A Phase II Trial of Pembrolizumab and Entinostat in Relapsed/Refractory Hodgkin Lymphoma

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Conflicts of interest

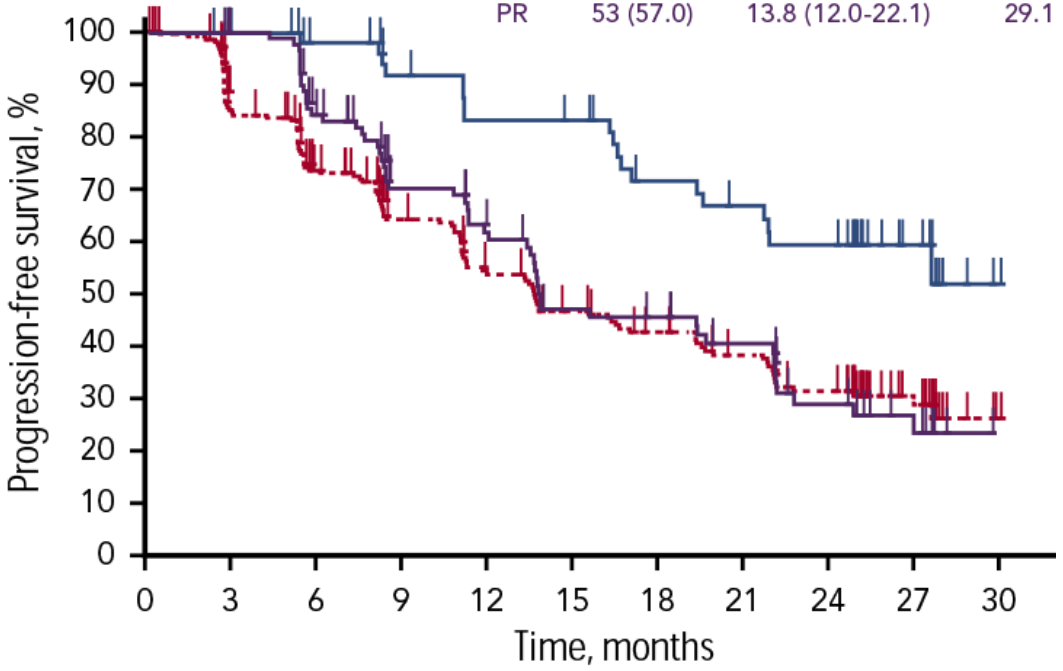
Honoraria: Merck, Pharmacyclics, and Bayer

