20TH INTERNATIONAL ULTMANN CHICAGO LYMPHOMA SYMPOSIUM

APRIL 21-22, 2023

Treating relapsed/ refractory Hodgkin lymphoma

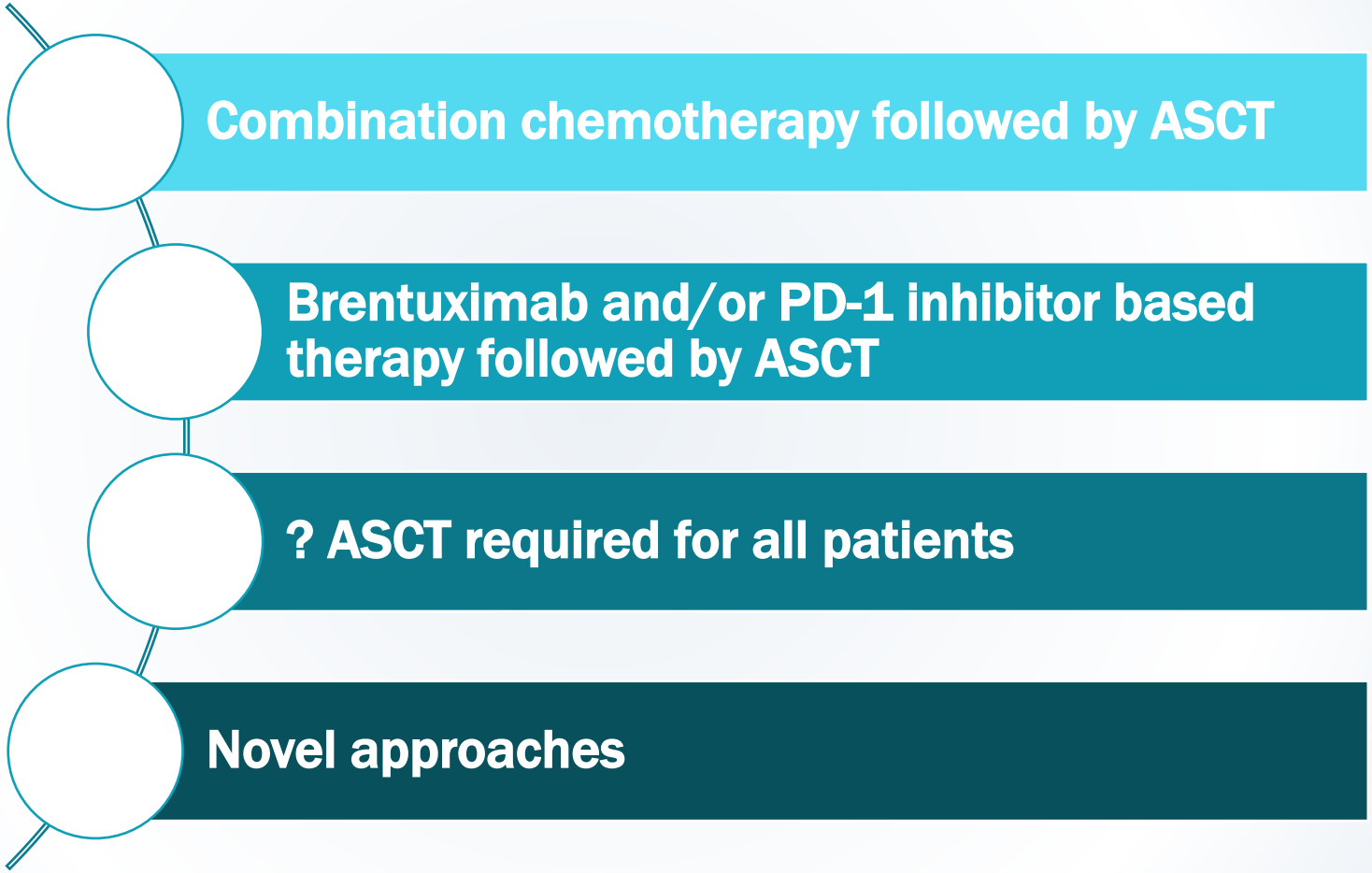
20TH ULTMANN
CHICAGO LYMPHOMA SYMPOSIUM

THE UNIVERSITY OF CHICAGO
MEDICINE & BIOLOGICAL SCIENCES

Disclosures

- **Consultancy: Seagen, Kite Pharma**
- **Speaker's Bureau/CME: Research to Practice**

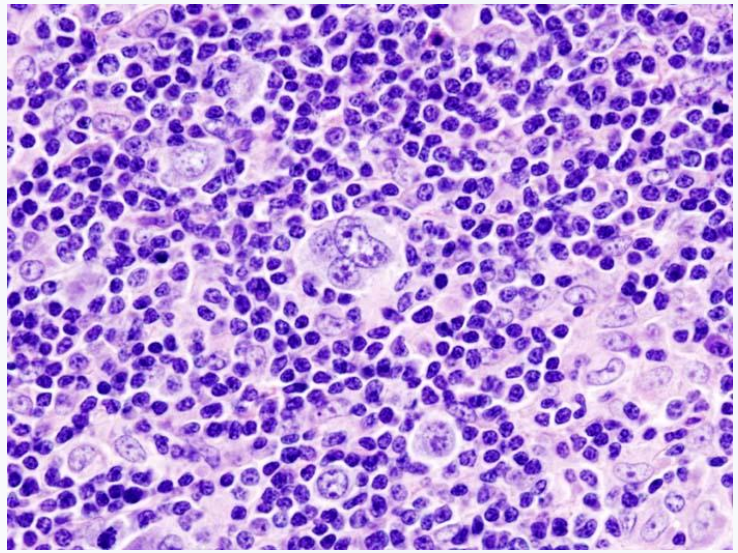
Past → Present → Future directions in relapsed cHL



10-30% of HL patients will relapse after initial therapy

10-20% of patients with stage I/II disease

25-30% of patients with stage III/IV disease

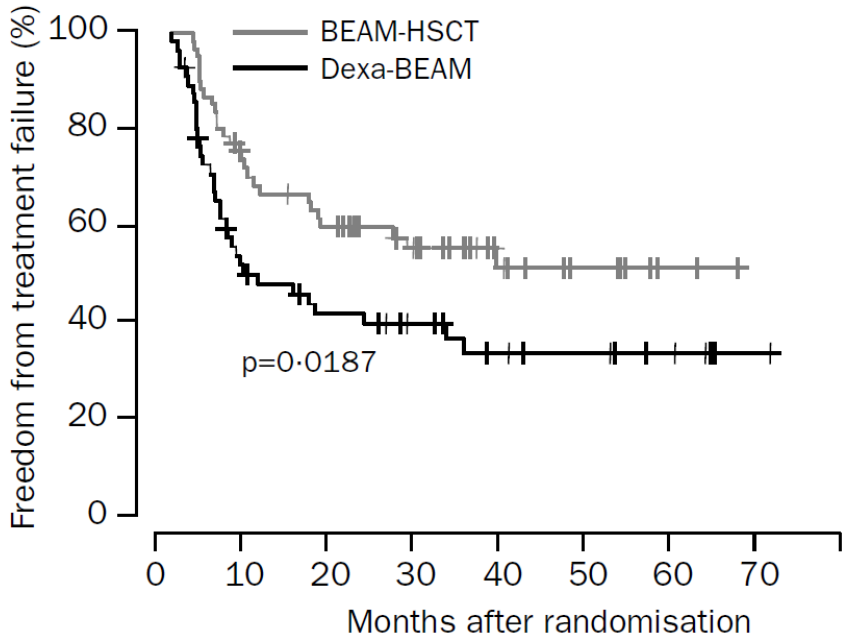


10-15% of patients are primary refractory

Importance of biopsy:

