Terapie cellulari nel linfoma di Hodgkin refrattario
Pros

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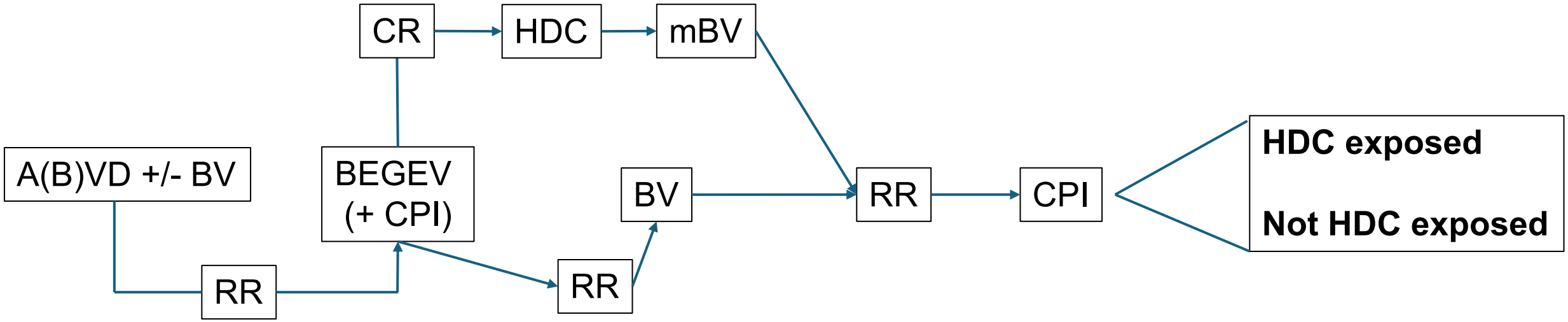
Palermo

Refractory HL



Refractory HL treated with CPI not exposed to HDC

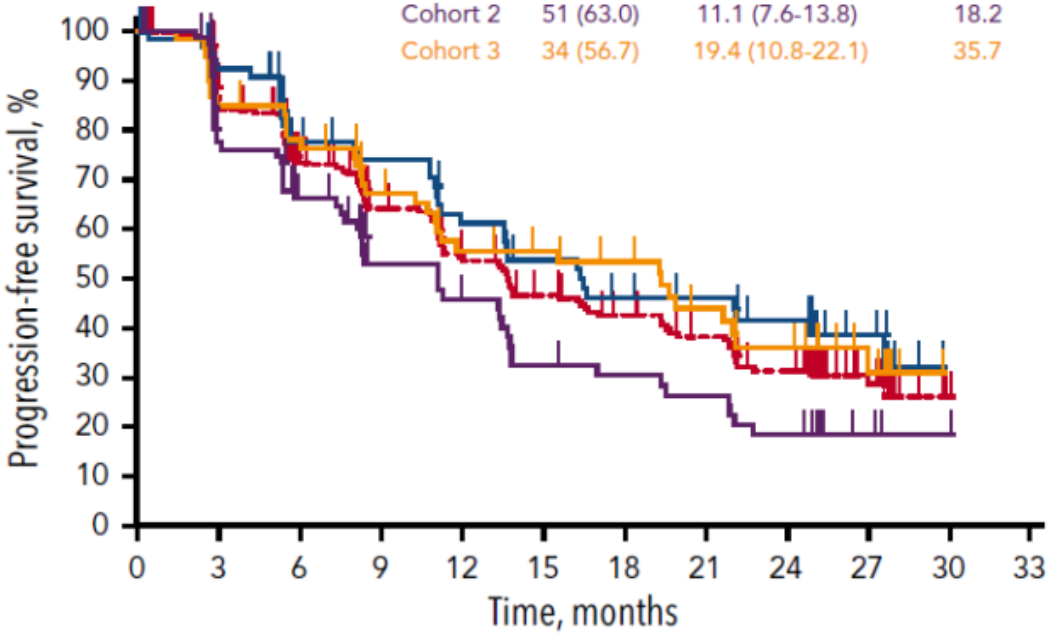
KEYNOTE 087

	Cohort 1 (n = 69): after ASCT/BV		Cohort 2 (n = 81): ineligible for ASCT and treatment failure with BV therapy		Cohort 3 (n = 60): no BV after ASCT		All patients (N = 210)	
	n (%)	95% CI*	n (%)	95% CI*	n (%)	95% CI*	n (%)	95% CI*
ORR	53 (76.8)	65.1-86.1	54 (66.7)	55.3-76.8	44 (73.3)	60.3-83.9	151 (71.9)	65.3-77.9
CR†	18 (26.1)	16.3-38.1	21 (25.9)	16.8-36.9	19 (31.7)	20.3-45.0	58 (27.6)	21.7-34.2
PR	35 (50.7)	38.4-63.0	33 (40.7)	29.9-52.2	25 (41.7)	29.1-55.1	93 (44.3)	37.5-51.3
SD	9 (13.0)	6.1-23.3	7 (8.6)	3.5-17.0	7 (11.7)	4.8-22.6	23 (11.0)	7.1-16.0
PD	5 (7.2)	2.4-16.1	18 (22.2)	13.7-32.8	9 (15.0)	7.1-26.6	32 (15.2)	10.7-20.8
No assessment	2 (2.9)	0.4-10.1	2 (2.5)	0.3-8.6	0 (0)	—	4 (1.9)	0.5-4.8

