Weill Cornell Medicine

What is the Standard of Care in Second Line Hodgkin Lymphoma?

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Disclosures

Research: Constellation, Genentech/Roche, Karyopharm

Consulting: ADC, BMS, GenMab, Karyopharm, Kite, Seagen

DSMB: Karyopharm

Introduction

- 75-85% of pts w/ classical Hodgkin lymphoma (cHL) are cured
- 15-25% pts relapse after / are refractory to 1st line therapy
- 2nd line therapy → ASCT is standard in pts who are candidates
- Regimens are evolving in the era of modern agents

Connors et al NEJM 2018
Ansell et al NEJM 2022

Linch et al Lancet 1993
Schmitz et al Lancet 2002

Second Line Classical Hodgkin Lymphoma (cHL) Scenarios

Candidate for ASCT

1. Prior ABVD
2. Prior Bv-AVD
3. Prior N-AVD

Not candidate for ASCT

1. Prior Bv → AVD → Bv
2. Prior N-AVD
3. Prior Bv/dacarbazine/other non-anthracycline regimen

Connors et al NEJM 2018
Ansell et al NEJM 2022

Herrera et al ASCO abstract 2023
Evens et al JCO 2018

Friedberg et al Blood 2024

Second Line HL Scenarios

Candidate for ASCT

1. Prior ABVD
2. Prior Bv-AVD

PD-1 blockade + chemotherapy

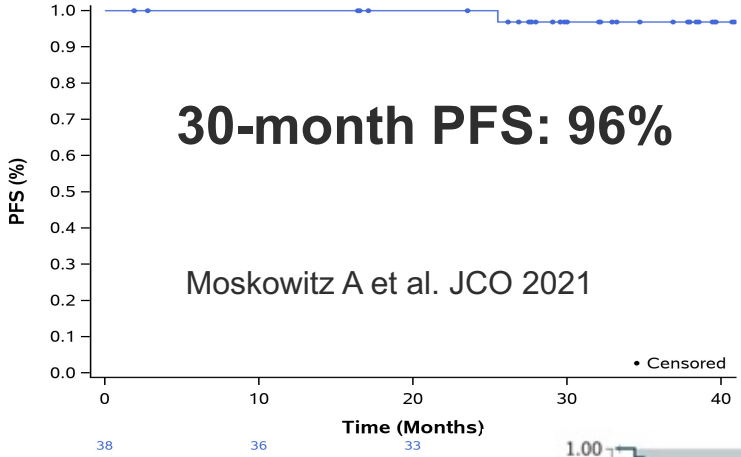
- Pembro-GVD
- Nivo → N-ICE or Pembro-ICE