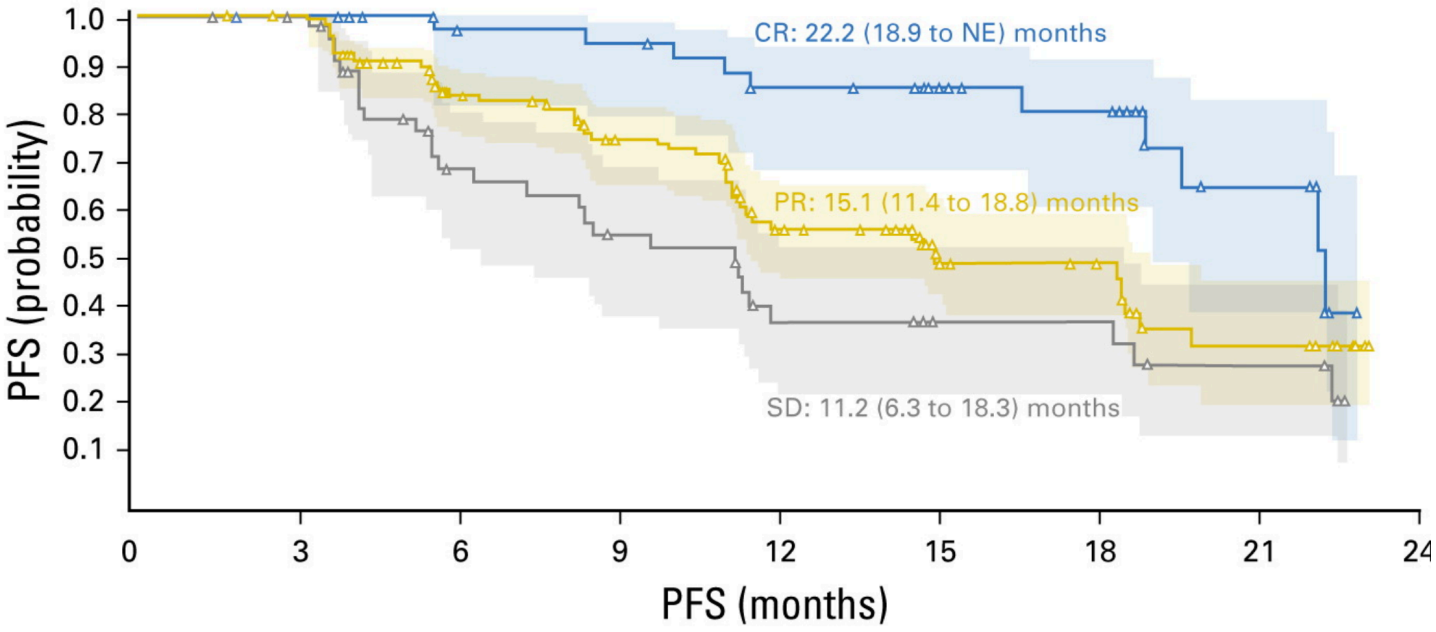
Research Funding: Merck, BMS, Janssen

CPI can result in durable responses in patients with CR

However, patients who accomplish a *PR or less have a median PFS of only ≤ 15 months*

