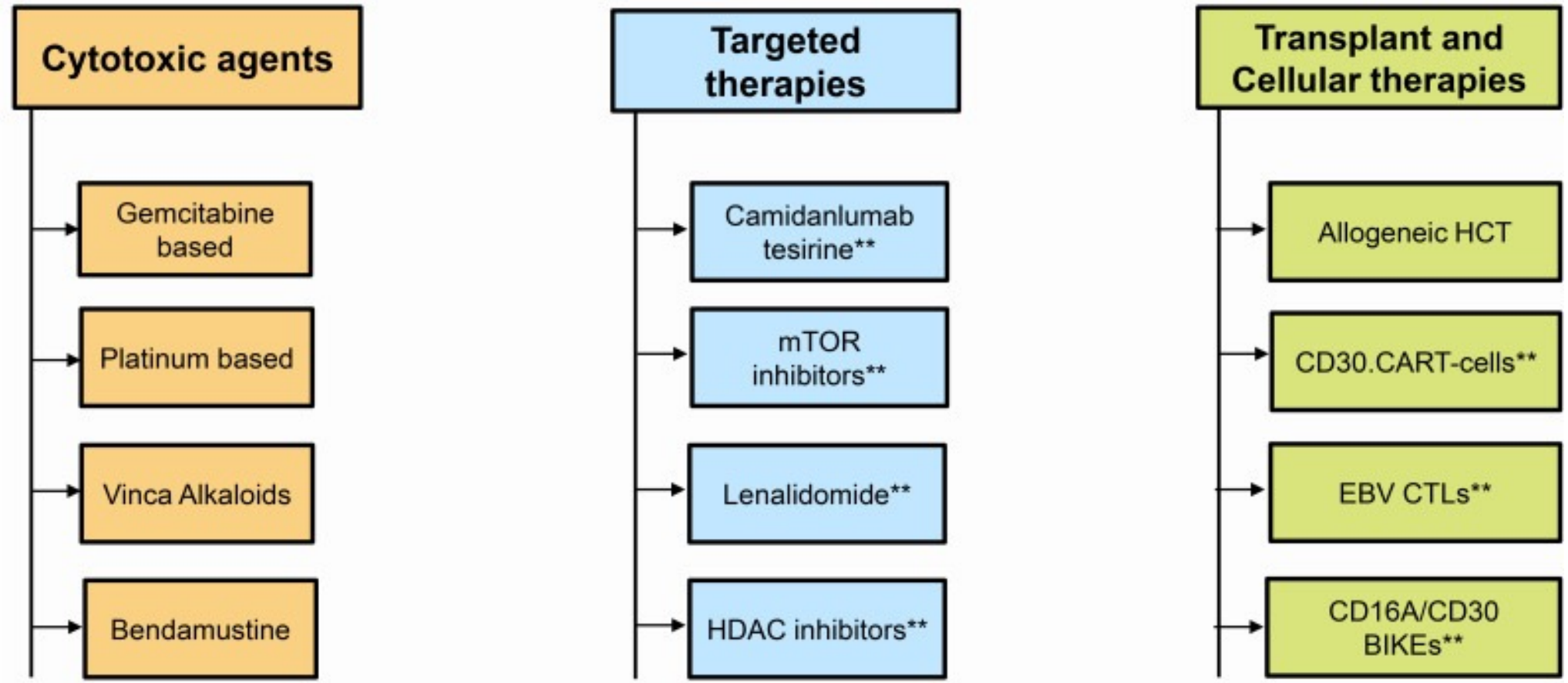
Figure 2: **Progression-free survival by blinded independent central review per International Working Group 2007 criteria**
Progression-free survival including (A) or excluding (B) clinical and imaging data following autologous HSCT or allogeneic HSCT. HSCT=haematopoietic stem-cell transplantation. HR=hazard ratio. HRs based on Cox regression model with Efron's method of tie-handling, with treatment as a covariate stratified by previous autologous HSCT (yes *vs* no) and classical Hodgkin lymphoma status after front-line therapy (primary refractory *vs* relapsed <12 months after completion of front-line therapy *vs* relapsed ≥12 months after completion of front-line therapy). One-sided p value based on log-rank test stratified by the same parameters as the HR.