- confirm relapsed HL
- r/o inflammation
- sarcoid
- r/o NHL or grey zone lymphoma

Two, small randomized studies led to adoption of ASCT: Improvement in treatment failure rates but not OS



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**

	Dexa-BEAM (n=21)	BEAM-HSCT (n=17)
Cause of death		
Hodgkin's disease	14	11
Early treatment-related toxic effect	6	1
Septicaemia after salvage therapy	0	1
Overwhelming post-splenectomy infection	0	1
Fibrosis of lung	0	1
Pneumococcal meningitis and pneumonia	0	1
Secondary leukaemia	0	1

Table 3: **Causes of death in chemosensitive patients at last follow-up**

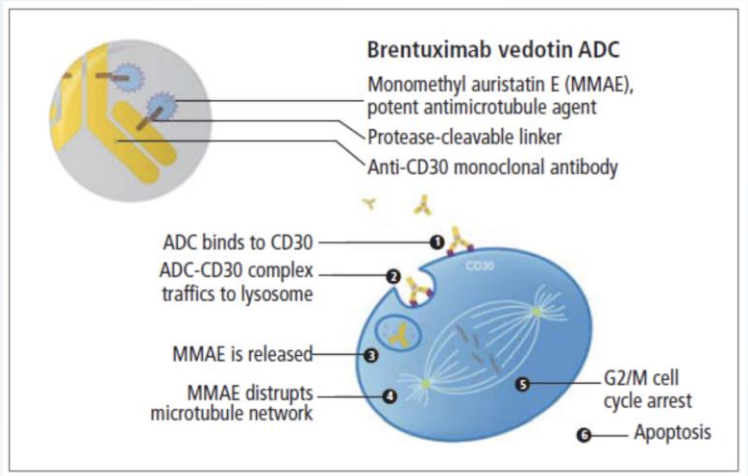
Schmitz et al. Lancet 2002

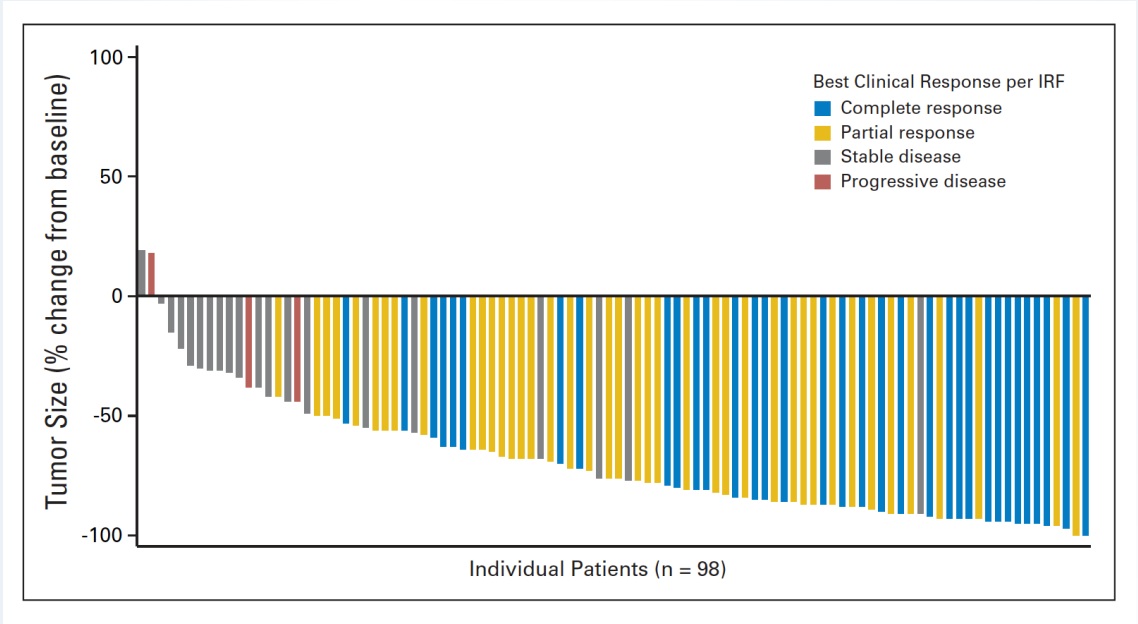
Pre-transplant PET prognostic for PFS after ASCT

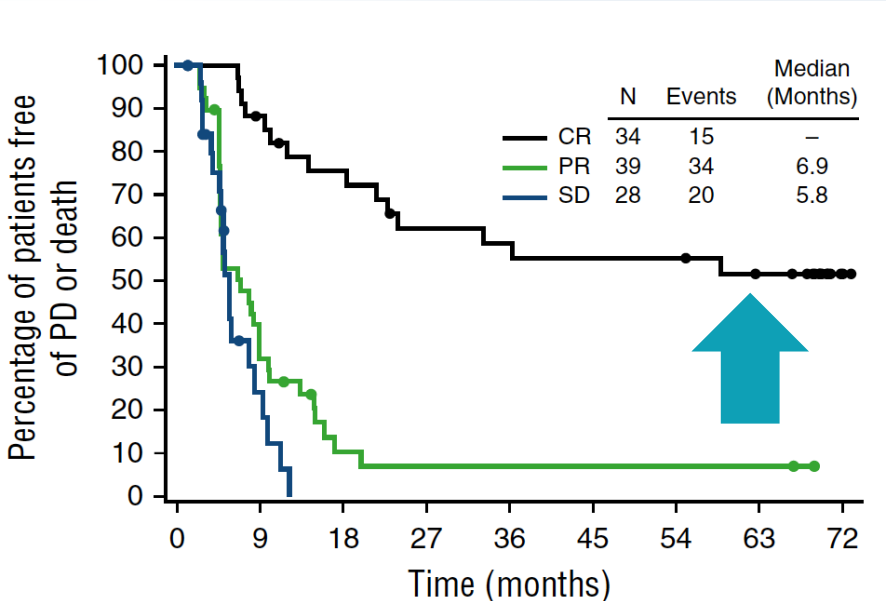
Regimen	n	CR	ref
ICE	97	60%	Moskowitz. Blood 2012
DHAP	102	21% (CT)	Josting. Ann Onc 2002
ESHAP	82	50%	Labrador. Ann Hem 2014
BeGV	59	73%	Santoro. Blood 2018

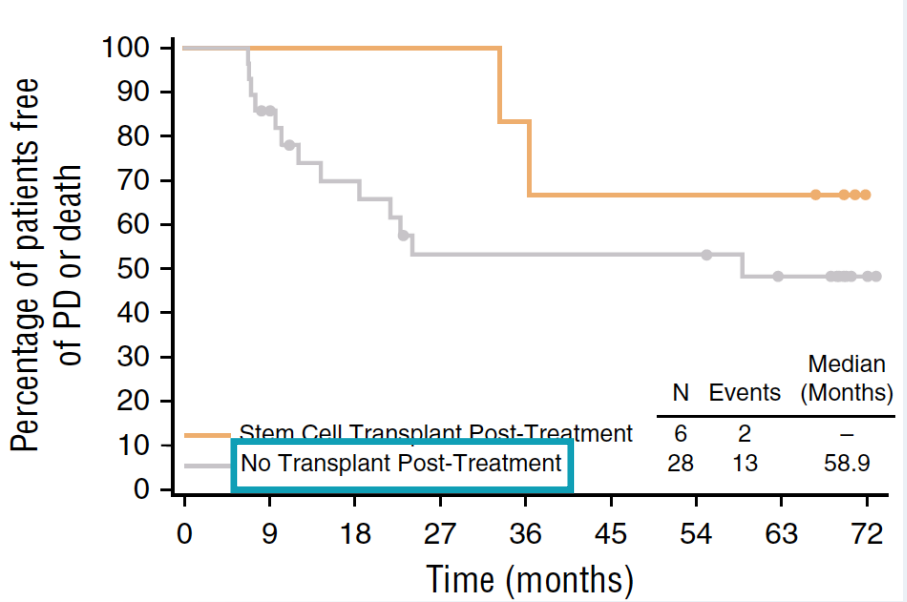
n	PET – PFS	PET + PFS	ref
105	4 yr PFS 77%	4 yr PFS 33%	Moskowitz. BJH 2010
153	5 yr PFS 75%	5 yr PFS 31%	Moskowitz. Blood 2010
97	4 yr PFS 80%	4 yr PFS 29%	Moskowitz. Blood 2012
111	5 yr PFS 79%	5 yr PFS 31%	Devillier. Hematologica 2012