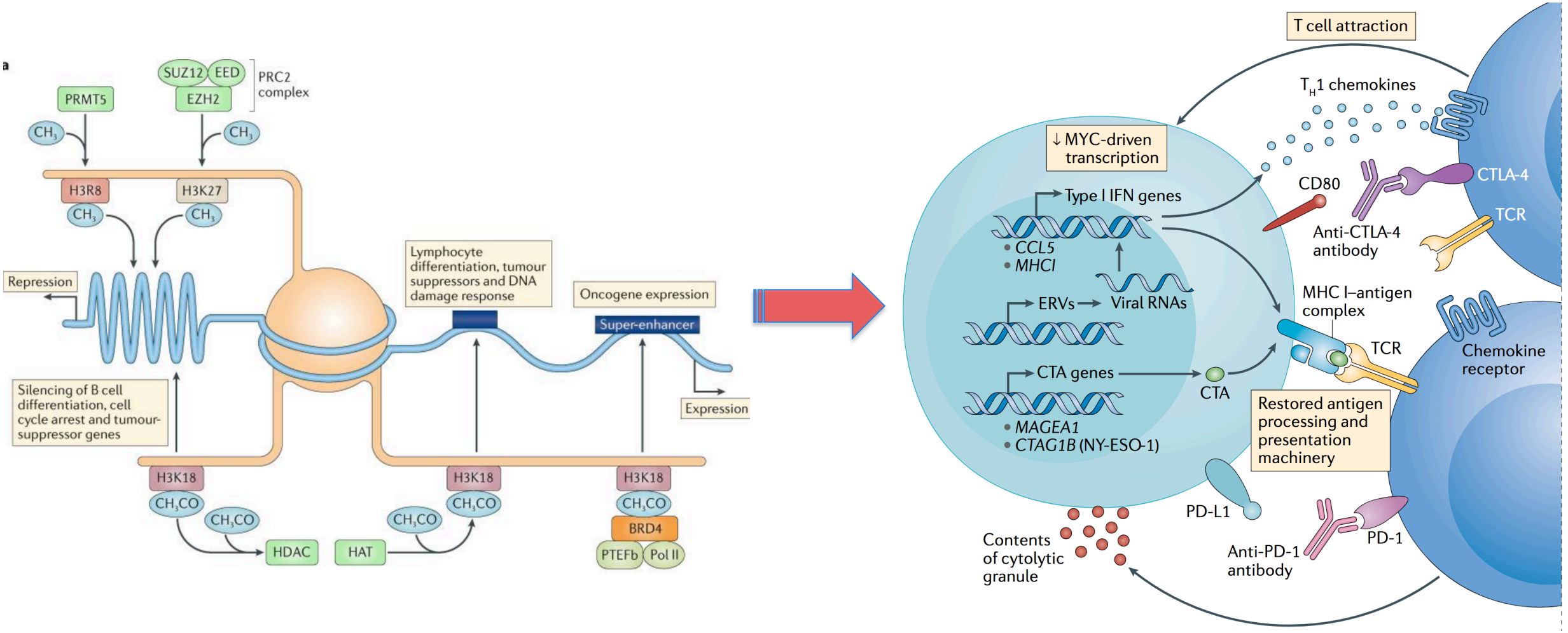
	Events, n (%)	PFS,* median (95% CI), mo	24-mo PFS,* %
All patients	120 (57.1)	13.7 (11.1-17.0)	31.3
CR	19 (32.8)	NR (21.7-NR)	59.5
PR	53 (57.0)	13.8 (12.0-22.1)	29.1