Kuruvila J. *Lancet Oncol*.2021



Takiar R *Cancers*. 2022

Treatment Options for Double Refractory Hodgkin lymphoma*



*Consider Radiation therapy in relapsed/refractory cHL patients with limited treatment options

**Investigational agents for treatment relapsed/refractory cHL

Epperla N. *Hematol Am Soc Educ*. 2021

Everolimus

1) 21 Years old girl, HL IIIB IPS 3. VI ABVD= Primary refractory
2) III ICE- PR- autoPBSCT- CR
3) 3 months- recidive
4) Brentuximab 7 cycles- progression
5) Everolimus 2 Years- PR with very good ECOG status
6) Nivo approved in Brazil- I switched to a more effective protocol
7) Clinical and CT progression after 6 months
8) Return everolimus= great response. PR
9) II Benda-brentuxi- CR- alo PBSCT
10) Nowadays: doctor specializing in Otorrino

Original article

Everolimus as a single agent in refractory or relapsed Hodgkin's lymphoma: the Brazilian Named Patient Program Experience

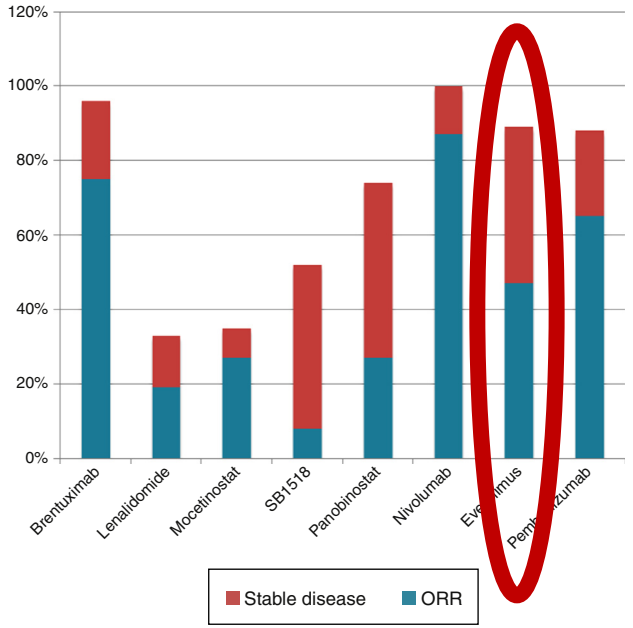
Talita Máira Bueno da Silveira da Rocha, Sergio Costa Fortier, Thais Rodrigues da Cunha Fischer, Guilherme Fleury Perini, Rafael Dezen Gaiolla, Laura Fogliatto, Marcia Torresan Delamain, Andressa Fragoso da Costa, Nelson Siqueira de Castro, Wolney Gois Barretos, Cármino Antonio de Souza, Valéria Buccheri, Carlos Sérgio Chiattone*

Faculdade de Ciências Médicas da Santa Casa de São Paulo (FCMSCSP), São Paulo, SP, Brazil

Table 1 – Patient characteristics ($n = 33$).

Characteristic	Number (%)
Stage at diagnosis	
Early	3 (9%)
Advanced	29 (87%)
NA	1 (3%)
Gender (male)	20 (60%)
Histologic type	
Classic	33 (100%)
First-line chemotherapy	
ABVD	31 (93%)
COPP	1 (3%)
BEACOPP	1 (3%)
Response to first treatment	
CR	19 (57.5%)
PR	7 (21.2%)
Refractory	7 (21.2%)
Number of lines of treatment	
Median	5
Range	3–7
Time between diagnosis until initial everolimus administration (months)	
Median	59
Range	14–111
Previous HSCT	
None	2 (6%)
Autologous	27 (81.8%)
Allogeneic	2 (6%)
Both	2 (6%)
Age at the time of initial everolimus administration	
Median	29
Range	20–70
Best everolimus response	
CR	2 (6%)
PR	13 (39.4%)
SD	14 (42.4%)
Progression	2 (6%)
NA	2 (6%)

NA: not assessable; ABVD: adryamicin, bleomycin, vinblastine and dacarbazine; COPP: cyclophosphamide, oncovin, procarbazine, prednisone; BEACOPP: bleomycin, etoposide, adriamycin, cyclophosphamide, oncovin, procarbazine, prednisone; CR: complete response; PR: partial response; SD: stable disease.