BV with long term responses in subset of complete responders









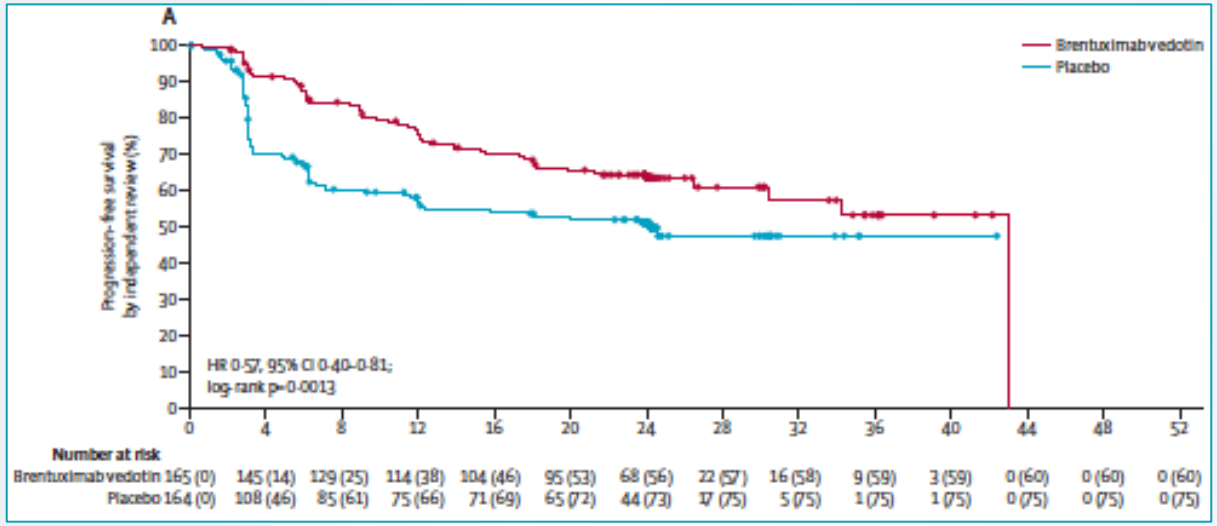
Younes et al. JCO 2012

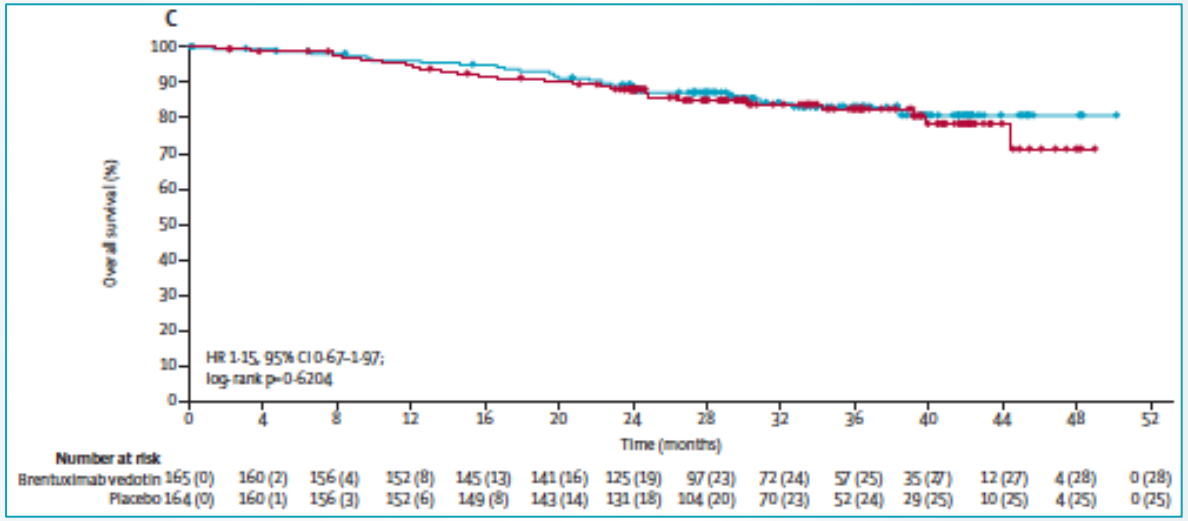
Chen et al. Blood 2016

Brentuximab containing salvage regimens with high CR rates

Regimen	n	CR	2-year PFS	ref
BV augmented ICE	45	27% BV 76% total	80% (EFS)	Moskowitz Lancet Onc 2015
BV bendamustine	82	73%	70%/63%	LaCasce Blood 2018
BV ESHAP	66	70%	71%	Garcia-Sanz Ann Onc 2019

Aethera: maintenance brentuximab vedotin after ASCT improves PFS in patients with high risk disease





? benefit in patients previously treated with BV

Moskowitz et al. Lancet. 2015

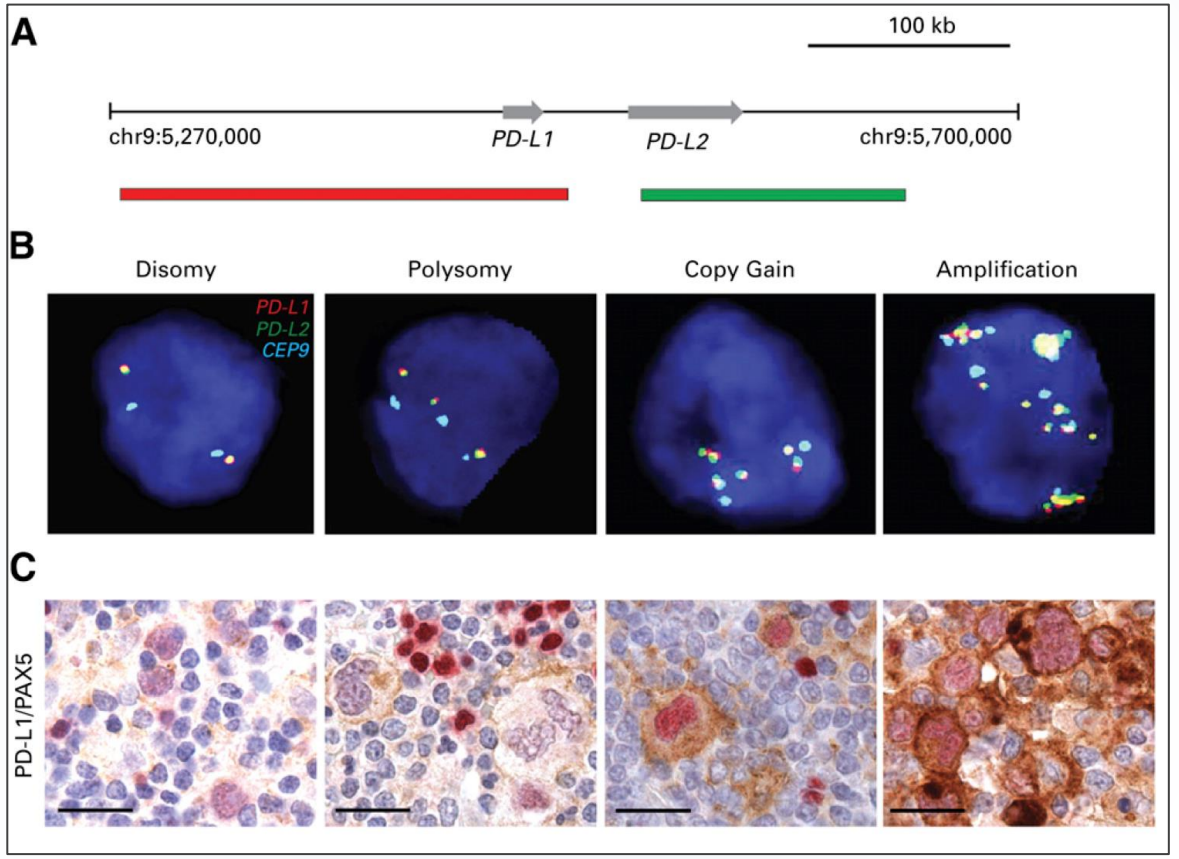
PD-1 inhibitors approved in relapsed/refractory HL

