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Educação
e Pesquisa



How to salvage a patient with Hodgkin's Lymphoma: what has changed and what hasn't

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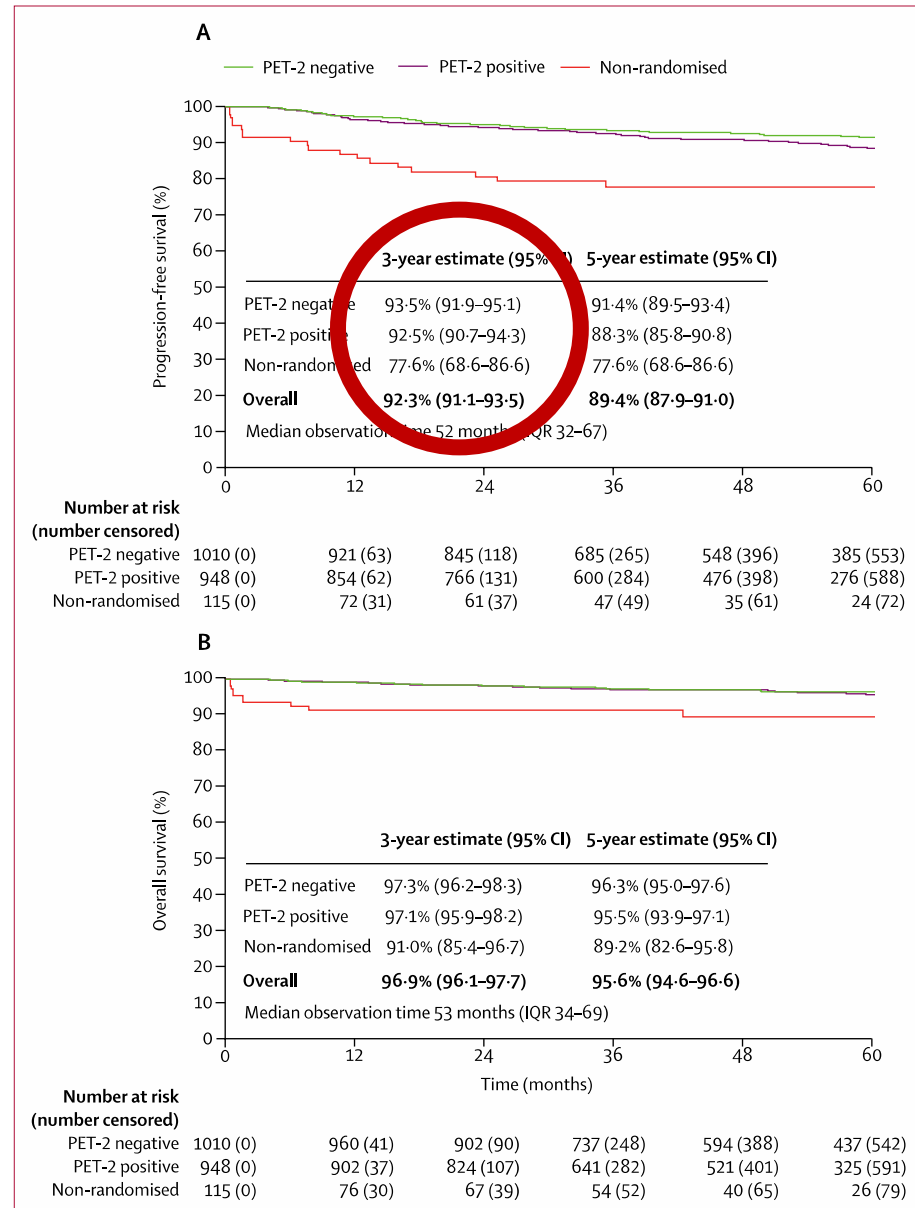
Faculdade Medicina Albert Einstein

Disclosure

No disclosure for this presentation

First line

HD18

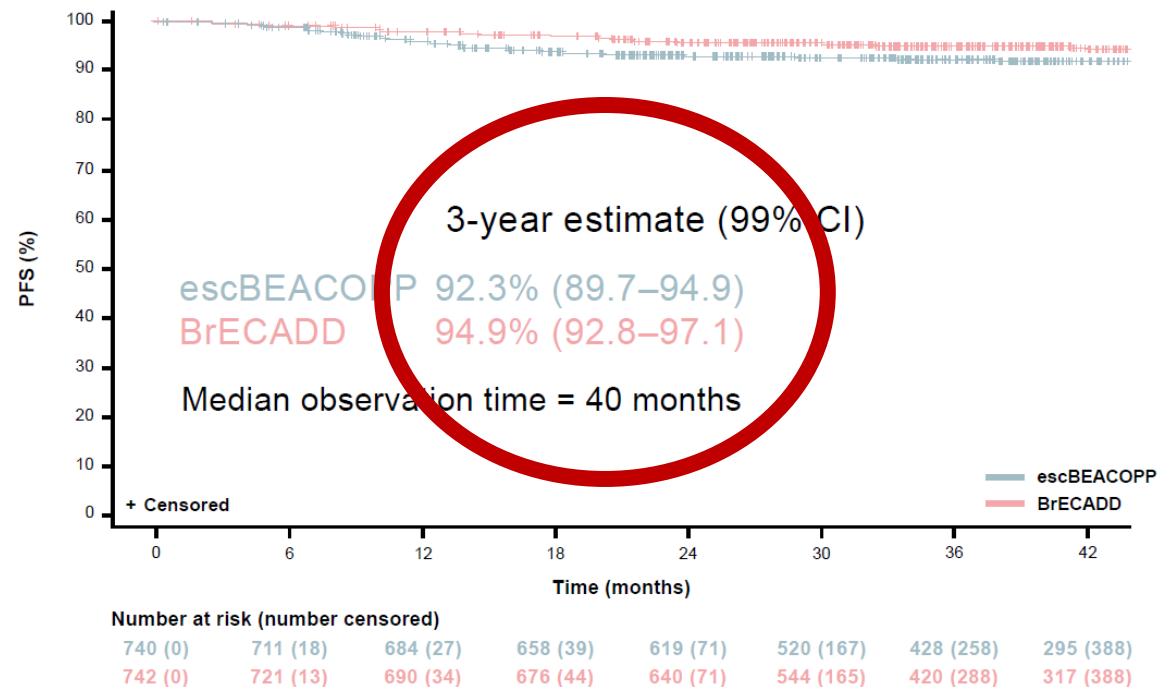


HD21 trial

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



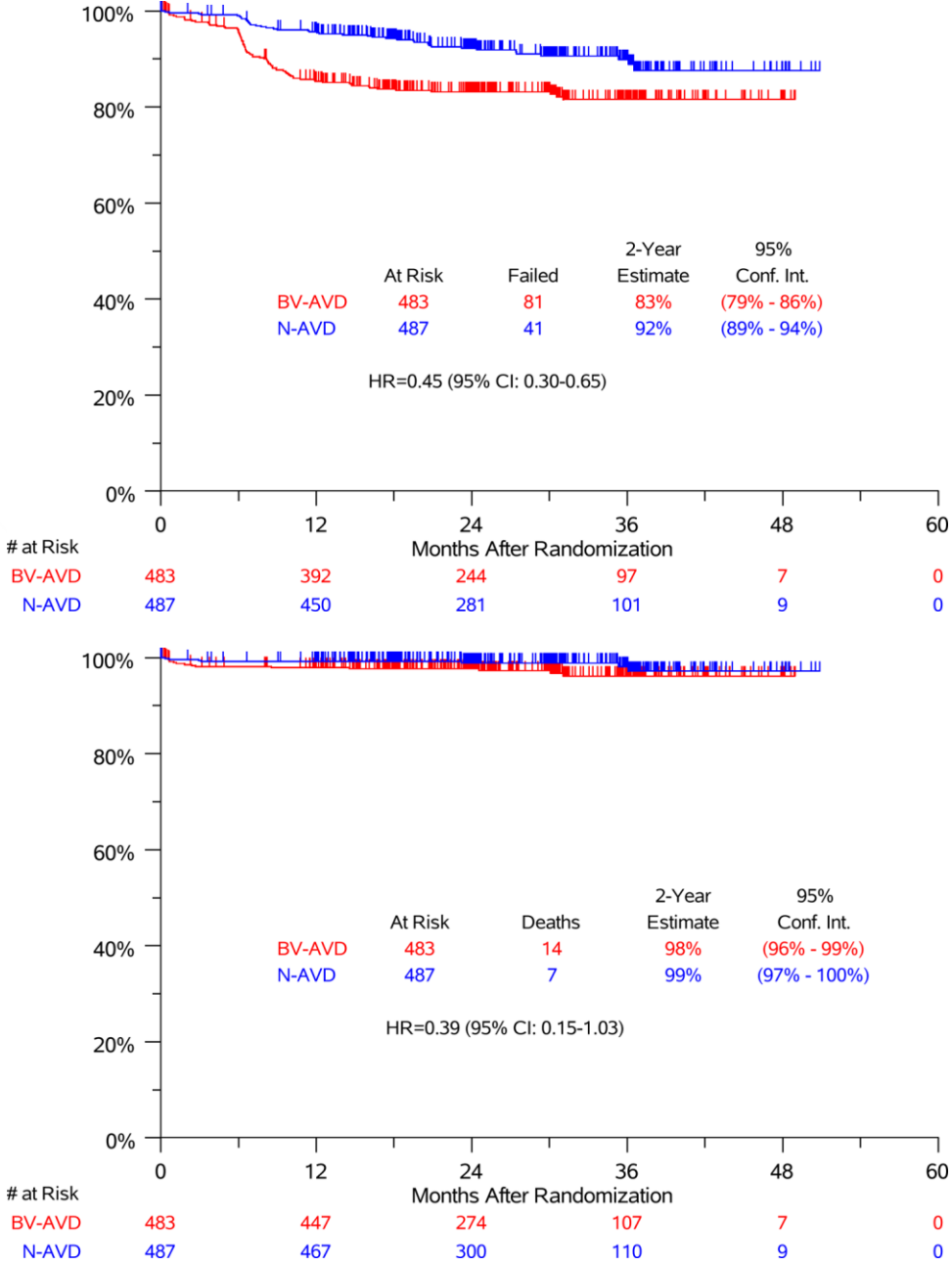


Figure 2:
(A) Progression-Free Survival and (B) Overall Survival in Modified Intent-to-treat Analysis Set

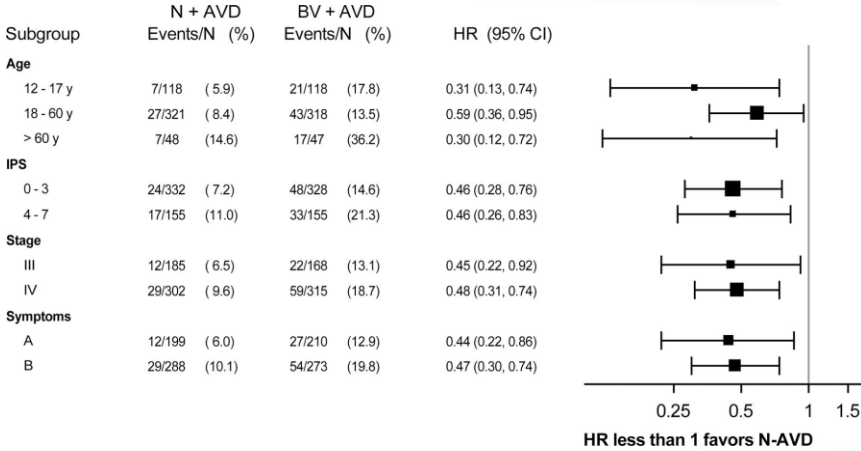
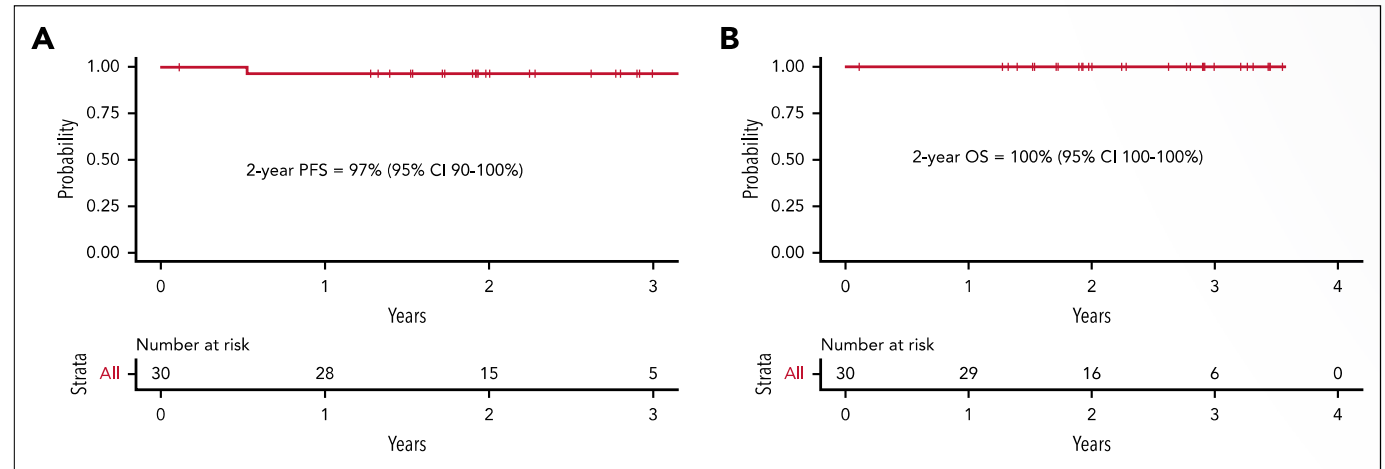


Figure 3:
Subgroup Analysis of Progression-Free Survival in Modified Intent-to-treat Analysis Set

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)



Refractory and recidive disease



Recidive AutoPBSCT

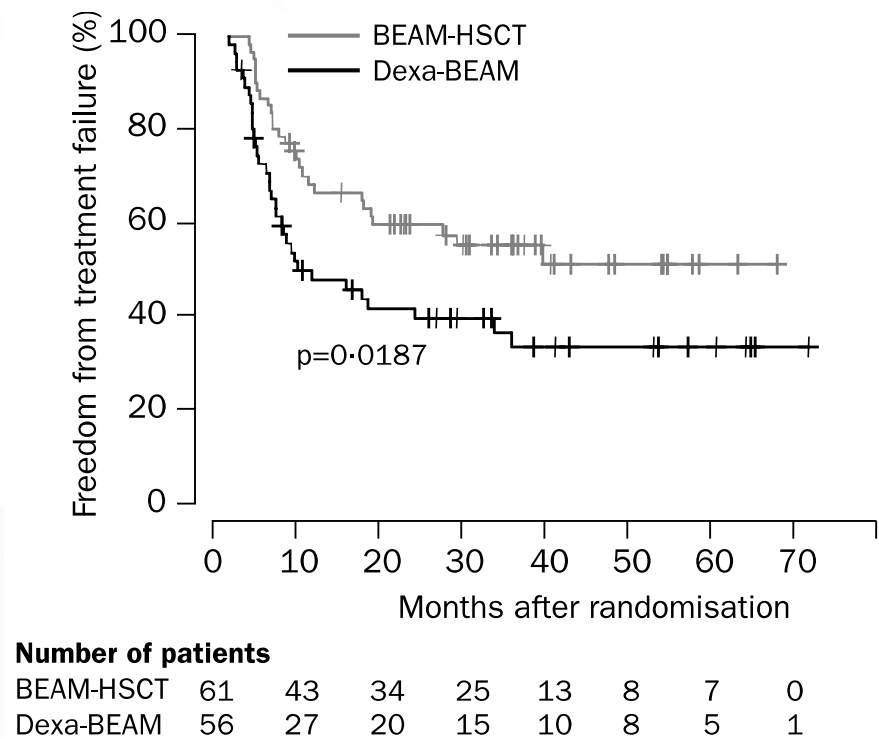
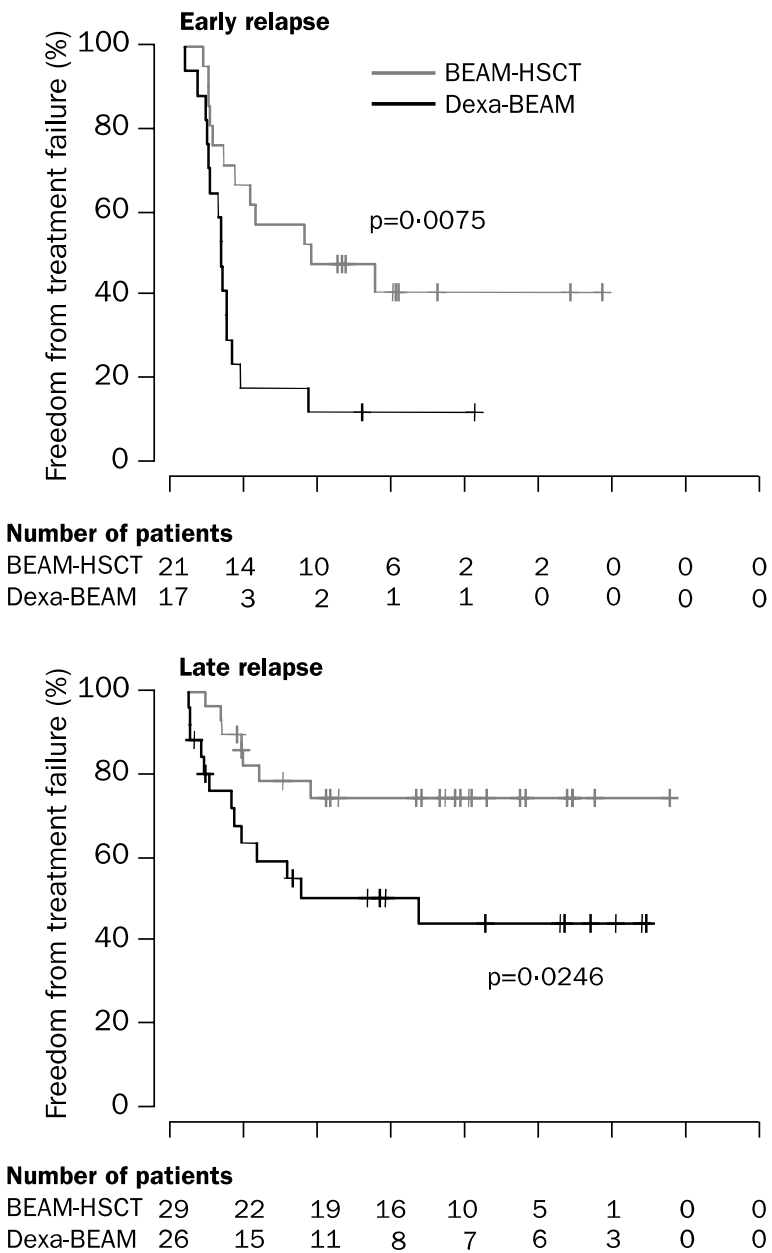


