Nivolumab in Hodgkin Lymphoma

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Chair, Lymphoma Group

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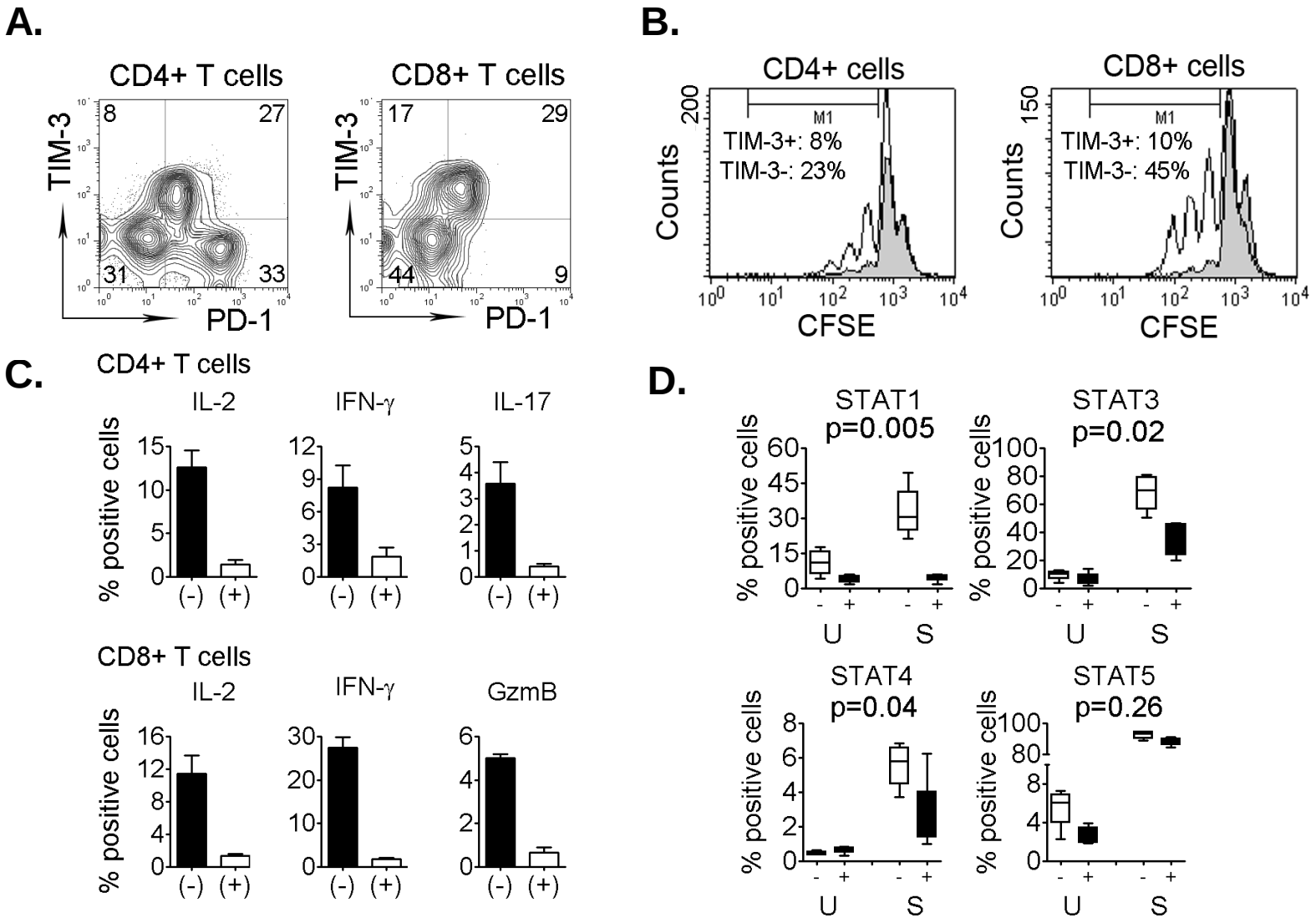
Conflicts of Interest

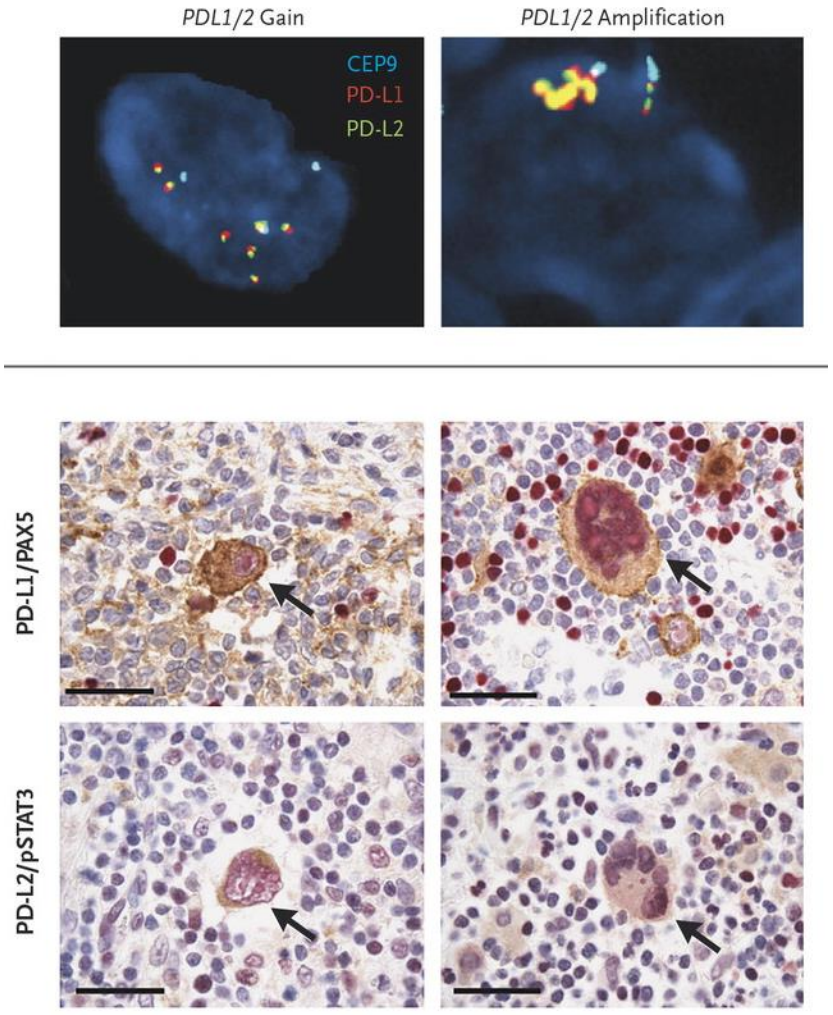
- Research Funding from –
  - Bristol Myers Squibb
  - Celldex Therapeutics
  - Seattle Genetics
  - Merck
  - Affimed