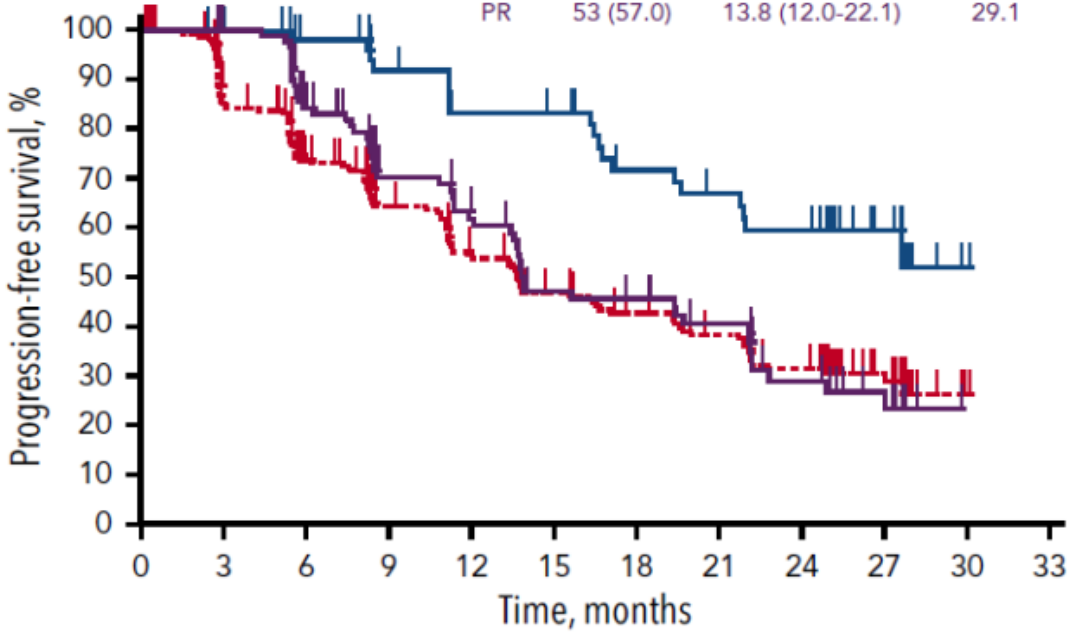
Chen, Blood 2019

Refractory HL treated with CPI not exposed to HDC

	Events, N (%)	PFS,* median (95% CI), mo	24-mo PFS,* %
All patients	120 (57.1)	13.7 (11.1-17.0)	31.3
Cohort 1	35 (50.7)	16.4 (11.3-27.6)	41.6
Cohort 2	51 (63.0)	11.1 (7.6-13.8)	18.2
Cohort 3	34 (56.7)	19.4 (10.8-22.1)	35.7



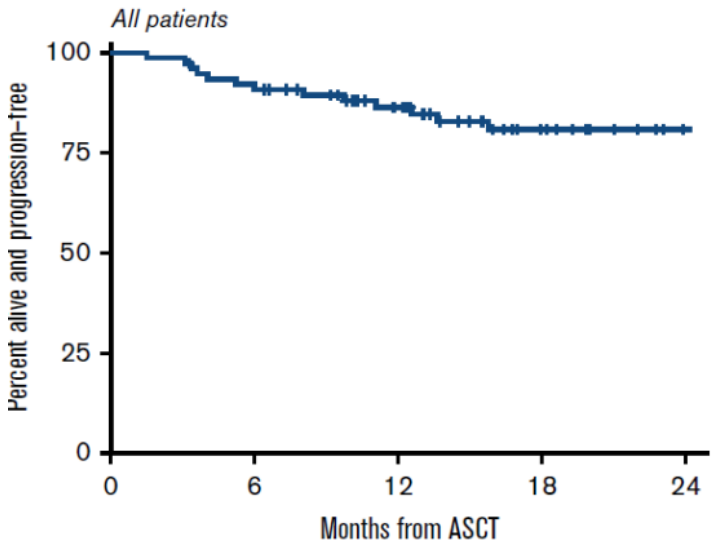
	Events, n (%)	PFS,* median (95% CI), mo	24-mo PFS,* %
All patients	120 (57.1)	13.7 (11.1-17.0)	31.3
CR	19 (32.8)	NR (21.7-NR)	59.5
PR	53 (57.0)	13.8 (12.0-22.1)	29.1