Figure 3: **Freedom from treatment failure for patients with relapsed chemosensitive Hodgkin’s disease**



Pre PBSCT

Early relapse: PFS 44% 4 years

Late relapse: PFS 72% 4 years

Table III

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

Covariates	Univariate		Multivariate	
	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

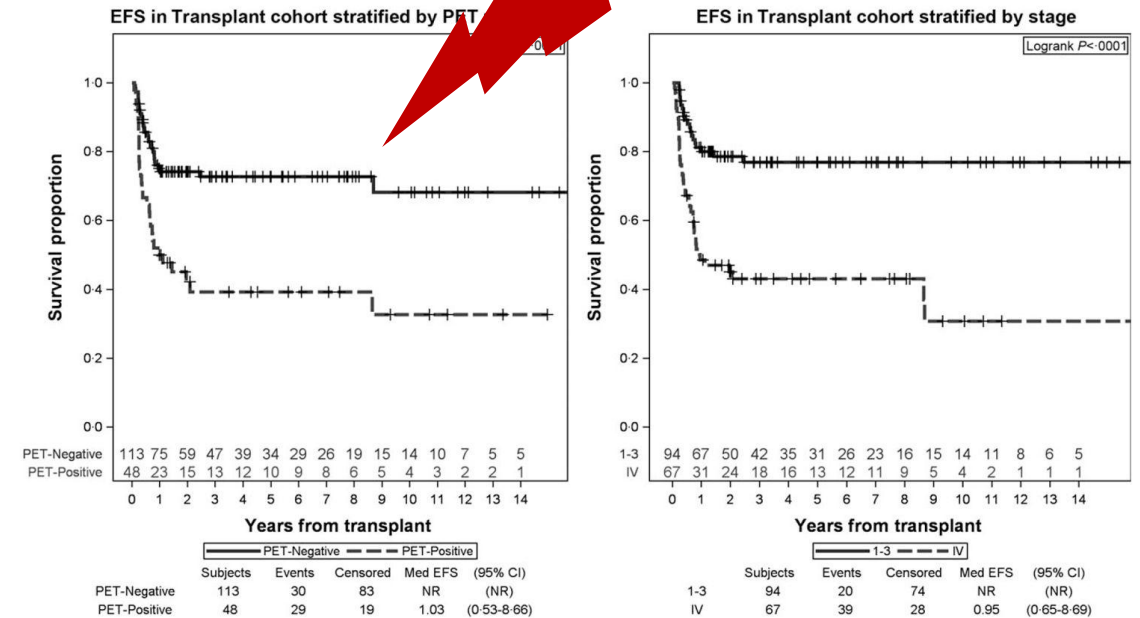


Fig 3.

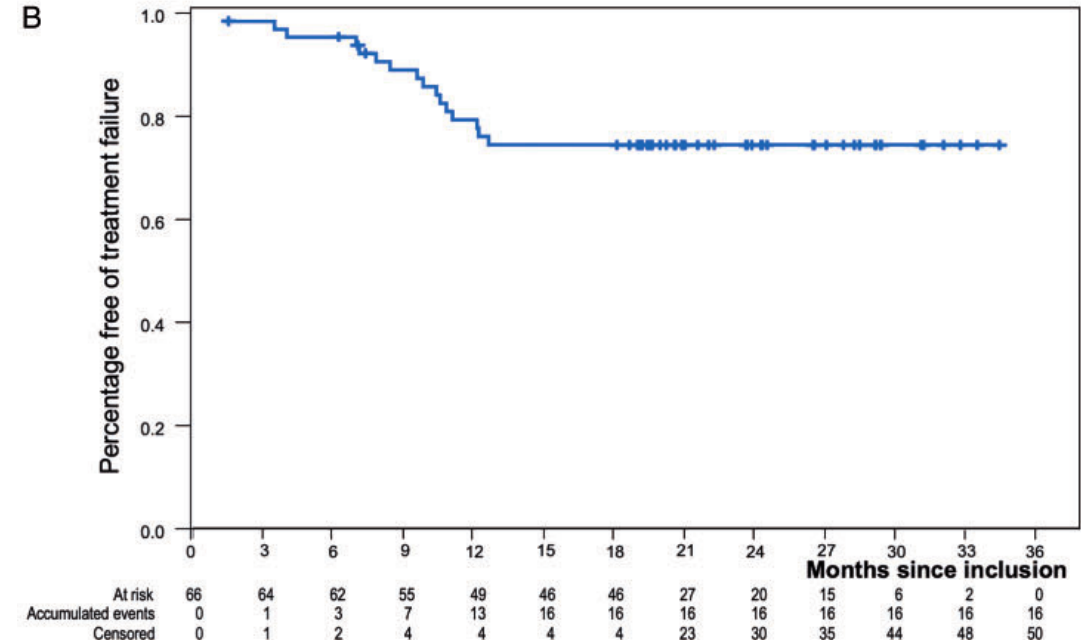
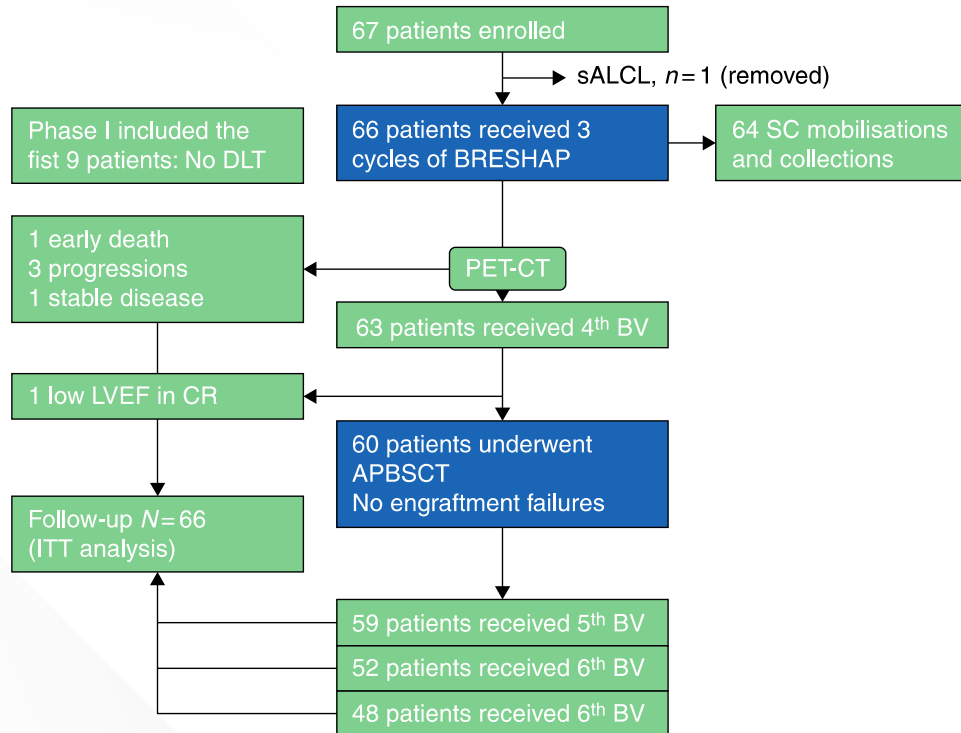
EFS by Significant Covariates. (a) by functional imaging prior to autologous stem cell transplantation (b) by Stage. EFS, event-free survival; PET, positron emission tomography; 95% CI, 95% confidence interval; NR, not reached.

Rescue chemotherapy

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

BV-ESHAP



71% CR

BV-benda

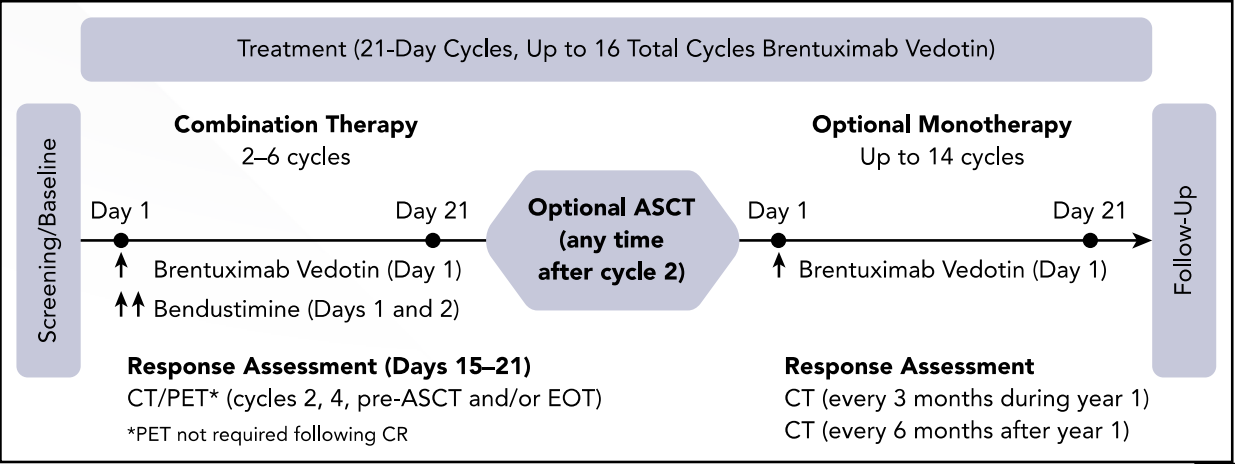
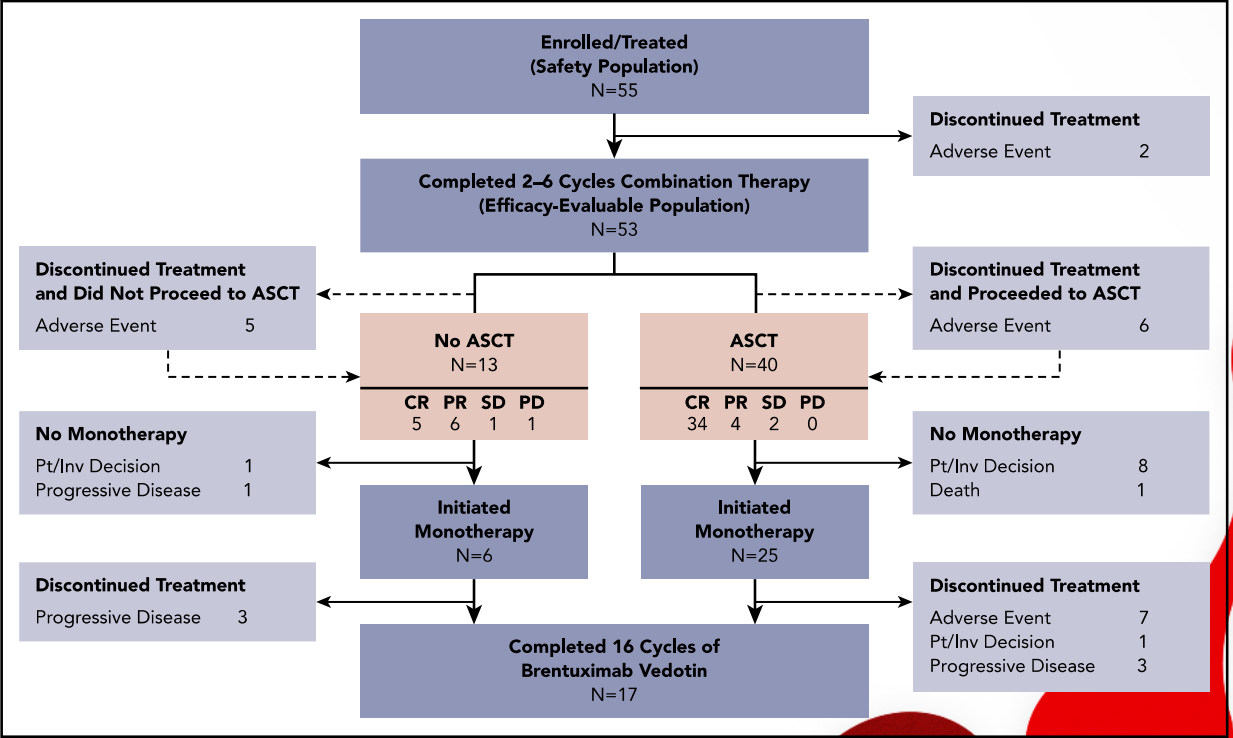


Figure 1. Study design. CT, computed tomography; EOT, End-of-Treatment; PET, positron emission tomography.



BV-benda

Table 1. Patient characteristics

Characteristic	N = 55
Age, median (range), y	36 (19-79)
Male, n (%)	24 (43.6)
White, n (%)	46 (83.6)
ECOG status, n (%)	
0	36 (65.5)
1	18 (32.7)
2	1 (1.8)
Months since HL diagnosis, median (range)	13.8 (3-98)
Disease stage at diagnosis, n (%)	
I	3 (5.5)
II	23 (41.8)
III	14 (25.5)
IV	15 (27.3)
Frontline therapy received, n (%)*	
ABVD†	50 (90.9)
Stanford V	3 (5.5)
AVD	1 (1.8)
VAMP	1 (1.8)
Response to frontline therapy, n (%)	
Primary refractory‡	28 (50.9)
Relapsed	27 (49.1)
CR > 1 y	17
CR ≤ 1 y	10
Prior cancer-related radiotherapy, n (%)	15 (27.3)
Baseline disease characteristics, n (%)	
B symptoms	12 (21.8)
Bulky disease§	5 (9.1)
Extranodal disease	17 (30.9)
Bone marrow involvement	9 (16.4)

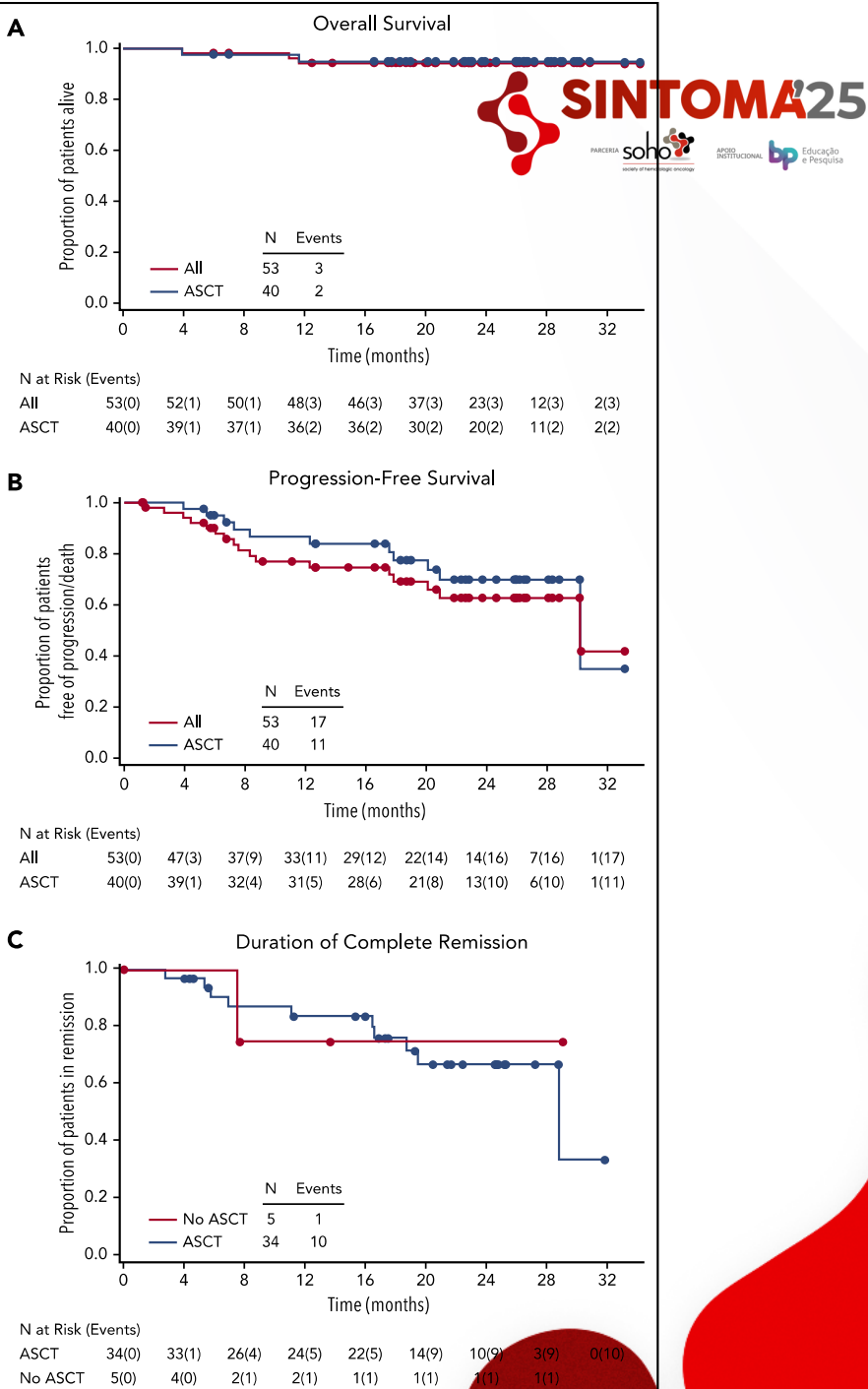
Table 2. Best response on combination therapy

Population	Best clinical response, n (%) [95% CI]				
	CR	PR	SD	PD	ORR*
Overall, N = 53	39 (73.6) [59.7, 84.7]	10 (18.9)	3 (5.7)	1 (1.9)	49 (92.5) [81.8, 97.9]
Response to frontline therapy					
Primary refractory, n = 28	18 (64.3) [44.1, 81.4]	6 (21.4)	3 (10.7)	1 (3.6)	24 (85.7) [67.3, 96.0]
Relapsed, n = 25	21 (84.0) [63.9, 95.5]	4 (16.0)	0 (0.0)	0 (0.0)	25 (100) [86.3, 100]
ASCT					
Yes, n = 40	34 (85.0) [70.2, 94.3]	4 (10.0)	2 (5.0)	0 (0.0)	38 (95.0) [83.1, 99.4]
No, n = 13	5 (38.5) [13.9, 68.4]	6 (46.2)	1 (7.7)	1 (7.7)	11 (84.6) [54.6, 98.1]

ORR, objective response rate. Other abbreviations are explained in Table 1.

*CR plus PR.