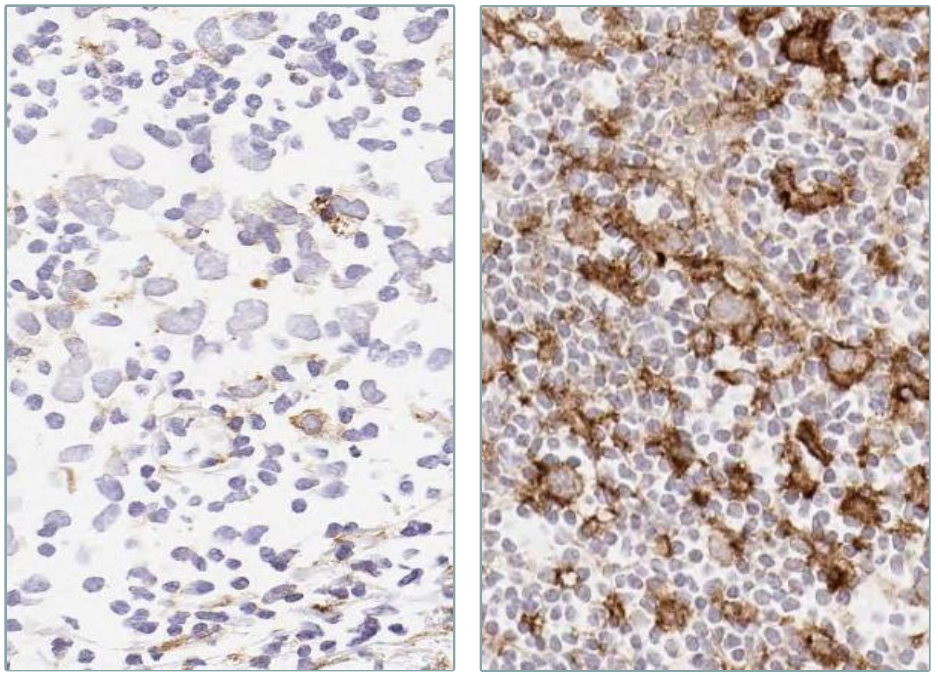
1. Exhausted intratumoral T-cells are poorly functional



Yang et al. J Clin Invest 2012;122(4):1271-82.

2. Increased PD-L1 and PD-L2 expression in Hodgkin Lymphoma



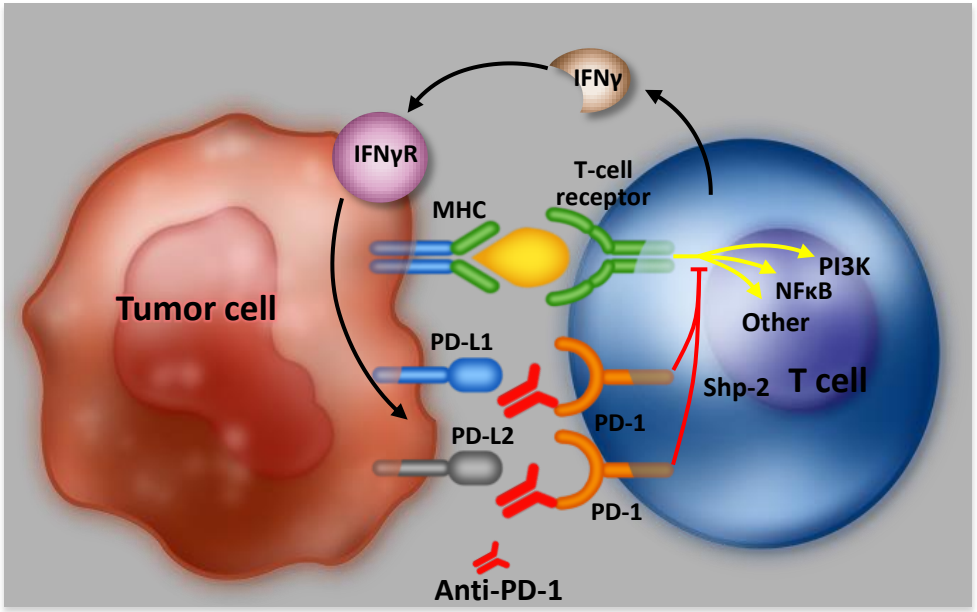


PD-L1 Negative PD-L1 Positive

Ansell et al. N Engl J Med. 2015;372:311-319
Roemer et al. ASH 2015 abstract #176
Moskowitz et al. ASH 2014, abstract 290

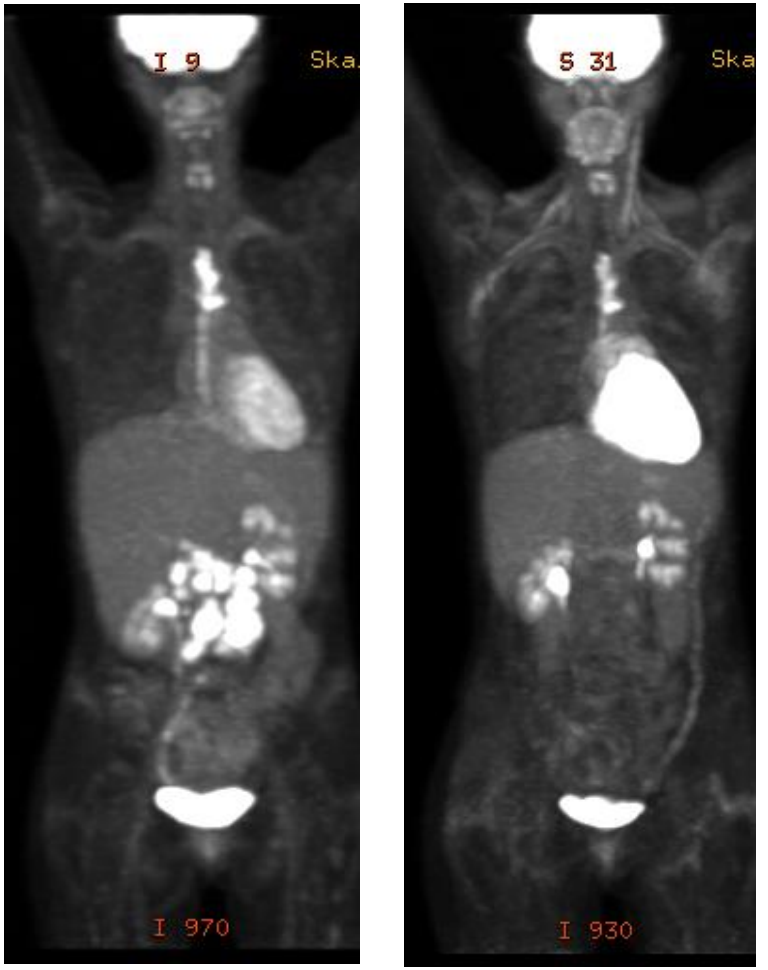
Does Immune Checkpoint Blockade work? Blocking PD-1 using nivolumab

