19th International Ultmann Chicago Lymphoma Symposium

Treatment of 1st relapsed classical Hodgkin lymphoma

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MEDICINE & BIOLOGICAL SCIENCES

Disclosures

- No relevant conflicts of interest

Outline

- Overview of strategy for 1st relapse of classical Hodgkin Lymphoma (cHL)
- Traditional Chemotherapy
- Incorporating Brentuximab Vedotin (BV)
- Incorporating Checkpoint Inhibitor (CPI)
- Maintenance therapy

Audience Response Question

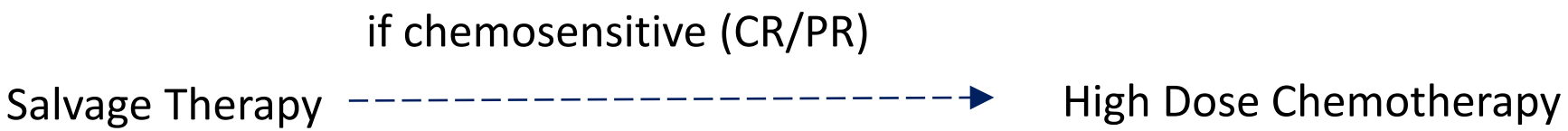
Which of the following is the standard of care treatment for classical Hodgkin lymphoma in 1st relapse?

A. Checkpoint inhibitor therapy alone
B. Brentuximab vedotin therapy alone
C. Salvage therapy followed by high dose chemotherapy/autologous stem cell transplant
D. Brentuximab vedotin plus checkpoint inhibitor therapy until remission obtained

General strategy for 1st relapse of cHL

Historically, ABVD has been frontline therapy for cHL and can cure a majority of patients

Second line therapy typically consists of chemotherapy salvage followed by consolidative high dose chemo and autologous stem cell transplant (HDT-ASCT) with the latter improving outcomes to salvage therapy alone



Rancea AU et al. Cochrane Database Syst Rev, 2013

Factors that predict success to 2nd line treatment

- The following factors at relapse have been shown to predict for worse outcome:
  - B symptoms
  - Extranodal disease
  - Initial remission duration < 1 year

- However, attaining a complete remission (CR) to salvage chemotherapy improves success rate.

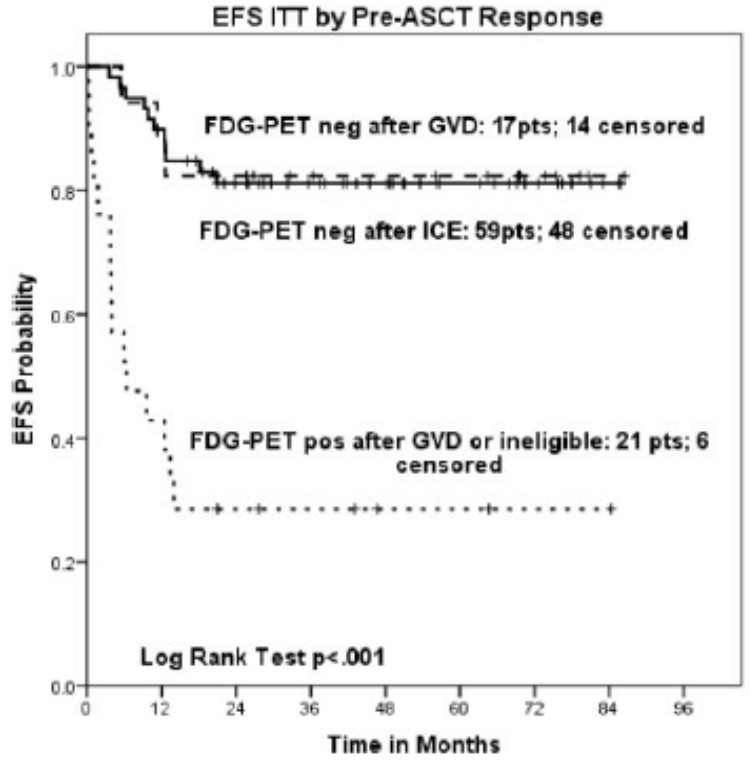
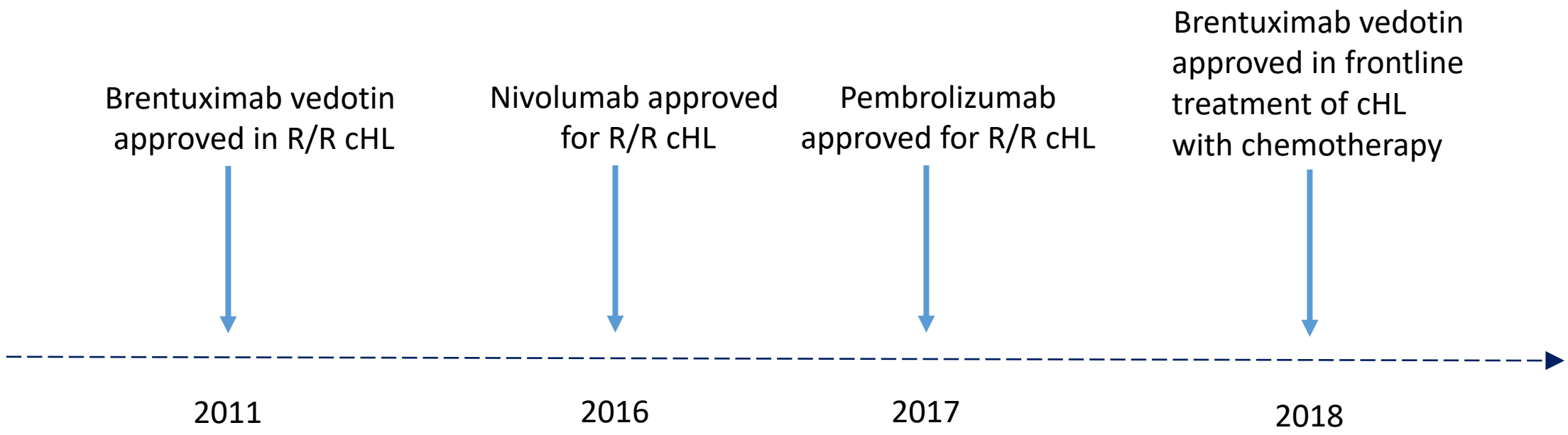


Figure 3. EFS intent to treat by pre-ASCT response.