LaCasce A. *Blood*. 2018



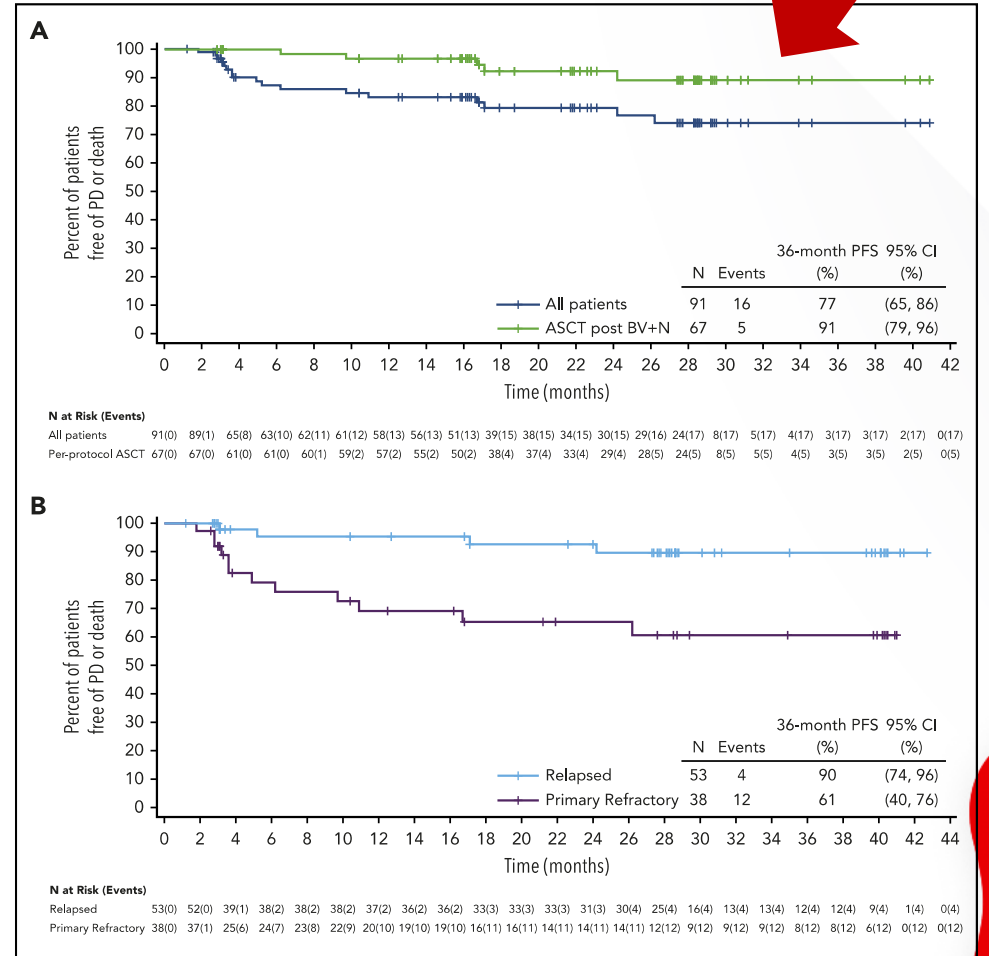
Brentuxi-Nivo

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)	

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)



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	5 (50%)
	BEACOPP esc	4 (40%)
	CHOEP	1 (10%)
Number of prior treatments before pembro-BV salvage	2	3 (30%)
	3	6 (60%)
	5	1 (10%)
First salvage therapy	DHAP	6 (60%)
	BEGEV	3 (30%)
	ICE	1 (10%)
Second salvage therapy	BEGEV	2 (20%)
	Bendamustine	2 (20%)
	ICE	1 (10%)
	BEACOPP esc	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.

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

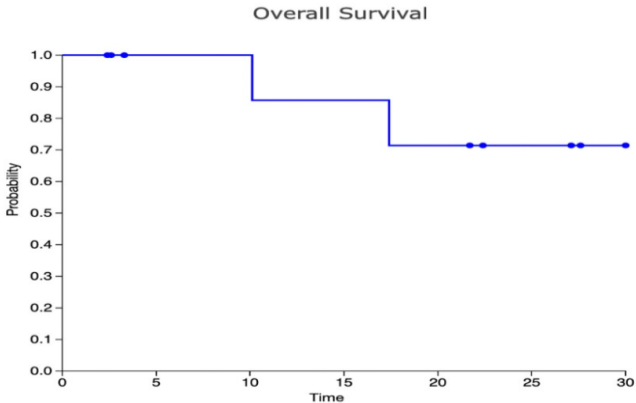
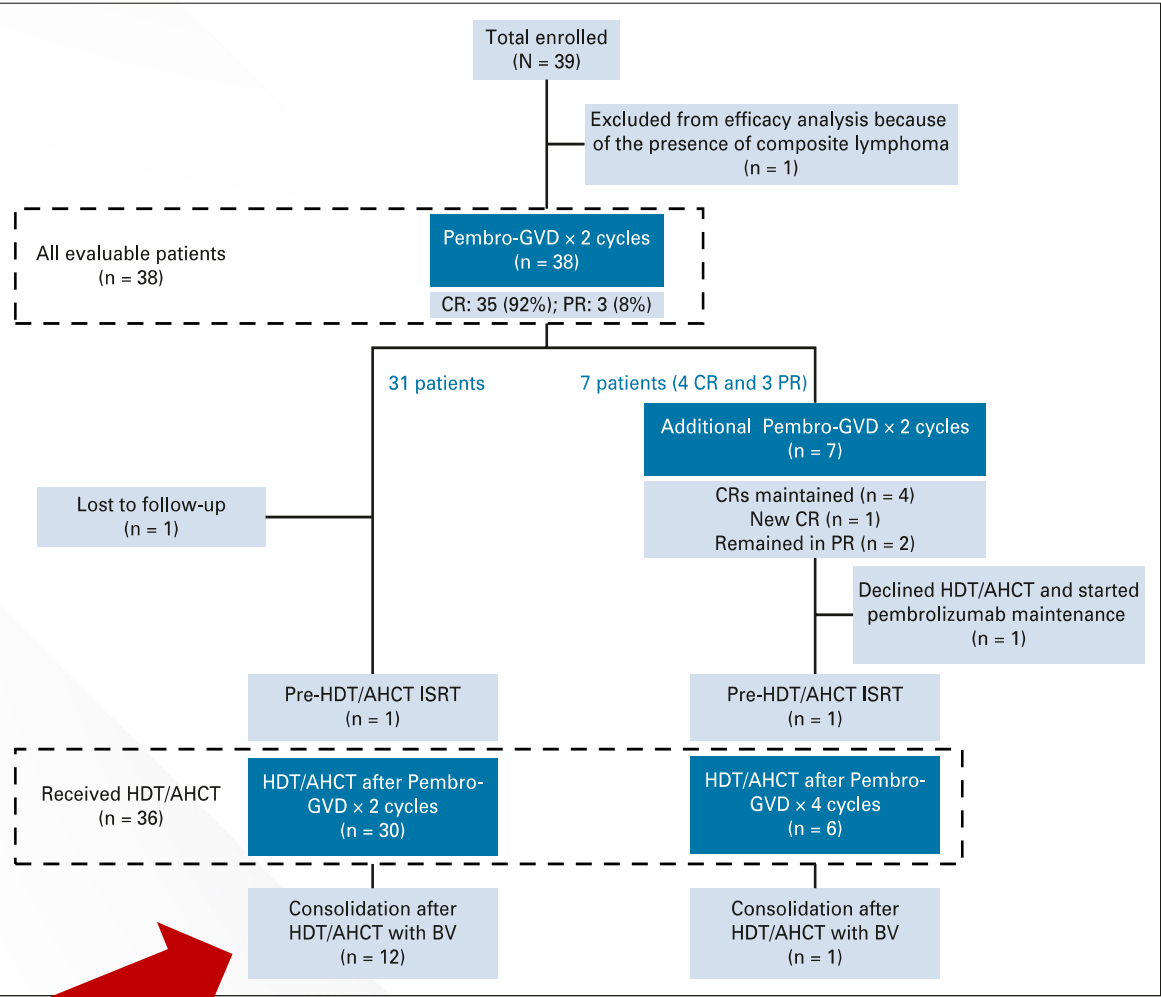


Figure 1. Kaplan-Meier curve for OS.

Pembro-GVD

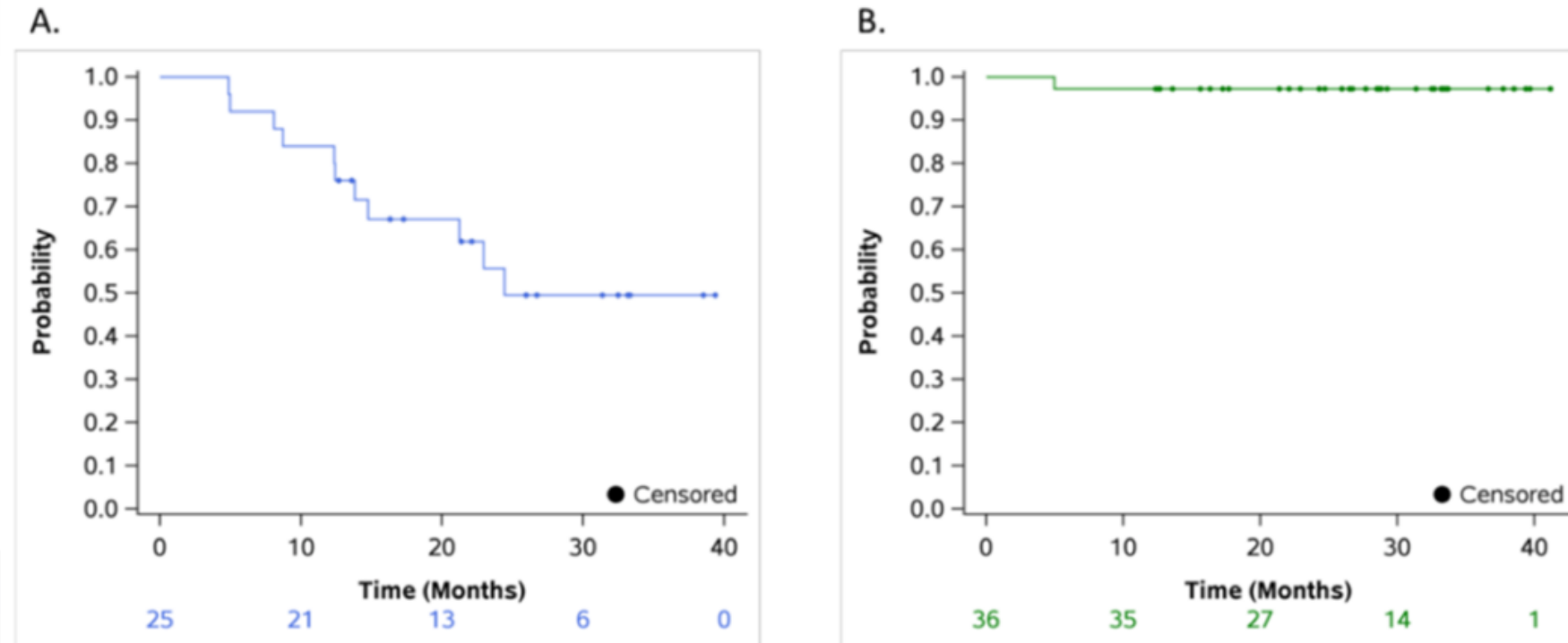
TABLE 3. Efficacy

Characteristic	Pembro-GVD × 2 (n = 38) ^a	Pembro-GVD × 4 (n = 7)	Pembro-GVD Overall (n = 38)
ORR, % (95% CI)	100 (91 to 100)	100 (59 to 100)	100 (91 to 100)
CR, % (95% CI)	92 (79 to 98)	71 (29 to 96)	95 (82 to 99)
PR, % (95% CI)	8 (2 to 21)	29 (4 to 71)	5 (1 to 18)
Best response, No. (%)			
CR	35 (92)	5 (71)	36 (95)
PR	3 (7.9)	2 (29)	2 (5.3)



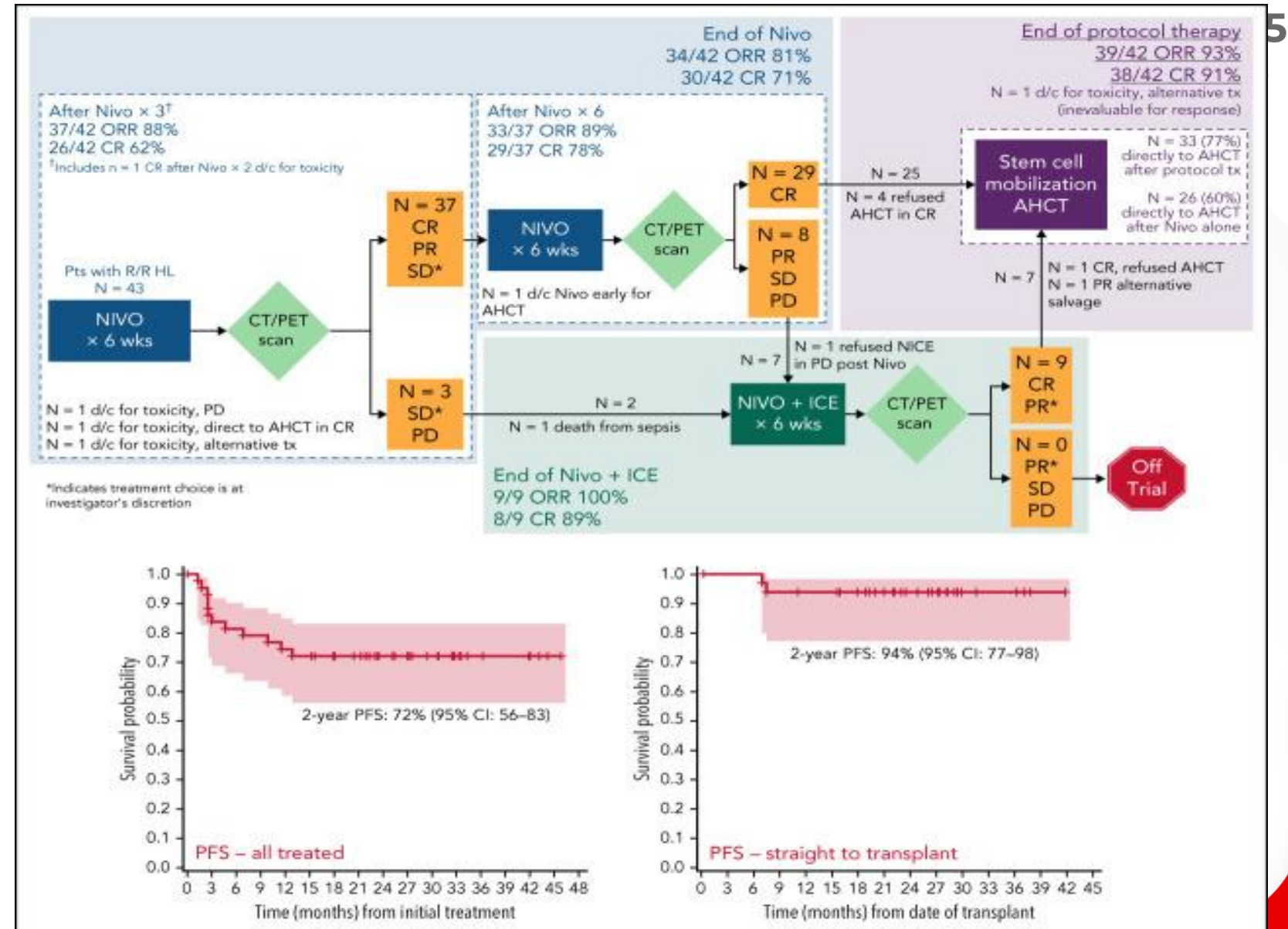
- 80% refractory disease ou <12 months recidive
- AUTO/TMO?

Pembrolizumab Maintenance Instead of Autologous Hematopoietic Cell Transplantation for Patients with Relapsed or Refractory Hodgkin Lymphoma in Complete Response after Pembrolizumab, Gemcitabine, Vinorelbine, and Liposomal Doxorubicin



Nivo- ICE

43 patients
44% primary refractory



Unfortunately there is no
Phase III trial to define the best
rescue regimen



Recidive after auto PBSCT

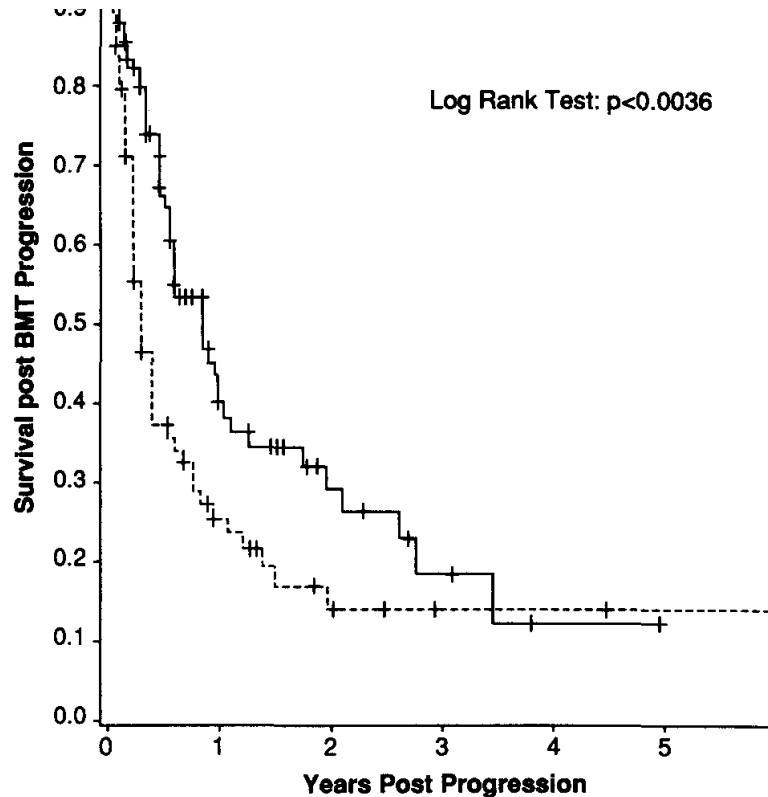


Fig 2. Overall survival for patients with progressive HD (—) compared with NHL (---). Tic marks indicate survival to the indicated interval.