Pembrolizumab
ORR 67-78%
CR 26-32%

Chen et al. Blood 2019

Nivolumab
ORR 65-73%
CR 12-29%

Armand et al JCO 2018

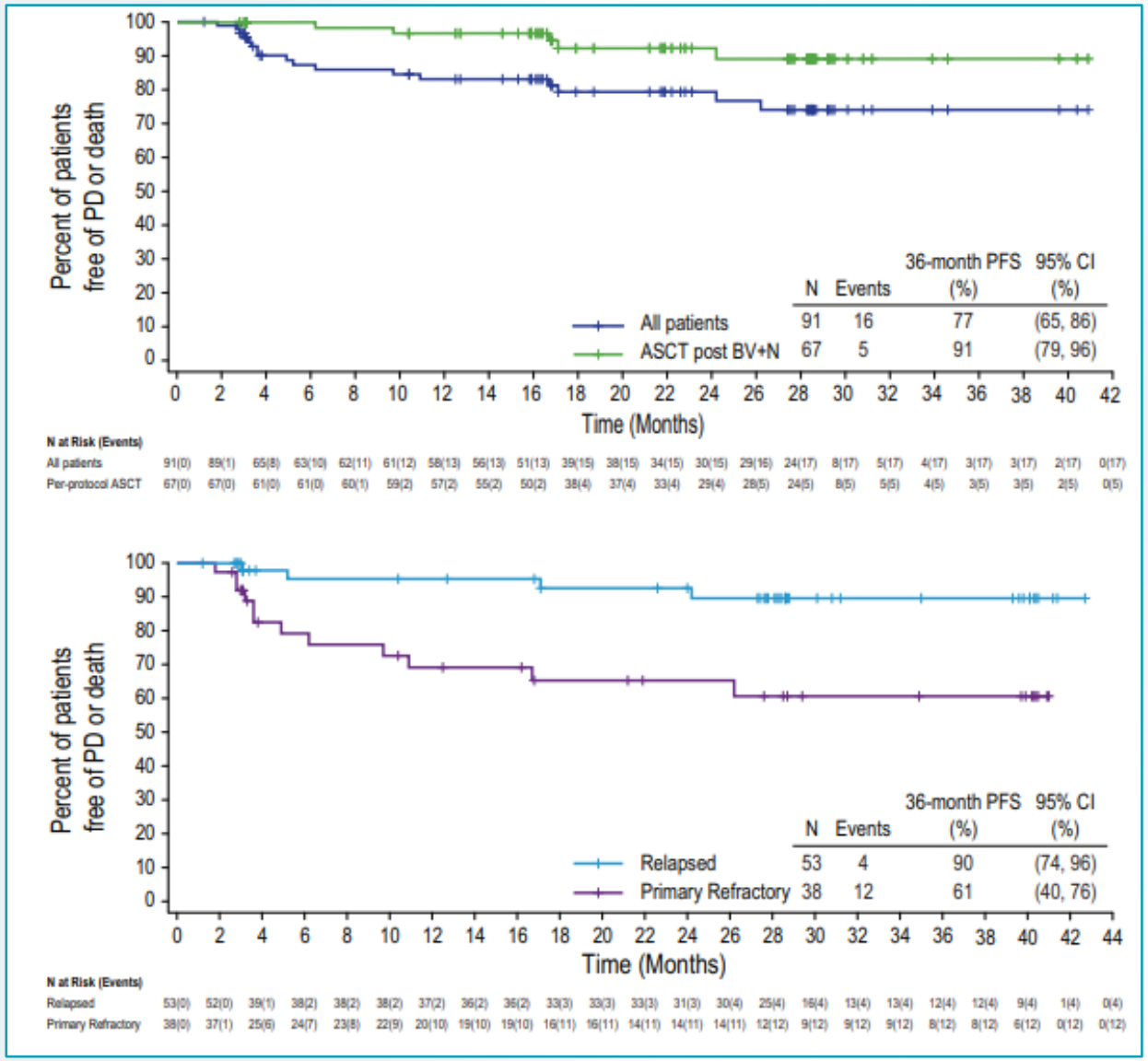


Grade 3-4 immune mediated AEs rare.

4-6% of patients discontinued therapy for toxicity.

Younes et al. Lancet Onc 2016

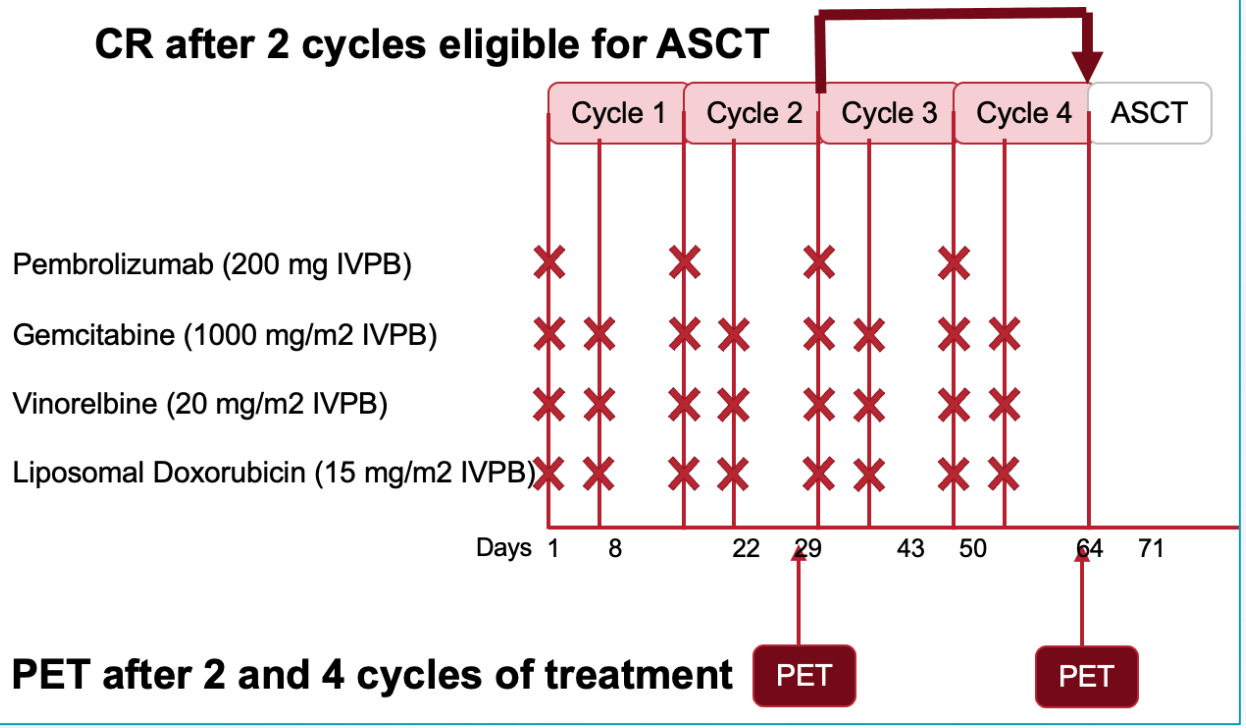
BV plus nivolumab with favorable PFS in first relapse