Chen et al., Blood 2019
Amand et al., J Clin Oncol. 2018

Epigenetic therapy can lead to "immune hot" state



Sermer et al., Nat Rev Clin Oncol. 2019
Topper et al., Nat Rev Clin Oncol. 2020

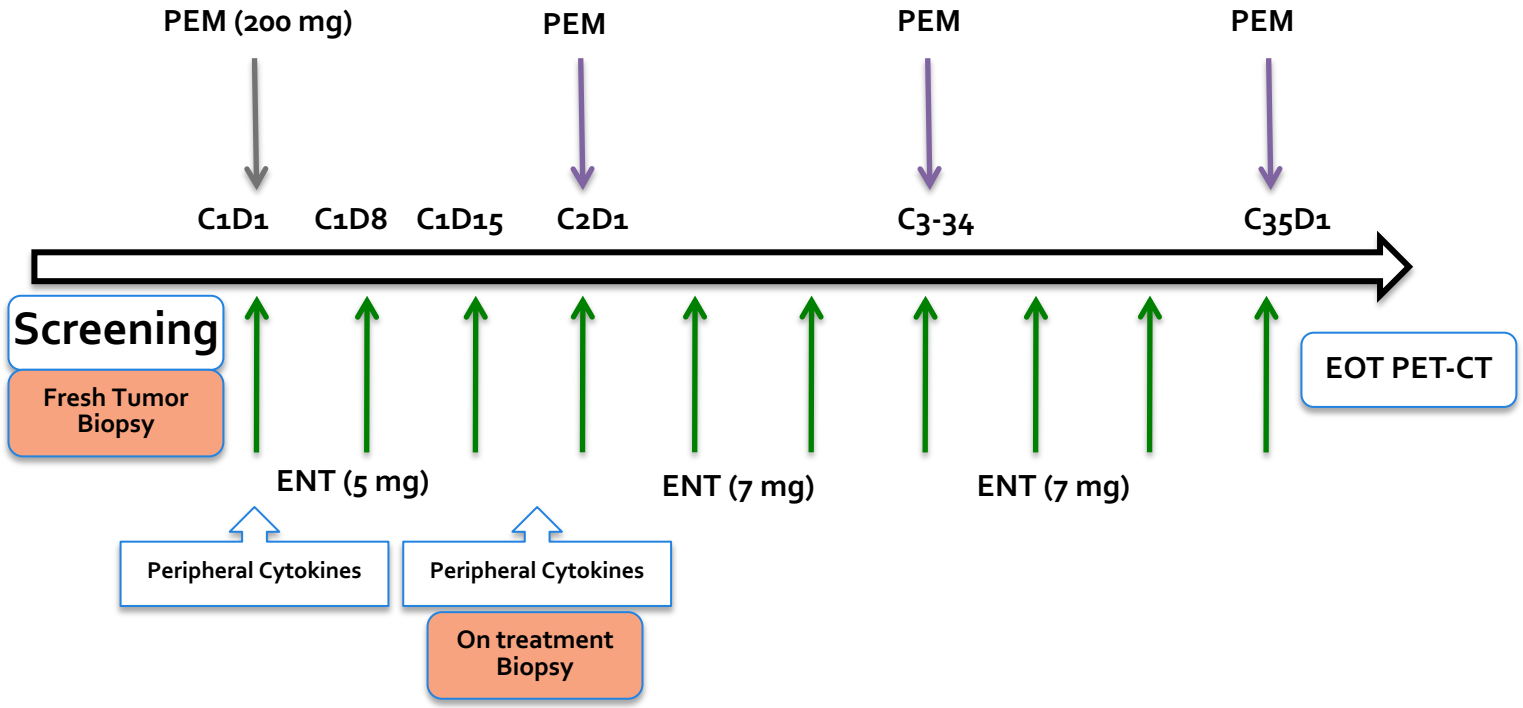
Patient Inclusion Criteria and Study Schema