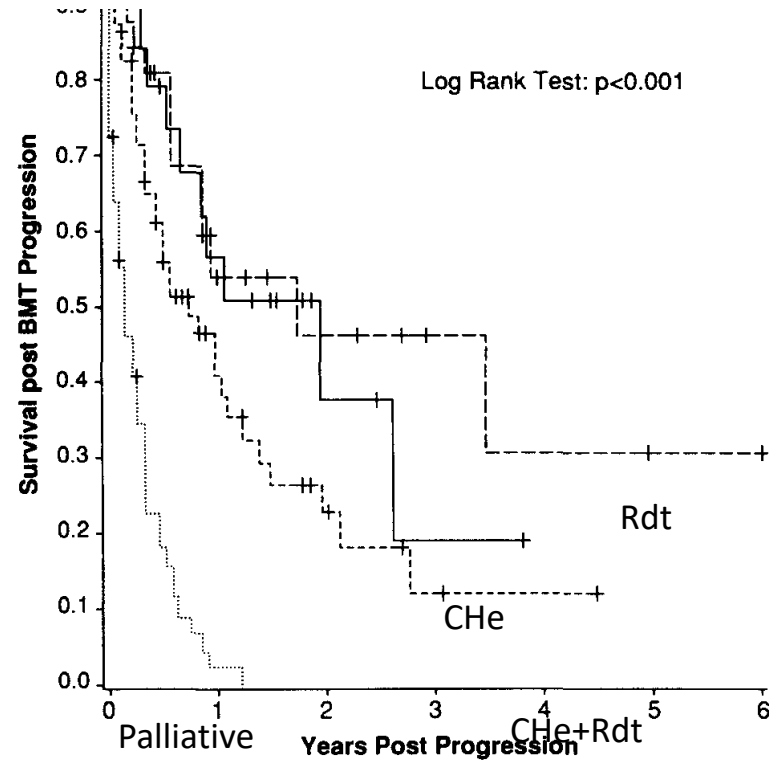
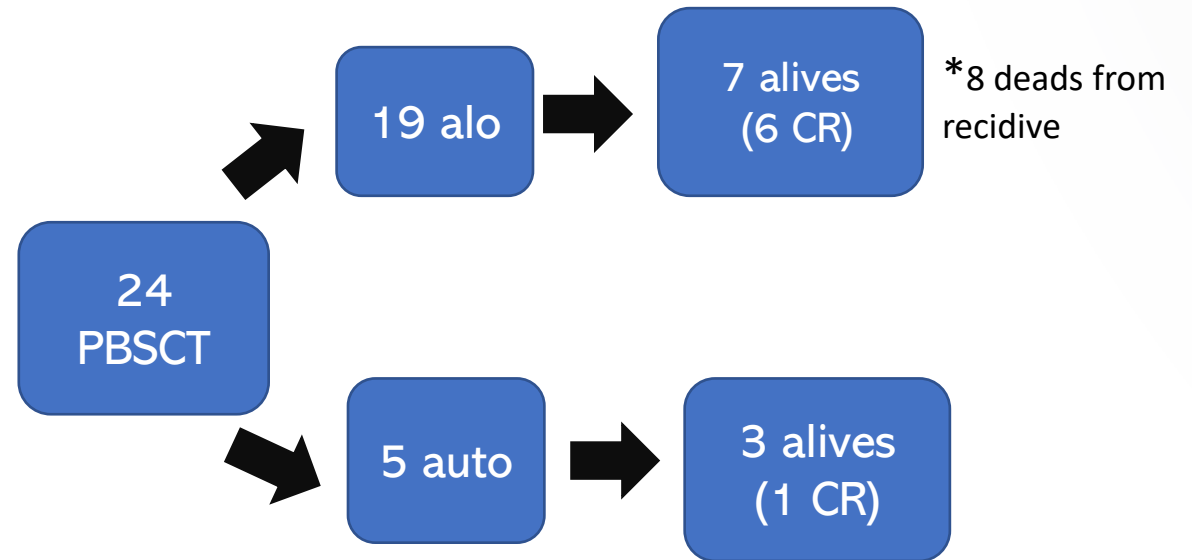


Fig 4. Overall survival for patients receiving chemotherapy (---), involved field irradiation therapy (....), combination chemotherapy and radiotherapy (—), or no therapy (— · —) after failure of ABMT. Tic marks indicate survival to the indicated interval.

of other large reports such as the report of Petersen et al¹⁸ that evaluated 101 patients from Seattle who received transplants for various types of lymphoma. In their study,

Recidive after auto PBSCT

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



Recidive after auto PBSCT

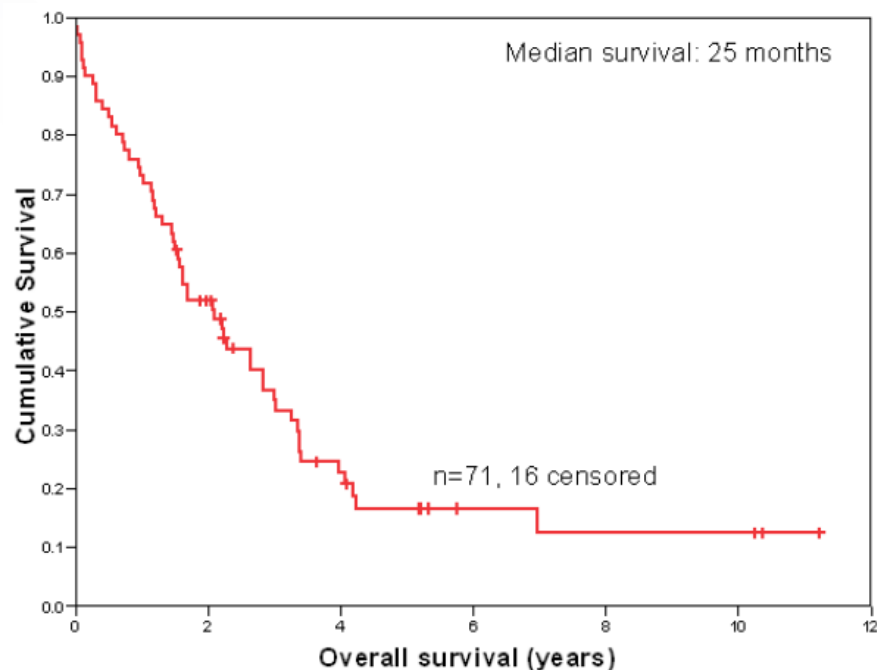


Fig1.
Overall Survival Following HDT-ASCT Failure

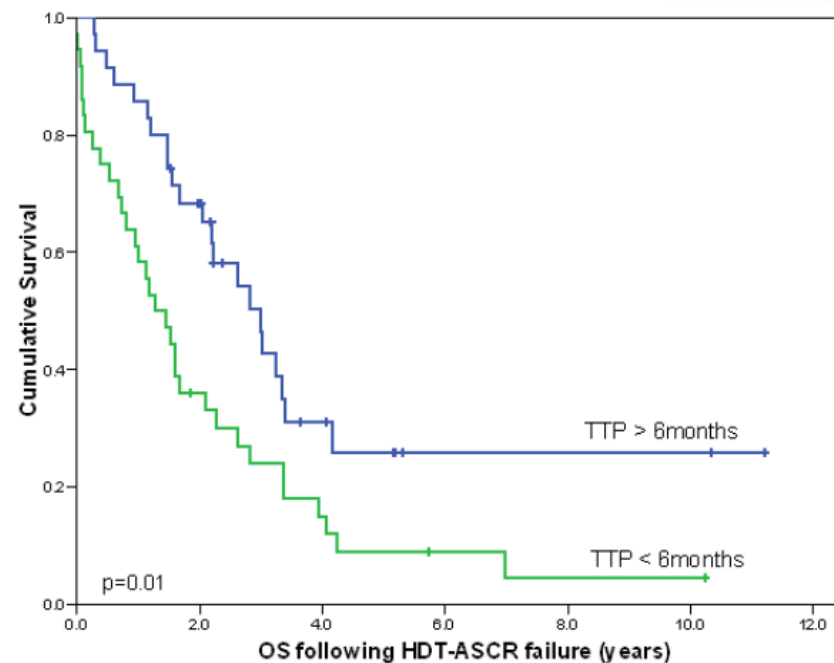
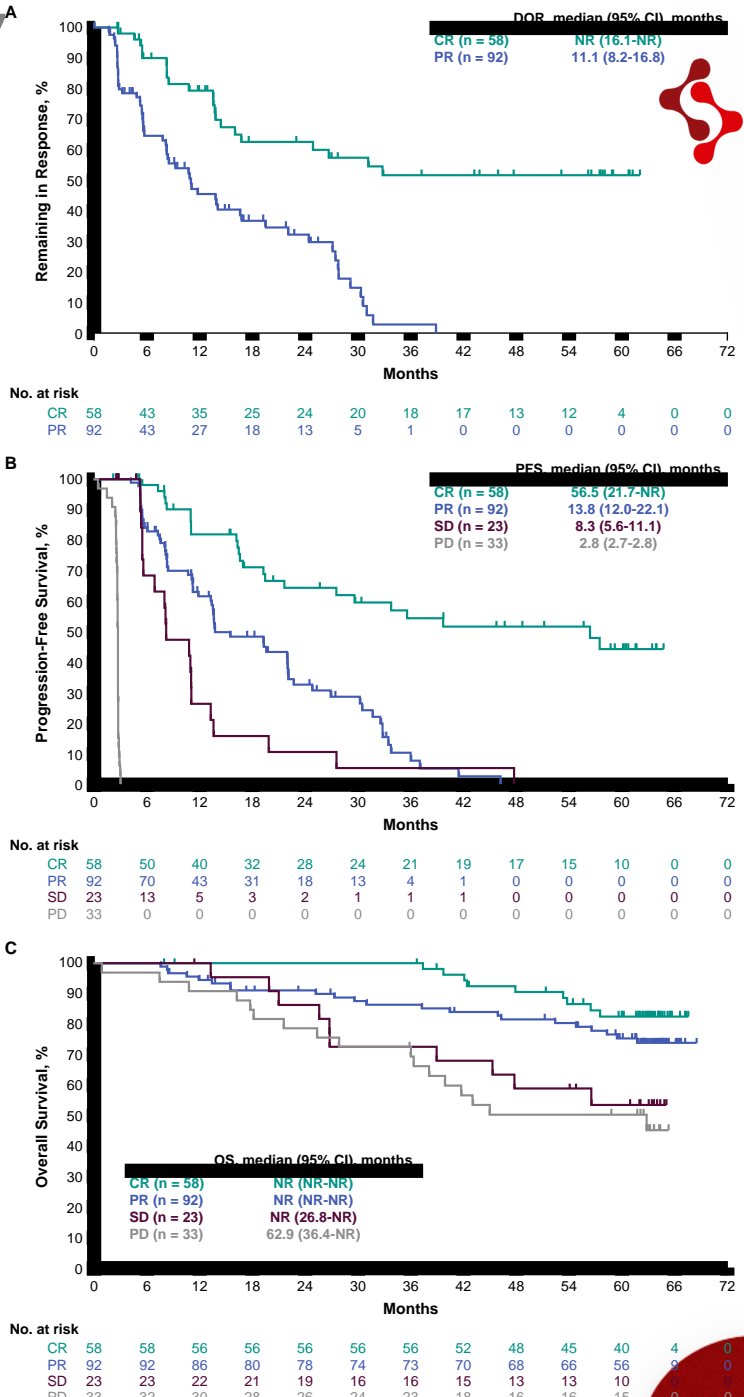
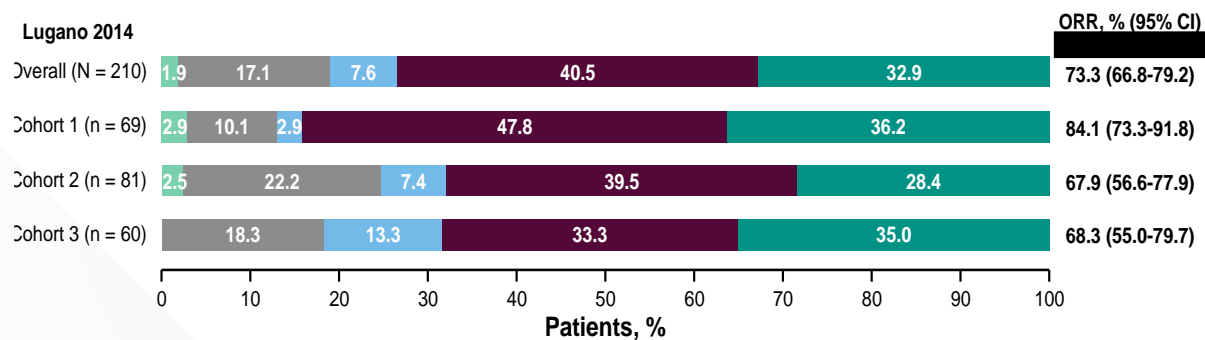


Fig2.
Survival following relapse within 6 months and after 6 months from HDT-ASCT

Pembro mono- 5 years keynote-087

Figure 3

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



Pembro mono- 5 years keynote-087



$\frac{1}{4}$ patients from original cohort are in remission after 4 years

$\frac{1}{2}$ patients with CR with pembro are still in CR after 4 years

PR: 13 months (only 3% are still in PR after 3 years)

Matching GR, response duration with Check-mate 205 (until progression): no benefit of doing more than 2 Years of imuno treatment

Pembro re-exposition

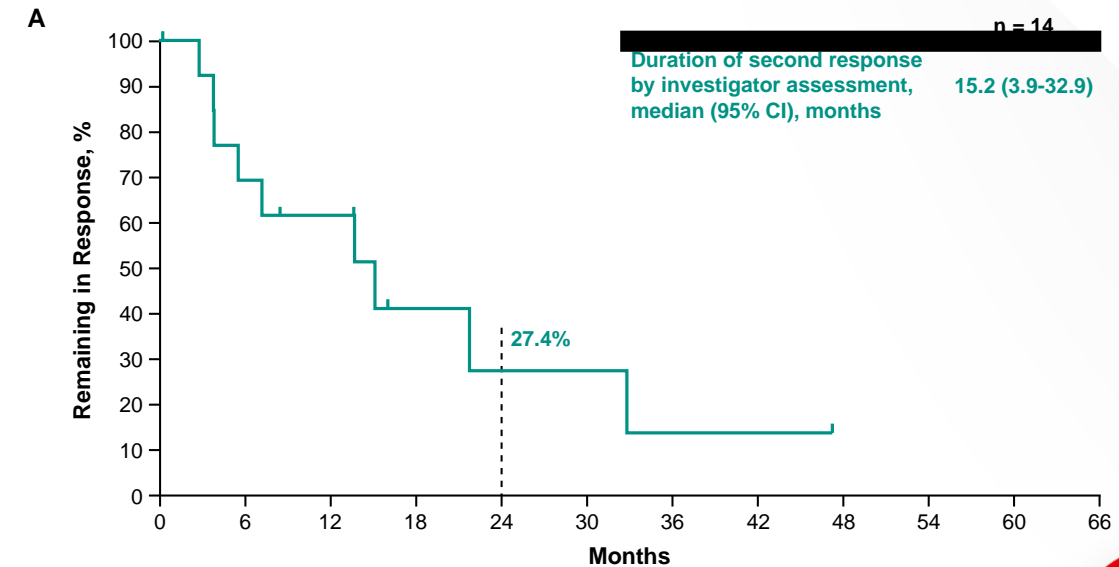
Table 1. Summary of overall response per the IWG 2007 criteria by investigator

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)

^aOne patient was not included because response data were not available at the time of data cutoff.

Figure 4



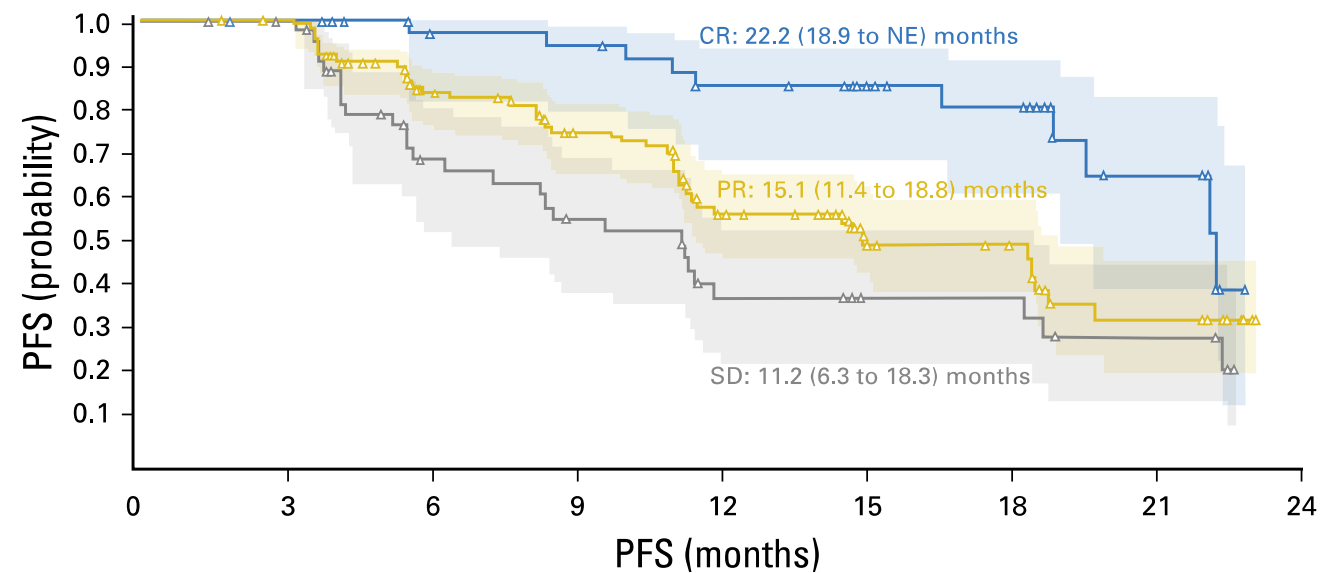
Nivolumab

Table 2. Objective and Best Overall Response per IRC

Response	Protocol-Specified Analysis by Cohort			
	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)	All patients (N = 243)
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)