Moskowitz CH, et al. Blood, 2001
Moskowitz CH, et al. Blood, 2012

Progress in treatment of cHL

- Brentuximab vedotin (anti-CD30 ADC) and nivolumab/pembrolizumab (CPI) are approved in R/R cHL past traditional 2nd line therapy
- Next steps have been to move these novel agents into earlier lines of therapy

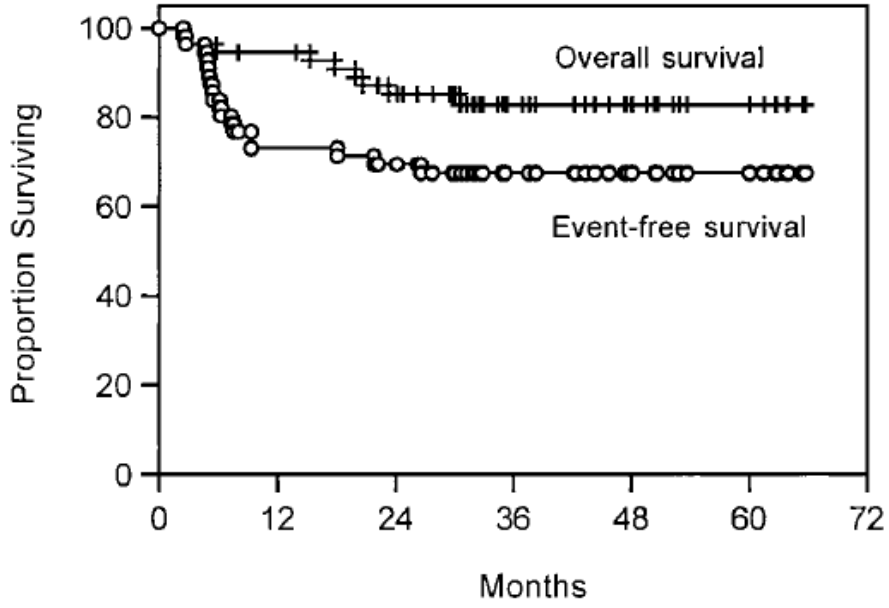


An Example of Traditional Chemotherapy

Ifosfamide/Carboplatin/Etoposide

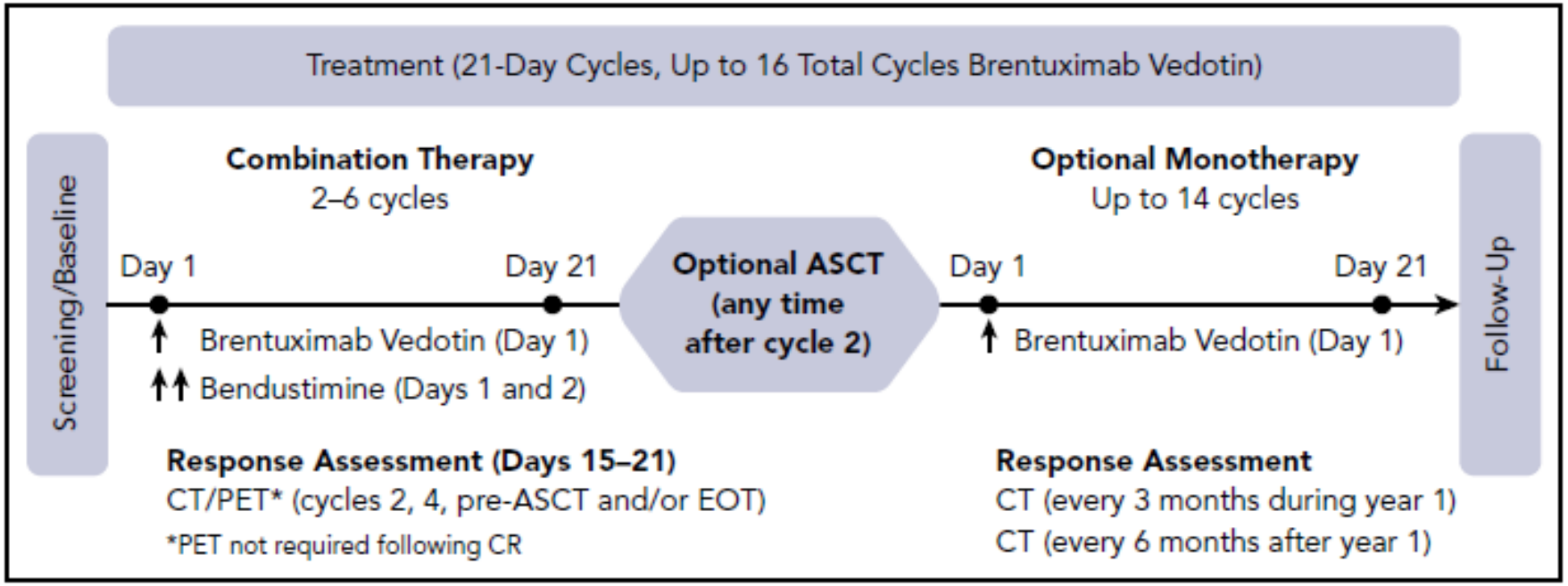
CR 26%, PR 59%
(CR rate may be underestimated
In a follow up study of ICE followed by GVD,
incorporating PET scan evaluation,
CR rate to ICE ~60%)