PD-1 blockade + Bv

- Nivo/Bv

PD-1 blockade + chemotherapy → ASCT

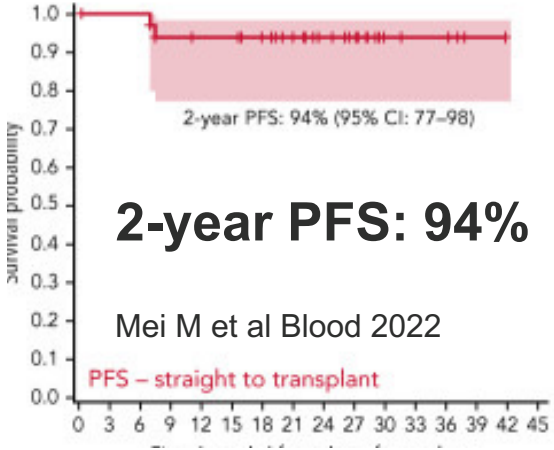
Pembro-GVD → ASCT



30-month PFS: 96%

Moskowitz A et al. JCO 2021

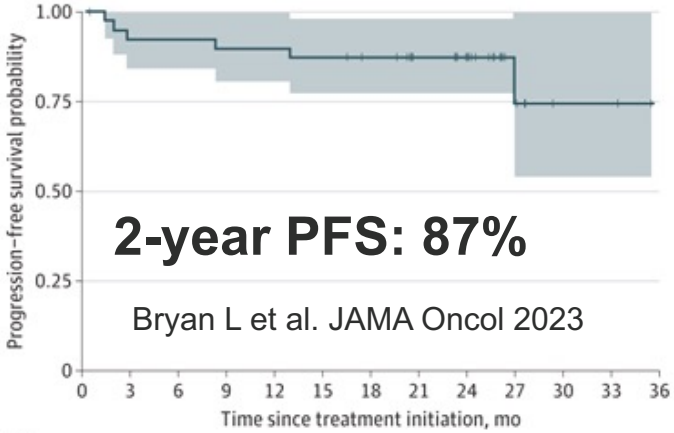
Nivo → N-ICE → ASCT



2-year PFS: 94%

Mei M et al Blood 2022

Pembro-ICE → ASCT



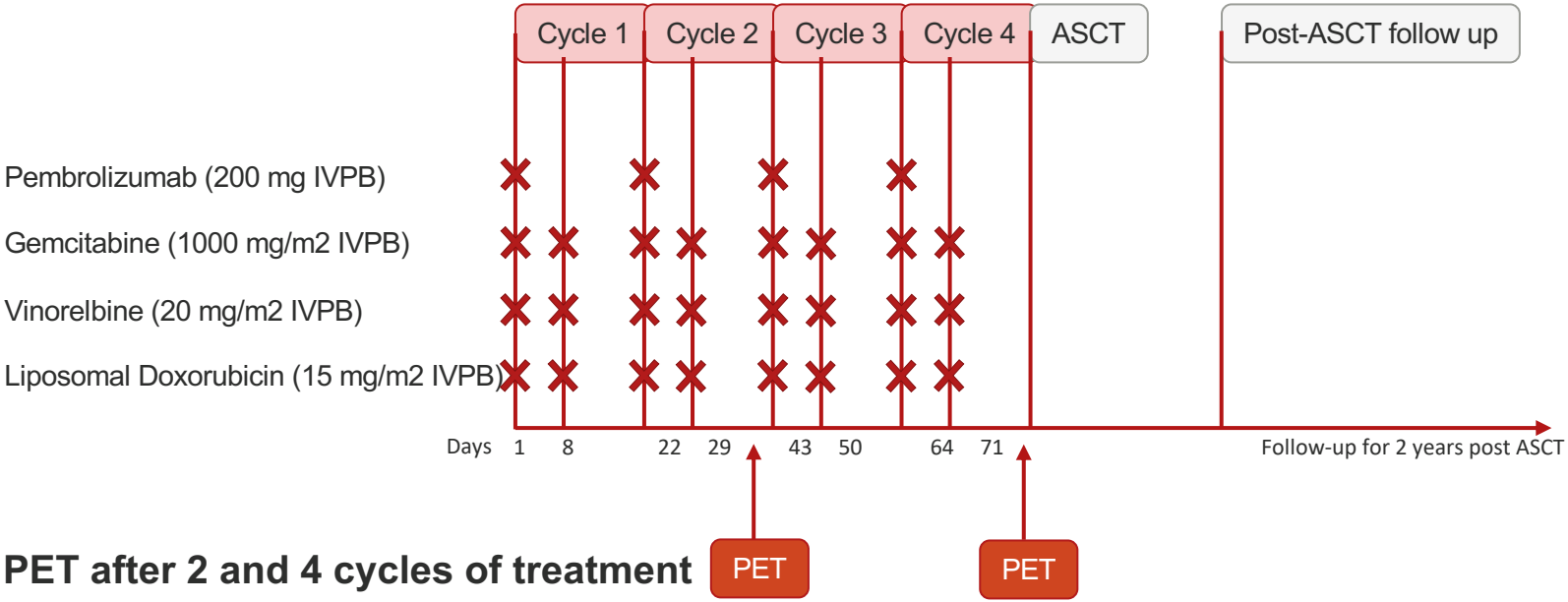
2-year PFS: 87%

Bryan L et al. JAMA Oncol 2023

Pembro-GVD

- **Eligibility**: relapsed or refractory cHL following 1-line of therapy
- **Primary endpoint**: CR (by Deauville 3) rate after 2-4 cycles

CR after 2 cycles eligible for ASCT



PET after 2 and 4 cycles of treatment

Moskowitz A et al. JCO 2021

Pembro-GVD

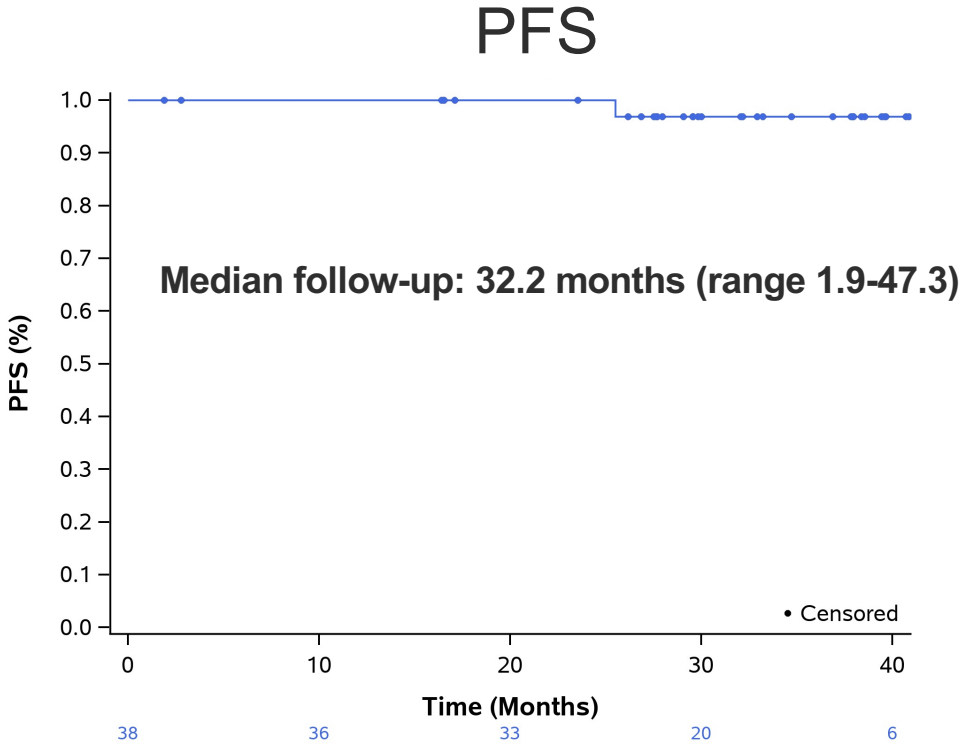
N=38 evaluable patients
- 41% primary refractory
- 31% extranodal disease

ORR: 100%

CR: 95% (92% after 2 cycles)

36 pts proceeded to ASCT

1 relapse



Updated from Moskowitz A et al. JCO 2021

Nivo → N-ICE

Nivolumab 240 mg every 2 weeks x 6 cycles

CR → ASCT

If PD at any point or PR at end → N-ICE x 2 cycles

Day 1: Nivolumab 240 mg, Etoposide 100 mg/m2
Day 2: Ifosfamide 5000 mg/m2, Carboplatin AUC 5, Etoposide 100 mg/m2
Day 3: Etoposide 100 mg/m2

N=43
44% primary refractory
37% extranodal disease

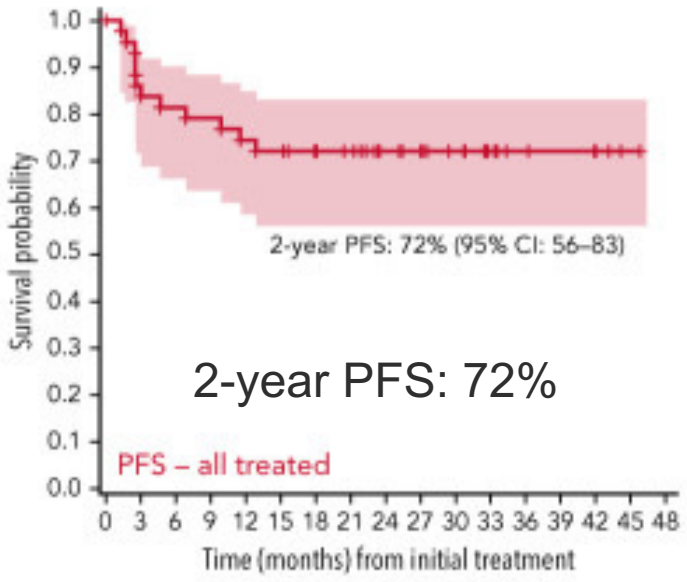
Mei M et al Blood 2022

Nivo → N-ICE

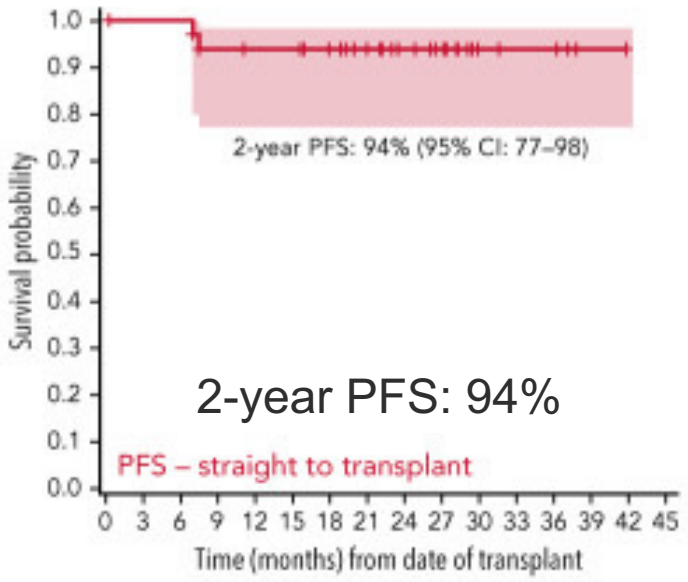
End of Nivo response
ORR: 81% (34/42)
CR: 71% (30/42)