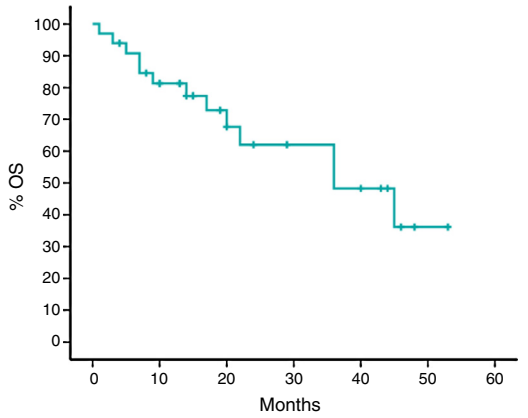
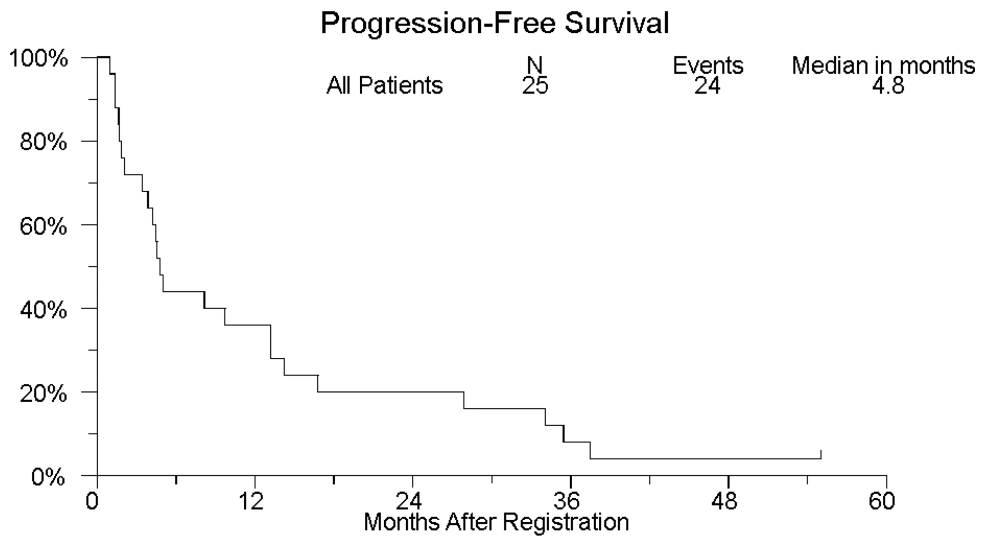


Figure 2 – Overall response in 33 eligible patients treated with everolimus. OS: overall survival.

Vorinostat

Median age (range)	41.6 (19.9–71.1)
Gender Male Female	14 (56%) 11 (44%)
Race White Other Missing	20 (83%) 4 (17%) 1
Performance status 0/1 2	12/12 (48%/48%) 1 (4%)
Disease Status Recurrent Refractory	13 (52%) 12 (48%)
Prior Treatment Bone Marrow Transplant Radiation Therapy Extensive (≥50% of body) Limited (<50% of body) Median # Chemotherapy Regimens (range)	11 (44%) 2 (8%) 16 (64%) 3 (2–5)

Best Response	**N (%)**
Complete response	0
Partial response	1 (4%)
Stable disease	12 (48%)
Progressive disease	8 (32%)
Assessment inadequate	4 (16%)