Key inclusion criteria:

- >2 prior regimens and ineligible for ASCT
- Prior allogeneic SCT allowed if no active GVHD and off all IS
- *Prior treatment with HDAC inhibitor or anti-PD1 antibody allowed if responded*

Study endpoint:

- 12-month PFS rate

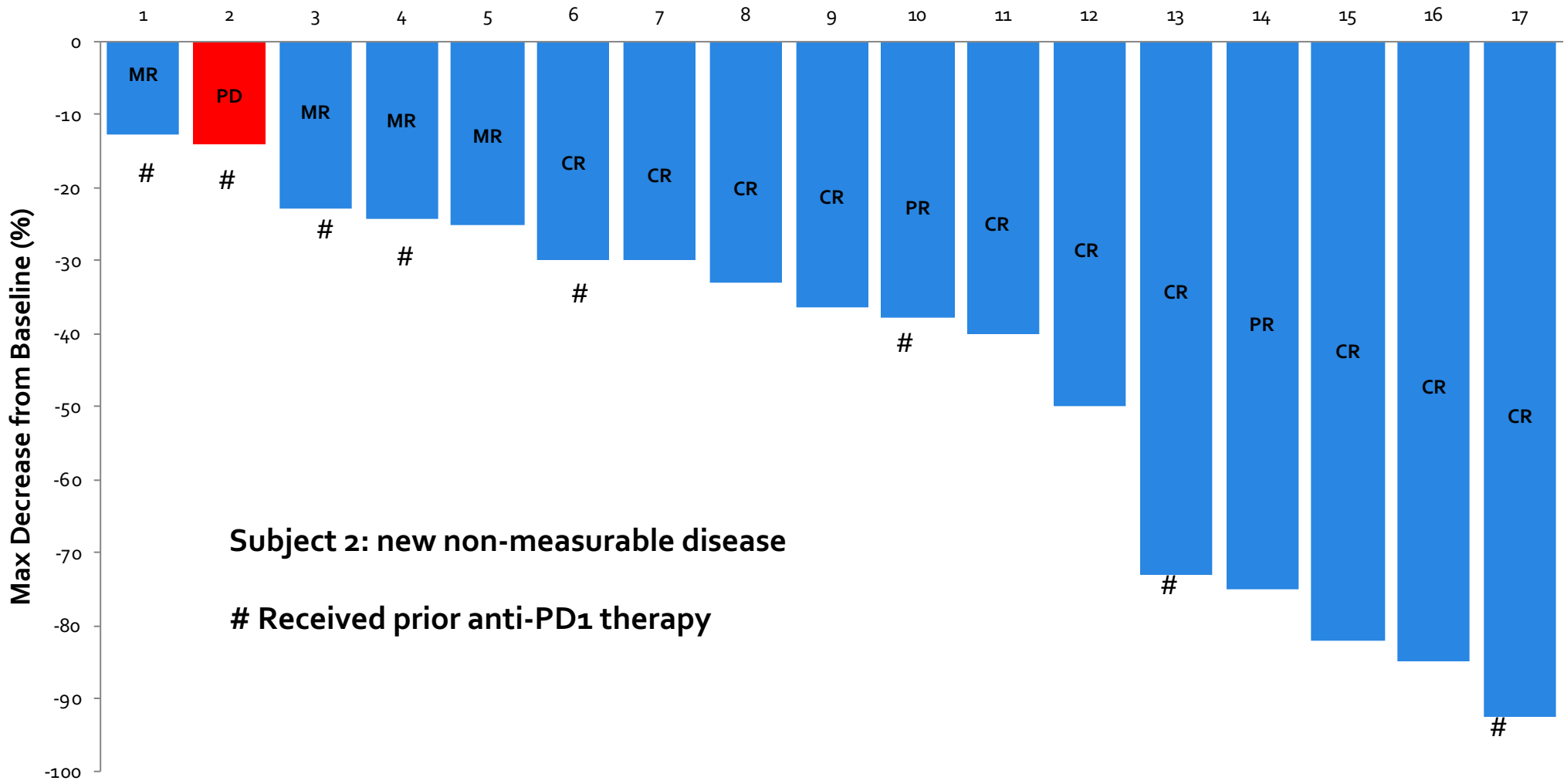


Younes et al., Ann Oncol. 2017