End of Nivo → N-ICE response
ORR: 93% (39/42)
CR: 91% (38/42)

PFS - all treated

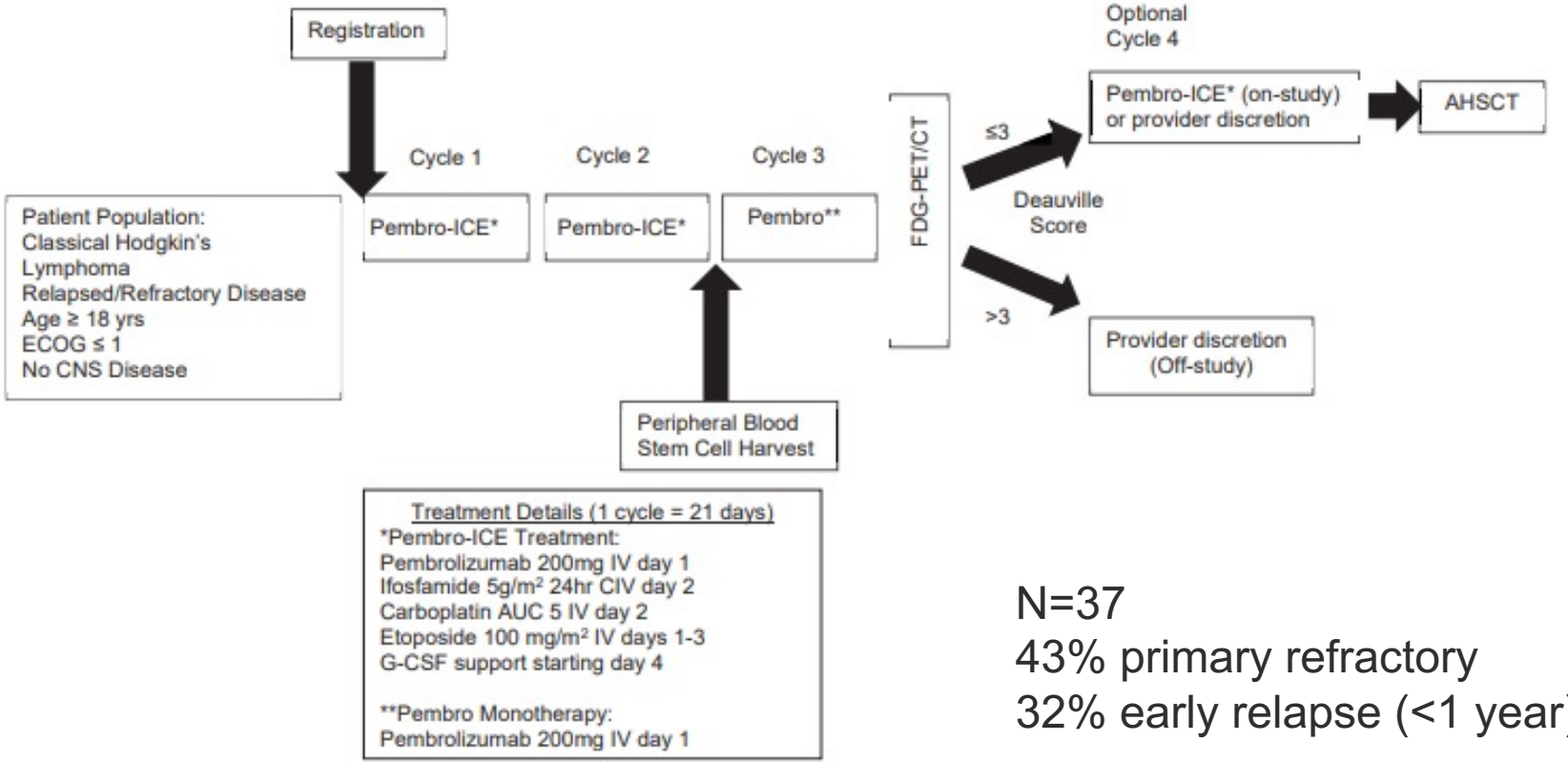


PFS - straight to transplant



Mei M et al Blood 2022

Pembro-ICE

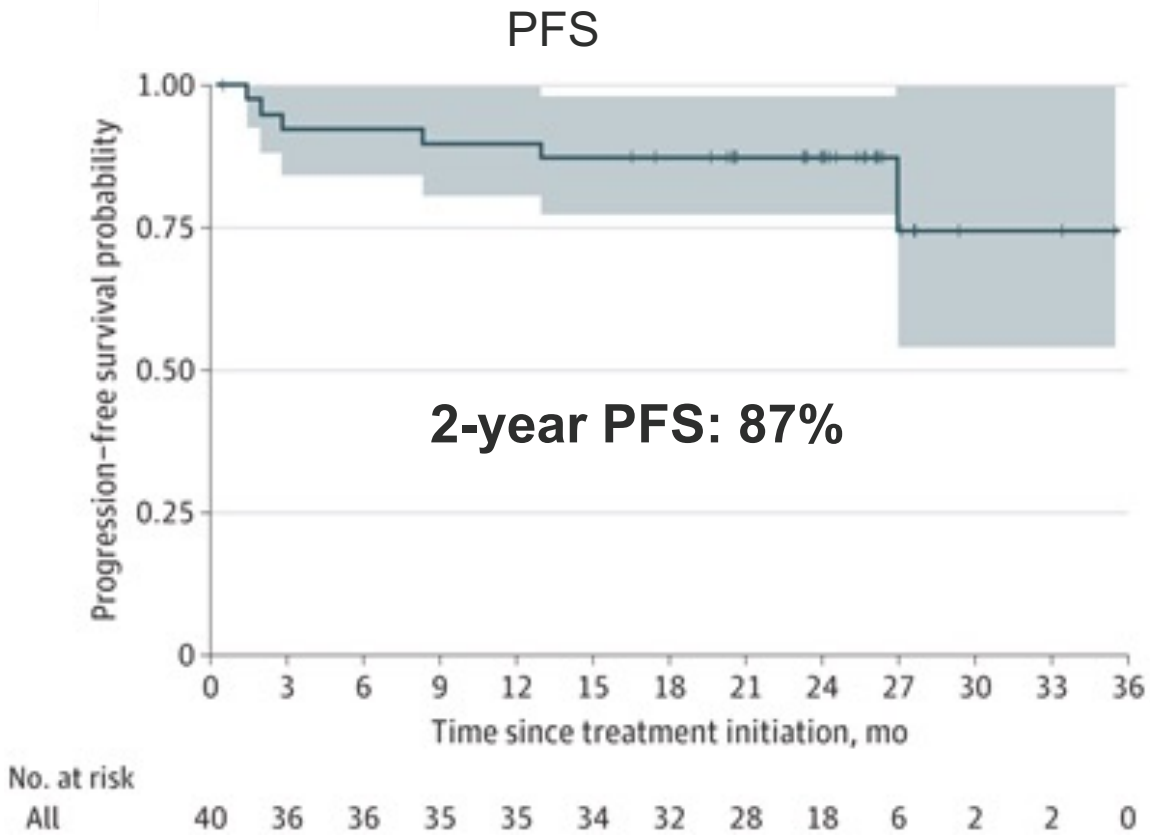


N=37
43% primary refractory
32% early relapse (<1 year)

Bryan L et al. JAMA Oncol 2023.