After 43 months median follow up,
EFS for transplanted population: 58%



Moskowitz CH, et al. Blood, 2001

Adding in BV to traditional chemotherapy

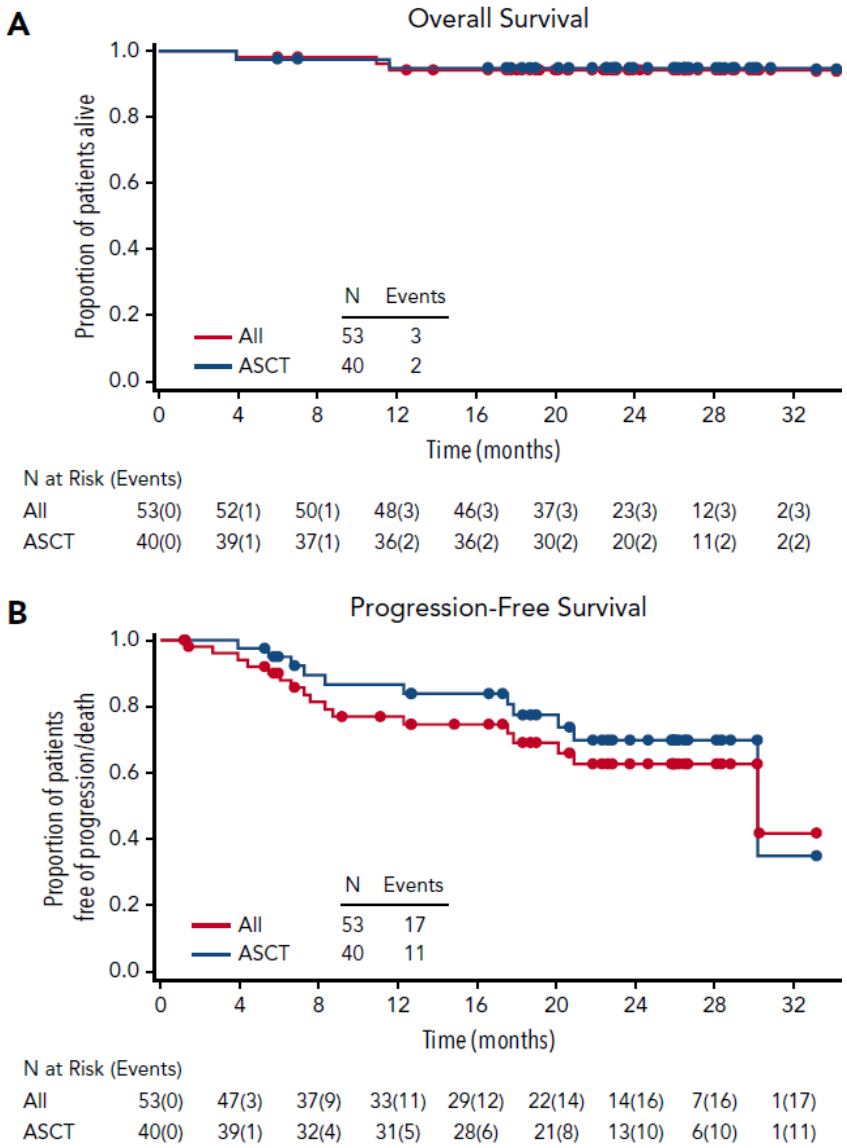


LaCasce AS, et al. Blood, 2018

BV-Bendamustine

Table 2. Best response on combination therapy

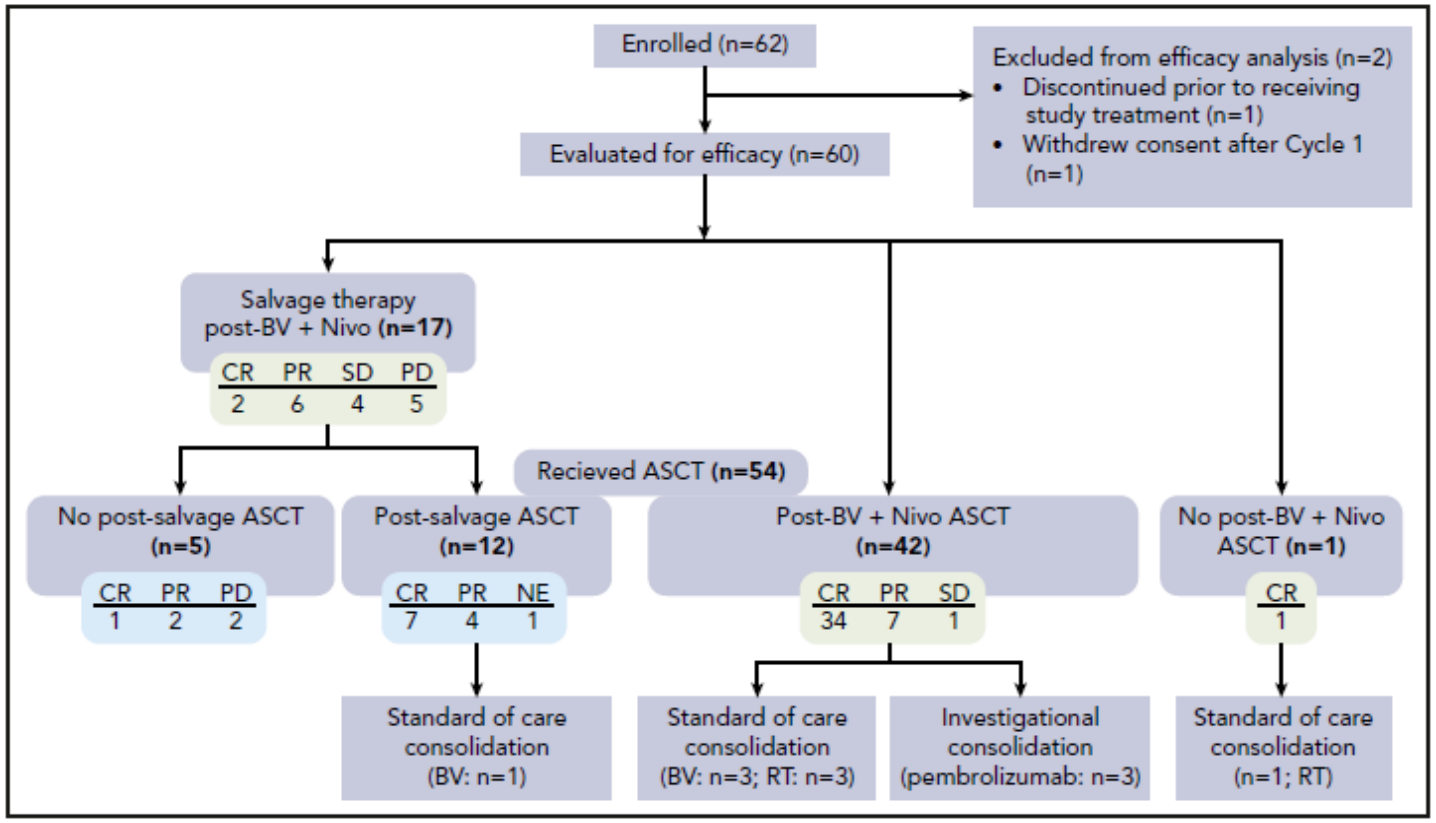
Population	Best clinical response, n (%) [95% CI]				
	CR	PR	SD	PD	ORR*
Overall, N = 53	39 (73.6) [59.7, 84.7]	10 (18.9)	3 (5.7)	1 (1.9)	49 (92.5) [81.8, 97.9]
Response to frontline therapy					
Primary refractory, n = 28	18 (64.3) [44.1, 81.4]	6 (21.4)	3 (10.7)	1 (3.6)	24 (85.7) [67.3, 96.0]
Relapsed, 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]