- PD-1 ligands are overexpressed in inflammatory environments and attenuate the immune response via PD-1 on immune effector cells.[1]
- PD-L1 expressed on malignant cells and/or in the tumor microenvironment suppresses tumor infiltrating lymphocyte activity.[2]

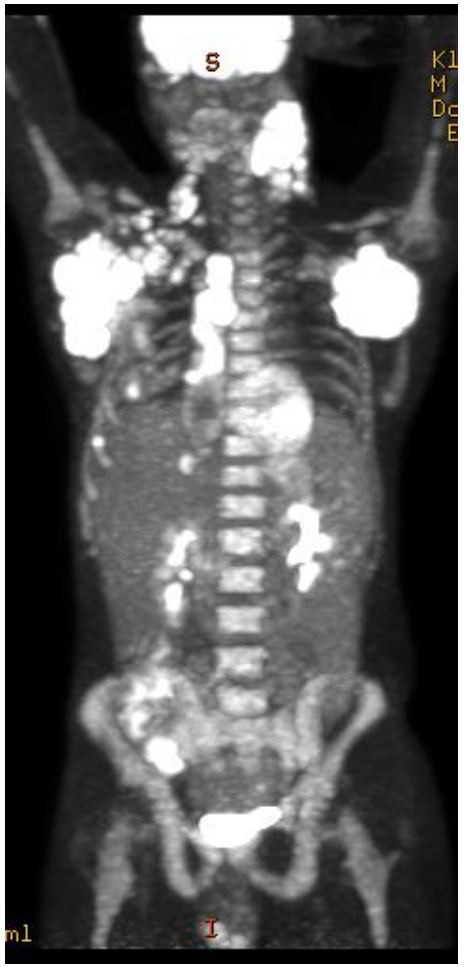


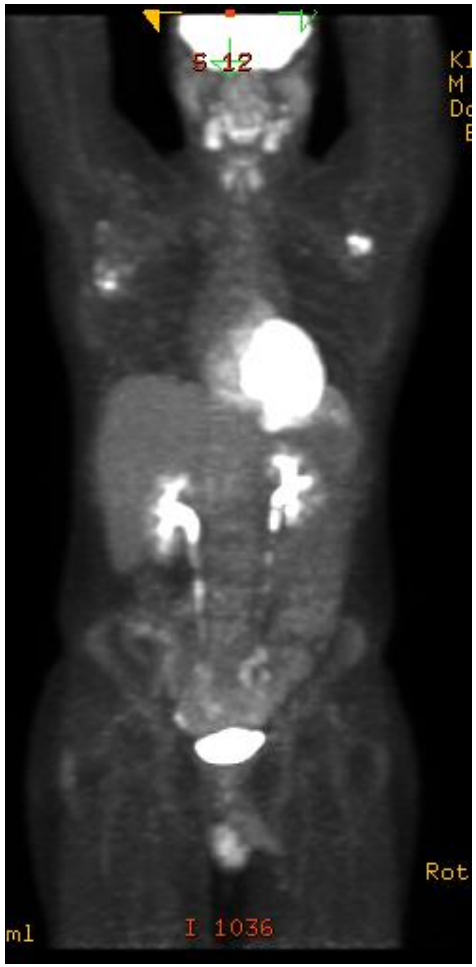
[1]Francisco LM et al. J Exp Med 2009;206:3015-29.
[2]Andorsky DJ et al. Clin Cancer Res 2011;17:4232-44

Does Blocking PD-1 with nivolumab work?