Pembro-ICE

ORR 97.3%
CR 87% (32/37)*
PR 11% (4/37)



Bryan L et al. JAMA Oncol 2023.

*2 pts with Deauville >3 had negative biopsy, proceeded to ASCT

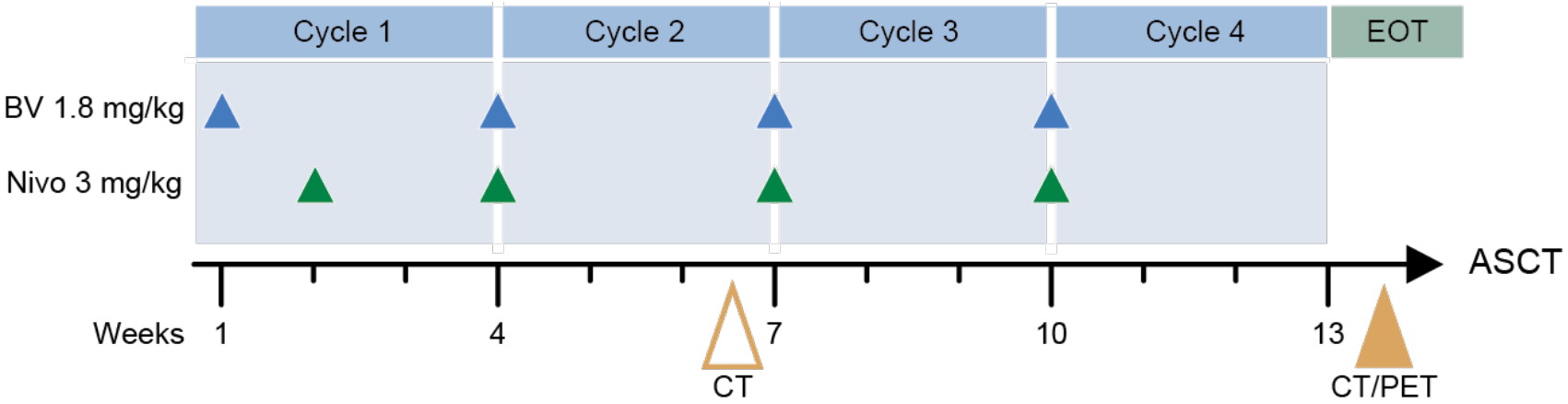
Second Line HL Scenarios

Candidate for ASCT

3. Prior N-AVD

- PD1 blockade + Bv
- Bv + chemotherapy
- PD1 blockade + chemotherapy

Bv-Nivo



91 pts received treatment, 86 completed
84 proceeded to ASCT (67 directly, 17 received additional therapy)

No patients had received prior Bv or PD1 blockade

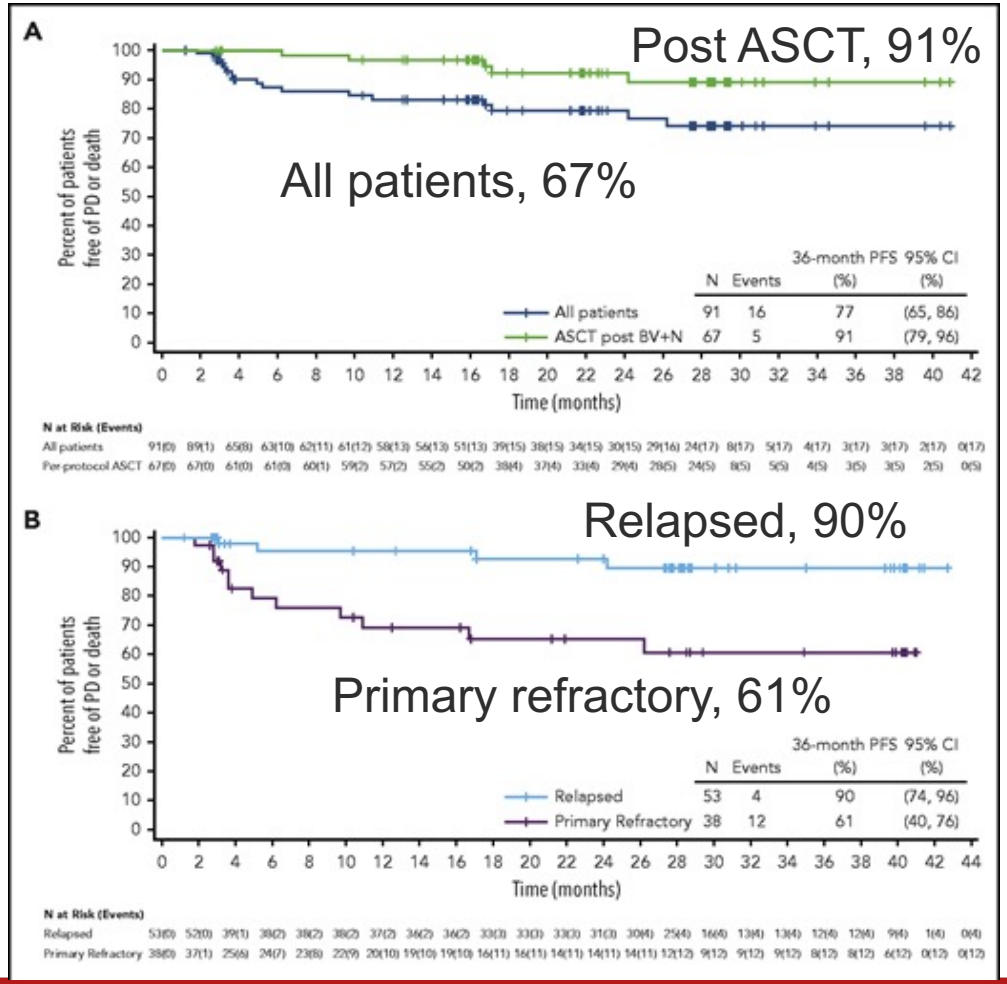
Herrera et al Blood 2018
Advani et al Blood 2021

Bv-Nivo

ORR: 85% (34/42)
CR: 67% (30/42)