Outpatient regimen
Minimal myelosuppression

Advani et al. Blood 2021

Pembrolizumab + GVD is highly active in second line



Disease status after frontline therapy	n=39
Refractory (no CR to frontline and progression ≤ 1 year)	16 (41)
Relapse (CR to frontline and remission duration ≤ 1 year)	15 (38)
Relapse (CR to frontline and remission duration > 1 year)	8 (21)

Moskowitz et al. JCO 2021

Early data promising with pembro-GVD in first relapse*

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)

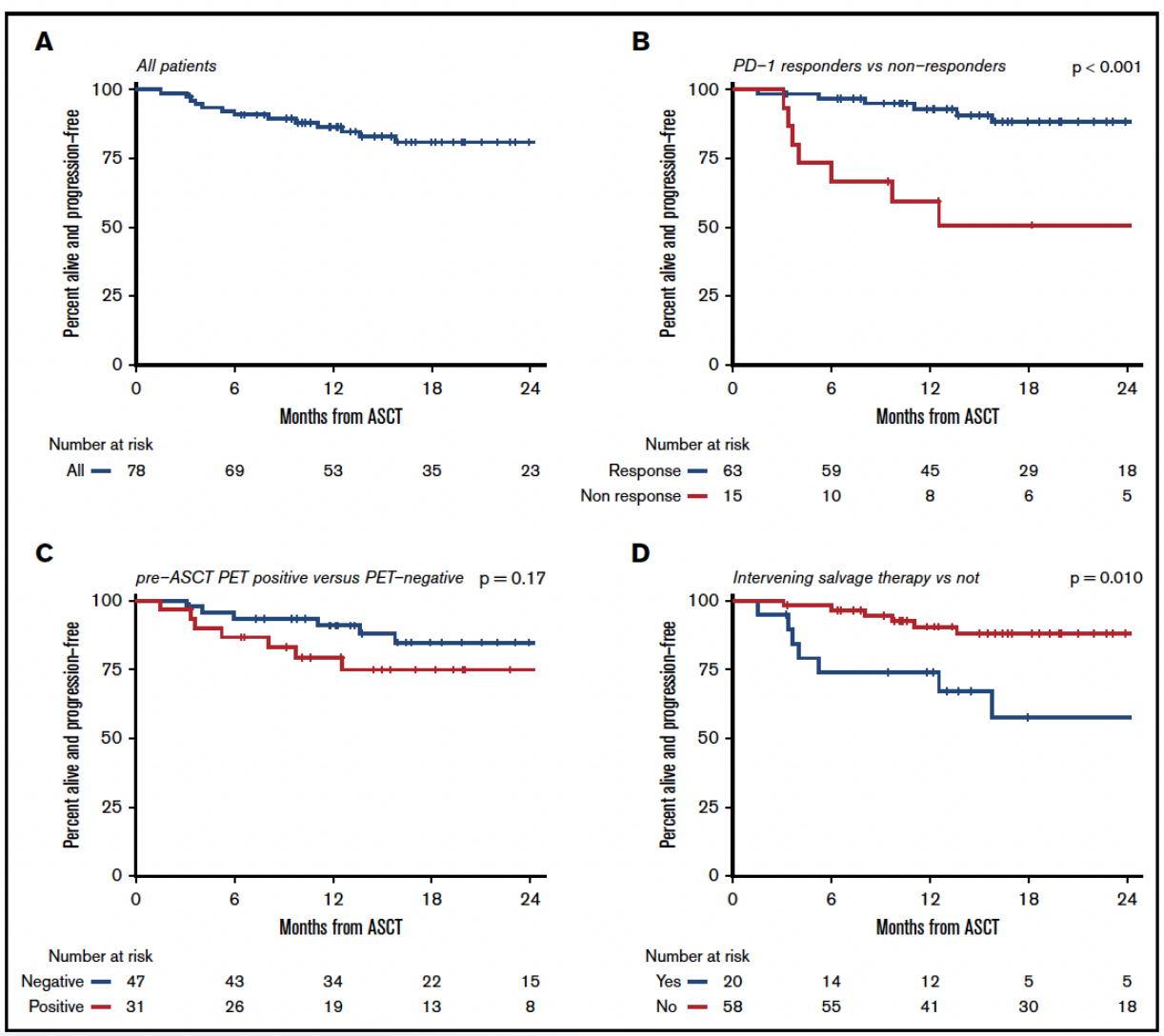
Toxicity:
13% required steroids
Mucositis - 41% (10% gr 3)
Engraftment syndrome in 68%

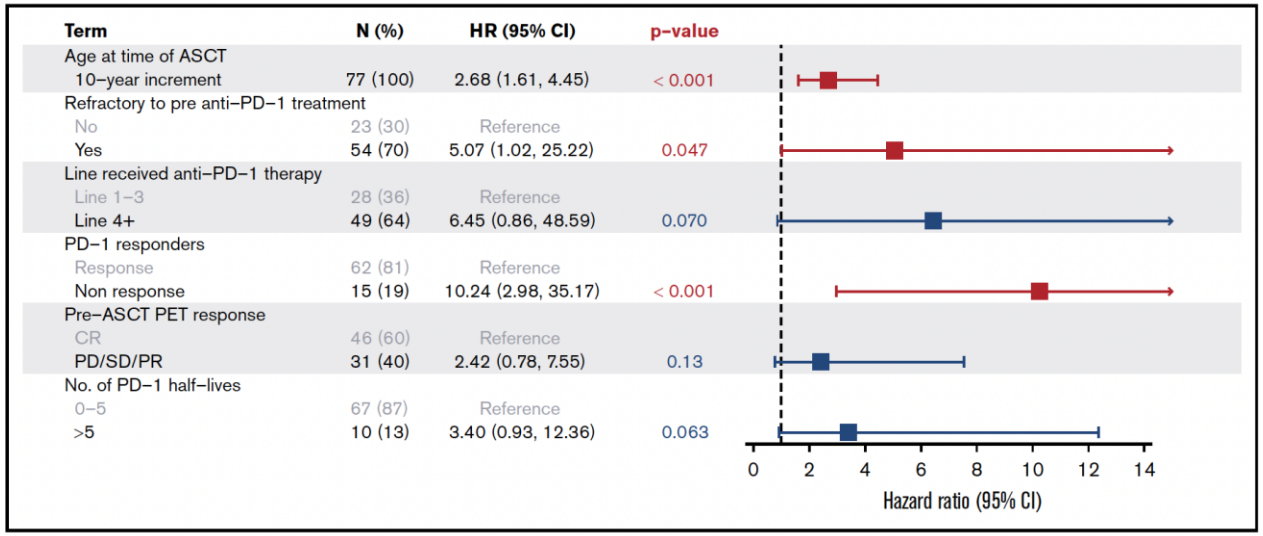
Median f/u 13.5 m, no relapses in patients who underwent ASCT