After a median follow up of 20.9 months,
2 year PFS 69.8% for patients who went to ASCT.

LaCasce AS, et al. Blood, 2018

BV-nivolumab

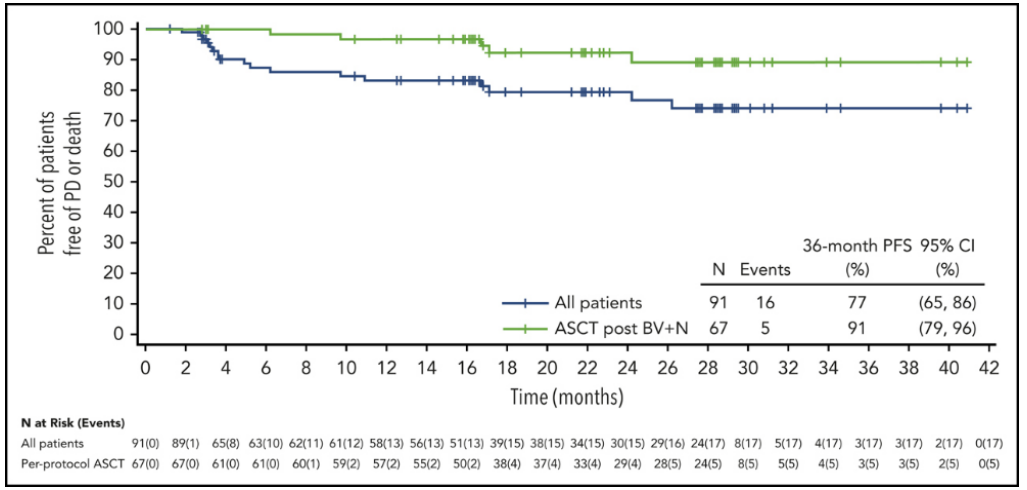


Herrera AF, et al. Blood, 2018

BV-nivolumab

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

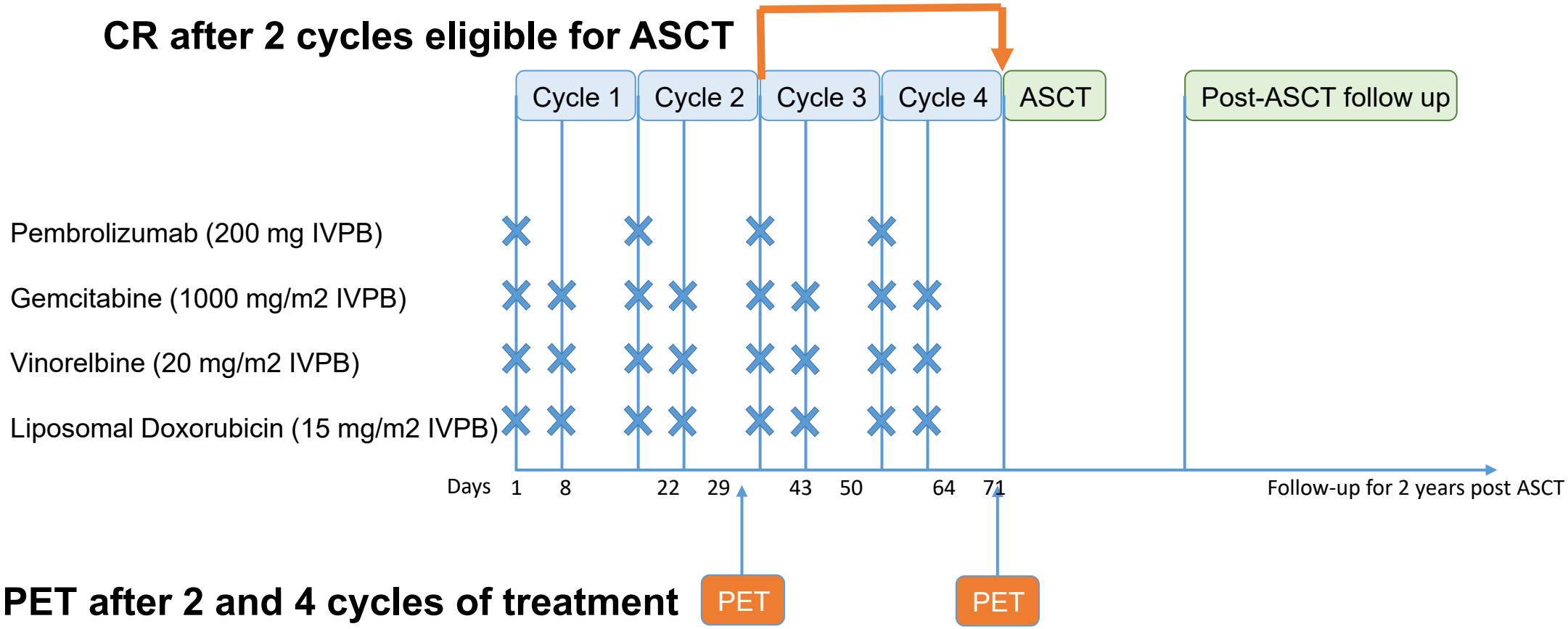
	All treated patients (n = 61)		Efficacy-evaluable patients (n = 60)	
	n (%)	95% CI‡	n (%)	95% CI‡
Objective response rate* (CR + PR)	50 (82)	70–90.6	50 (83)	71.5–91.7
Complete metabolic response (CMR/CR) Deauville score = 1 Deauville score = 2 Deauville score = 3 Deauville score = 5†	37 (61) 14 (23) 15 (25) 7 (11) 1 (2)	47.3–72.9	37 (62) 14 (23) 15 (25) 6 (10) 21 (2)	48.2–73.9
Partial metabolic response (PMR/PR) Deauville score = 4 Deauville score = 5	13 (21) 7 (11) 6 (10)	11.9–33.7	13 (22) 7 (12) 6 (10)	12.1–34.2
No metabolic response (NMR/SD) Deauville score = 5	5 (8) 5 (8)	2.7–18.1	5 (8) 5 (8)	2.8–18.4
Progressive disease (PMD/PD) Deauville score = 5	4 (7) 4 (7)	1.8–15.9	4 (7) 4 (7)	1.8–16.2
Clinical progression	1 (2)		1 (2)	
NE	1 (2)		0	