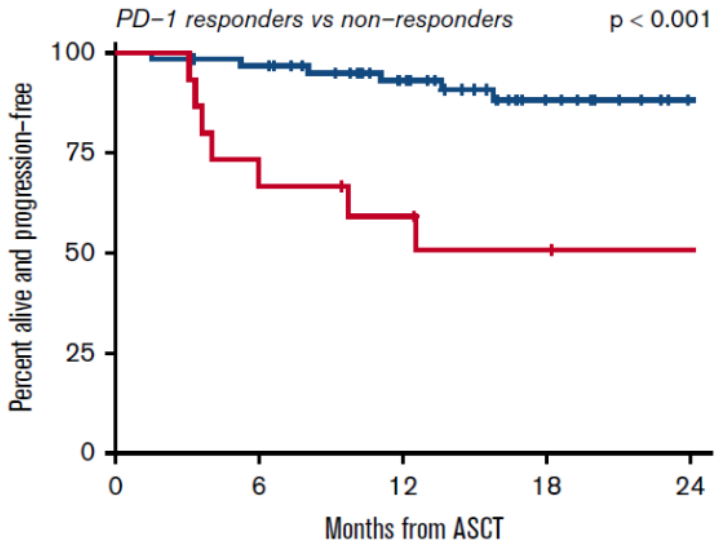


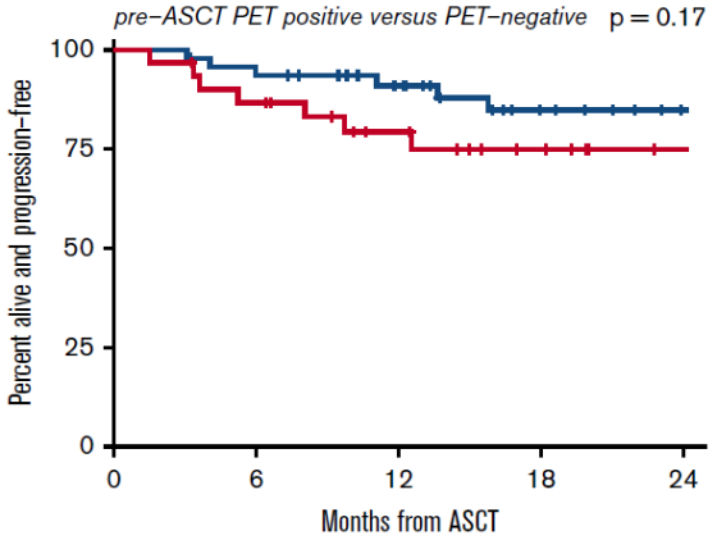
Chen, Blood 2019

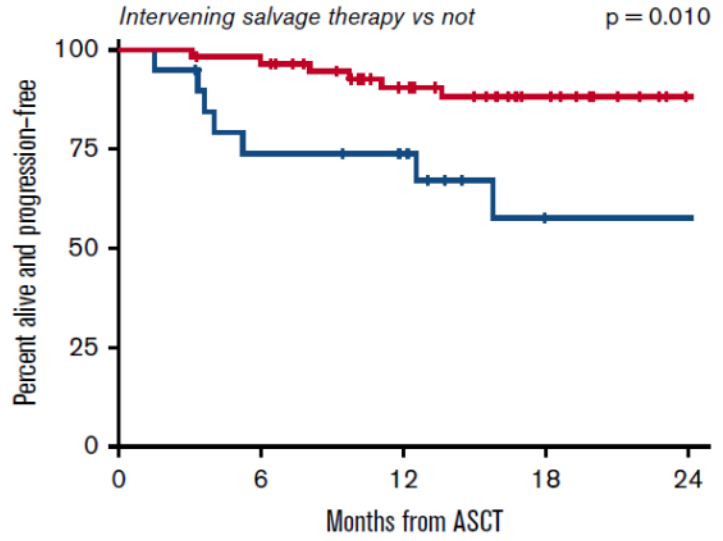
Refractory HL treated with CPI not exposed to HDC

- N= 78
- ORR CPI alone: 80% (CR 42%)
- ORR CPI +: 100% (CR 58%)
- 26% received CT after CPI
- Median time last CPI-HDC 52 days