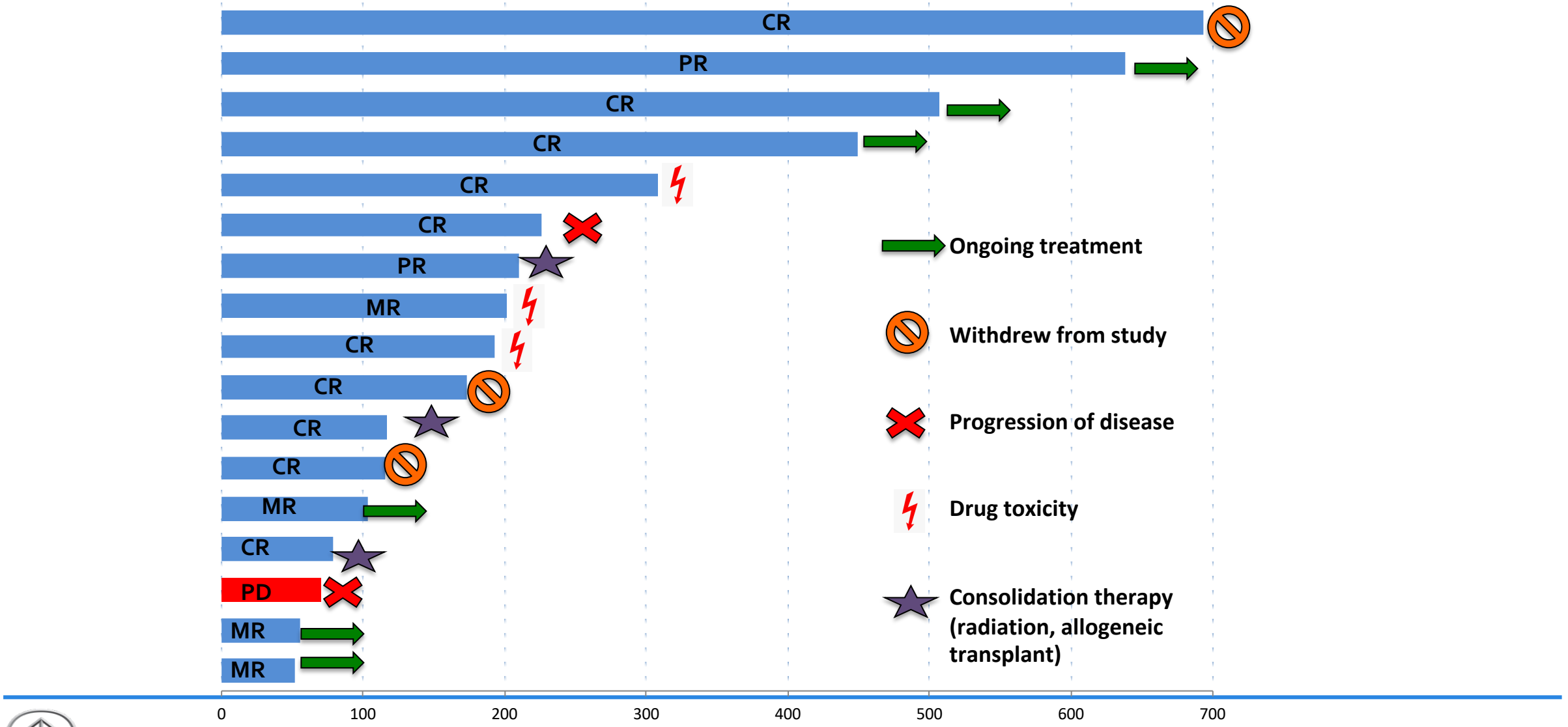
Patient characteristics

Total Number	17
Age	34 (21-77)
Gender Male Female	 10 (59%) 7 (41%)
ECOG 0 1	 10 (59%) 7 (41%)
Number of prior lines	4 (2-17)
Refractory to last therapy	7 (41%)
Prior autologous stem cell transplant	11 (65%)
Prior checkpoint inhibitor	8 (47%)
Prior HDAC	3 (18%)