*off label

Moskowitz et al. JCO 2021

PD-1 before ASCT associated with favorable PFS



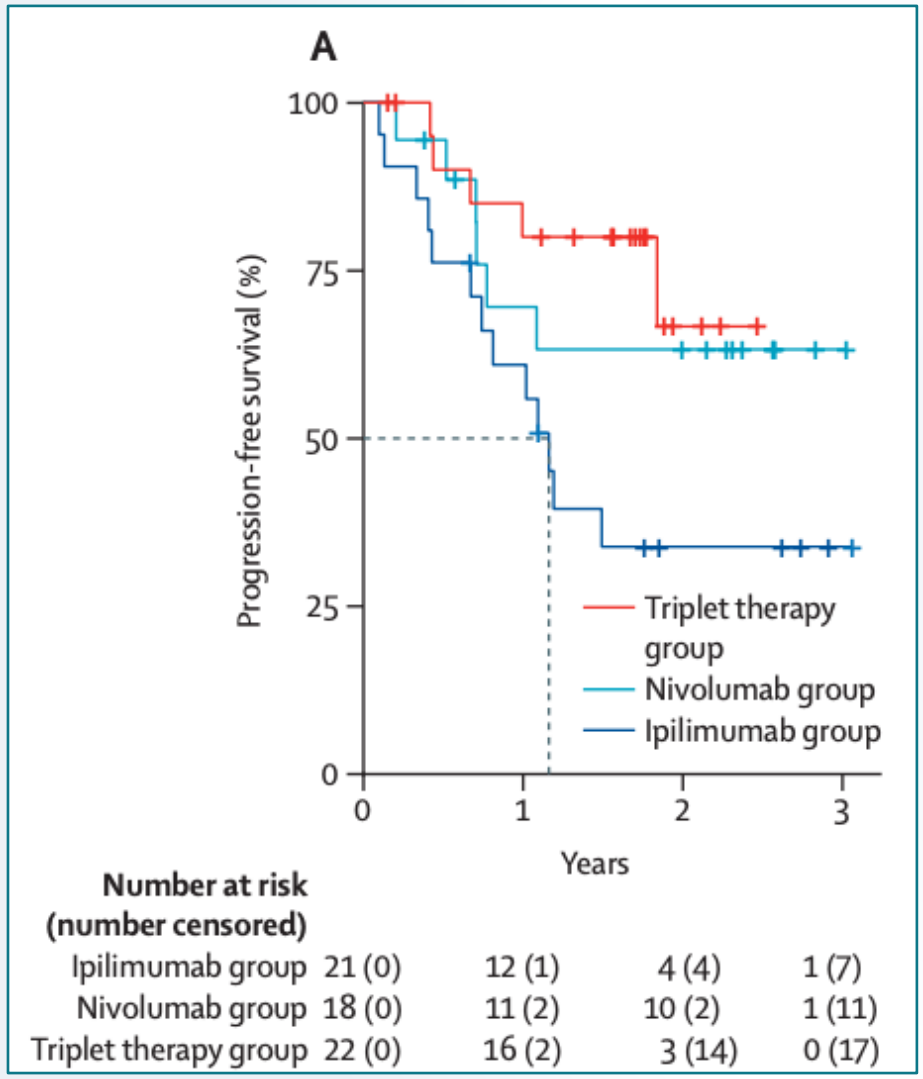


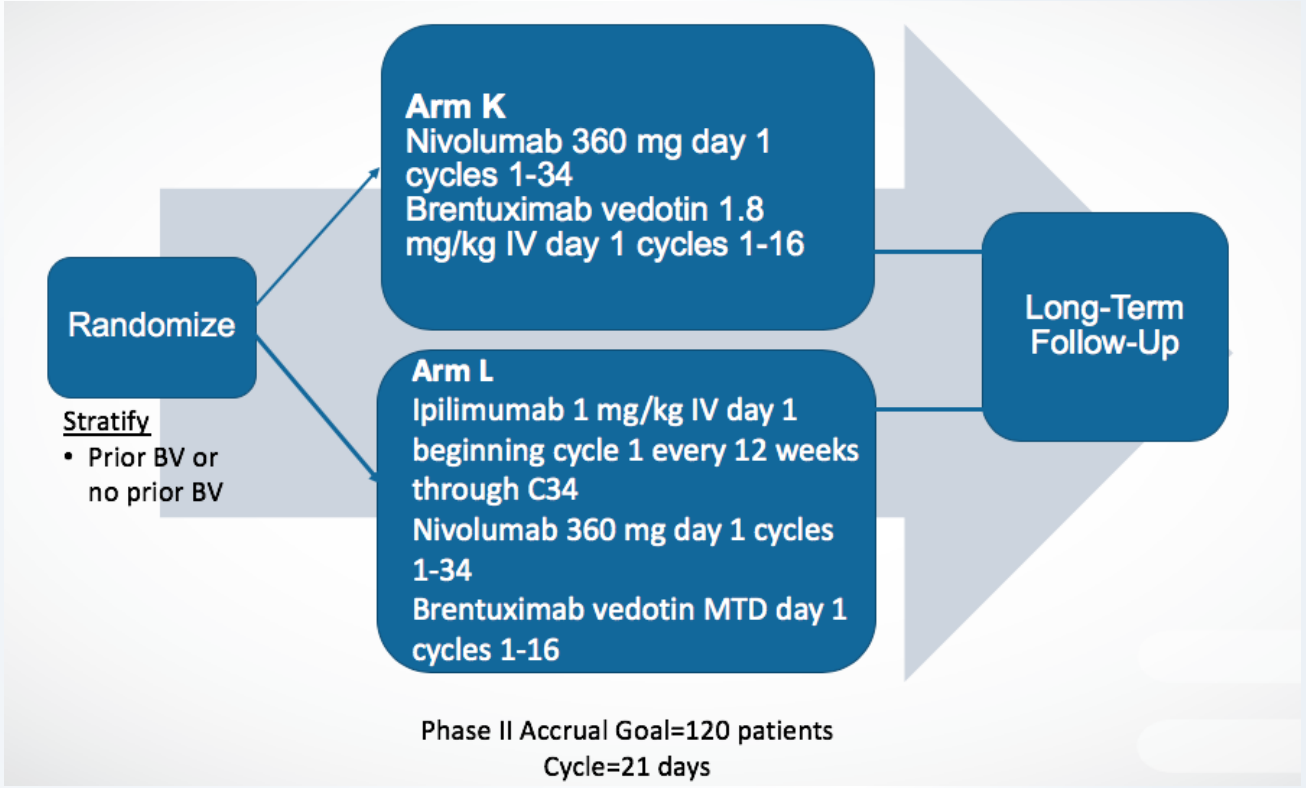
Merryman et al. Blood Adv 2021

Is ASCT necessary in all patients?