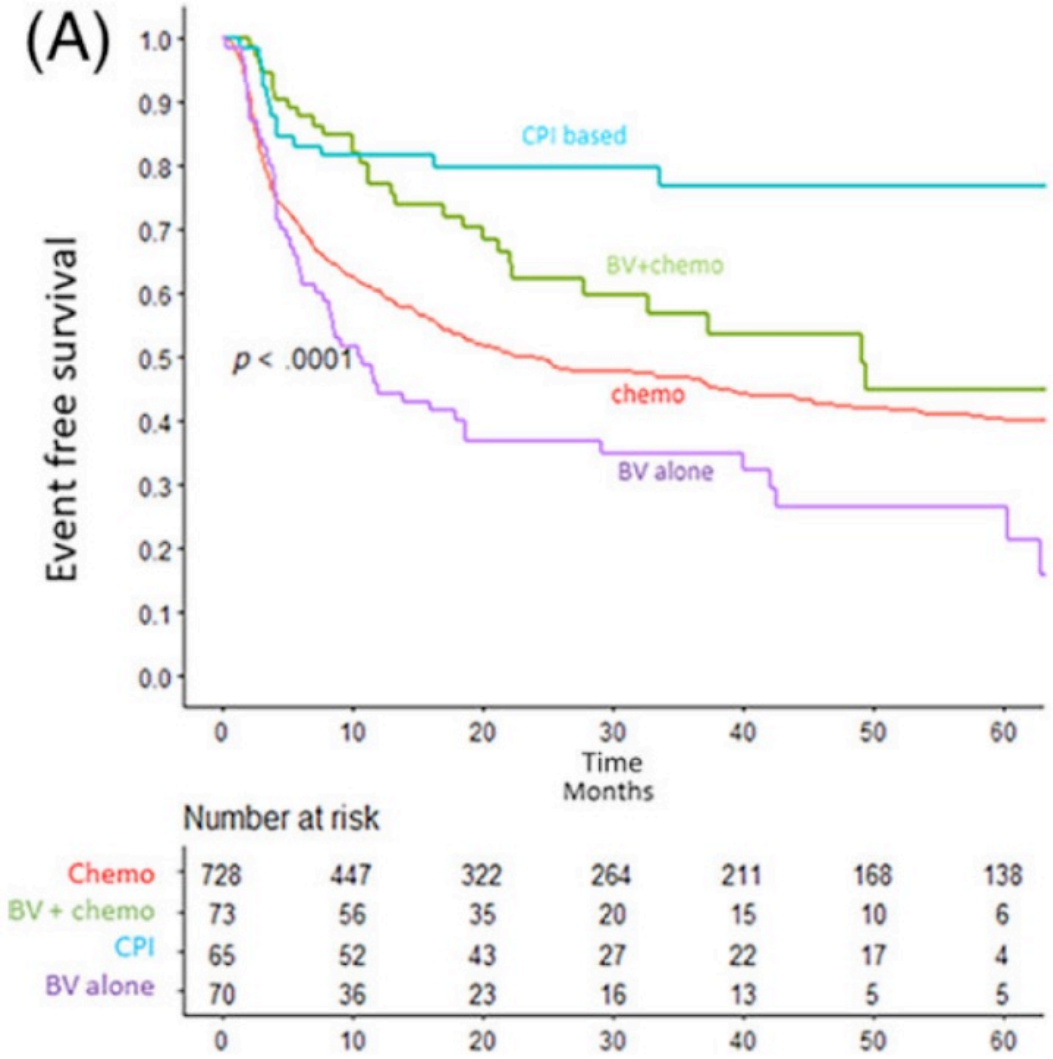






Merryman, Blood Adv 2021

Refractory HL treated with CPI no exposed to HDC



Desai, AJH 2023

Refractory HL treated with CPI and exposed to HDC

Armand, Blood Adv 2020

Refractory HL treated with CPI and exposed to HDC

Table A4. Characteristics of Patients Who Proceeded to Allo-HCT and Characteristics of Allo-HCT