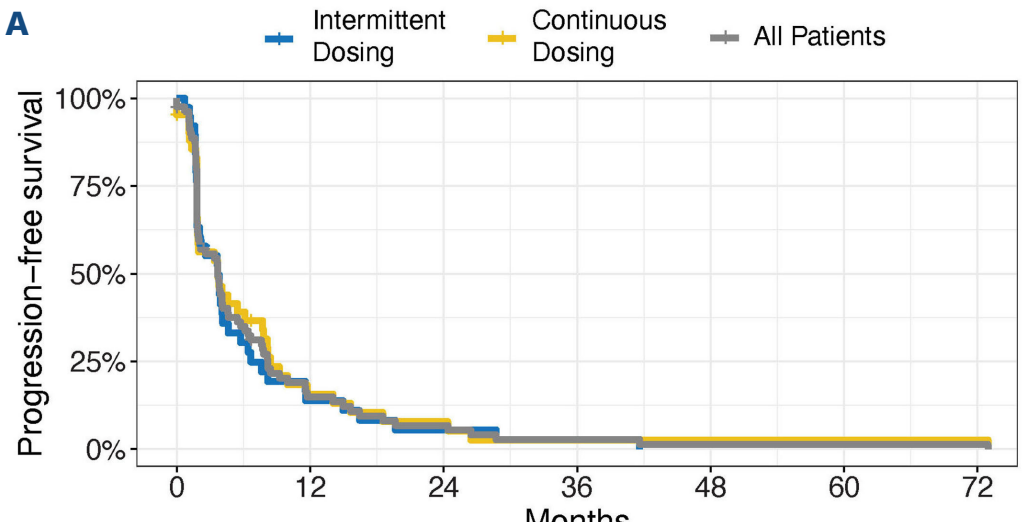


Kirschbaum M. *Leuk Lymphoma*. 2012

Lenalidomida

Table 1. Response rates for entire cohort and per protocol response-evaluable patients for interrupted and continuous cohorts.

Type of response	Entire cohort			Response-evaluable patients		
	Interrupted N=38	Continuous N=42	Combined N=80	Interrupted N=36	Continuous N=36	Combined N=72
CR*, N (%)	1 (2.6)	3 (7.2)	4 (5.0)	1 (2.8)	3 (8.3)	4 (5.5)
PR*, N (%)	6 (15.7)	9 (21.4)	15 (18.8)	6 (16.6)	9 (25.0)	15 (20.8)
SD ≥6 months*, N (%)	6 (13.2)	6 (14.3)	12 (15.0)	6 (16.6)	6 (16.7)	12 (16.7)
ORR (CR+PR)**, N (%)	7 (13.2)	12 (28.6)	19 (23.8)	7 (19.4)	12 (32.4)	19 (26.4)
Disease control rate** (CR+PR+SD ≥6 months), N (%)	13 (34.2)	18 (42.9)	31 (38.5)	13 (36.1)	18 (48.6)	31 (43.1)