Best clinical response

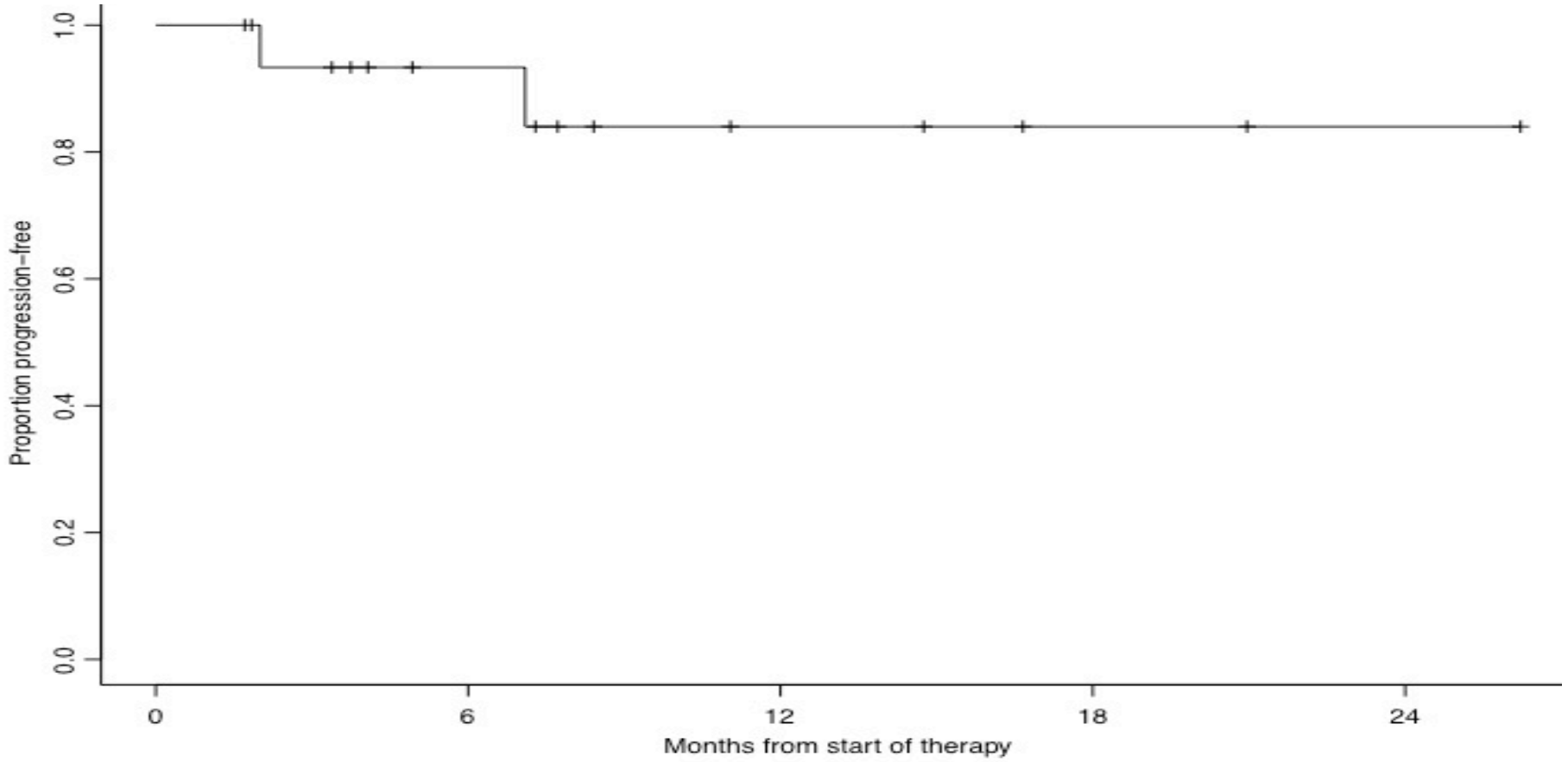


Duration of treatment (in Days)



Progression-free survival

12-month PFS was 84% and the median PFS was not reached



Toxicities

Serious Adverse Events

- 2 cases of pericardial effusions
- 1 case of HLH
- 1 case of bullous dermatitis

Immune-related Adverse Events (all ≤ grade 2)

- 3 cases of hypothyroidism
- 3 cases of hepatitis
- 2 cases of pneumonitis

Toxicity	All grade AEs	Grade 3 or 4 AEs
Thrombocytopenia	17 (68%)	8 (32%)
Neutropenia	16 (64%)	13 (52%)
Fatigue	10 (40%)	1 (4%)
Nausea/vomiting	10 (40%)	0
Muskuloskeletal	8 (32%)	1 (4%)
Abdominal pain	6 (24%)	1 (4%)
Peripheral edema	5 (20%)	1 (4%)
Hypophosphatemia	5 (20%)	0
Anemia	4 (16%)	2 (8%)
Mucositis	4 (16%)	0
Rash	3 (12%)	1 (4%)
Dysgeusia	3 (12%)	0
Fever	3 (12%)	0
Effusions	3 (12%)	2 (8%)
Hypothyroidism	3 (12%)	0
Transaminase elevation	3 (12%)	0
Dizziness	3 (12%)	0

Conclusions

- The combination of pembrolizumab with entinostat was overall well tolerated and demonstrated a promising CR rate in a heavily pre-treated patient population
- Responses were observed irrespective of prior HDAC-I or CPI therapy and appear durable
- Longer follow-up will be needed to confirm these data