42 year old female – Hodgkin lymphoma

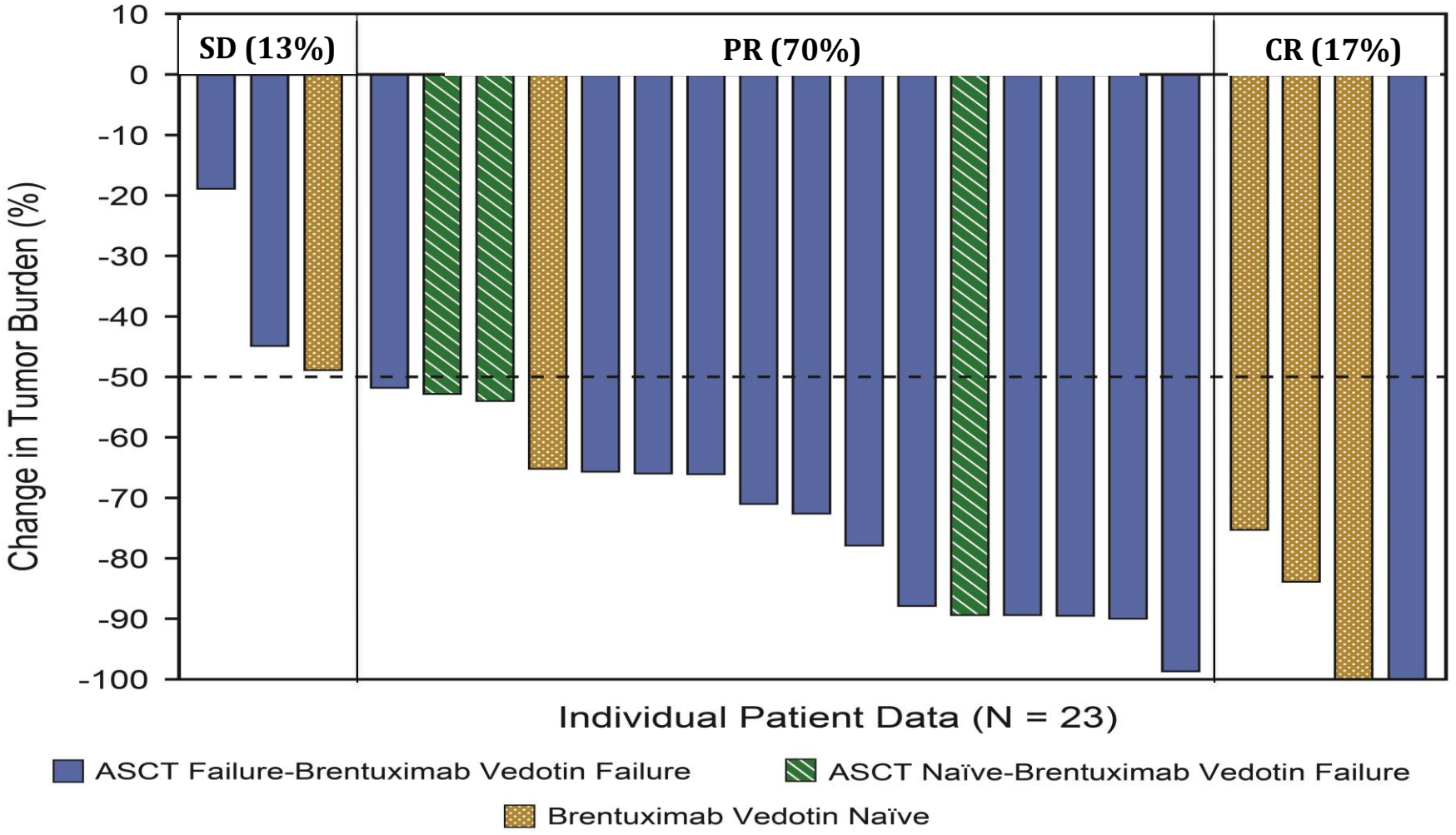




26 year old male – Hodgkin lymphoma

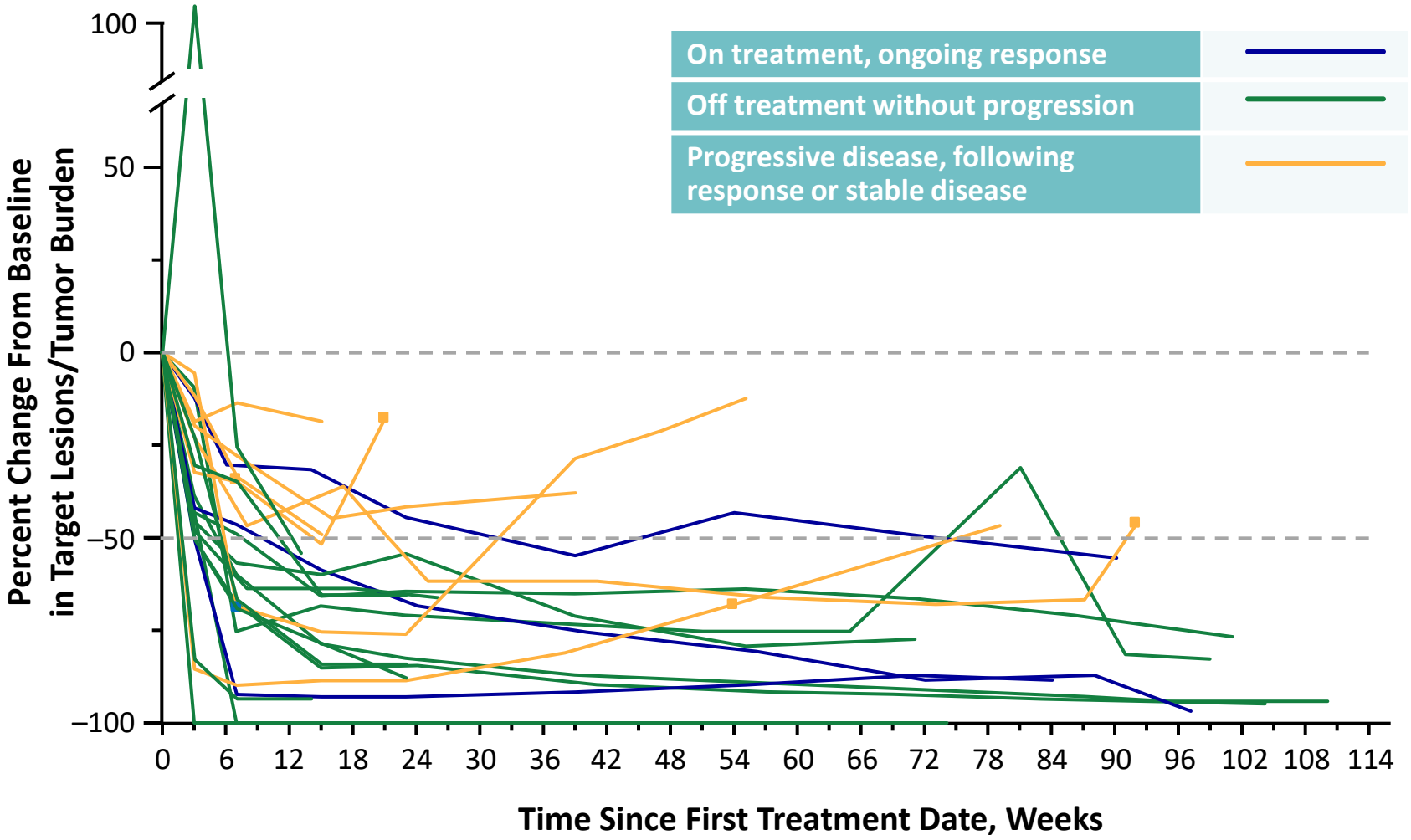
Courtesy of SM Ansell, Mayo Clinic

Hodgkin Lymphoma – Phase 1 data with nivolumab



Ansell et al. N Engl J Med. 2015;372(4):311-9.