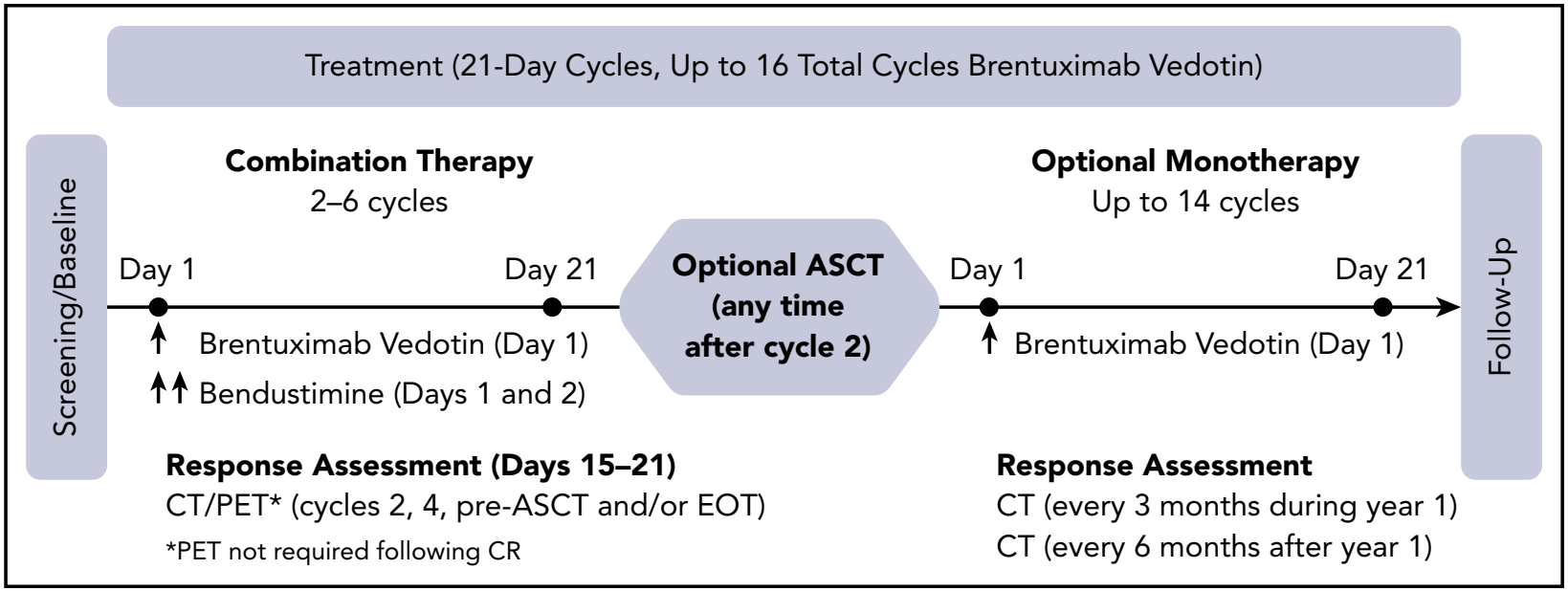
6 pts with
Deauville 4-5
Considered CR
(5 negative bx,
1 w/ no site to bx)