Herrera AF, et al. Blood, 2018
Advani RH, et al. ASH 2021

Adding CPI to chemotherapy (Pembro-GVD)

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

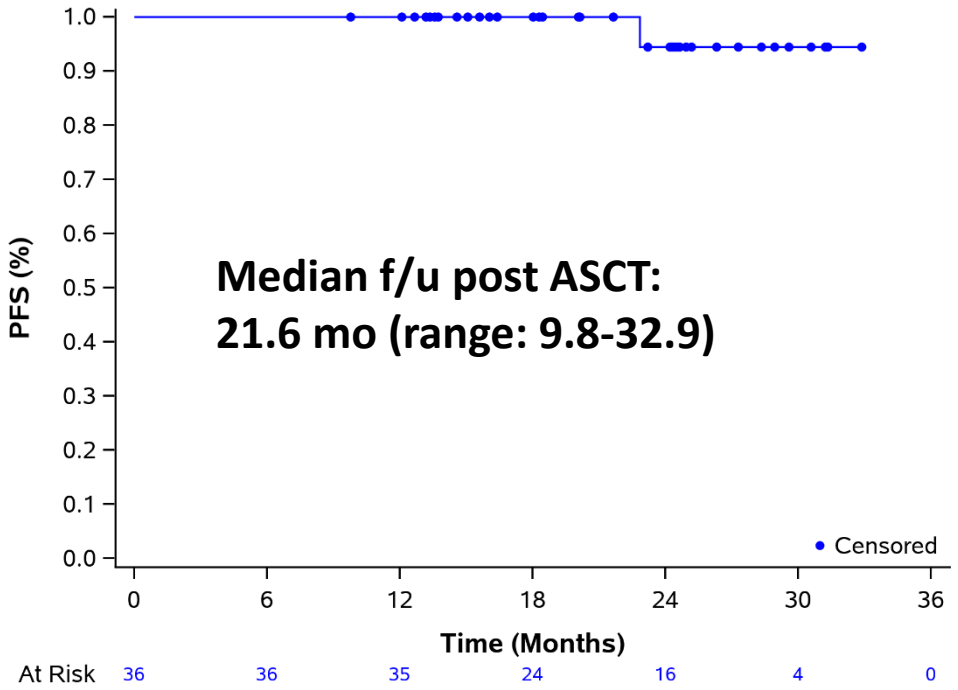


Courtesy of Dr Alison Moskowitz

Moskowitz AJ, et al. ASH 2020

Adding CPI to chemotherapy (Pembro-GVD)

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)



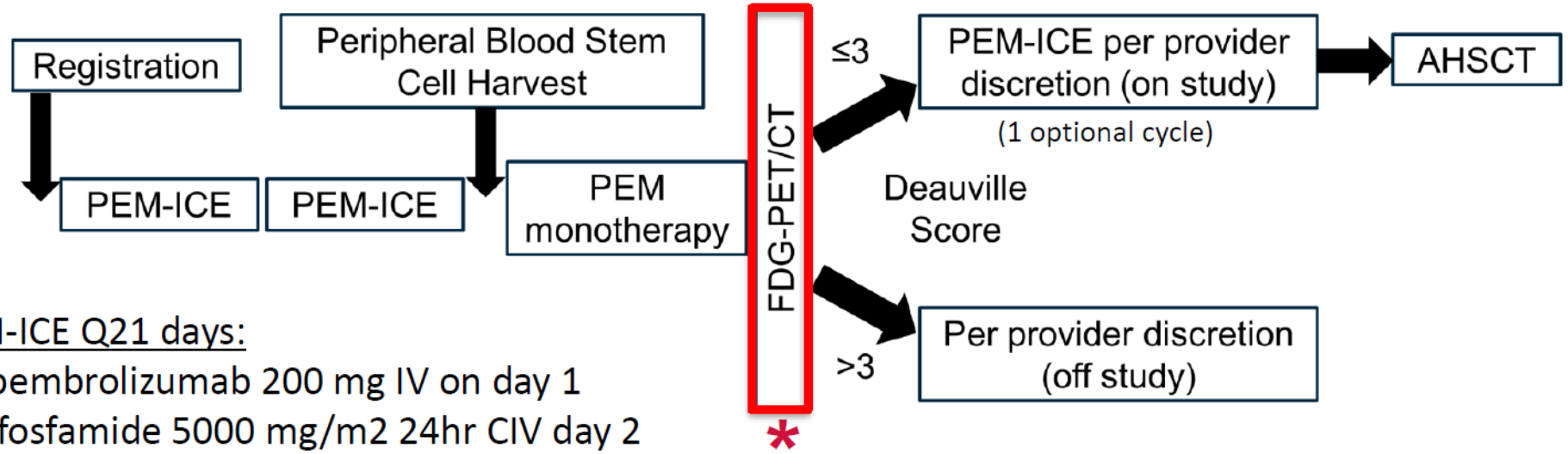
- 36 pts proceeded to ASCT
- 1 relapse

Moskowitz AJ, et al. JCO 2021

Adding CPI to chemotherapy (Pembro-ICE)

Trial Schema:

Key enrollment criteria:
Age >18 years
Medically fit for AHSCT
Relapsed/refractory classic Hodgkin lymphoma
Exclusions: >2 prior regimens, prior PD-1 inhibitor exposure, history of autoimmune disease, known CNS involvement.