PFS 16,6 months

C

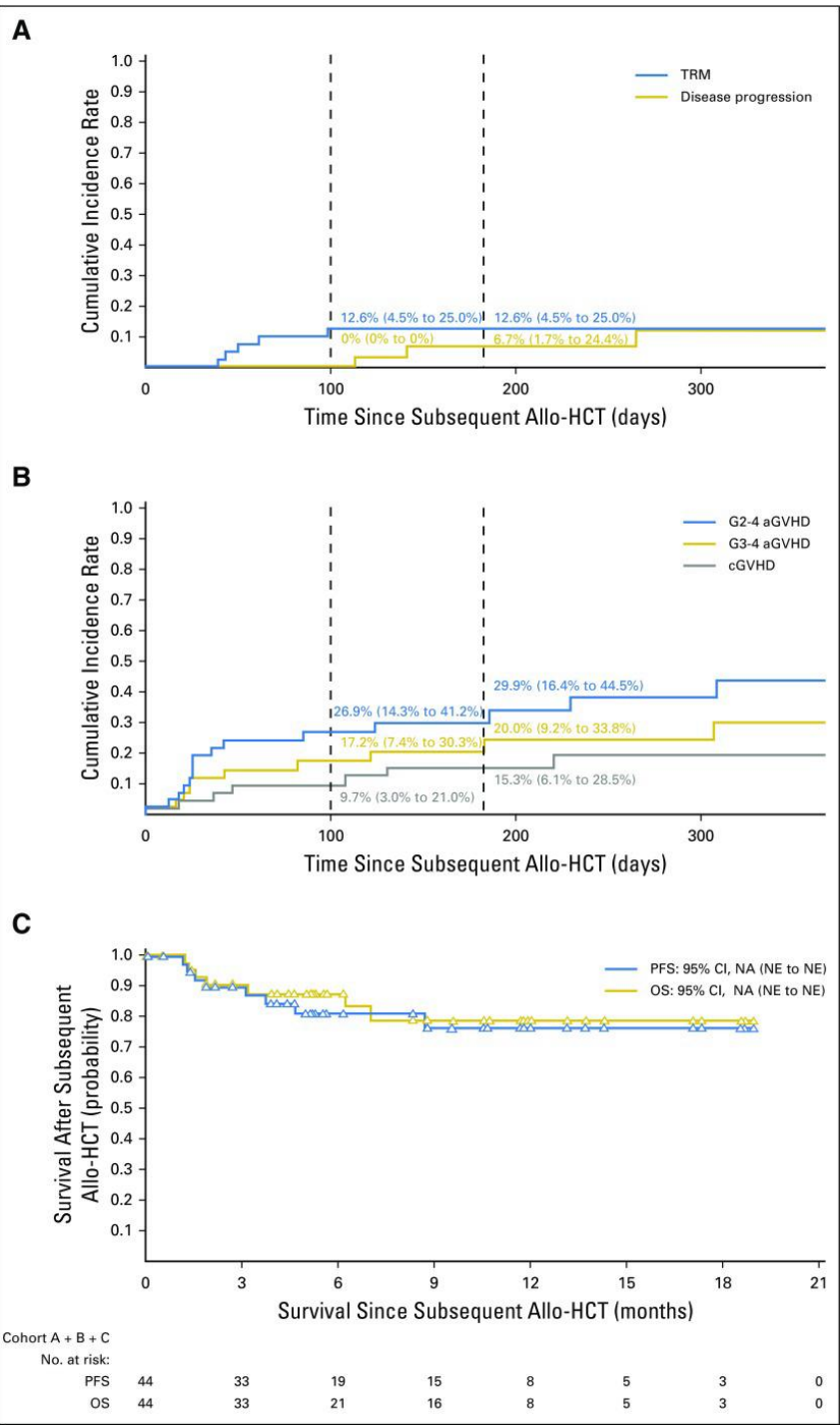


No. at risk:

CR	40	40	33	32	27	20	16	7	0
PR	128	126	89	71	46	25	21	8	0
SD	47	44	25	19	11	8	8	5	0

Nivolumab

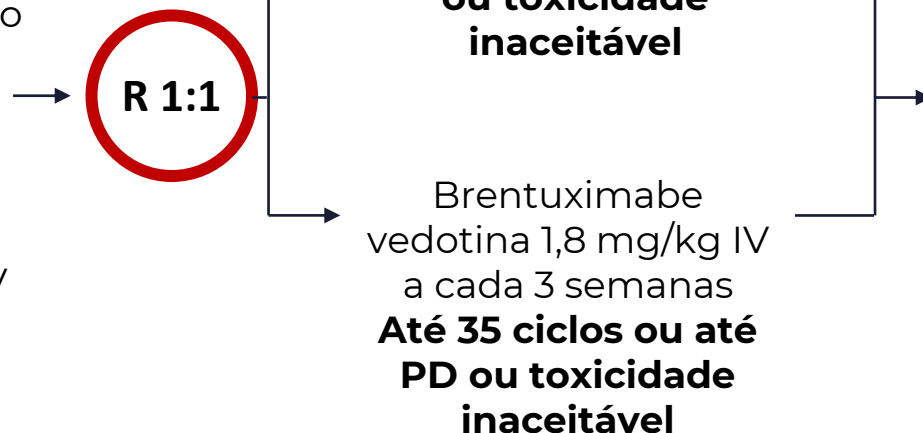
Alo: 44 patients



KEYNOTE-204

Crítérios-Chave de Elegibilidade

- LHc refratário ou recidivado
- Recidiva pós TCTH autólogo e falha em uma linha de terapia anterior
- Doença mensurável pelos critérios do IWG 2007¹
- PS ECOG 0-1
- Pacientes tratados com BV e pacientes que não foram tratados com BV eram elegíveis



- A resposta foi avaliada a cada 12 semanas pelos Critérios Revisados de Resposta para Linfoma Maligno do IGW de 2007¹
- EAs foram avaliados a cada 12 semanas ao longo do período de estudo, e a cada 12 semanas durante o acompanhamento

Fatores de Estratificação

- TCTH autólogo anterior (sim *versus* não)
- *Status* após terapia de 1L (refratário *versus* recidivado primário < 12 meses *versus* recidivado ≥ 12 meses após final da terapia de 1L)

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

Keynote-204

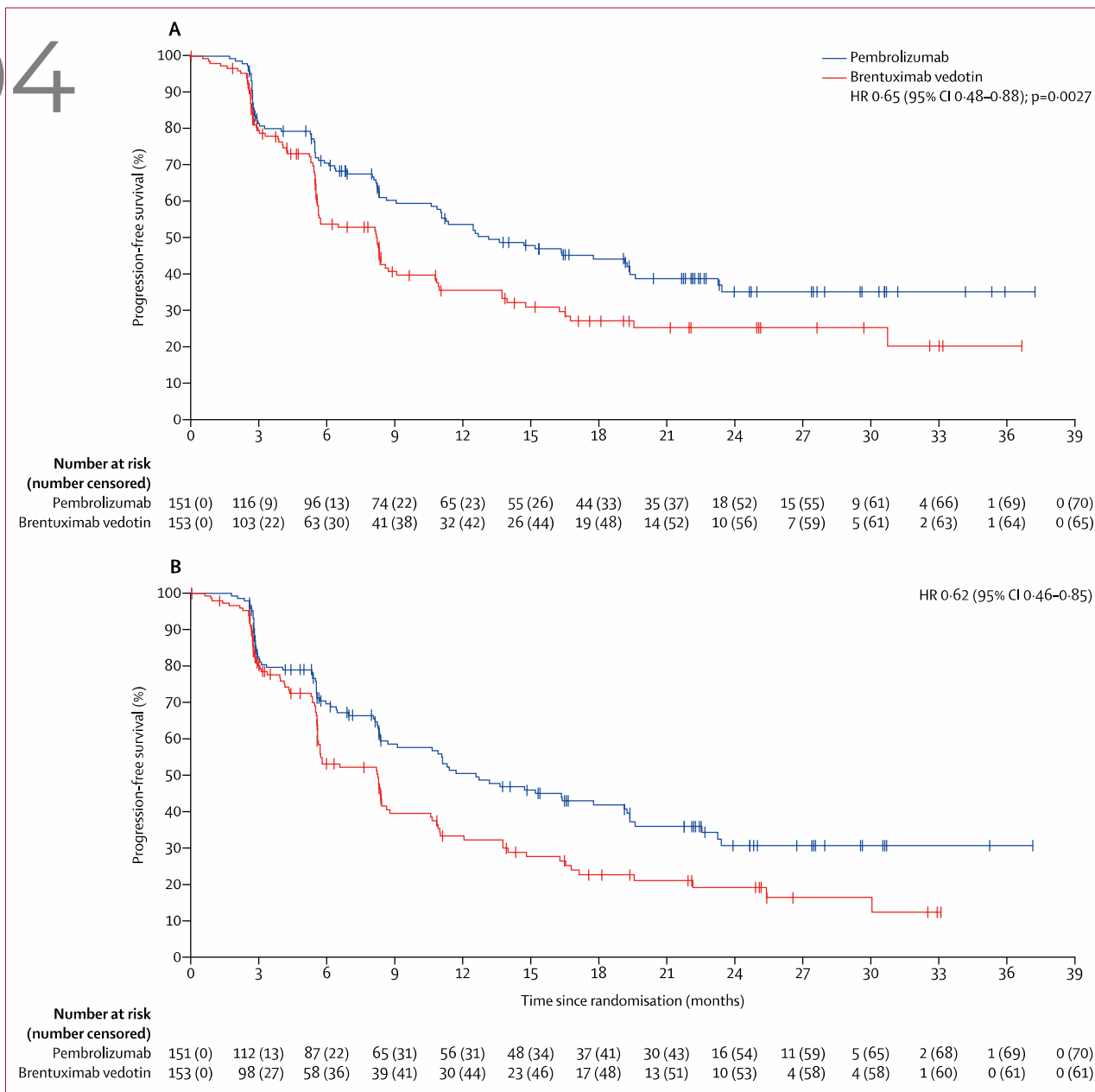


Figure 2: Progression-free survival by blinded independent central review per International Working Group 2007 criteria

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.

Double refractory

Table 3. Double Refractory Characteristics.

	All patients <i>n</i> = 173
Age At DR/INT, (median, range)	40 (19–90)
DR/INT	
Double Refractory	127 (73.4)
Intolerant	46 (26.6)
Years From Diagnosis, (median, range)	3.4 (0.5–23.1)
Prior LOT (median, range)	5 (1–13)
Prior ASCT at DR/INT	
Yes	86 (49.7)
No	87 (50.3)
Treatment After DR/INT	
Yes	153 (88.4)
No	20 (11.6)
BV Therapy After DR/INT	
Yes	41 (23.7)
No	132 (76.3)
Anti-PD-1 Therapy After DR/INT	
Yes	63 (36.4)
No	110 (63.6)

Treatment characteristics for patients with DR/INT classic Hodgkin lymphoma.
DR Double Refractory, INT Intolerant, LOT Lines of Therapy, ASCT Autologous Stem Cell Transplant, BV Brentuximab Vedotin.

Table 2. Initial BV and Anti-PD-1 Therapy.

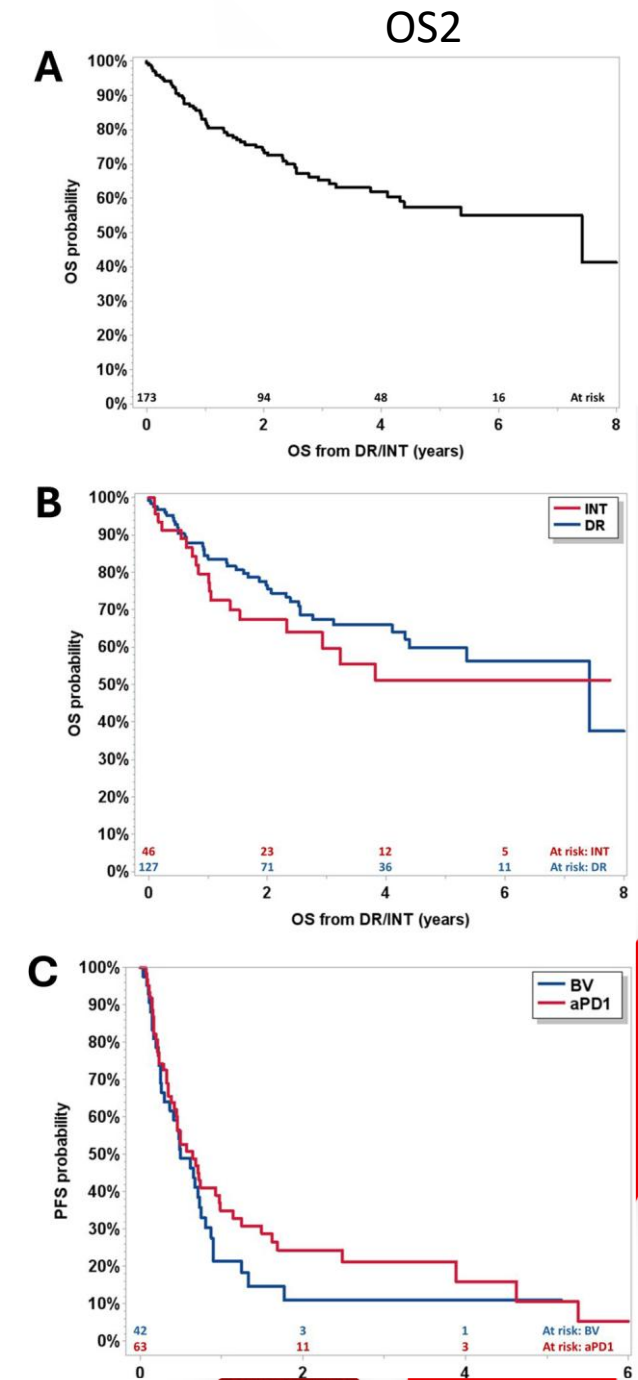
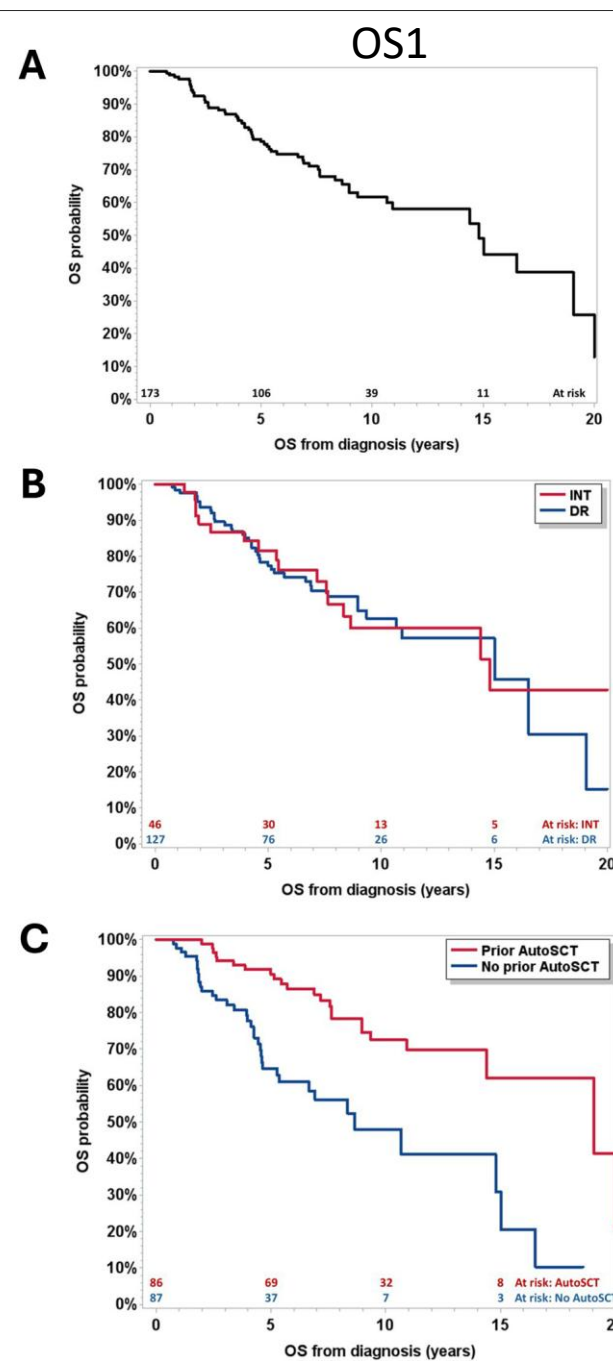
	Brentuximab Vedotin <i>n</i> = 173		Anti-PD-1 <i>n</i> = 173
Prior LOT (median, range)	2 (0–7)	Prior LOT (median, range)	3 (0–12)
Regimen		Regimen	
BV	105 (60.7)	Anti-PD-1	134 (77.4)
BV + Chemo	43 (24.9)	Anti-PD-1 + Chemo	2 (1.2)
BV + Anti-PD-1	25 (14.4)	BV + Anti-PD-1	25 (14.5)
		Other Combination	12 (6.9)
Best Response		Best Response	
CR	37 (21.4)	CR	32 (18.5)
PR	60 (34.7)	PR	63 (36.4)
SD	21 (12.1)	SD	33 (19.1)
PD	45 (26.0)	PD	37 (21.4)
Unknown	10 (5.8)	Unknown	8 (4.6)
PFS (days, median, 95% CI)	166 (138–187)	PFS (days, median, 95% CI)	225 (179–265)

Treatment characteristics for initial brentuximab vedotin and anti-PD-1 therapy.
BV Brentuximab Vedotin, LOT Lines of Therapy, Chemo Chemotherapy, CR Complete Response, PR Partial Response, SD Stable Disease, PD Progressive Disease, PFS Progression Free Survival, CI Confidence Interval.