36-month PFS



Herrera et al Blood 2018
Advani et al Blood 2021

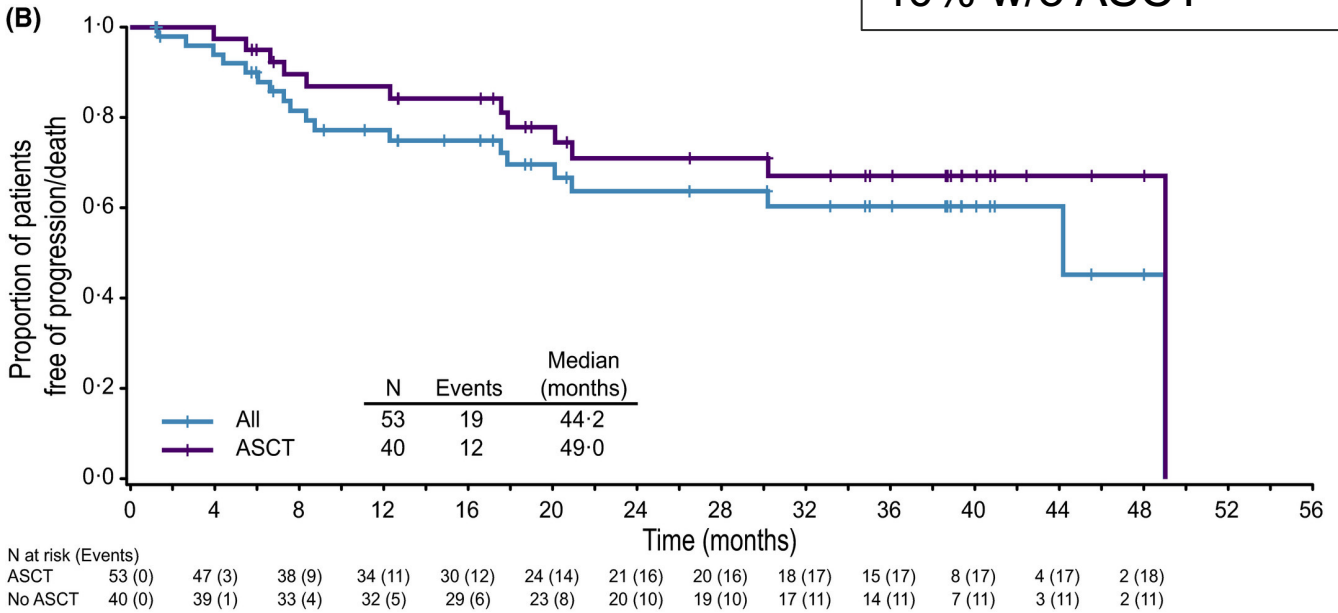
Bv-bendamustine



Bv-bendamustine

3-year PFS
60% overall
67% w/ ASCT
40% w/o ASCT

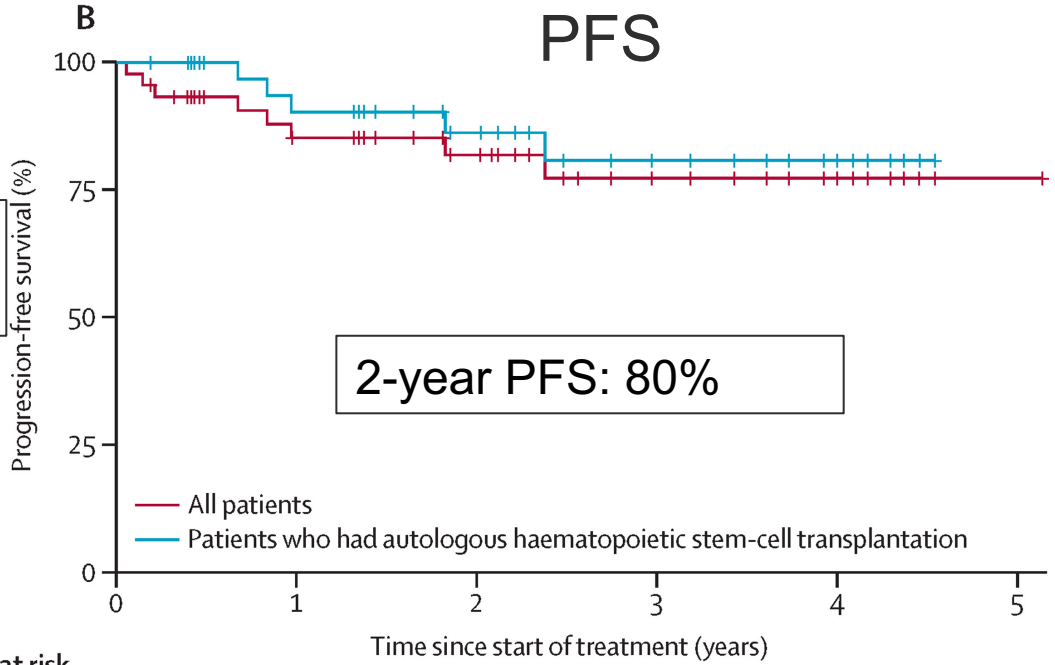
Median PFS



LaCasce A et al Blood 2018
LaCasce A et al BJH 2020

Bv-ICE

ORR 91% (39/43)
CRR 74% (32/43)



Number at risk (number censored)						
All patients	45 (0)	31 (8)	23 (15)	13 (24)	7 (30)	1 (36)
Patients who had autologous haematopoietic stem-cell transplantation	37 (0)	28 (6)	20 (13)	12 (20)	6 (26)	0 (32)

Lynch et al Lancet Hematol 2021.

Considerations in 2nd line cHL

Can we retreat with PD1 inhibitor if it was received in 1st line?

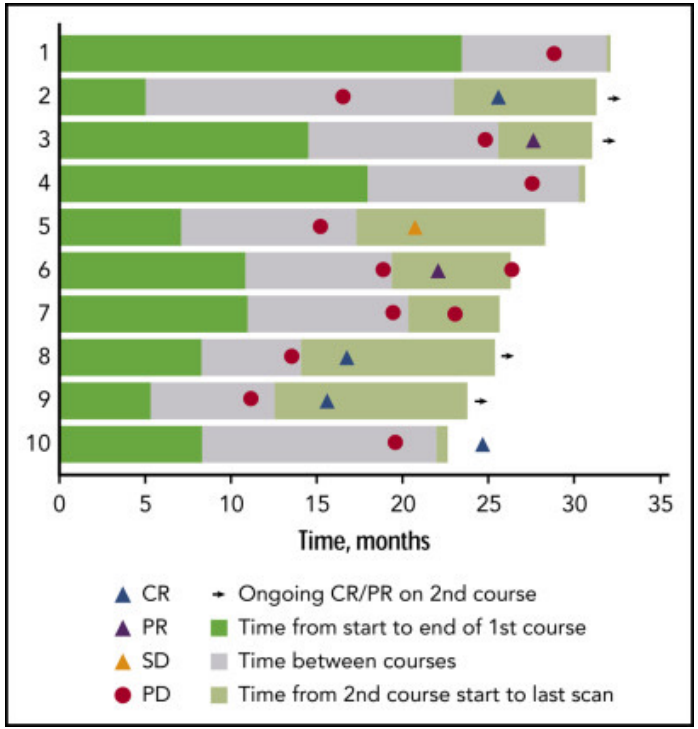
Should we switch from one PD1 inhibitor to the other?

Is PET complete metabolic response (CMR) necessary before ASCT?

Should we give maintenance therapy after ASCT?

Retreatment with PD1 inhibitor

Pembrolizumab in KEYNOTE-087



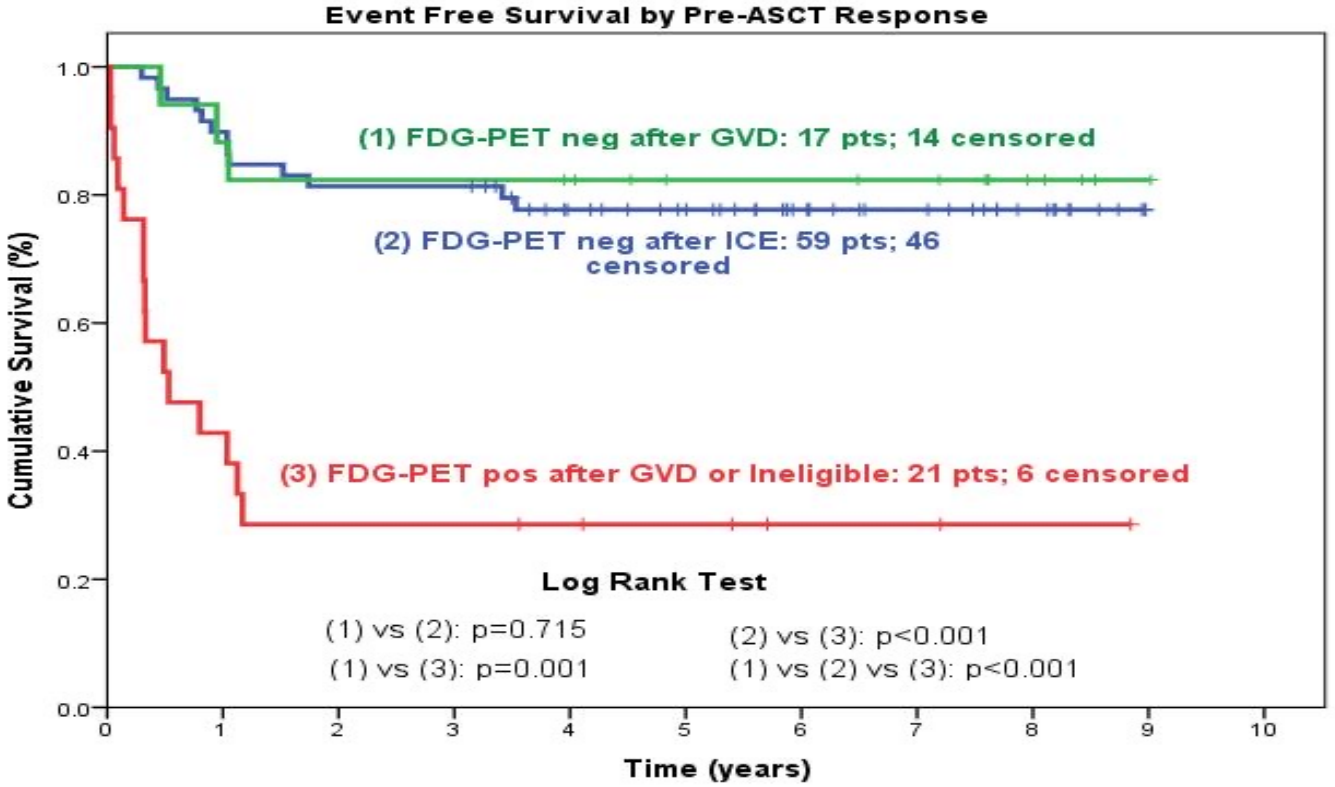
ORR 75% (6/8)
4 CR, 2 PR

Nivolumab

ORR 67% (6/9)
3 CR, 3 PR

Chen et al. Blood 2019.
Fedorova et al Ann Hematol 2021.