PEM-ICE Q21 days:

- pembrolizumab 200 mg IV on day 1
- ifosfamide 5000 mg/m2 24hr CIV day 2
- carboplatin AUC 5 IV day 2
- etoposide 100 mg/m2 IV days 1-3

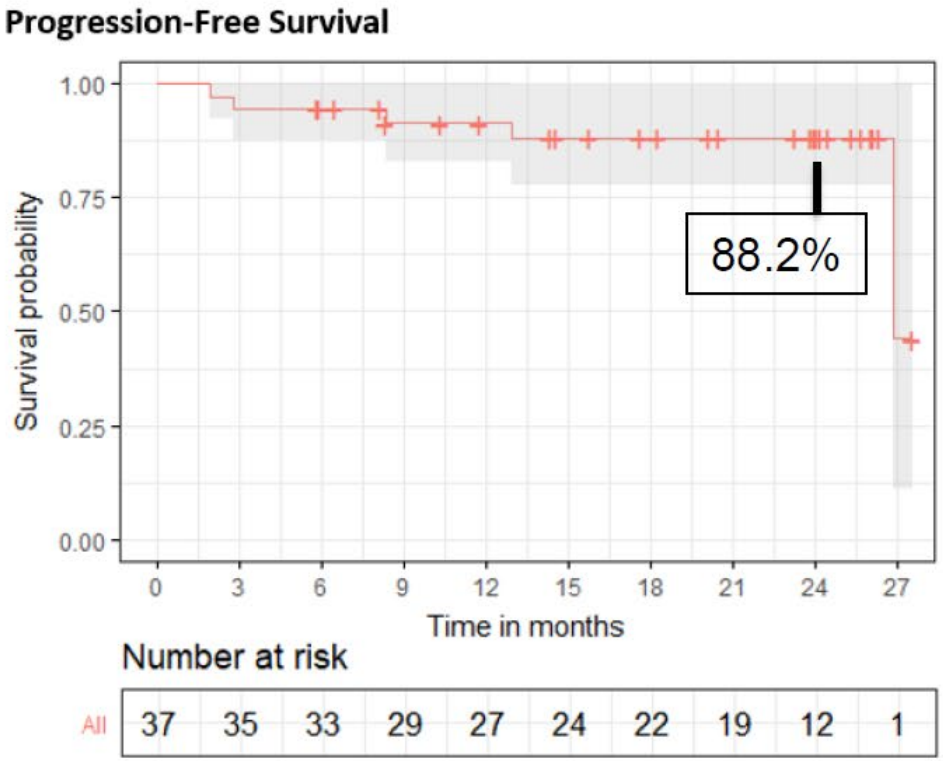
NCT03077828

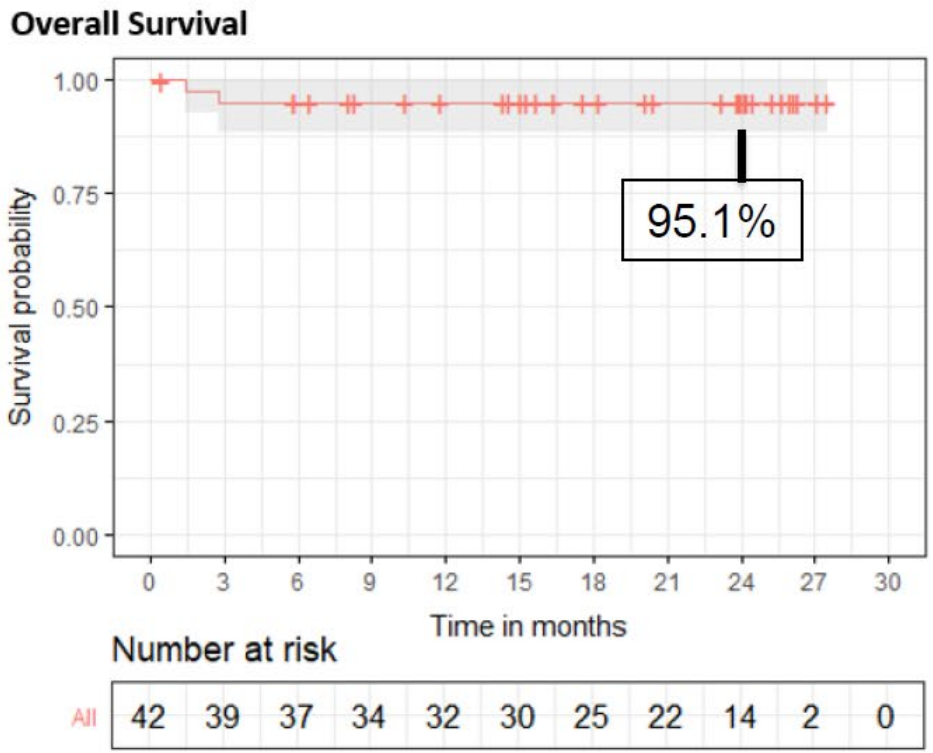
Courtesy of Dr Locke Bryan

Bryan LJ, et al. ASH 2021

Adding CPI to chemotherapy (Pembro-ICE)