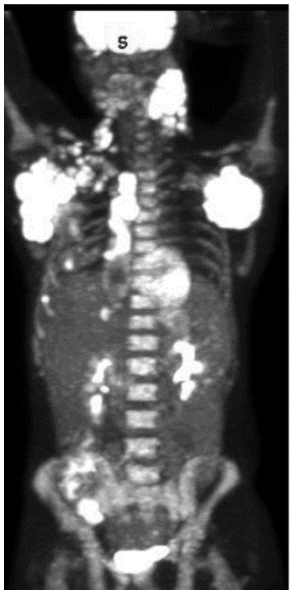
Nivolumab - Durability of Response



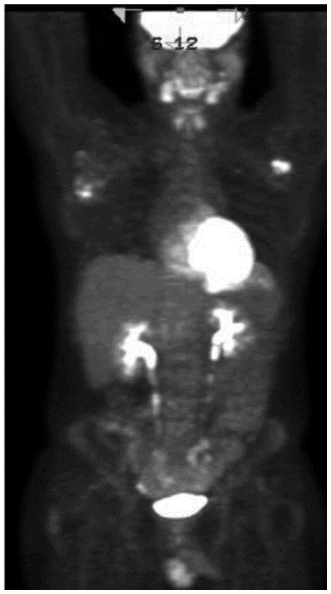
■ First occurrence of new lesion

Ansell et al. ASH 2015, abstract 583

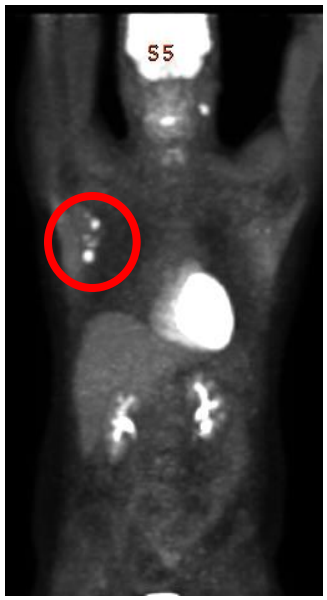
Retreatment With Nivolumab



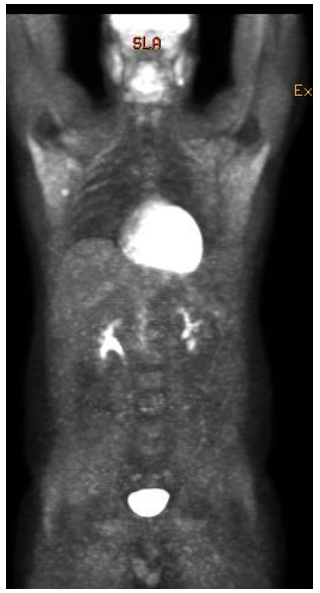
Pretreatment



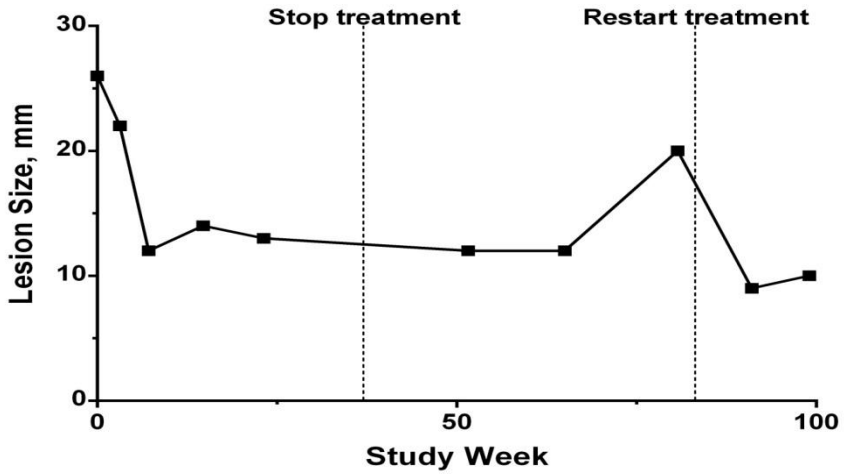
6 weeks posttreatment



Progression when therapy stopped



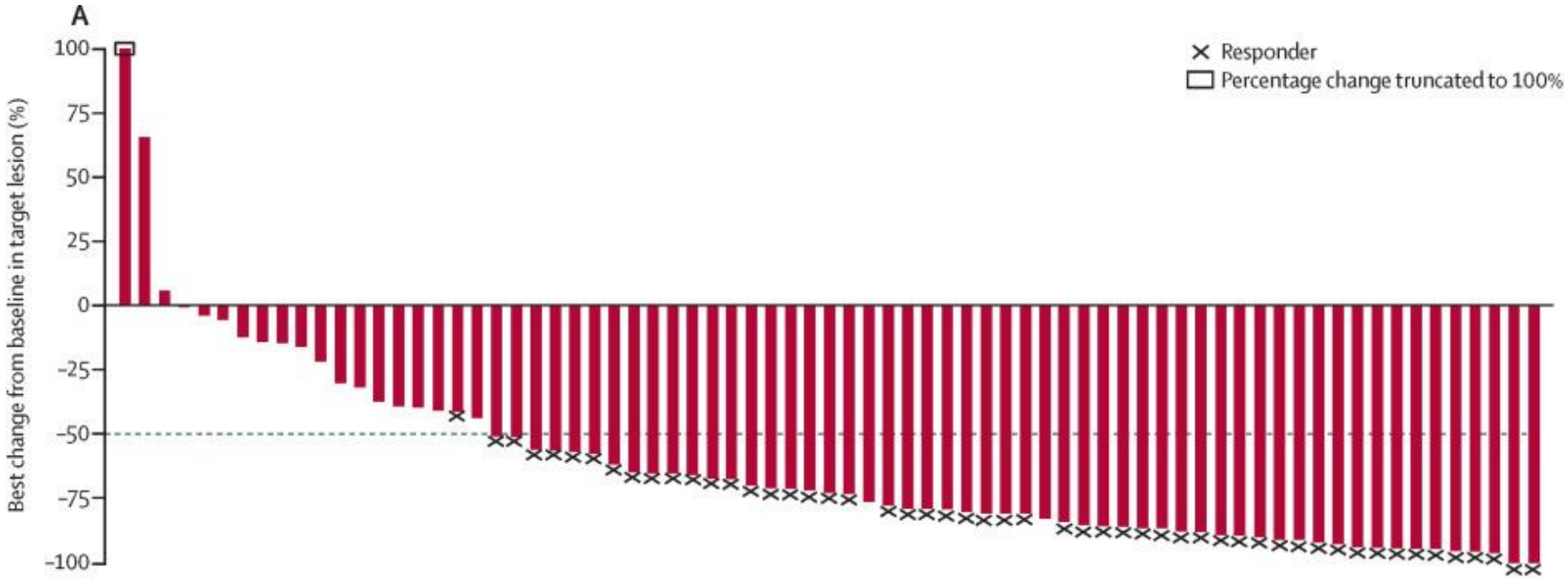
6 weeks post-second course of therapy



Ansell et al. Haematologica 2016; 101(s5): P090

Nivolumab for classical Hodgkin's lymphoma: a multicentre, multicohort, single-arm phase 2 trial (Cohort B).