PET CMR prior to ASCT was gold standard

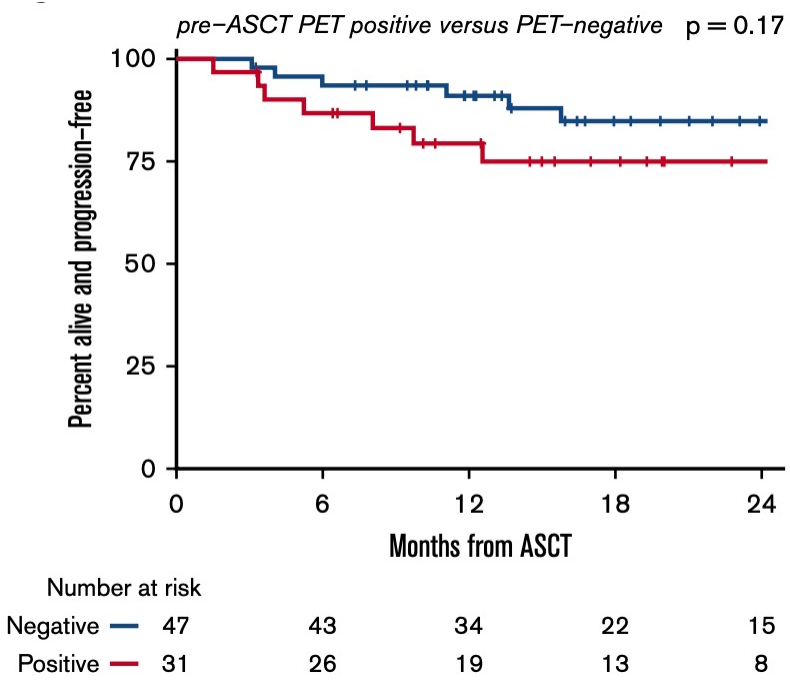


→ Immunotherapies can result in increased uptake in absence of progression

Moskowitz CH et al. Blood 2012;119:1665-70

Cheson et al. Blood 2016.

With PD1 blockade, PET CMR before ASCT may not be necessary



Retrospective study of pts with R/R cHL

N=78, median therapies 3

58 pts with PD-1 blockade as most recent therapy before ASCT

PET-positive 18-mo PFS 91% (N=25)
PET-negative 18 mo-PFS 86% (N=33)

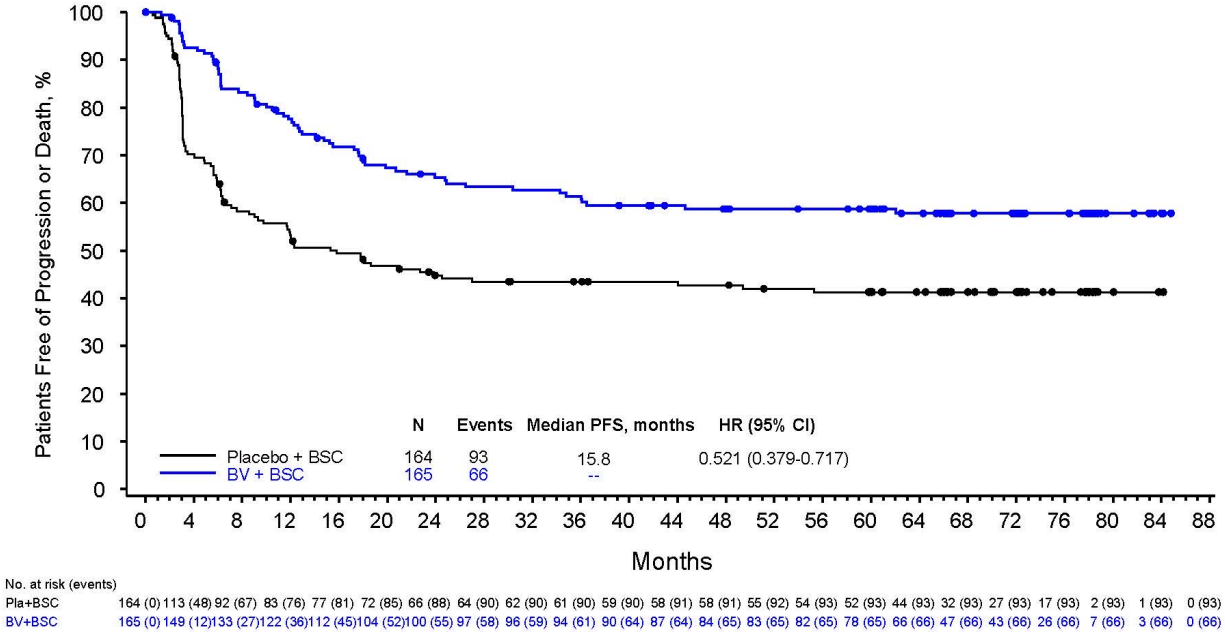
P = 0.87

Merryman et al. Blood Advances 2021.

Post-ASCT Bv maintenance?

AETHERA: Phase III study evaluating post-transplant **maintenance BV** for high risk