Results: Outcomes





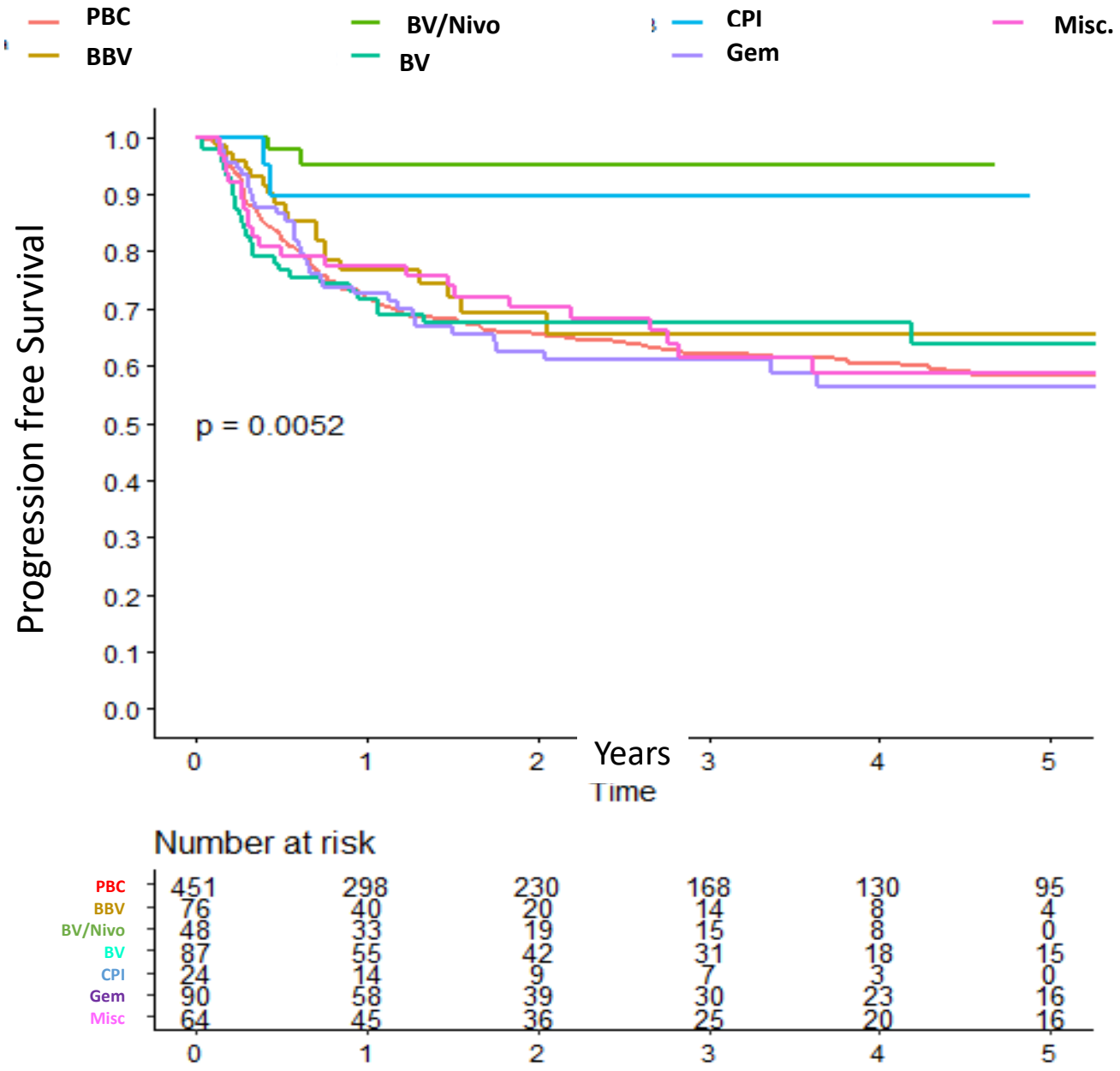
CR rate: 86.5%
Median f/u 27 mo

Courtesy of Dr Locke Bryan

Bryan LJ, et al. ASH 2021

Retrospective comparison of salvage strategies

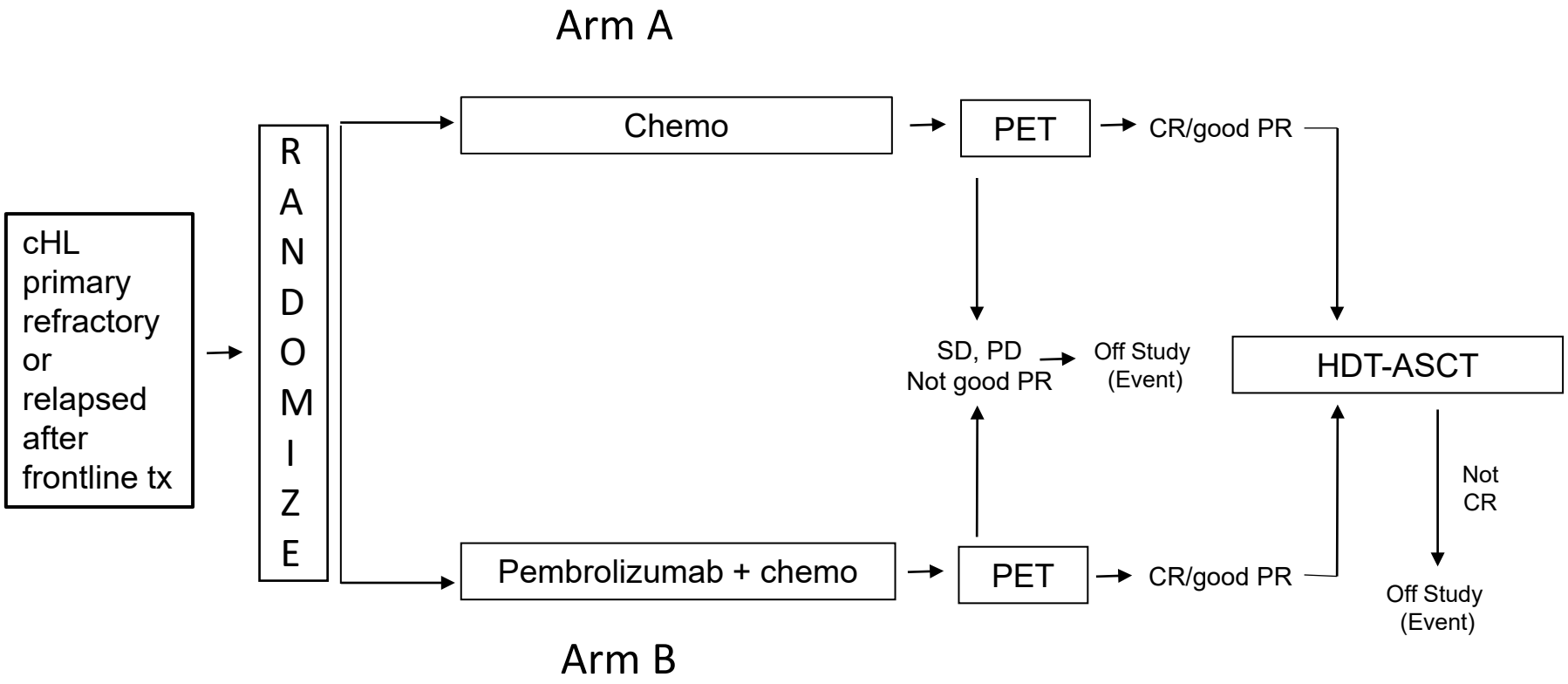
Pre-ASCT ST (N)	2 Year PFS % (CI_{95})	P value
PBC (451)	65.4 (61.9-68.9)	ref
BBV (76)	69.3 (60.2-78.4)	NS
BV/Nivo (48)	***95.2 (91.7-98.7)***	***<0.01***
BV (87)	67.6 (60-75.2)	NS
CPI (24)	***89.7 (82.1-97.3)***	***<0.01***
Gem (90)	62.6 (54-71.2)	NS
Others (64)	70.3 (62-78.6)	NS