Double refractory

OS1: 14,9 Years (19,1 auto X 8,6)
OS2: 7,4 years

Voorhees T. *Blood Cancer Journal*. 2025



Double refractory

OS1: 14,9 Years (19,1 auto X 8,6)
OS2: 7,4 years

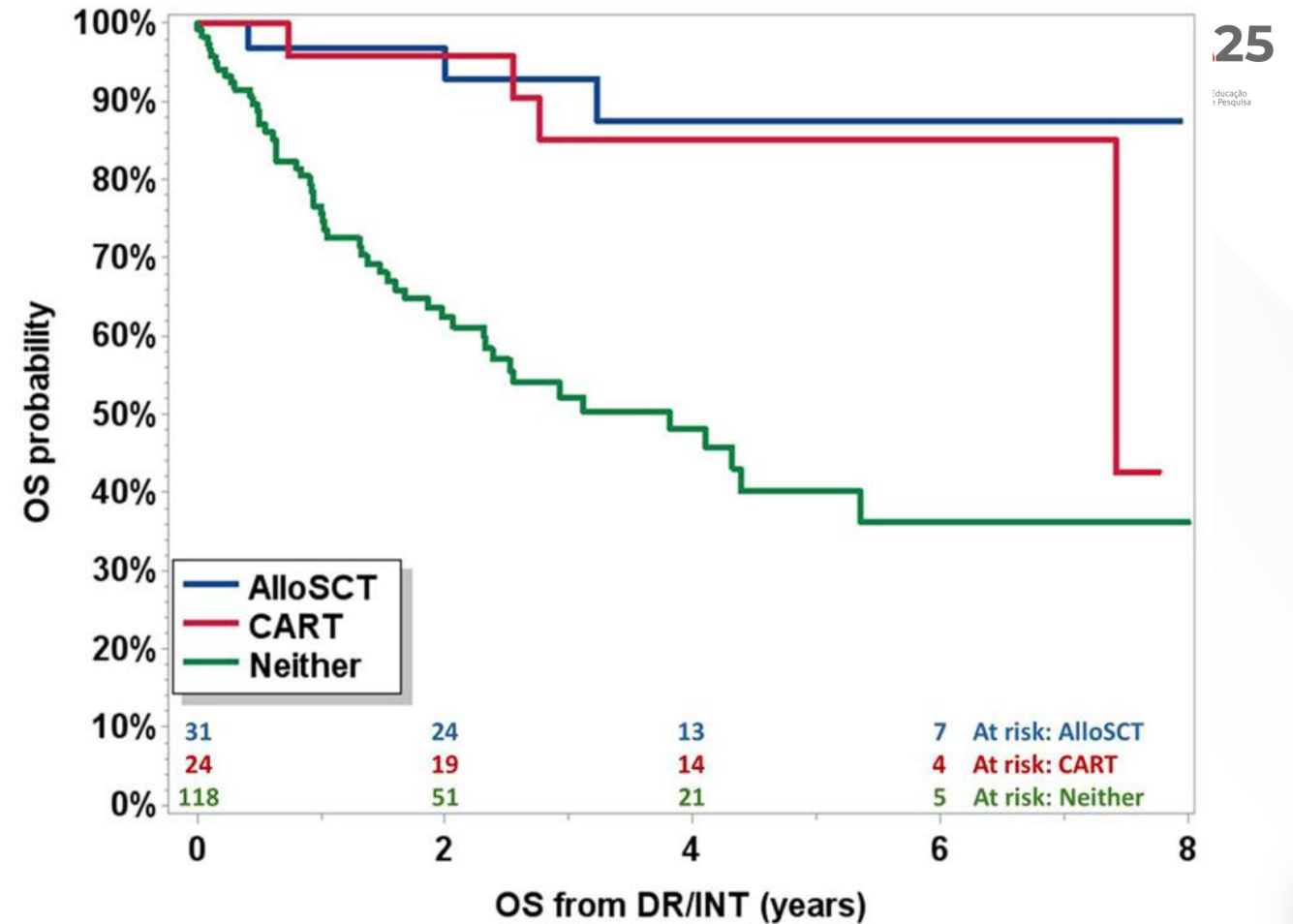


Fig. 3 Overall survival from the time of DR/INT (OS-2) stratified by subsequent AlloSCT (blue), CD30.CAR-T cell therapy (red), or neither therapy (green).

Allo in HL

Table 3 Studies of reduced intensity conditioning (RIC) allogeneic hematopoietic cell transplantation in patients with HL

Study	No. of patients (N)	Type of graft/donor	Conditioning	GVHD	Survival	NRM	Relapse
Robinson et al. [39]	285	BM (n = 57) and PB (n = 228) TCD (48.1%)	RIC: fludarabine based or TBI based	Acute GVHD Grade II–IV: 30% at d + 100 Chronic GVHD: 42% at 3 yr	3-yr OS 29% 3-yr PFS 25%	21.1% at 3 yr	59% at 5 yr
Sureda et al. [35]	168	MAC BM = 33 PB = 46 RIC BM = 15 PB = 74	MAC (n = 79) RIC (n = 89)	D + 100 acute GVHD: MAC 53%, RIC 33% 1-yr chronic GVHD: MAC 33%, RIC 33%	5-yr MAC OS 22%, PFS 18% RIC OS 28%, PFS 23%	1-yr NRM MAC 46% RIC 23%	MAC 30.4% RIC 57.3%
Sarina et al. [38]	122 in donor arm; (104 patients in HCT)	PBSC = 90 BM = 13 PBSC + BM = 1 MRD = 57 MUD = 33 Haplo = 14	RIC: fludarabine based or thiotepa based	Acute GVHD: 27% Chronic GVHD: 41.1%	2-yr PFS 31% OS 57%	2-yr NRM 12.7%	54%
Thompson et al. [37]	38 in RIC arm	PBSC = 31 BM = 7 MRD 24 MUD 14	RIC: fludarabine/melphalan/alemtuzumab	Grade II–IV acute GVHD: 16% Chronic GVHD: 13% (n = 5)	5 yr PFS 34% OS 51%	5-yr NRM 19%	55.2% (n = 21)
Peggs et al. [32]	49	PBSC 37 BM = 12 MRD = 31 MUD = 18	Fludarabine/melphalan/alemtuzumab	Acute GVHD: 16% Chronic GVHD: 14% (n = 7)	4-yr PFS 55.7% OS 39%	16.3% at d + 730 (higher NRM than MUD)	43%
Alvarez et al. [41]	40	MRD: 38 MUD: 2 PBSC: 3 BM: 37	RIC: fludarabine/melphalan	Grade II–IV acute GVHD: 42% Extensive chronic GVHD: 47%	2-yr PFS 32% OS 48%	1-yr TRM 25%	27.5% (received DLI for relapse)
Anderlini et al. [43]	58	MRD: 25 MUD: 33 PBSC: 28 BM: 30	RIC: fludarabine/melphalan/antithymocyte globulin	D + 100 acute GVHD: MRD 12%, MUD 19% Chronic GVHD: MRD 57%, MUD 85%	2-yr PFS 32% OS 64%	2-yr TRM 15%	55% at 2 yr
Majhail et al. [42]	21	MRD: 9 UCB: 12	RIC: fludarabine/busulphan/TBI or fludarabine/cytosan/TBI	Severe acute GVHD: 33% 1-yr chronic GVHD: MRD 33%, UCB 100%	2-yr PFS MRD 20% UCB 25% 2-yr OS MRD 51% UCB 48%	D + 180 TRM MRD 22% UCB 25%	Not reported
Devetten et al. [40]	148	BM: 39 PB: 104 MUD: 110 MMUD: 33	RIC: 94 NMA: 49	Grade II–IV acute GVHD: 60% at d + 100 Chronic GVHD: 68% at 2 yr	2-yr OS 37% PFS 20%	2-yr TRM 33%	47% at 2 yr

Note. BM = bone marrow; DLI = donor lymphocyte infusion; GVHD = graft-versus-host disease; MAC = myeloablative conditioning; MMUD = mismatched unrelated donor; MRD = matched related donor; NMA = nonmyeloablative; NRM = nonrelapse mortality; OS = overall survival; PB = peripheral blood; PBSC = peripheral blood stem cells; PFS = progression-free survival; RIC = reduced intensity conditioning; TBI = total body irradiation; TRM = transplant-related mortality; UCB = umbilical cord blood.

Allopos 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	
<u>Reduced intensity conditioning (RIC)</u>	<u>38 (97%)</u>
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%)
<u>Myeloablative conditioning (MAC)</u>	<u>1 (3%)</u>
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%)

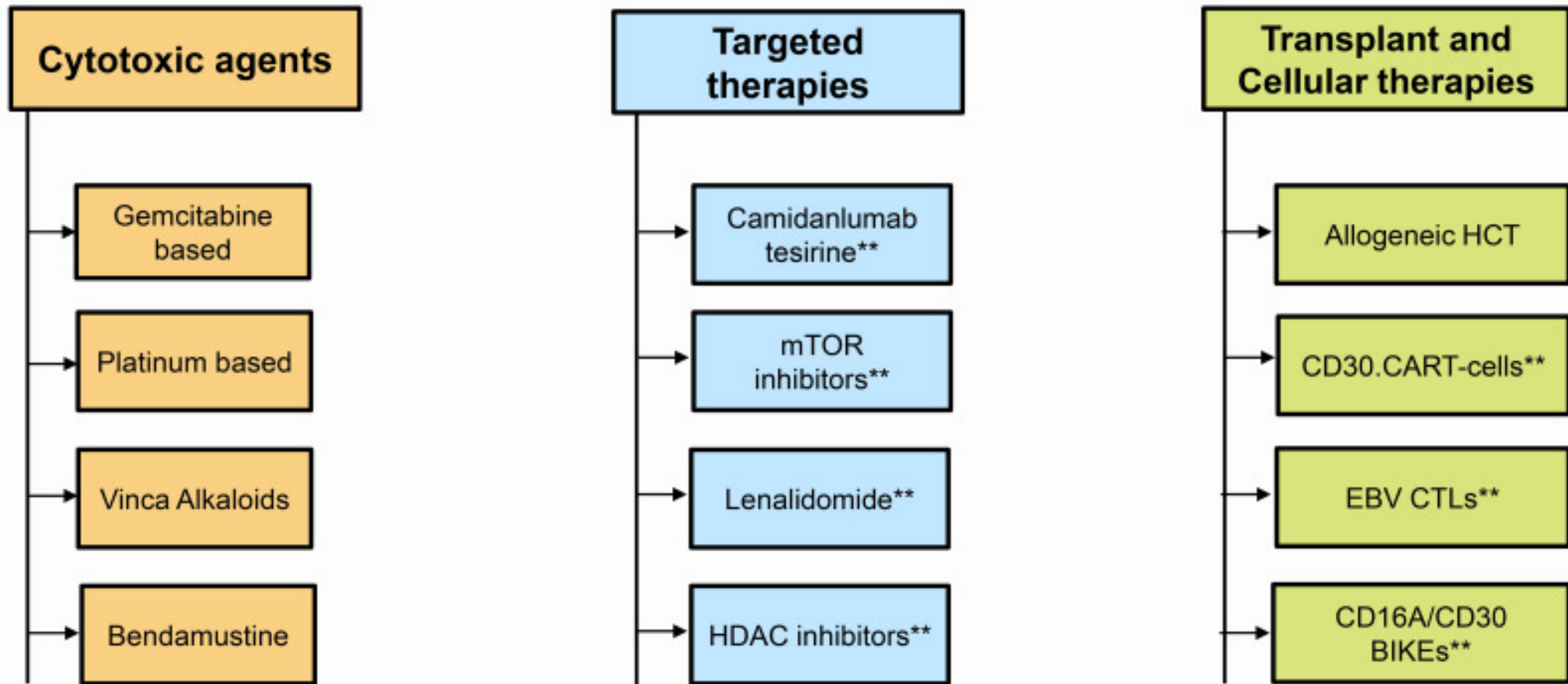
Table 2: Toxicity, Outcomes, and Deaths

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)		
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

Treatment Options for Double Refractory Hodgkin lymphoma*

OMA'25

APRO INSTITUCIONAL
bp Educação e Pesquisa



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

**Investigational agents for treatment relapsed/refractory cHL

Brentuxi-Benda (1 day)

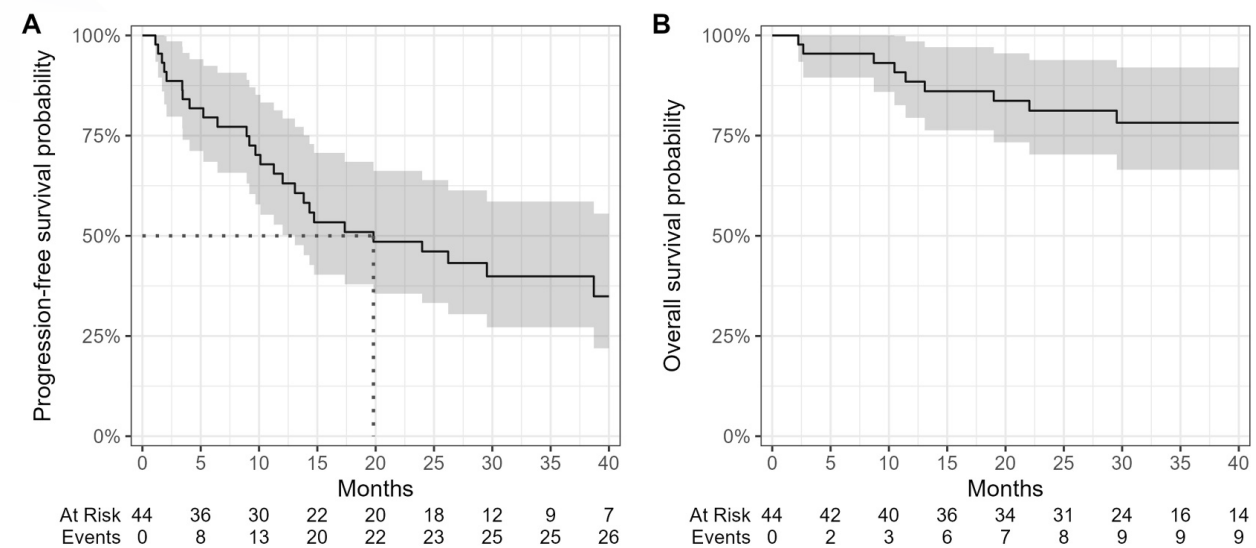


FIGURE 1 | (A) Progression-free survival, (B) Overall survival estimated with Kaplan–Meier curves.

ORR 84%
CR 73%

TABLE 1 | Detailed adverse events.

	Total n (%)
Grade 3–4 neutropenia	3 (7%)
Febrile neutropenia	1 (2%)
Need for GCSF	8 (18%)
Grade 3–4 thrombopenia	2 (4%)
Need for platelet transfusion	1 (2%)
Need for red cells transfusion	3 (7%)
Other infections	3 (7%)
Non-documented septic shock	1 (2%)
Pyelonephritis	1 (2%)
Non-severe COVID infection	1 (2%)
Peripheral sensory neuropathy	7 (16%)
Grade 1	6 (14%)
Grade 3	1 (2%)
Infusion-related reaction (IRR)	16 (36%)
Grade 1	6 (14%)
Grade 2	7 (16%)
Grade 3	3 (7%)
Resolution after pre-medication	8
Patients with any grade 3 adverse event	10 (23%)
Interruption for toxicity	3 (7%)
Adaptation for toxicity	8 (18%)
Diminution of treatment dose	1 (2%)
Bendamustine alone interruption	2 (4%)
BV alone interruption	5 (11%)
Cause of adaptation	
IRR	3 (7%)
Neuropathy	1 (2%)
Infection	1 (2%)
Constipation	1 (2%)
Worsening oedemato-ascitic syndrome on pre-existing cirrhosis	1 (2%)
Deaths under treatment	1 (2%)

Everolimus

Table 2 Best overall response to everolimus treatment

Best overall response, n (%)	N = 57
Complete response	5 (8.8)
Partial response	21 (36.8)
Stable disease	20 (35.1)
Progressive disease	9 (15.8)
Unknown	2 (3.5)

Table 1 Baseline demographics and disease characteristics

Characteristic, n (%)	N = 57
Age, years, median (range)	32.0 (19.0–77.0)
Sex, n (%)	
Male	24 (42.1)
Female	33 (57.9)
Race, n (%)	
White	44 (77.2)
Black or African American	8 (14.0)
Asian	1 (1.8)
Pacific Islander	3 (5.3)
Other	1 (1.8)
ECOG performance status, n (%)	
0	32 (56.1)
1	23 (40.4)
2	2 (3.5)
Hodgkin lymphoma classification, n (%)	
Classical nodular sclerosis	52 (91.2)
Classical mixed cellularity	3 (5.3)
Other	2 (3.5)
Stage at diagnosis, n (%)	
I	2 (3.5)
II	20 (35.1)
III	18 (31.6)
IV	17 (29.8)
Number of previous regimens, median (range)	4 (1–17)
Previous treatment, n (%)	
AHSCT	38 (66.7)
Gemcitabine-containing regimen	32 (56.1)
Vinorelbine-containing regimen	23 (40.4)
Vinblastine-containing regimen	55 (96.5)
Disease progression during previous therapy, n (%)	38 (66.7)
Time from diagnosis to first recurrence/relapse, months, median (range)	11.1 (0.6–80.0)
Time from diagnosis to most recent recurrence/relapse, months, median (range)	38.9 (7.0–221.4)

Unless otherwise noted, all data are presented as n (%)

AHSCT autologous hematopoietic stem cell transplantation, ECOG Eastern Cooperative Oncology Group



Original article

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

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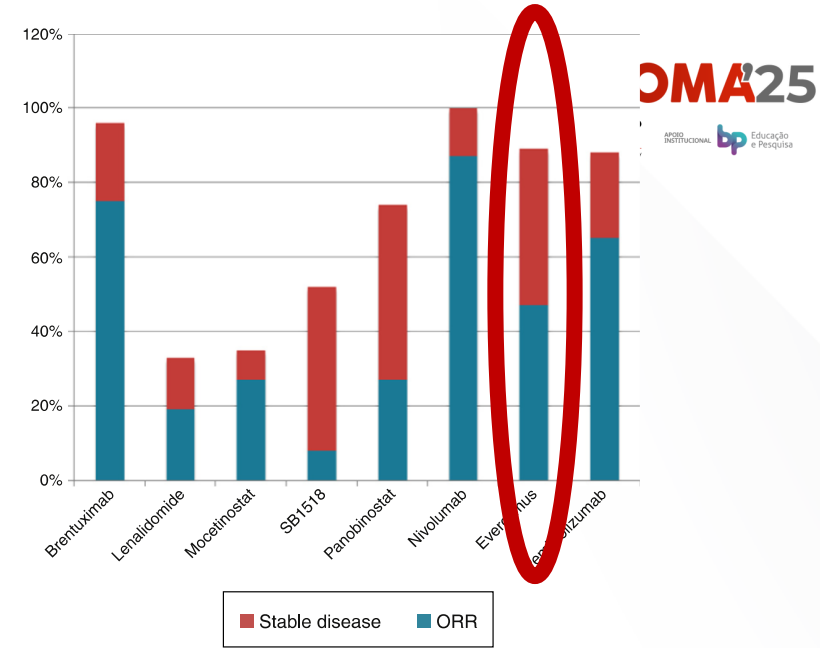


Table 1 – Patient characteristics (n = 33).

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

CR	2 (6%)
PR	13 (39.4%)
SD	14 (42.4%)
Progression	2 (6%)
NA	2 (6%)

NA: not assessable; HSCT: hematopoietic stem cell transplantation; ABVD: adriamycin, 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.