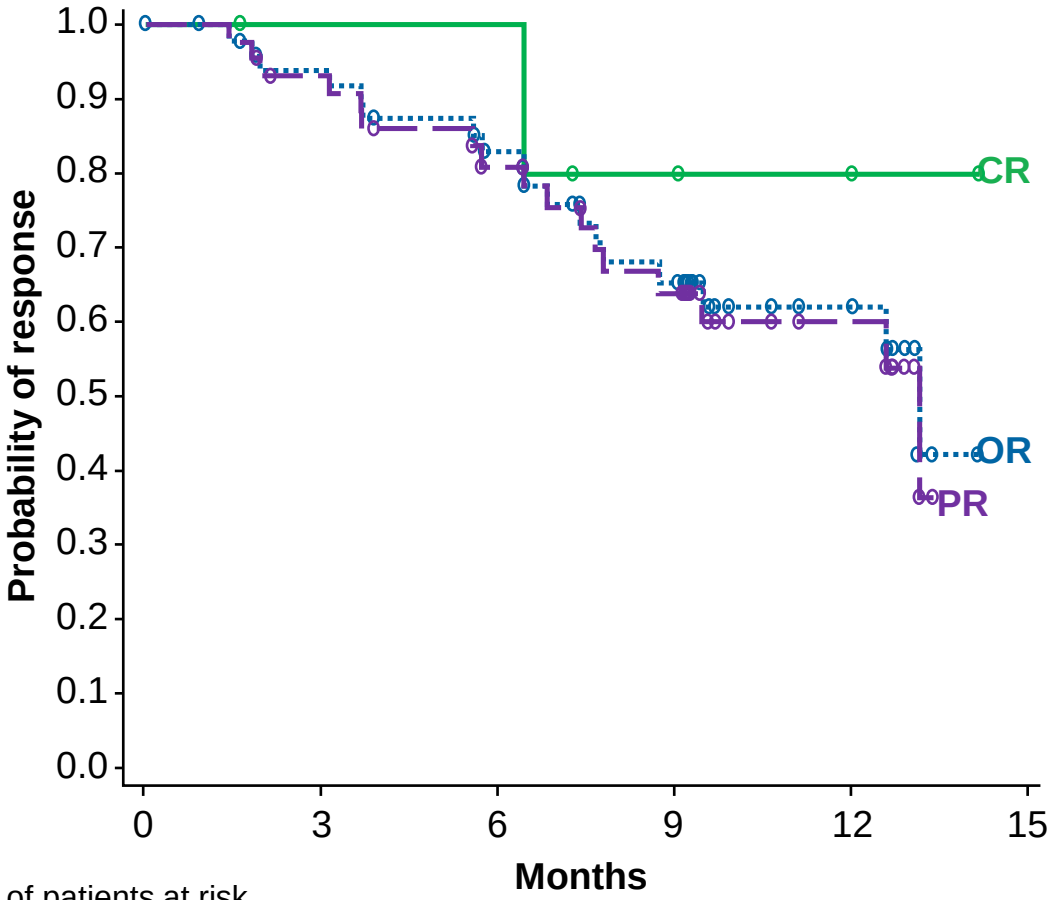
80 patients – failed ASCT and BV
66% ORR



Younes et al. Lancet Oncol. 2016 2016 Sep;17(9):1283-94.

Duration of Response by Best Response

Cohort B: Nivolumab After BV Post-ASCT



No. of patients at risk

CR	6	5	5	3	2	0
PR	48	39	31	22	10	0
OR	54	44	36	25	12	0

Database lock	Oct 2015	Apr 2016
Median follow-up, mo (range)	**9** (2–12)	**15** (2–19)
ORR, n (%)	**53 (66)**	**54 (68)**
Median DOR, mo (95% CI)	**8** (7, NR)	**13** (9, NR)
Median DOCR, mo (95% CI)	**5** (NR, NR)	**NR** (5, NR)
Median DOPR, mo (95% CI)	**8** (7, NR)	**13** (8, NR)

Timmerman et al. ASH 2016 abstract #1110

Best Overall Response

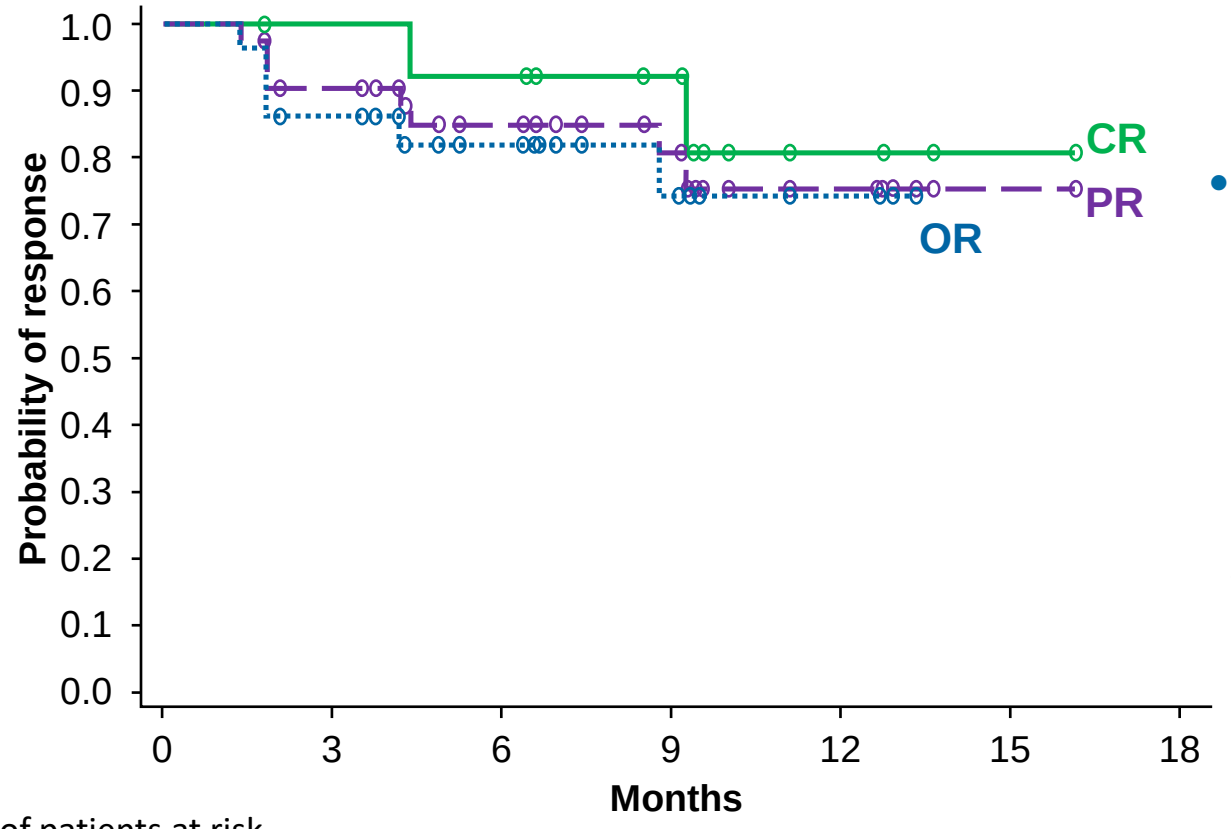
Cohort A: Nivolumab in BV-Naïve Post-ASCT Patients