Courtesy of Dr Sanjal Desai

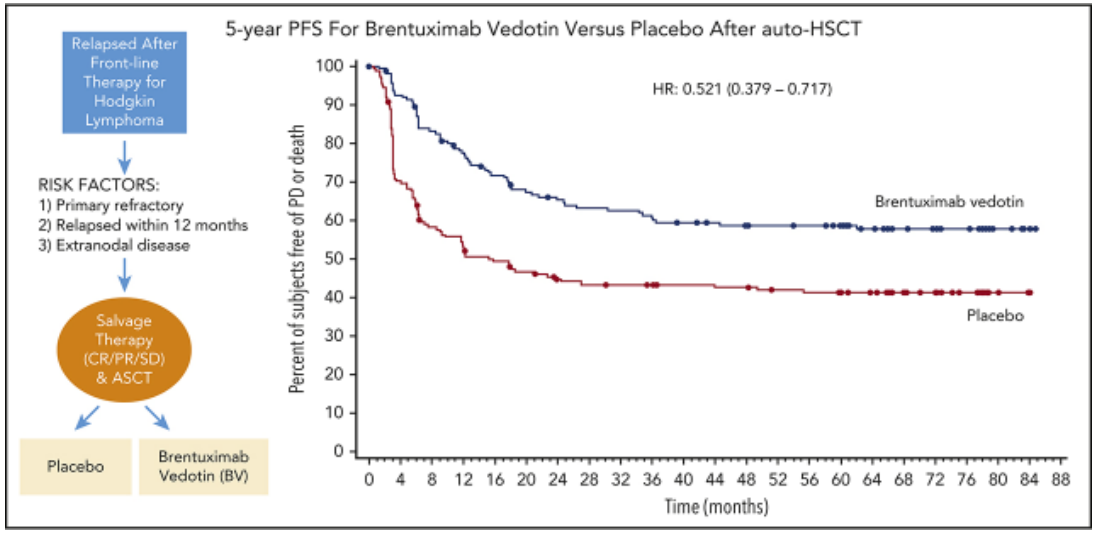
Desai SH, et al. ASH 2021

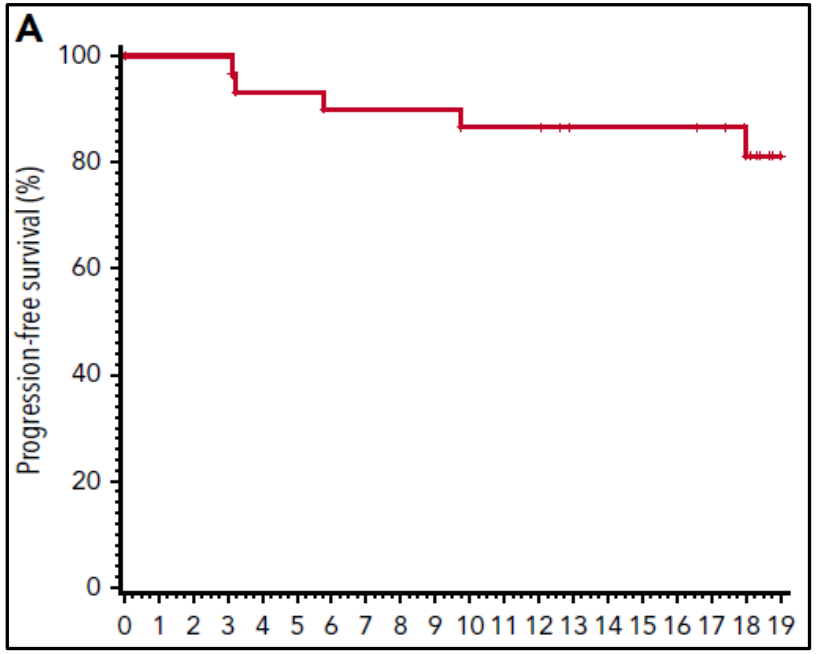
EA4211:
Phase 3 study to compare chemo vs CPI/chemo



Primary Endpoint: 2 year event free survival

Maintenance after HDT-ASCT





BV q3 weeks for up to 16 cycles
5 yr PFS: 59% vs 41%

Peripheral Neuropathy in 67%
90% improved, 73% completely

Pembrolizumab 200 mg q 3 weeks x 8 cycles
18 month PFS: 82%

30%: at least one grade 3 AE

Armand P, et al. Blood, 2019
Moskowitz CH, et al, Blood 2018

Future Directions

- The current standard remains salvage therapy followed by HDT-ASCT
- EA4211 will be an intergroup trial comparing salvage with CPI/chemo vs chemo in a phase 3 setting to determine if CPI/chemo is superior
- This trial will also potentially elucidate whether CR to salvage is as critical when CPI is used in the salvage regimen

- Once we have longer term data on checkpoint inhibitor combinations in 2nd line setting and know the durability of responses, we may ask the question of whether consolidative HDT-ASCT is necessary

Audience Response Question

Which of the following is the standard of care treatment for classical Hodgkin lymphoma in 1st relapse?

A. Checkpoint inhibitor therapy alone
B. Brentuximab vedotin therapy alone
C. Salvage therapy followed by high dose chemotherapy/autologous stem cell transplant
D. Brentuximab vedotin plus checkpoint inhibitor therapy until remission obtained