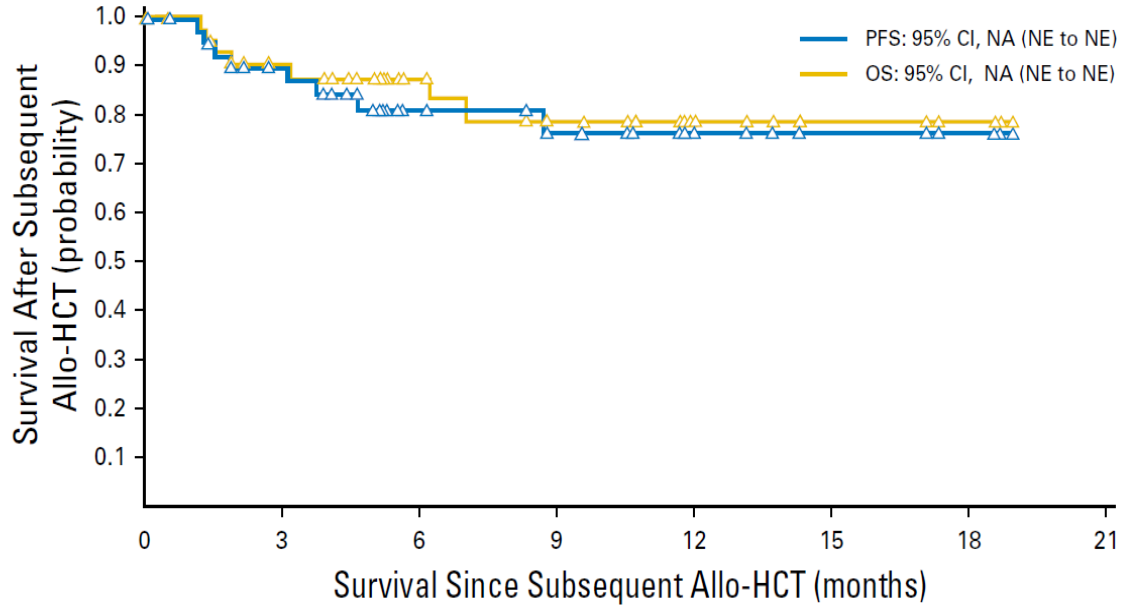
Characteristic	BV Naïve: Cohort A (n = 9)	BV After Auto-HCT: Cohort B (n = 14)	BV Before and/or After Auto-HCT: Cohort C (n = 21)	
Characteristics of patients who proceeded to allo-HCT				44
Median nivolumab doses received (IQR)	11 (8–14)	10 (8–17)	13 (10–16)	11
BOR to nivolumab				
Complete remission	2 (22)	1 (7)	4 (19)	
Partial remission	4 (44)	6 (43)	14 (67)	
Stable disease	1 (11)	7 (50)	2 (10)	
Progressive disease	2 (22)	0	1 (5)	
Discontinued nivolumab as a result of disease progression	3 (33)	5 (36)	2 (10)	
Therapeutic intervention after nivolumab and before allo-HCT	4 (44)	6 (43)	2 (10)	25%
Median time from last nivolumab dose to allo-HCT, months (IQR)	4.2 (1.6–6.2)	1.4 (1.0–4.2)	1.5 (1.2–3.3)	
Disease status at allo-HCT				47%
Complete remission	4 (44)	7 (50)	10 (48)	21%
Partial remission	4 (44)	6 (43)	9 (43)	11%
UTD/not reported	1 (11)	1 (7)	2 (10)	
Allo-HCT characteristics				
HCT source				
Peripheral blood	8 (89)	10 (71)	14 (67)	
Bone marrow	0	3 (21)	6 (29)	
Unknown/not reported	1 (11)	1 (7)	1 (5)	
Donor type				16%
HLA-identical relative	2 (22)	2 (14)	5 (24)	27%
≥ 2 HLA-mismatched haploidentical relative	2 (22)	3 (21)	7 (33)	47%
Unrelated	4 (44)	8 (57)	9 (43)	
Unknown	1 (11)	1 (7)	0	
Preparative regimen				
MAC	1 (11)	1 (7)	0	
Non-MAC	5 (56)	10 (71)	19 (90)	
Unknown/not reported	3 (33)	3 (21)	22 (10)	

NOTE: Data presented as No. (%) unless otherwise indicated.
Abbreviations: allo-HCT, allogeneic hematopoietic cell transplantation; auto-HCT, autologous hematopoietic cell transplantation; BOR, best overall response; BV, brentuximab vedotin; HLA, human leukocyte antigen; IQR, interquartile range; MAC, myeloablative conditioning; UTD, unable to determine.