MEPED

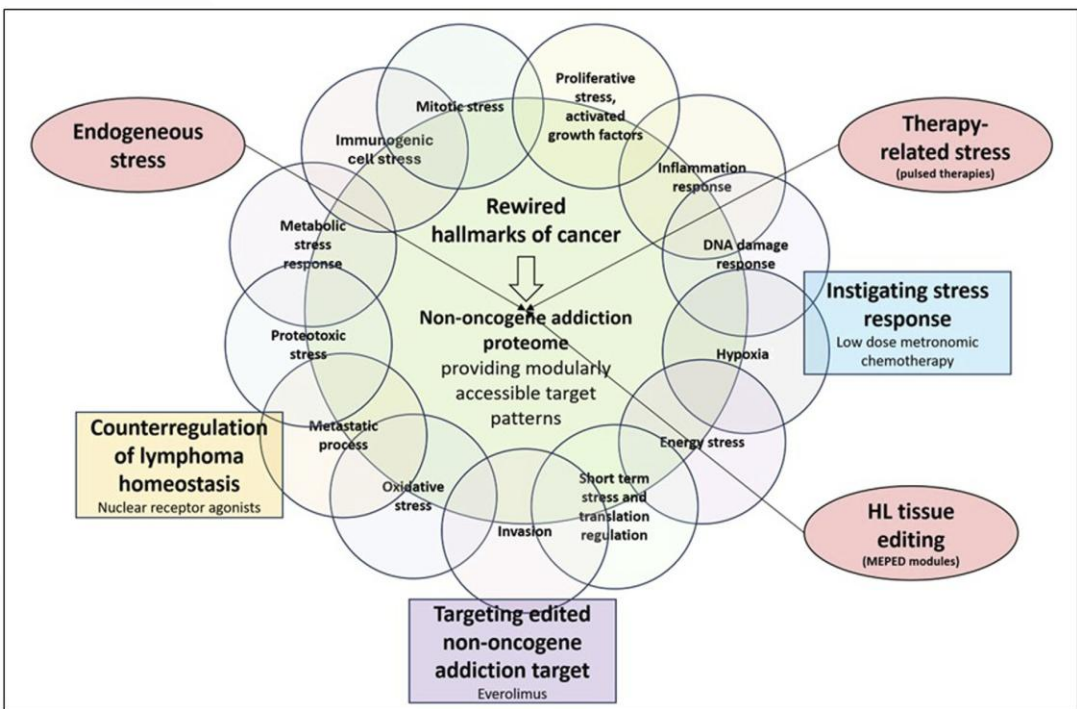


FIGURE 2
Communicatively integrating, counterregulating, and inhibiting non-oncogene addiction targets, while instigating HL stress response enables durable long-term responses in relapsed/refractory Hodgkin's lymphoma (r/r HL).

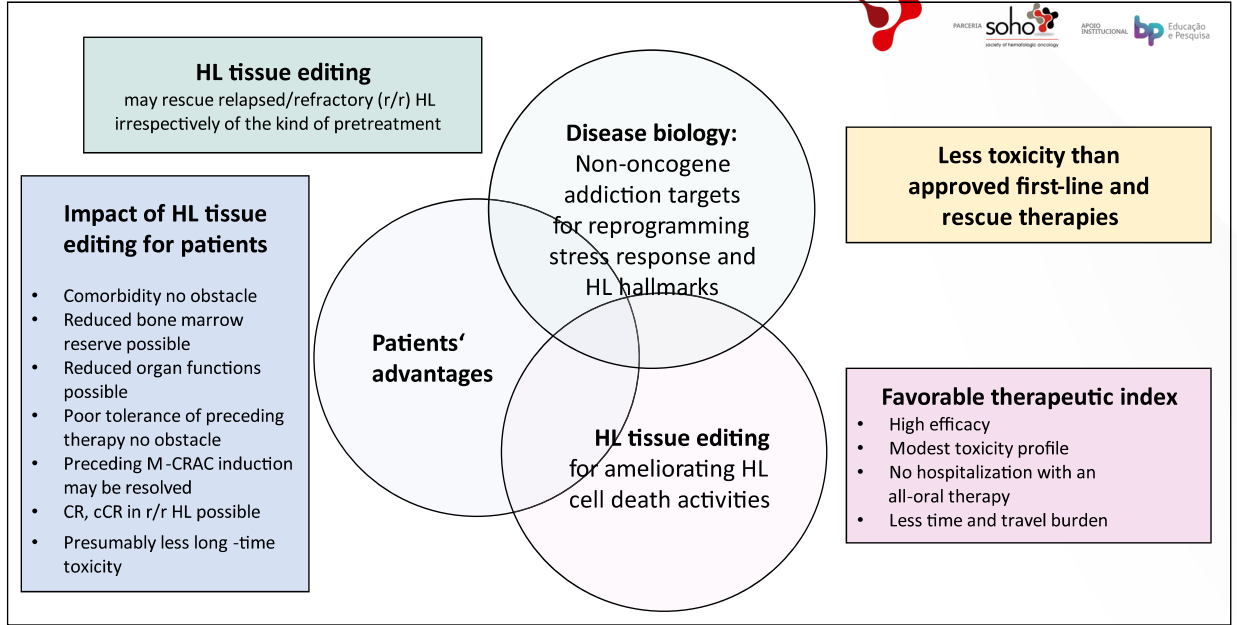


FIGURE 1
Hodgkin's lymphoma (HL) tissue editing with MEPED: impact of target selection on patient performance status.

TABLE 1 MEPED schedule: concerted transcriptional modulation combined with the induction of stress response.

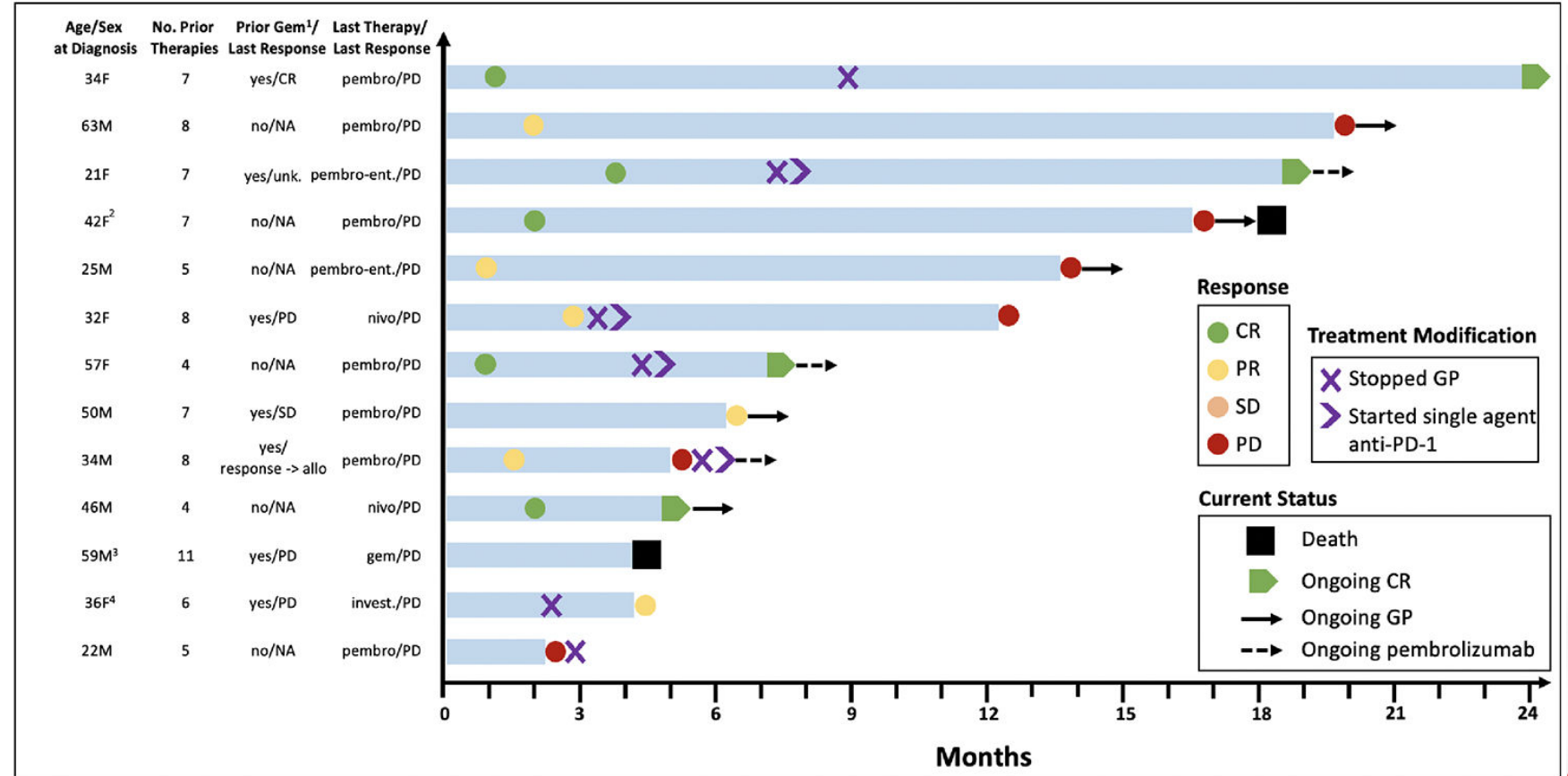
Drug of MEPED schedule	Dose (mg)	Day application per cycle	Comments
Treosulfan ^a	250	1–28	Mild antiemetic on demand
Pioglitazone ^a	45	1–28	-
Dexamethasone ^a	0.5	1–28	-
Etoricoxib ^a	60	1–28	-
Everolimus ^a	15	1–28	To achieve nadir level of 15 ng/mL

^aScheduled dose reductions.

7 patients- 6 CR

Pembro+ gencitabine

13 patients



Radiotherapy

Immunomodulators

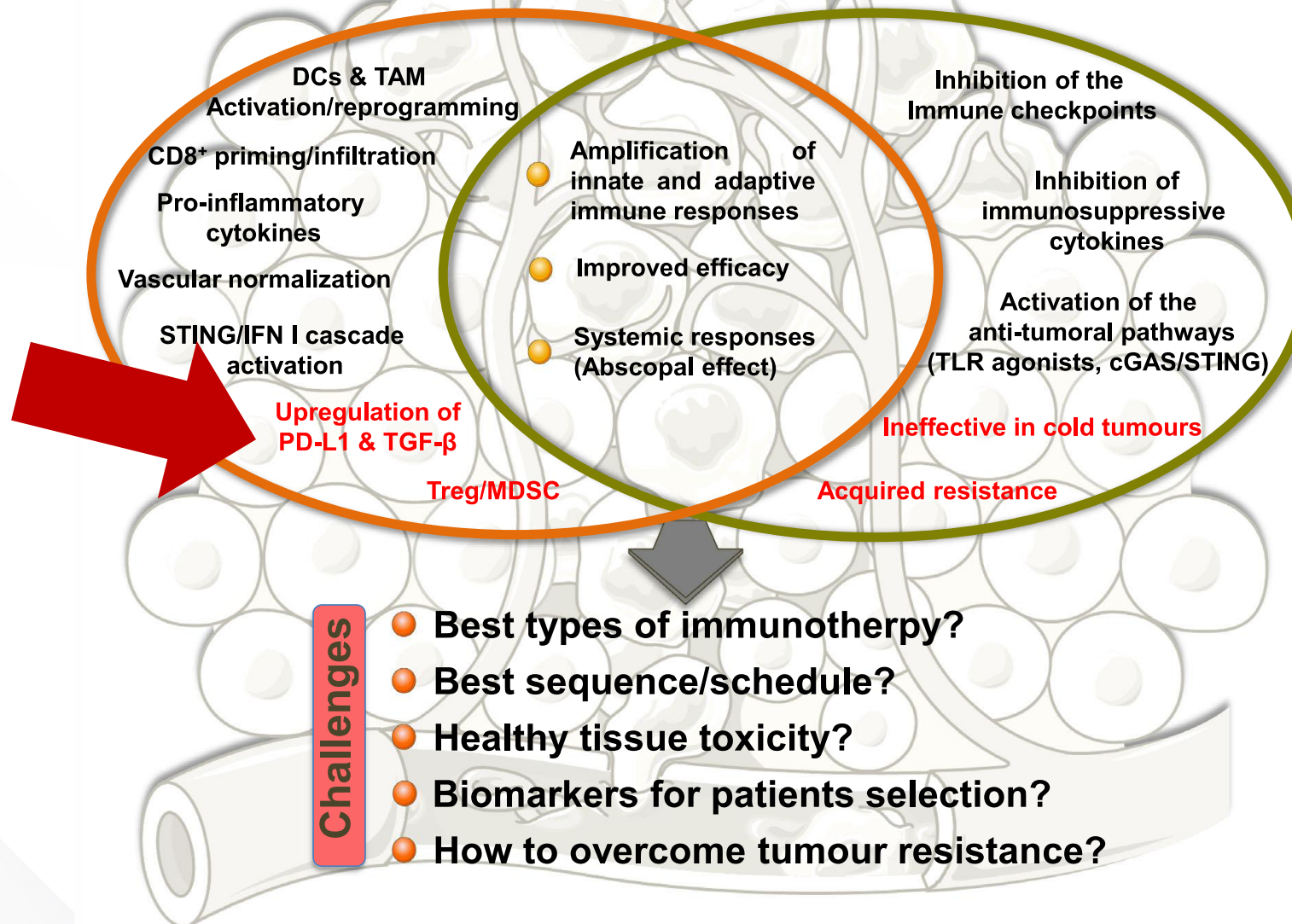
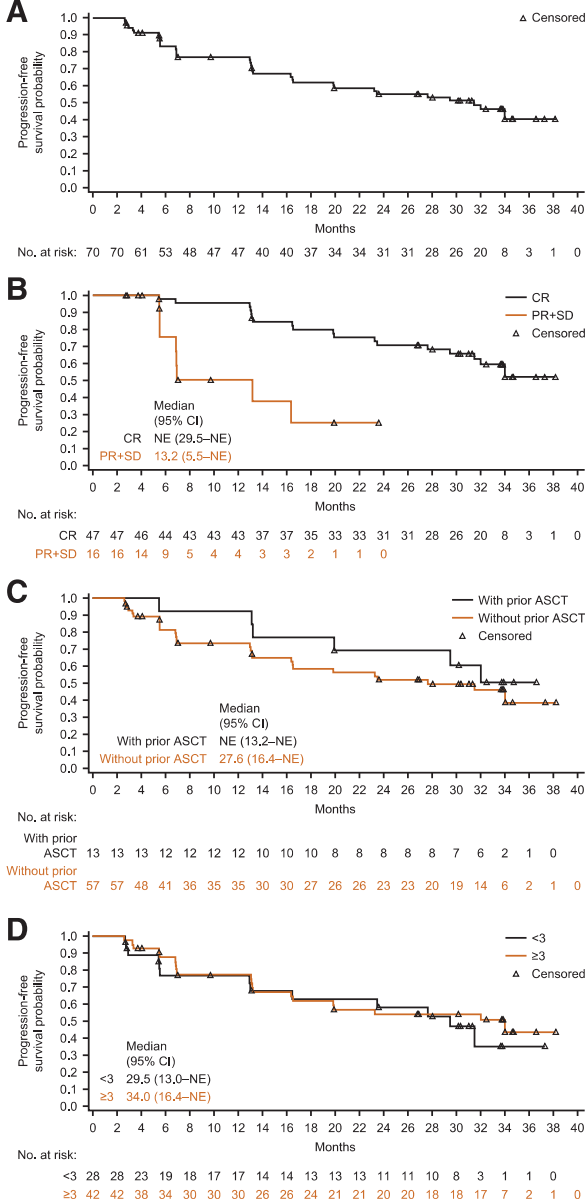


Fig. 2. Strengths, weaknesses and challenges of radiotherapy and immunotherapy combinations.

Tislelizumab

OR 87%
CR 67,1%
PR 20%



B

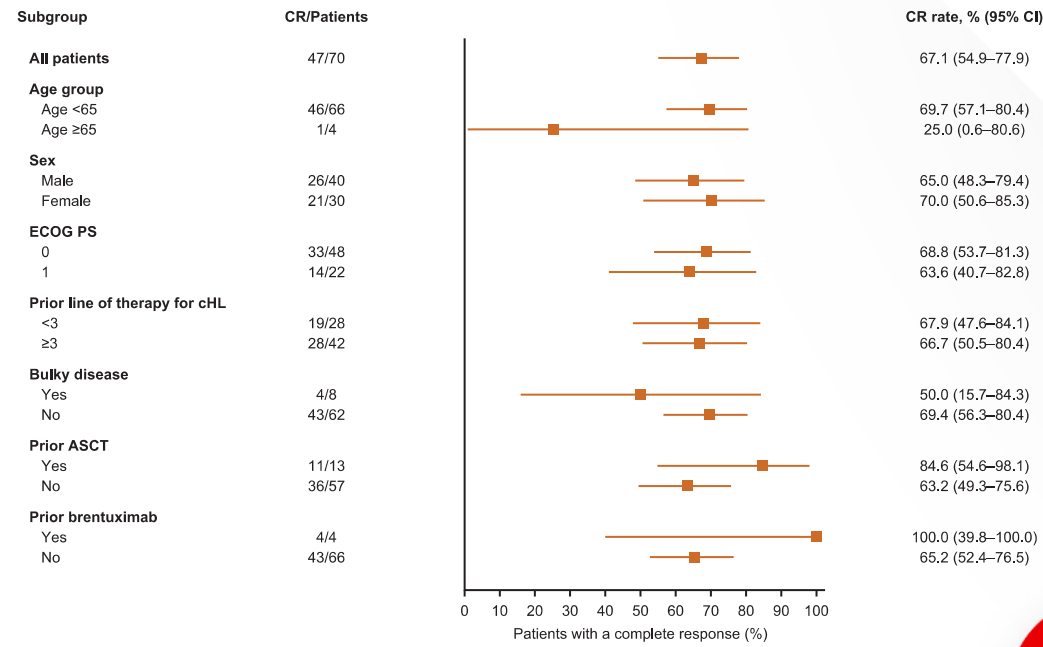


Figure 2. Progression-free survival by independent review committee per the Lugano classification. **A**, All treated patients. **B**, Patients achieving CR or PR + SD. **C**, Patients with/without prior ASCT. **D**, Patients with different number of lines of prior therapies (<3 vs. ≥3). ASCT, autologous hematopoietic stem cell transplant; CI, confidence interval; CR, complete response; NE, not estimable; PR, partial response; SD, stable disease.