	Cohort A (n = 63)
	IRRC assessed
ORR, n (%)	43 (68)
95% CI	55, 79
CR, n (%)	14 (22)
PR, n (%)	29 (46)
SD, n (%)	13 (21)
PD, n (%)	7 (11)

Timmerman et al. ASH 2016 abstract #1110

Duration of Response by Best Response

Cohort A: Nivolumab in BV-Naïve Post-ASCT Patients



No. of patients at risk

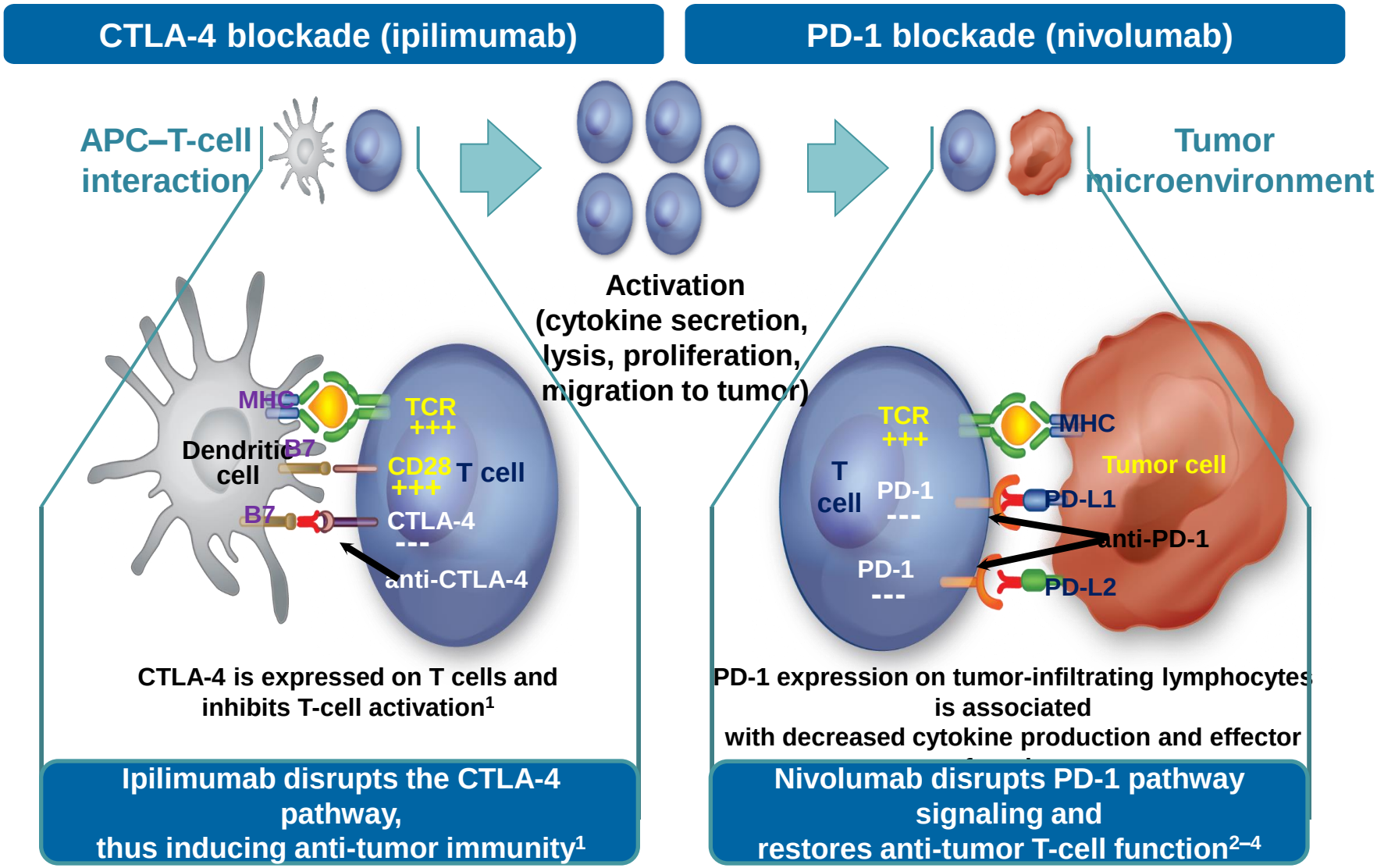
CR	14	13	12	9	3	1	0
PR	29	24	16	10	3	0	0
OR	43	37	28	19	6	1	0

- Durable responses in both complete and partial responders

Database lock	Jun 2016
Median duration of follow-up, mo (range)	**14** (1–20)
Median DOR, mo (95% CI)	**NR** (NR, NR)