Armand, JCO 2018

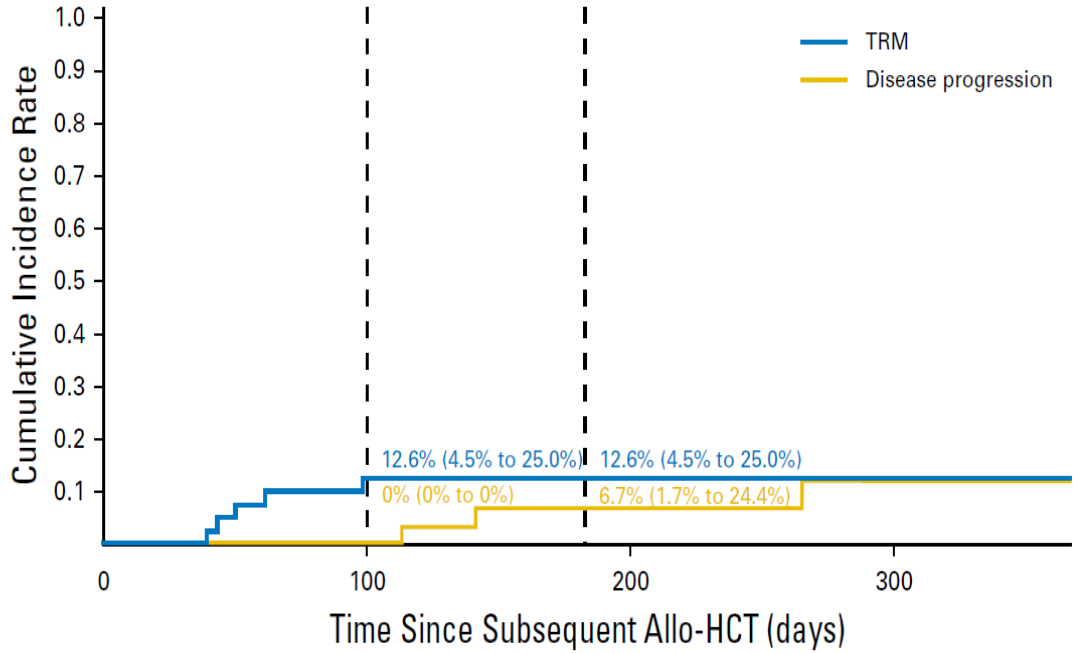
Refractory HL treated with CPI and exposed to HDC

C



Cohort A + B + C No. at risk:								
PFS	44	33	19	15	8	5	3	0
OS	44	33	21	16	8	5	3	0

A



Armand, JCO 2018

Refractory HL treated with CPI and exposed to HDC

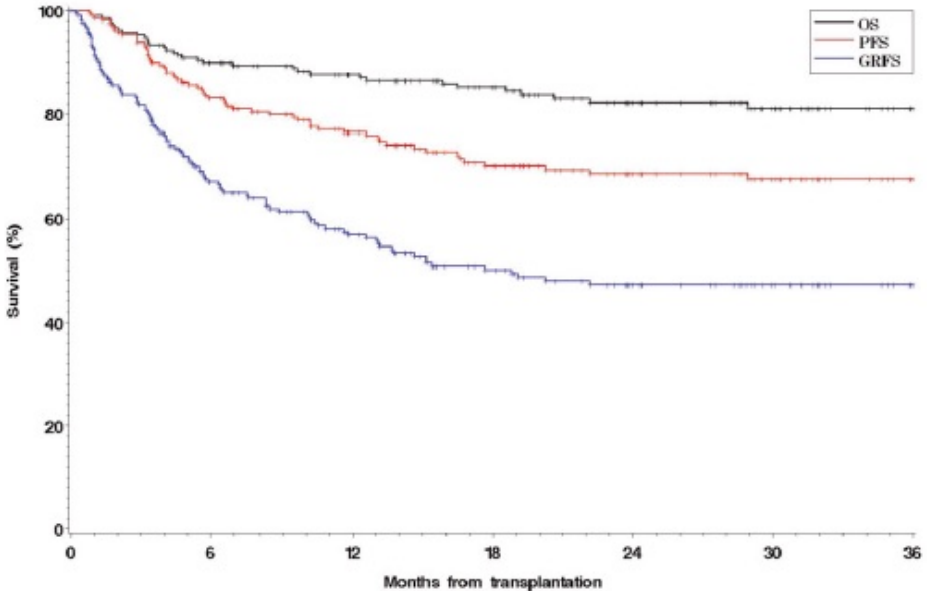
Variable	PFS		OS		GRFS	
	HR	p	HR	p	HR	p
Age						
≤50	**3.1**	**0.001**	**3.0**	**0.012**	**2.7**	**0.0002**
>50						
Status at allo						
No CR	0.5	**0.012**	0.6	0.12	0.7	0.14
CR						
Doses of PD1						
1-9 (or unknown)	0.8	0.49	0.6	0.14	0.7	**0.039**
10+						
Groups						
No/No						
Haplo/PTCY	**0.4**	**0.005**	**0.6**	0.29	**0.4**	**0.0002**
No/PTCY	**0.3**	**0.022**	**0.1**	**0.023**	**0.4**	**0.009**
BOR to PD1						
CR/PR/SD	**2.2**	**0.044**	1.3	0.68	**2.0**	**0.024**
PD						