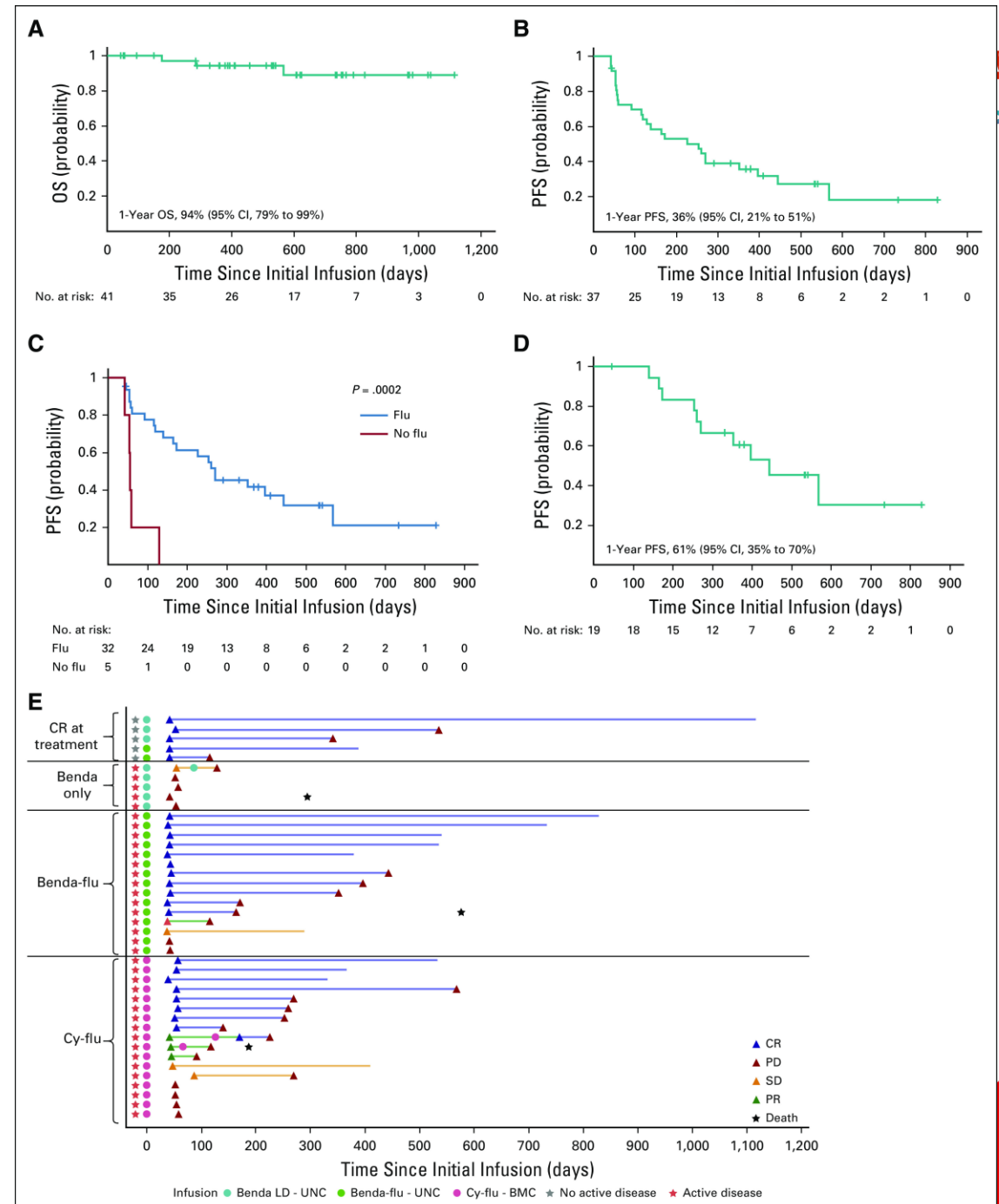
CART anti30

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.



CART Metanalysis

Table 2 Efficacy outcomes of anti-CD30 CAR-T cell therapy in R/R cHL

Efficacy	Incidence	95% CI	P
ORR	0.57	0.36–0.76	0.50
CR	0.34	0.13–0.64	0.29
PR	0.32	0.15–0.55	0.12
SD	0.27	0.14–0.46	0.002

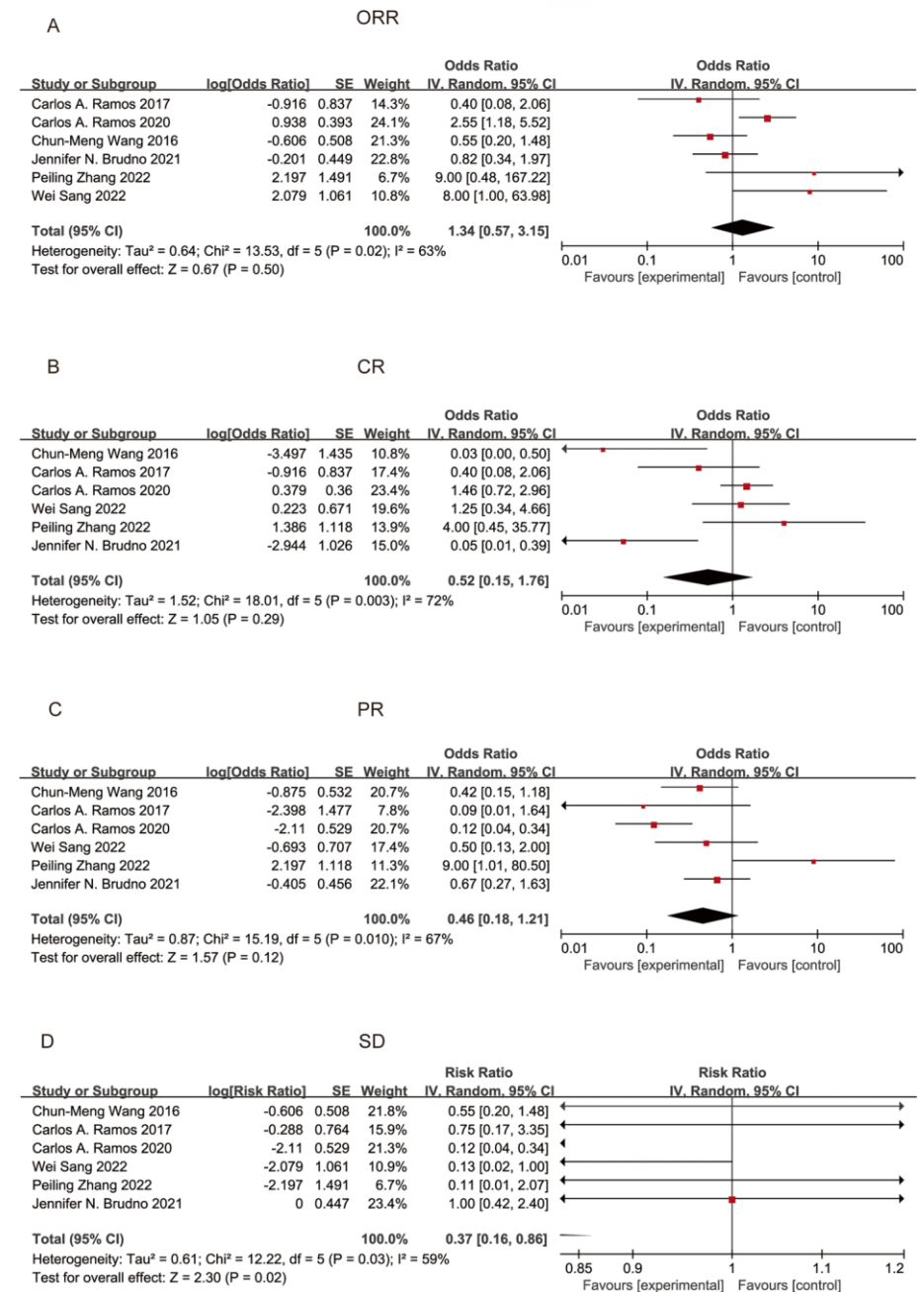


Fig. 2 Forest plots of pooled ORR (A), CR (B), PR (C), and SD (D) in this meta-analysis

CART metanalysis

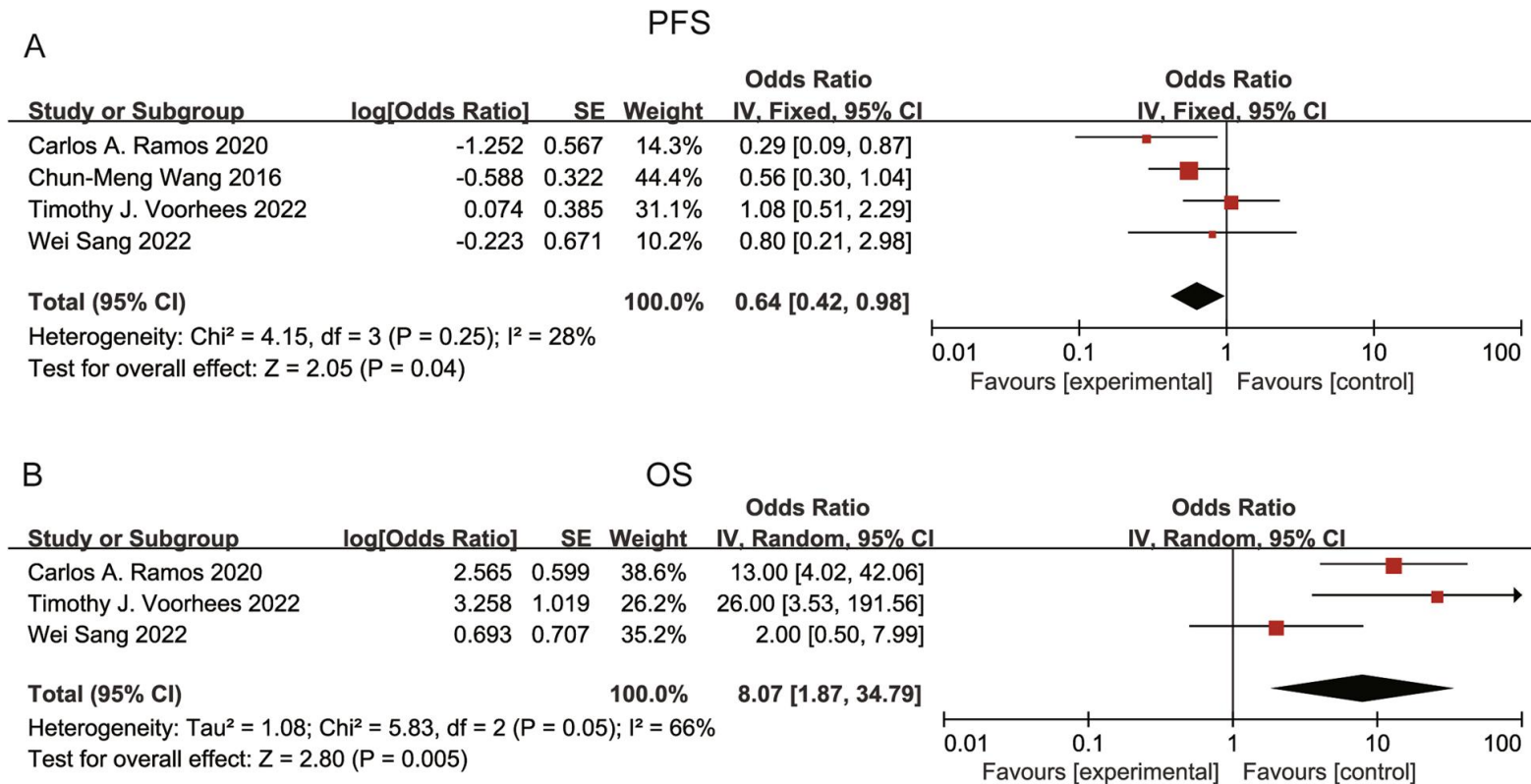
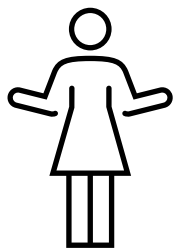
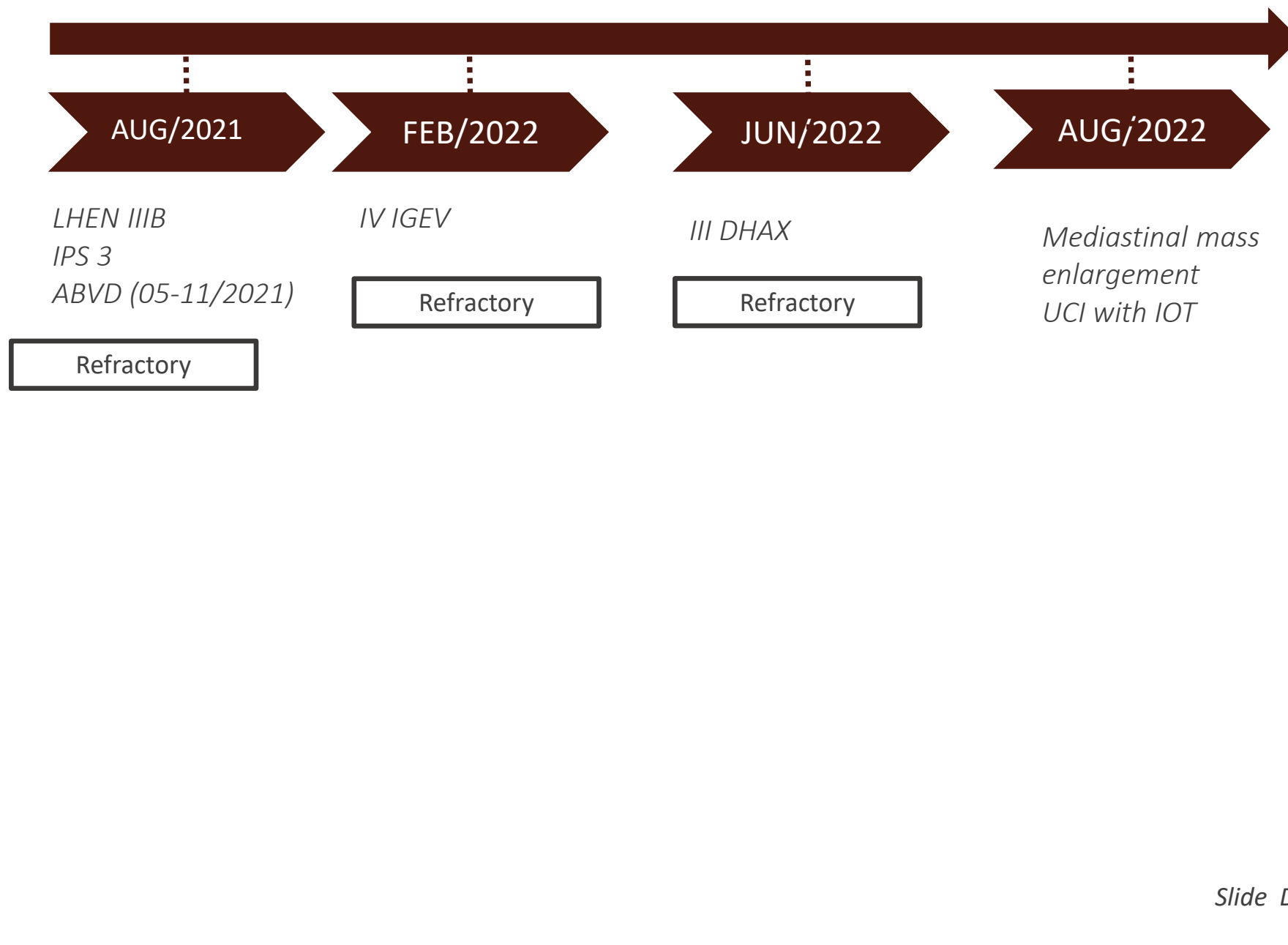
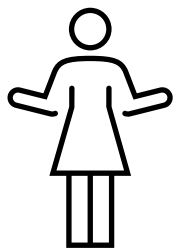


Fig. 3 Forest plots of pooled PFS (A) and OS (B) in this meta-analysis



2021: 27 years,
feminine, no
medical history





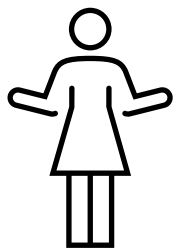
2021: 27 years,
feminine, no
medical history



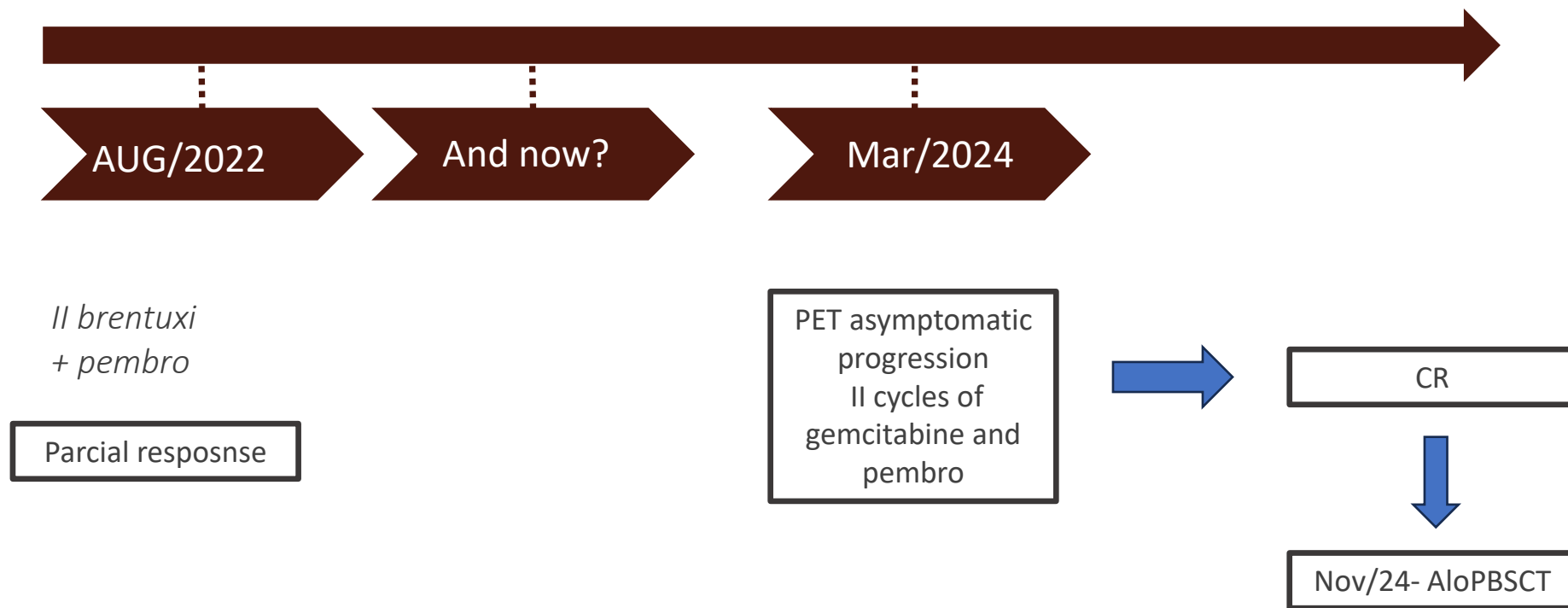
*Il brentuxi
+ pembro*

Parcial Response

What to do with a
PR after Immuno?



2021: 27 years,
feminine, no
medical history



Conclusions

Rare disease

After imuno?

PBSCT is in check?

Cure or chronic disease?





Obrigada

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