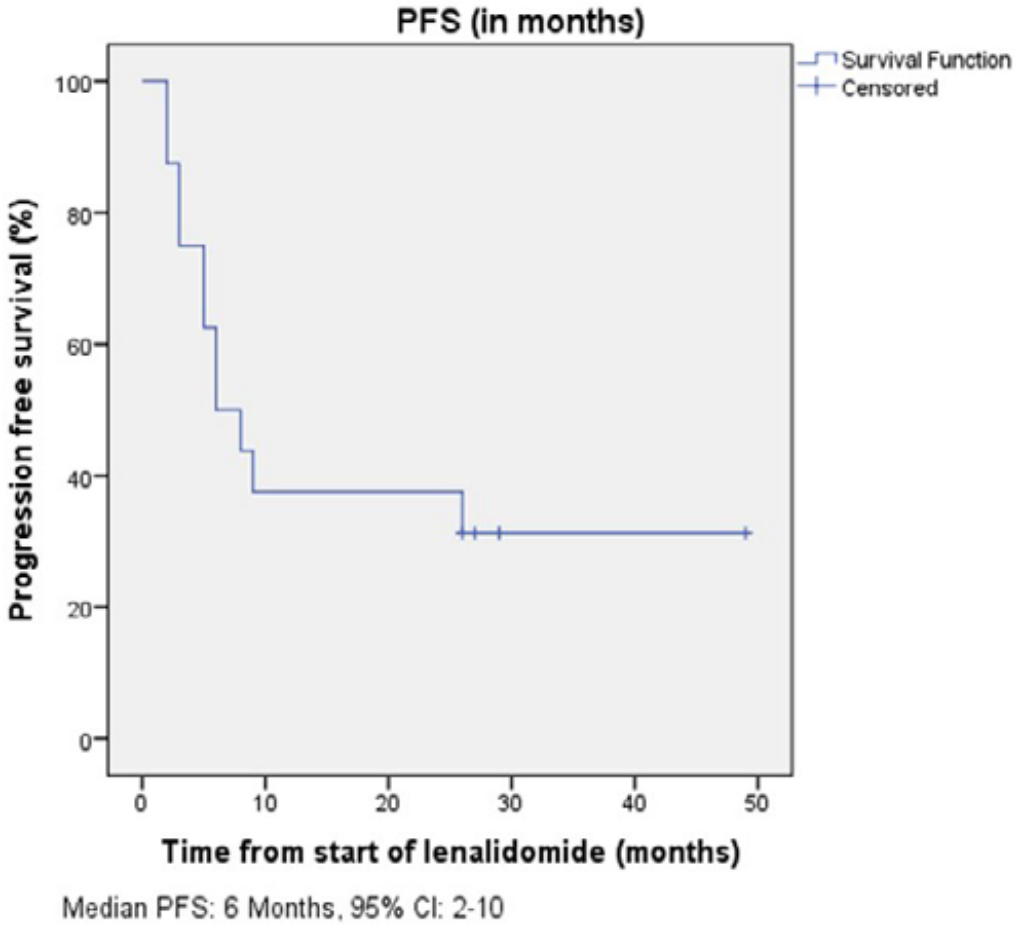
Fehniger T. *Haematologica*. 2024

Lenalidomide pos auto

Table 2. Responses in the entire study cohort of 16 patients

Response rate (N=16)		
Type of Response	Number	Percentage
CR	4	25
PR	4	25
ORR (CR+PR)	8	50
SD>6 Months	1	6.3
Clinical benefit rate (CR+PR+SD>6 Months)	9	56.3
SD<6 Months	1	6.3
PD	6	37.5

CR, complete response; ORR, overall response rate; PR, partial response; SD, stable disease; PD, progressive disease



