

New Drugs In Hematology

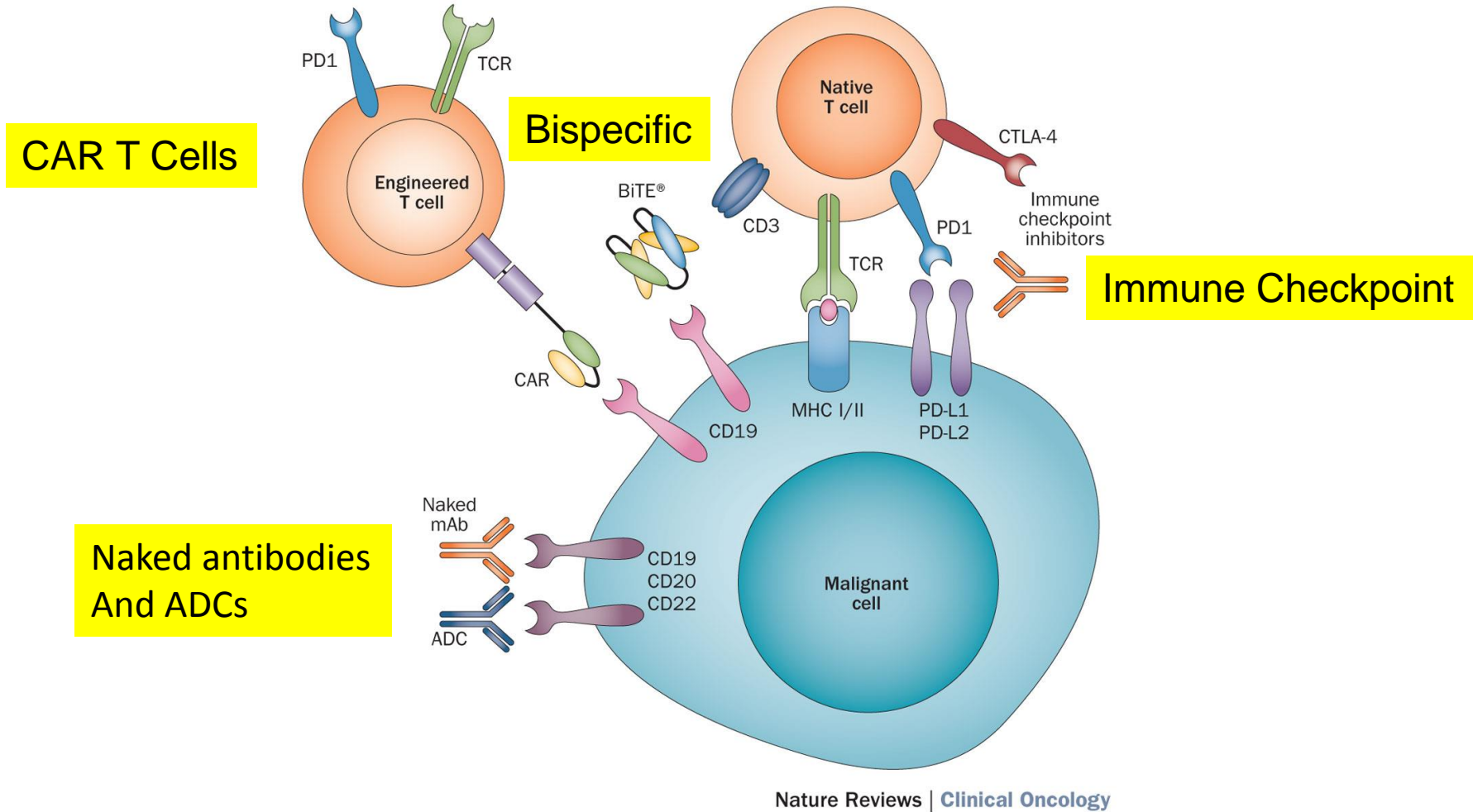
Hodgkin Lymphoma
Nivolumab

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Monday, May 9, 2016

2:10-2:25 p.m

immunotherapy modalities



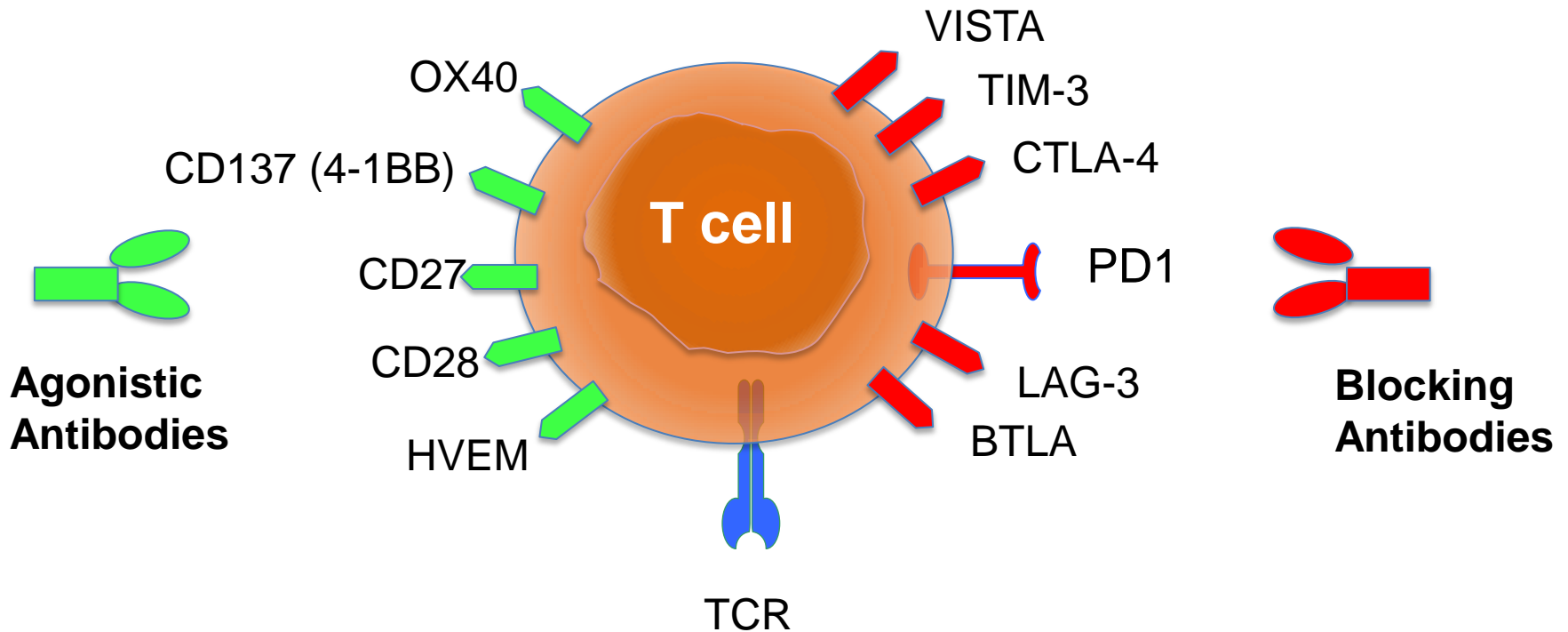
Batlevi, C. L. *et al.* (2015) Novel immunotherapies in lymphoid malignancies