- Outcomes post ASCT after PD-1 promising
- No plateau in patients with refractory HL s/p PD-1
- ? maintenance strategies
- On-going trials testing BV-nivo
- Pembro-GVD

BV-nivo vs BV-ipi-nivo in PD-1 naïve relapsed/refractory HL

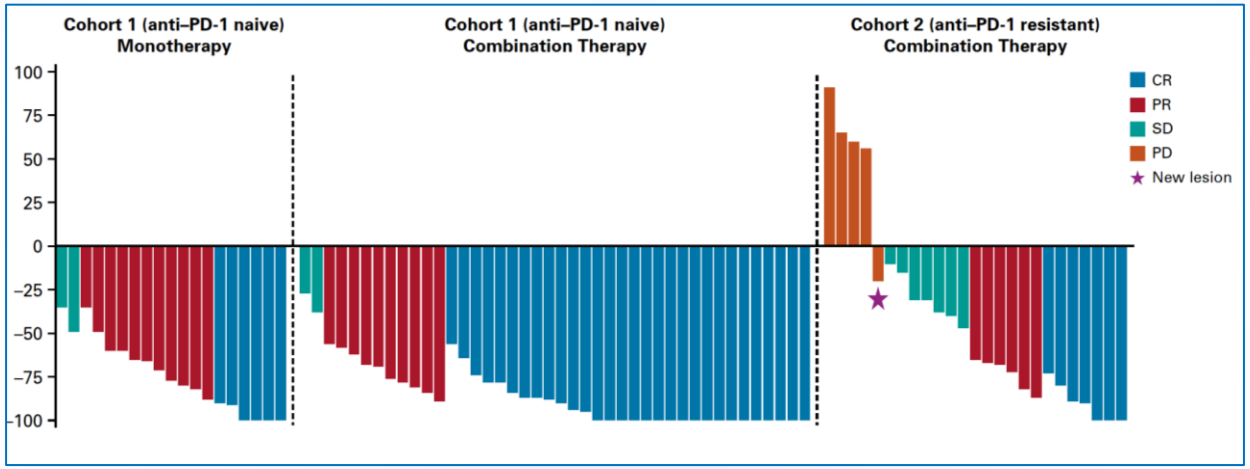




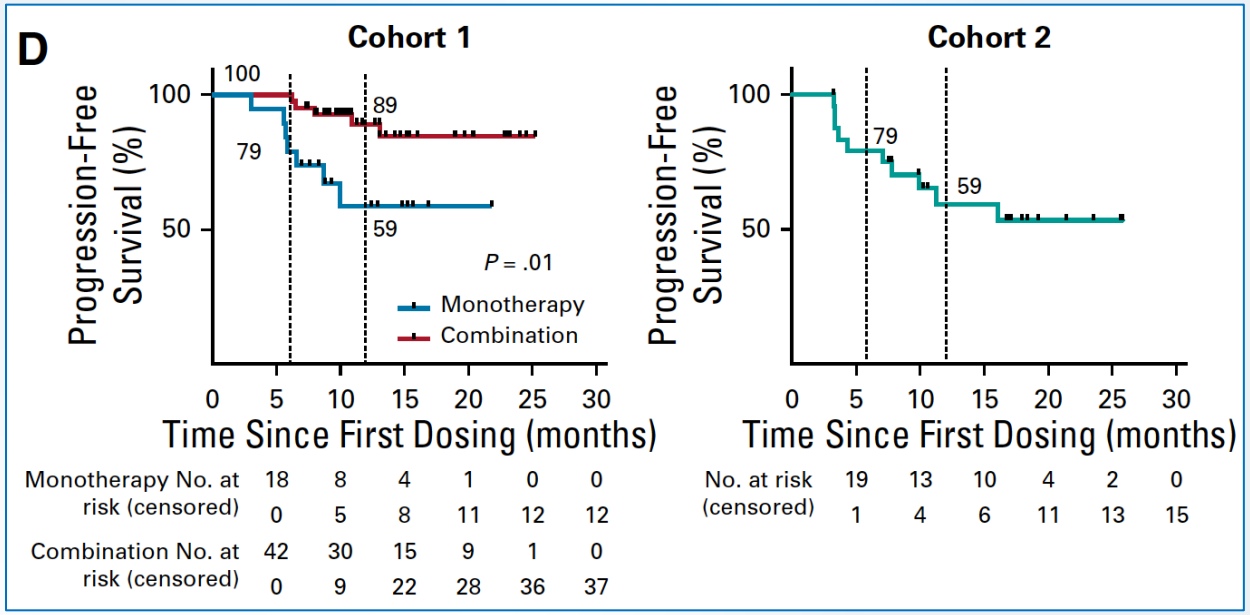
Grade 3-4 AE:
Ipilimumab 43%
Nivolumab 16%
Combo 50%
2 deaths (nivo and triplet)

Diefenbach et al. Lancet Heme 2020

PD-1 inhibitor plus decitabine active in relapsed/ref HL



Grade 3-4 toxicities occurred in 37% of pts on combination therapy (37% leukocytopenia, 3% thrombocytopenia)



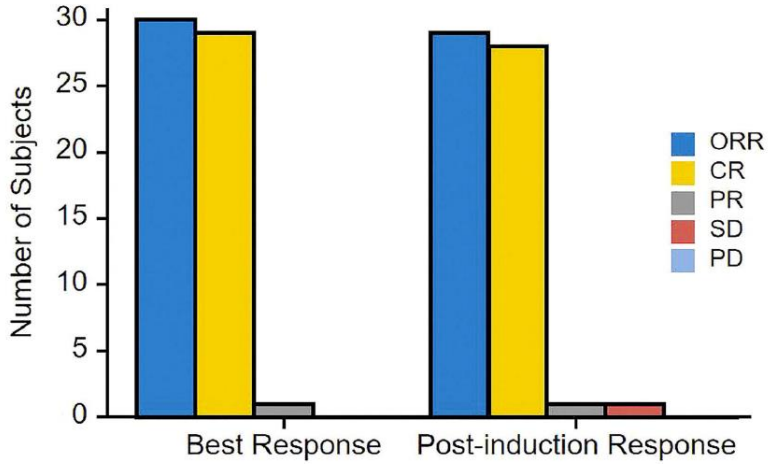
Nie et al. JCO 2019

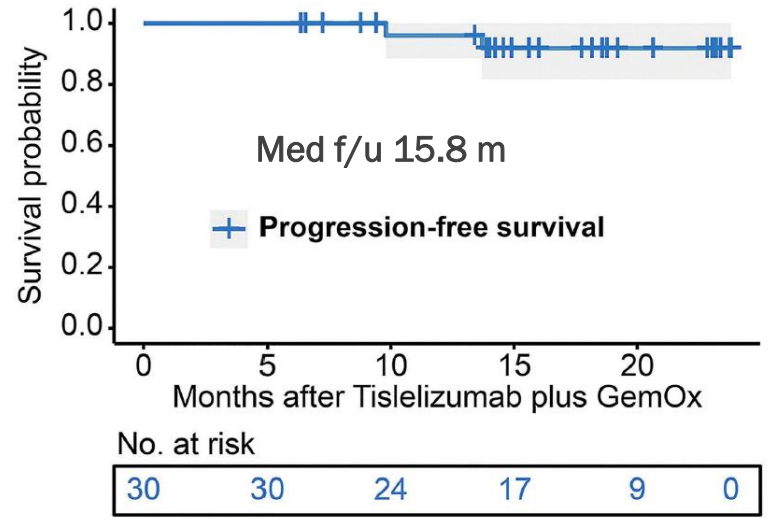
Tislelizumab with gemcitabine and oxaliplatin

Accessed for eligibility (N = 32)

Characteristics	N = 30
Previous lines of therapy, n (%)	
1 prior line	17 (56.7)
2 prior lines	4 (13.3)
≥3 prior lines	9 (30.0)
Prior chemotherapy, n (%)	30 (100)
ABVD	30 (100)
BEACOPP	2 (6.7)
GDP	4 (13.3)
ICE	4 (13.3)
IGEV	3 (10.0)
GVD	2 (6.7)
Others	2 (6.7)
Prior radiotherapy, n (%)	4 (13.3)
Prior ASCT, n (%)	5 (16.7)
Prior brentuximab vedotin, n (%)	2 (6.7)
Prior PD-1 antibody, n (%)	4 (13.3)
Prior PD-L1 antibody, n (%)	2 (6.7)
Response to PD-1/PD-L1 antibody*, n (%)	
Partial remission	2 (33.3)
Stable disease	2 (33.3)
Disease progression	2 (33.3)
Disease status, n (%)	
Relapsed after first-line chemotherapy	10 (33.3)
Refractory to first-line chemotherapy	20 (66.7)
Refractory to the most recent therapy	20 (66.7)