Kumbhalwar K. *Blood Cell Therapy*. 2023

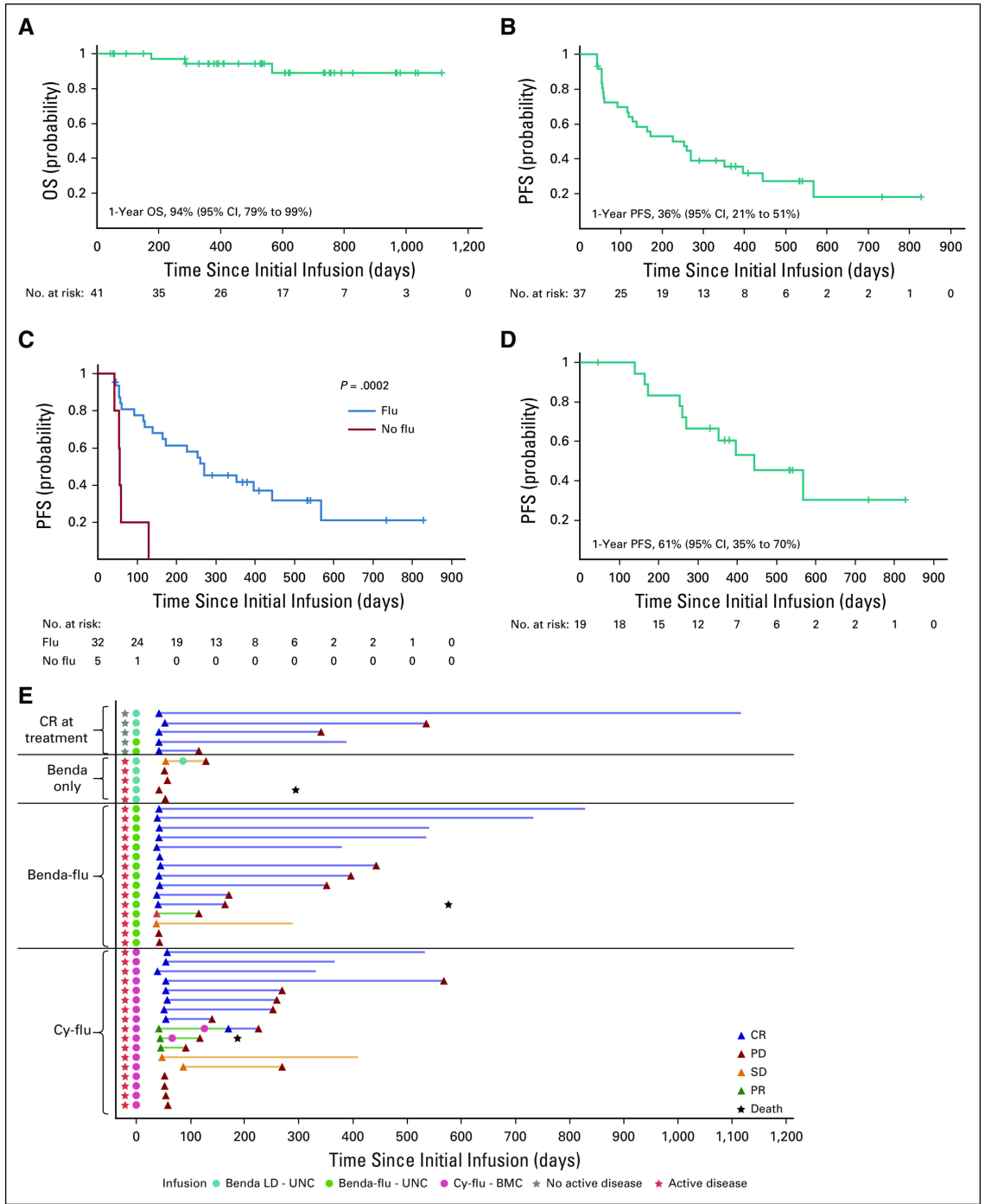
CART anti30

TABLE 3. Clinical Responses in Patients With Measurable Disease at the Time of Treatment

Response	All Patients (N = 37)	Benda (n = 5)	Benda-Flu (n = 15)	Cy-Flu (n = 17)
ORR				
CR + PR	23 (62)	0 (0)	12 (80)	11 (65)
Response rate				
CR	19 (51)	0 (0)	11 (73)	8 (47)
PR	4 (11)	0 (0)	1 (7)	3 (18)
SD	4 (11)	1 (20)	1 (7)	2 (11)
PD	10 (27)	4 (80)	2 (13)	4 (24)

NOTE. Data are No. (%).

Abbreviations: benda, bendamustine; CR, complete response; cy, cyclophosphamide; flu, fludarabine; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease.



Ramos C. *JCO*. 2020

Camindelumab- anti CD25

Response rates in the entire rel/ref cHL patients and at 45 μg/kg and 30 μg/kg			
Response rates	Total (n=75)	45 μg/kg (n=37)	30 μg/kg (n=18)
ORR	71%	87%	50%
CR rate	40	49%	28%
Response rates by prior PD-1 inhibitors (45 μg/kg cohort)			
Response rates	No prior PD-1 inhibitors (9/11)	≤4 months from prior PD-1 inhibitor (14/15)	>4 months from prior PD-1 inhibitor (9/11)
ORR	82%	93%	82%
CR rate	55%	47%	46%

Abbreviations: rel/ref. – relapsed or refractory, cHL – classical Hodgkin lymphoma, ORR – overall response rate, CR – complete response, PD-1 - programmed death-1

TEAEs	Total *n* =77 (%)	45 μg/kg *n* =37 (%)	30 μg/kg *n* =20 (%)
Patients with any Grade≥3 TEAEs	51 (66)	25 (68)	12 (60)
GGT increased	13 (17)	3 (8)	2 (10)
Maculopapular rash	13 (17)	8 (22)	2 (10)
ALT increased	7 (9.1)	3 (8)	0
Anemia	6 (7.8)	3 (8)	2 (10)
AST increased	5 (6.5)	1 (3)	0
GBS/radiculopathy	5 (6.5)	3 (8)	1 (5)
Lipase increased	4 (5.2)	3 (8)	1 (5)
Patients with any TEAE leading to treatment discontinuation	26%	27%	20%

Abbreviations: TEAEs - treatment-emergent adverse events, GGT - gamma glutamyl transferase, ALT - alanine aminotransferase, AST – aspartate aminotransferase, ALP - alkaline phosphatase, GBS - Guillain-Barré syndrome