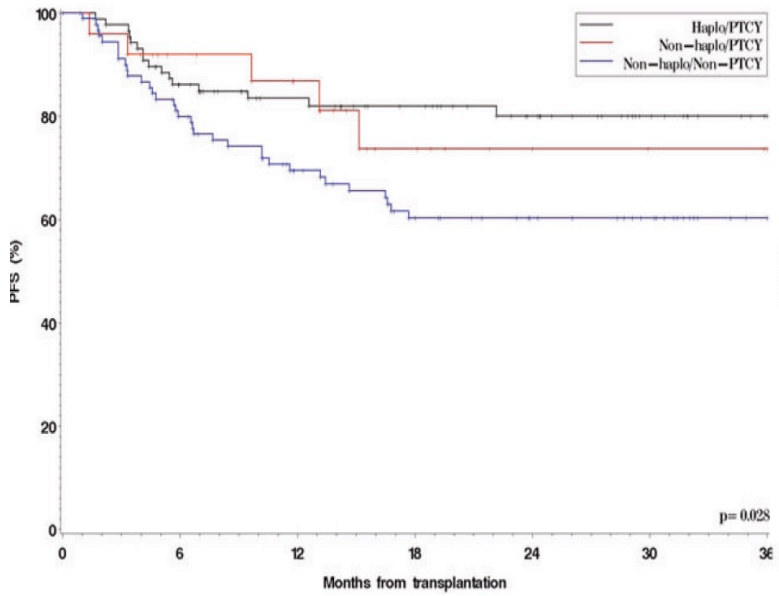
Variable	CIR		NRM		aGVHD		cGVHD	
	HR	p	HR	p	HR	p	HR	p
Age								
≤50								
>50	1.9	0.26	2.5	0.069				
Status at allo								
No-CR								
CR	0.4	**0.018**	0.7	0.38				
Intervening salvage								
no								
Yes	2.9	**0.003**	0.7	0.34				
Groups								
No/No								
Haplo/PTCY	0.2	**0.006**	0.7	0.4	0.7	0.12	0.5	**0.026**
No/PTCY	0.7	0.53	0.2	**0.056**	0.5	0.07	0.2	**0.011**
Doses of PD-1								
1-9 (or unknown)								
10+					1.0	0.99	0.6	**0.036**
Days to alloHCT								
0-80								
81+					0.6	**0.041**	0.7	0.14

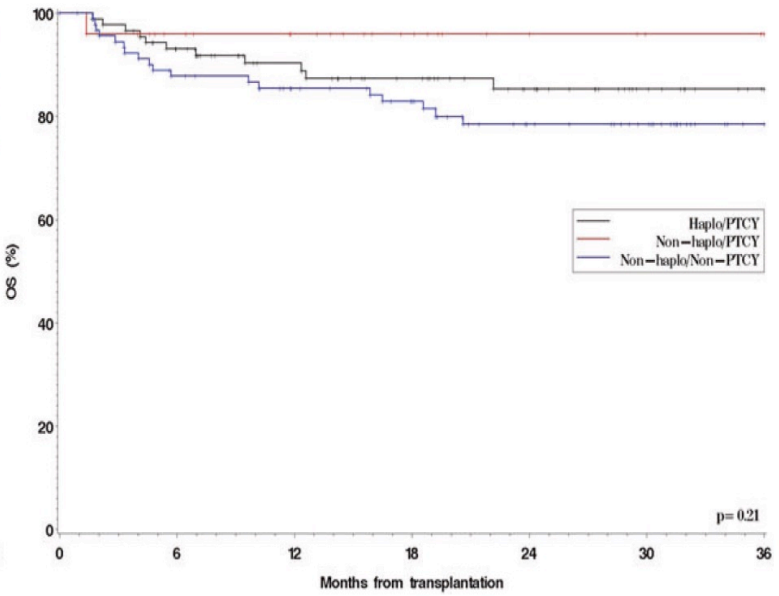
100-day CI SOS: 3%
2y NRM 14%
aGVHD 2-4: 37%