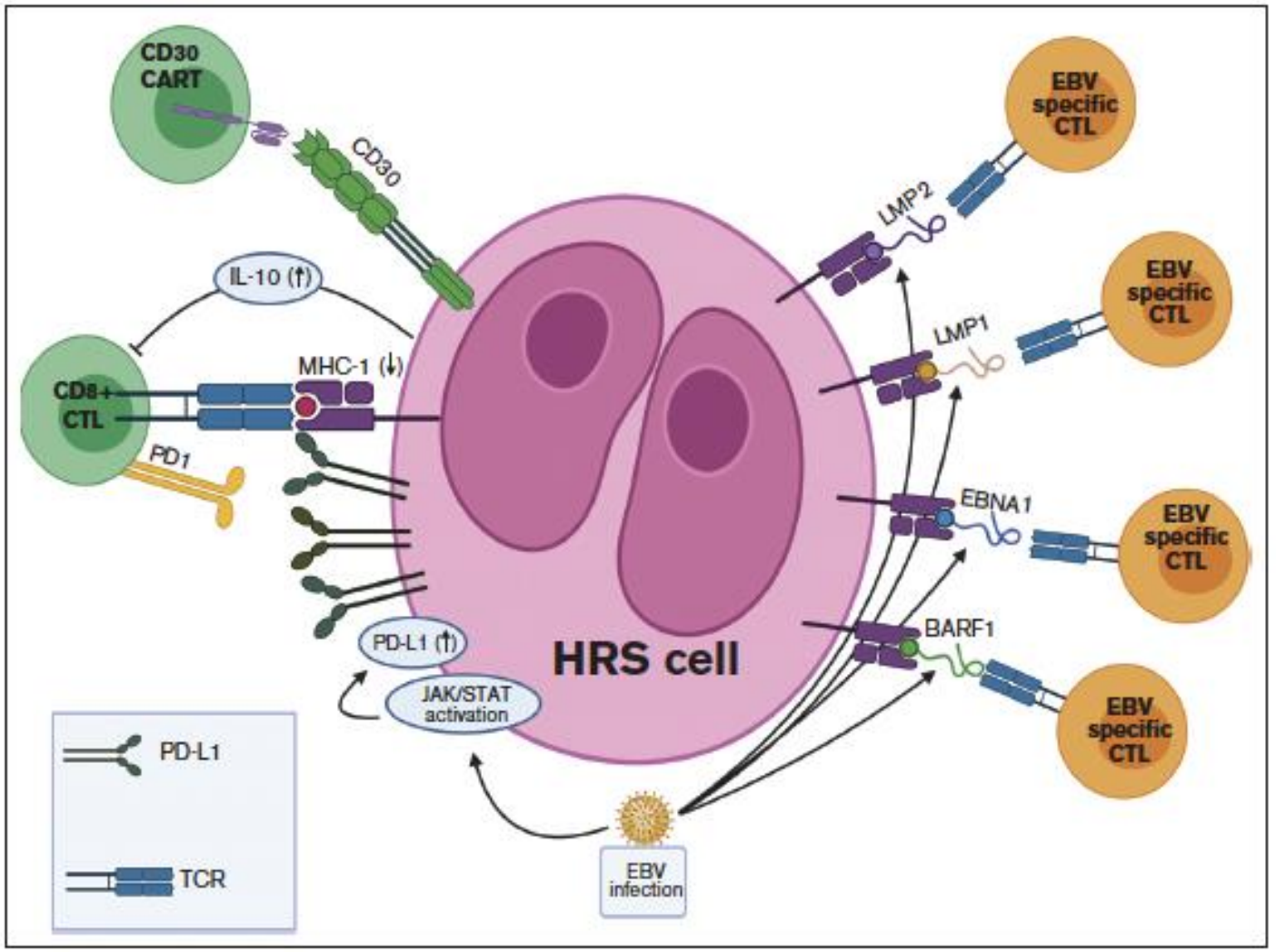
Maintenance ongoing (N = 24)





Ding et al. Hematologica 2023

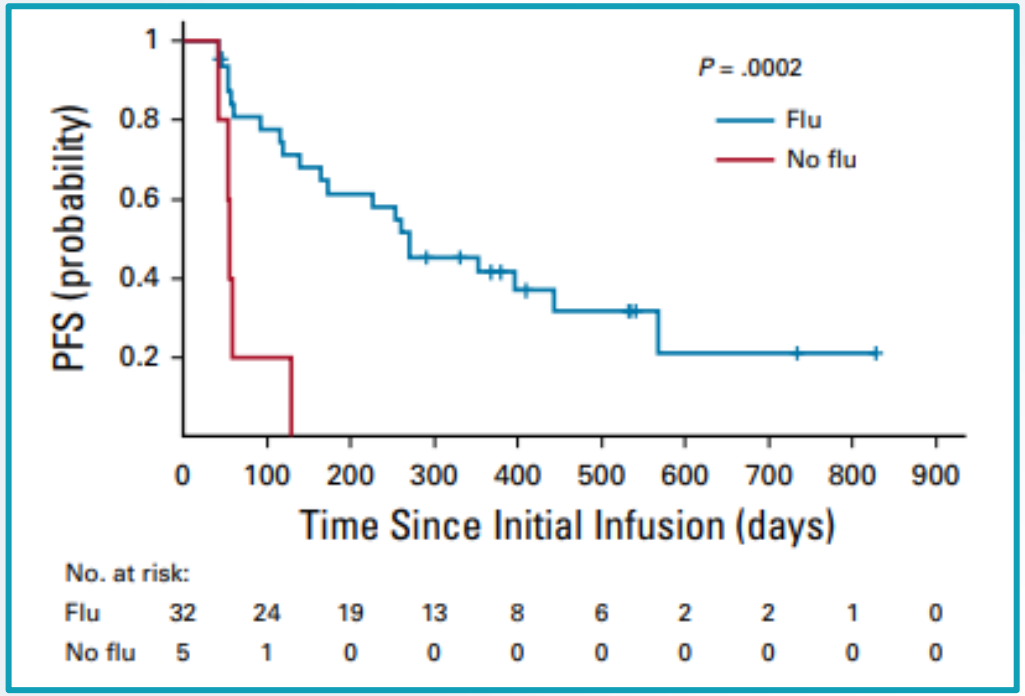
Adoptive T-cell therapy for cHL



Ho et al. Blood Adv 2021

CD30 CAR-T in relapsed/refractory HL

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)



On-going trials:

Allogeneic CD30.CAR-EBVSTs in Patients With Relapsed or Refractory CD30-Positive Lymphomas

CD30 CAR T Cells, Relapsed CD30 Expressing Lymphoma (RELY-30) (RELY-30)

Study of CAR-T Cells Expressing CD30 and CCR4 for r/r CD30+ HL and CTCL

Ramos et al. JCO 2020


THANK
YOU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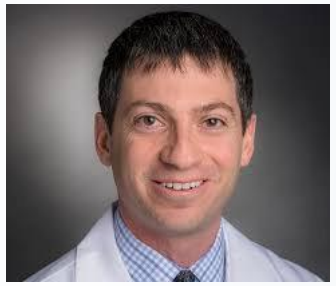
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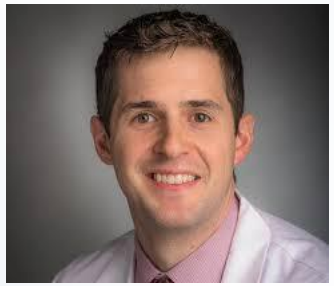
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