*observed in at least 5% of patients

Epperla N. *Curr Hematol Malig Report*. 2021

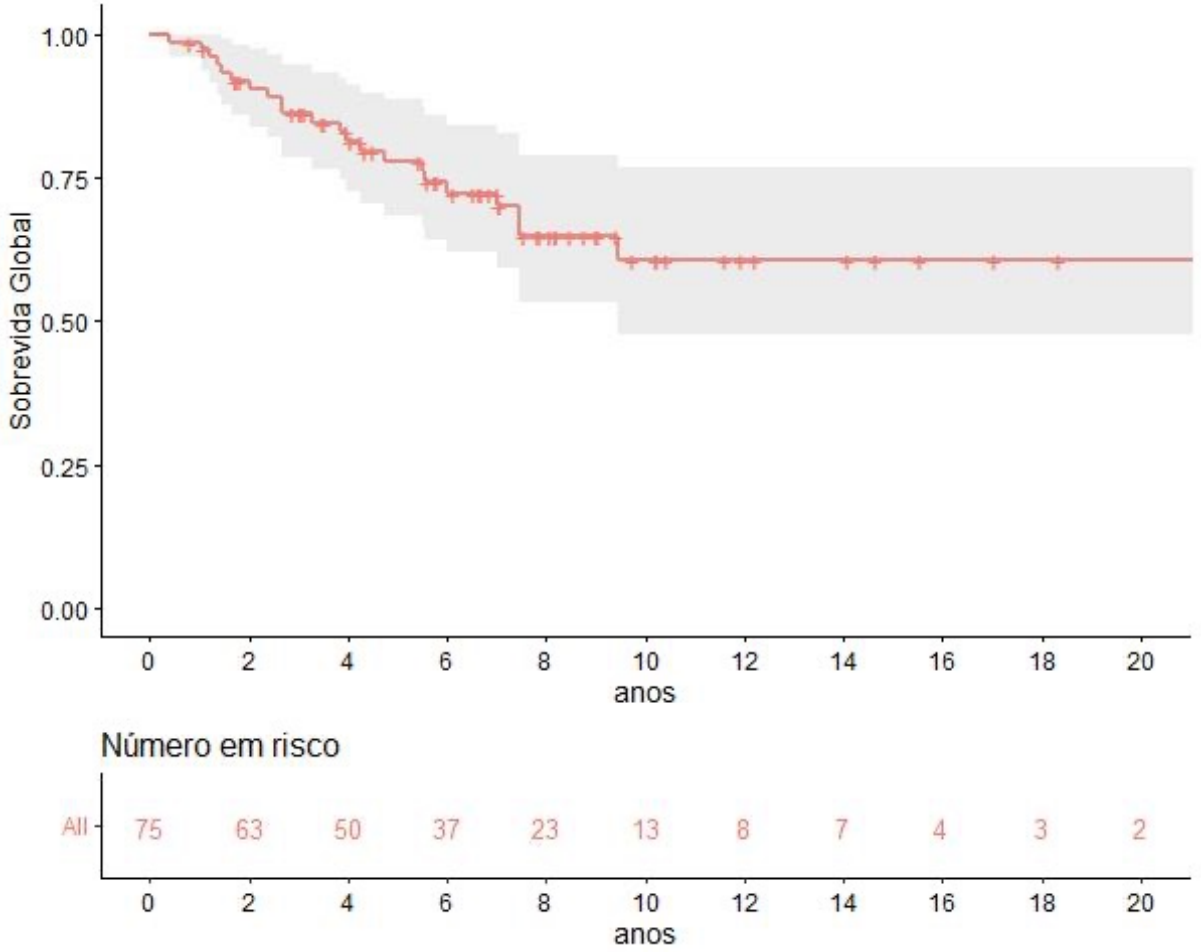
Cohort Santa Casa Recidive Patients

	N 80
Median Age	27 (13-74)
Gender	53% Male
Recidive (73)	34% <12 months
B symptons (74)	32%
Stage (75)I	1,3%
II	29%
III	21%
IV	48%
Bulky (72)	30%
IPS (58) >2	50%
Auto-PBSCT	45%
Immunotherapy	12,5%

Cohort Santa Casa
Recidive patients

FUP: 93 months

4 aloPBSCT- all alive in CR
Death: 23 (no data)
OS 5 Years: 77,9%
OS 10 Years: 60,7%



Conclusions

- Rare disease
- After imuno?
- PBSCT is in check?
- Cure or chronic disease?

Gracias!

talita.rocha@accamargo.org.br