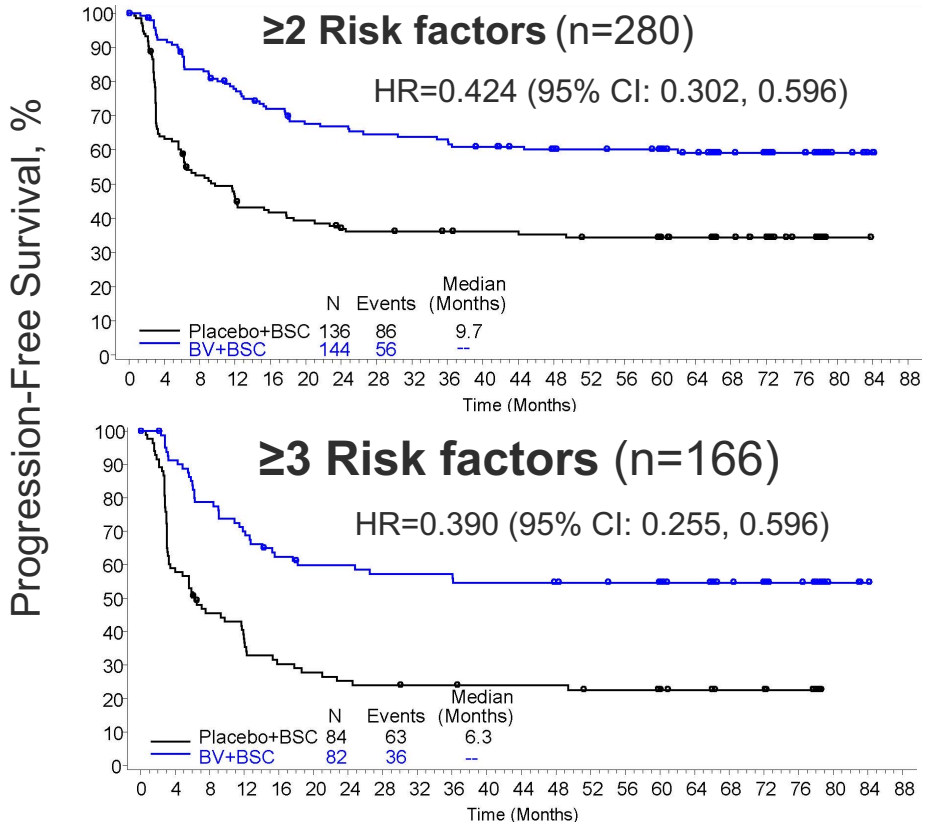
Risk factors: **Relapse w/n 1 year of initial treatment, primary refractory disease, extranodal disease at time of relapse**



5-Year PFS Rates	
BV=59%	Placebo=41%
HR=0.521	

Moskowitz CH, et al. Lancet 2015;385:1853-62
Moskowitz CH, et al. ISHL 2018

Consider Bv maintenance for ≥2 Risk factors



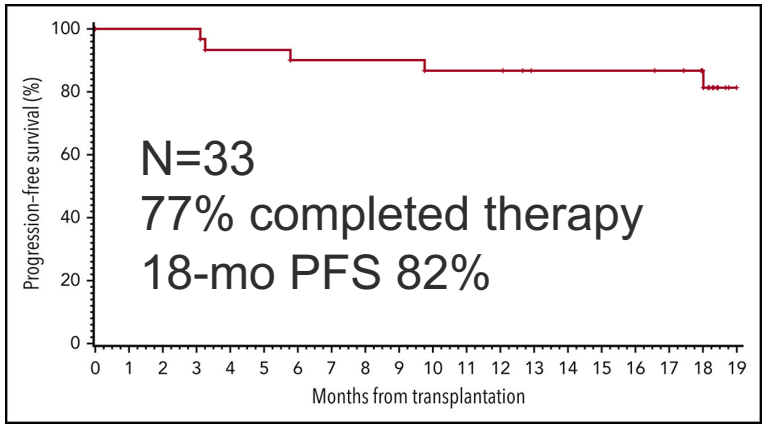
Risk Factors

- Primary-refractory HL or relapse <12 months from completion of frontline therapy
- PR or SD as best response to salvage therapy pre-ASCT
- ≥2 previous salvage therapies
- Extranodal disease at pre-ASCT relapse
- B symptoms after failure of frontline therapy

Moskowitz CH, et al. Lancet 2015;385:1853-62
Moskowitz CH, et al. ISHL 2018

Maintenance strategies with PD1 blockade

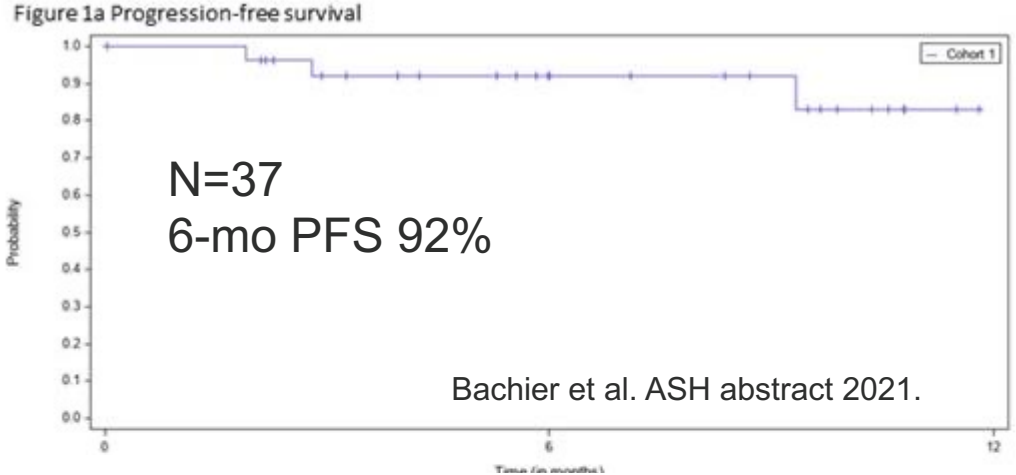
Pembrolizumab maintenance (8 cycles)



N=33
77% completed therapy
18-mo PFS 82%

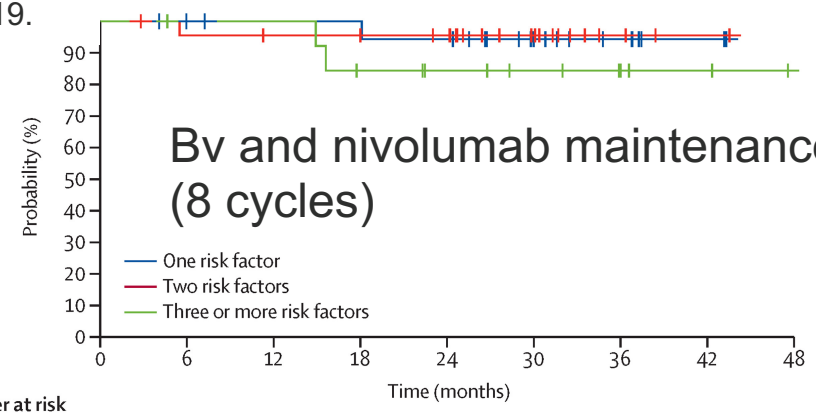
Armand et al. Blood 2019.

Nivolumab maintenance (12 cycles)



N=37
6-mo PFS 92%

Bachier et al. ASH abstract 2021.



Bv and nivolumab maintenance
(8 cycles)

N=59
49% completed therapy
18-mo PFS 94%

Herrera A et al. Lancet Haematology 2023.

Considerations in 2nd line cHL

Can we retreat with PD1 inhibitor if it was received in 1st line?

YES

Should we switch from one PD1 inhibitor to the other?

UNCLEAR

Is PET CMR necessary prior to ASCT?

PROBABLY NOT (when PD1 inhibitor used)

Should we give maintenance therapy after ASCT?

YES, IN HIGH RISK

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