Merryman, Leukemia 2021

Refractory HL treated with CPI and exposed to HDC







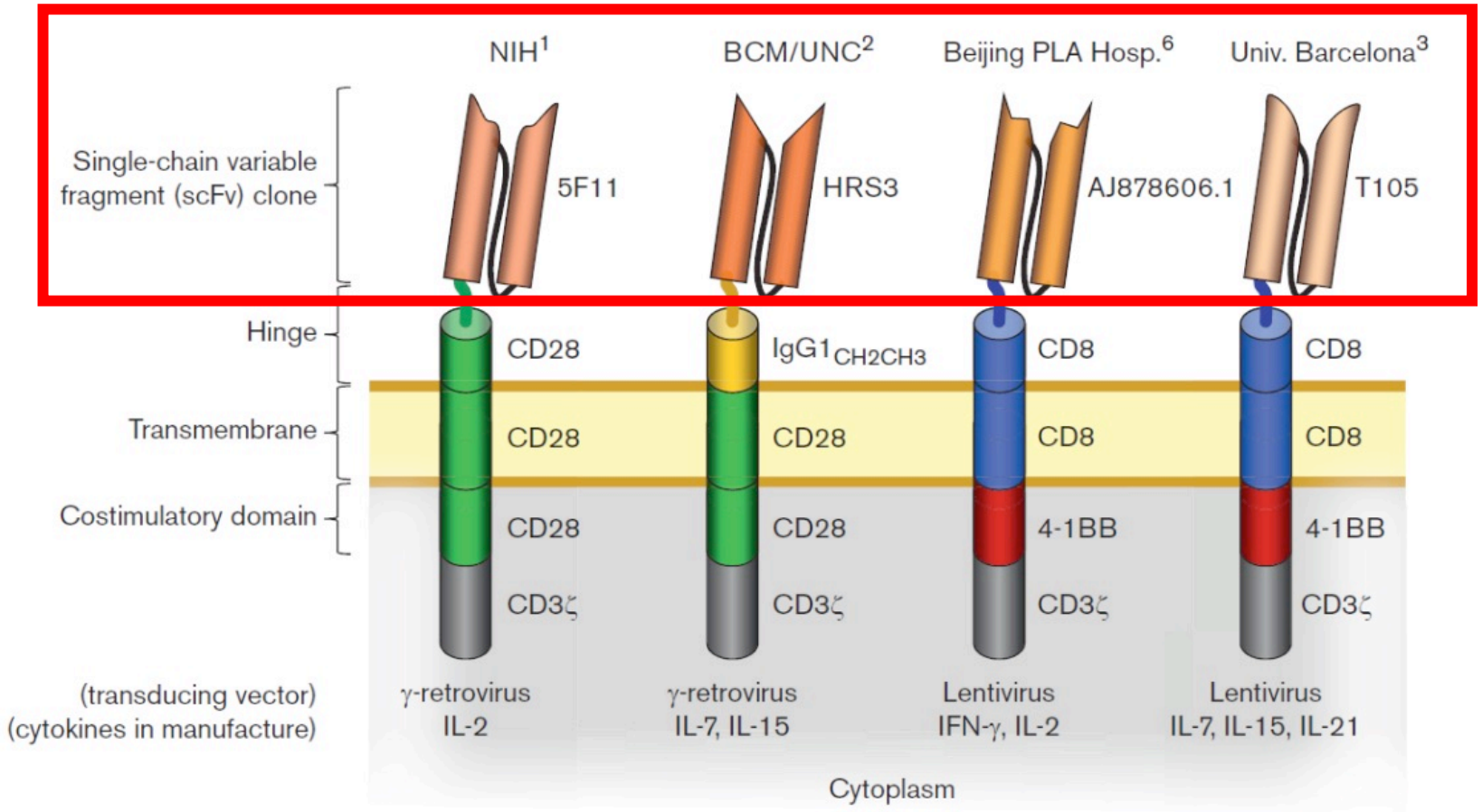
Merryman, Leukemia 2021

CAR-T in refractory HL treated

	Wang 2017	Svoboda 2018	Ramos 2020	Brudno 2024
n	18	4	41	21
Antigen	CD30	CD19	CD30	CD30
Transfection	Lentivirus	Electroporation	Retrovirus	Lentivirus
Disease	CD30+ lymphoma	HL	HL	CD30+ lymphoma
LD	FC+GMC+PC	Cy -4 to -1 and +7	FC Benda Benda+F	FC
Dose	1-3x10e7/kg	7.4x10e5- 2.1x10e6/kg In 6 infusions	2x10e7/m2-2x10e8/m2 1x10e8/m2-2x10e8/m2	0.3x10e6-9x10e6/kg In 1-3 infusions
Tox	CRS G1 100% Skin rash 11%	/	CRS G1 24% Skin rash 48%	CRS G1-3 55% Skin rash 43%
ORR	39% (CR 0%)	50%	72% (CR 59%)	43% (CR 5%)

GMC= gemcitabine, mecloretamine, cyclophosphamide
PC= placlitaxel, cyclophosphamide

CAR-T in refractory HL treated



- ✓ Few patients
- ✓ Heterogenous disease
- ✓ Different cellular products
- ✓ Variable CD30 CART tumor infiltration
- ✓ Few HL cells in suppressive TME

Grover, Blood Adv 2024

Conclusions

- Cellular therapies, autologous and allogeneic transplantation have a prominent role in the treatment landscape of RR HL.
- In absence of randomized or prospective studies, HDC and autologous stem cell infusion, should be strongly considered in patients in response after CPI.
- Similarly, an allogeneic stem cell transplantation must be proposed to patients pre-treated with HDC and CPI.
- The improvement of first line therapy with the introduction of BV and CPI, probably will reduce the number of refractory patients.