Timmerman et al. ASH 2016 abstract #1110

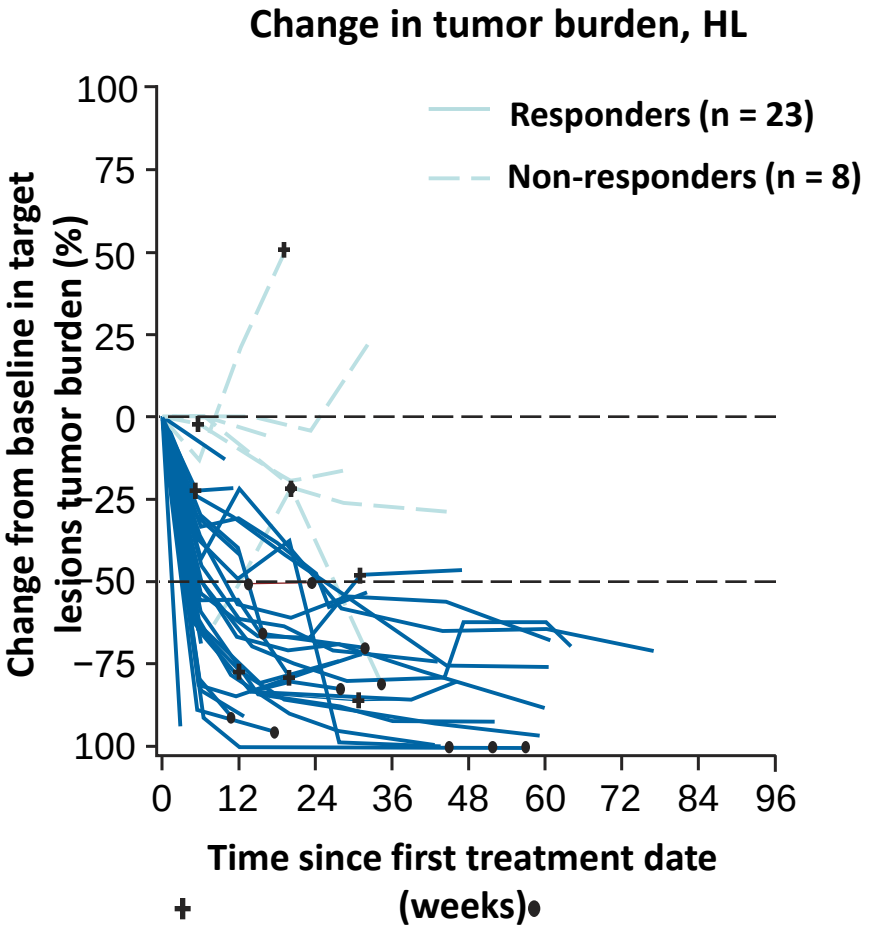
Nivolumab and Ipilimumab Mechanism of Action



Ansell et al. ASH 2016 abstract #183

Nivolumab + Ipilimumab – Hodgkin Lymphoma

	HL (N = 31)
ORR, n (%)[a]	23 (74)
Complete response	6 (19)
Partial response	17 (55)
Stable disease	3 (10)
Relapsed or progressive disease	3 (10)
Median duration of OR, months (range)	NR (0.0+, 13.4+)
	Transplant naïve[b] (n = 18)
ORR, n (%)	12 (67)



[a]Response was not reported for 2 (6%) patients with HL

bTransplant-naïve patients are a subset of the total number of patients with HL; a total of 13 transplant-naïve patients were chemoresistant and 3 were ineligible for the procedure

NR = not reached; + = censored value

Ansell et al. ASH 2016 abstract #183

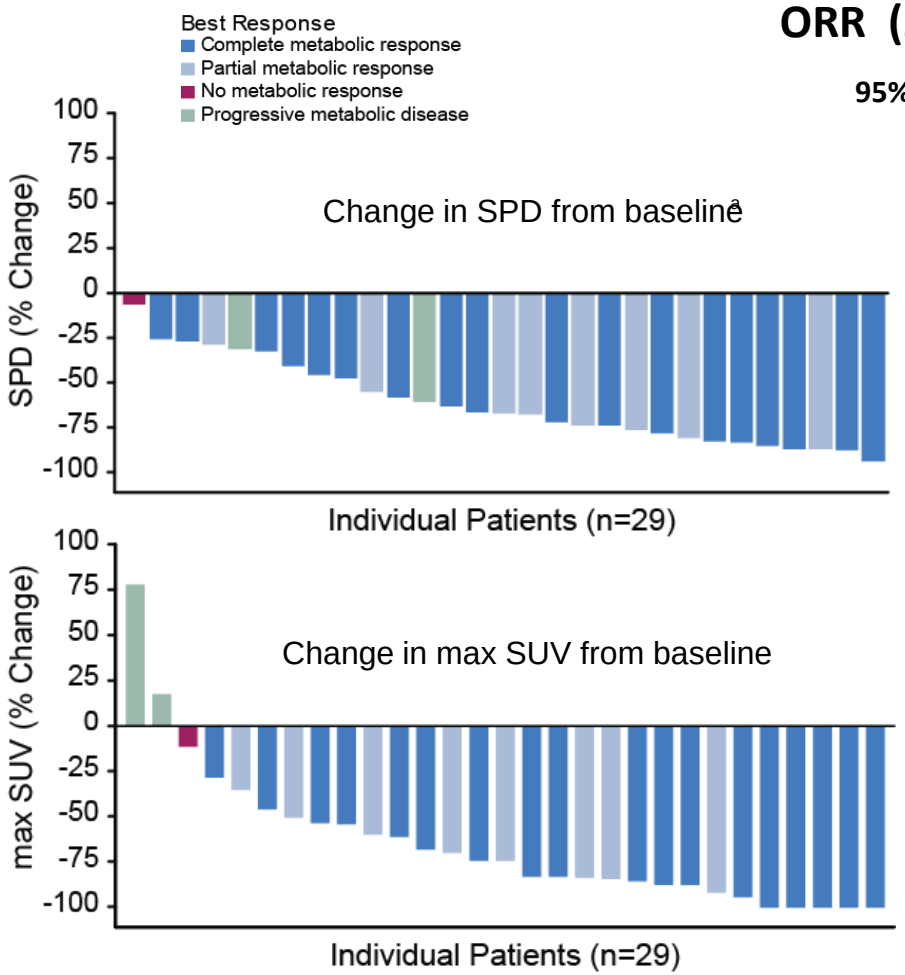
Nivolumab + Brentuximab vedotin

ORR (26/29) = 90%

95% CI: 72.6, 97.8

CmR (18/29) = 62%

95% CI: 42.3, 79.3



[a] Cycle 2 SPD reported for 1 patient

Deauville score (N=29)

	5-Point Score	n (%)	Total
CmR	1	8 (28)	18 (62)
	2	6 (21)	
	3	3 (10)	
	Missing	1 (3)	
PmR	4	6 (21)	8 (28)
	5	2 (7)	
NmR	5	1 (3)	3 (10)
PmD	5	2 (7)	2 (7)

Herrera et al. ASH 2016 abstract #1105

BV and Nivolumab is Highly Active

Evaluable Patients (n = 12)	ORR
ORR	12/12 (100%)
CR	8/12 (66%)
PR	4/12 (34%)

2 of 2 patients with prior BV evaluable= CR

NYU Langone MEDICAL CENTER

Diefenbach et al. ASH 2016 abstract #1106

ECOG-ACRIN cancer research group
Reshaping the future of patient care

Conclusions

- Optimizing immune function is the new therapeutic “frontier” in Hodgkin lymphoma
- Immune checkpoint inhibitors such as nivolumab hold real promise in Hodgkin lymphoma.
- Incorporating promising immunologic agents such as nivolumab into combination approaches will be the next clinical challenge.