Nat. Rev. Clin. Oncol. doi:10.1038/nrclinonc.2015.187

Therapeutic Activation of Autologous T Cells

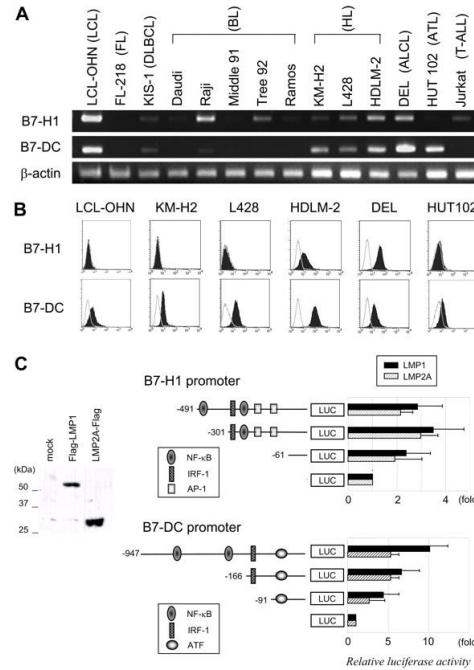
Targeting Immune Checkpoints

Activating Receptors

Inhibitory Receptors

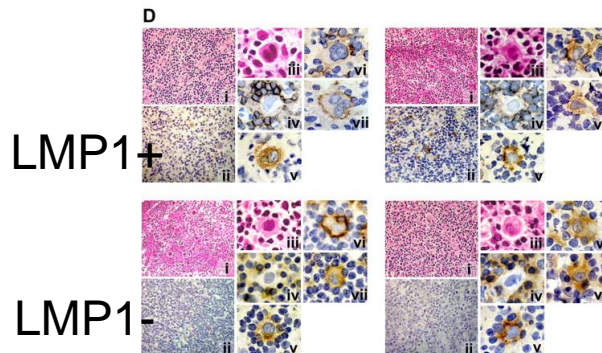


Expression and gene regulation of PDL-1 (CD273) and PDL-2 (CD274) in Hodgkin Lymphoma



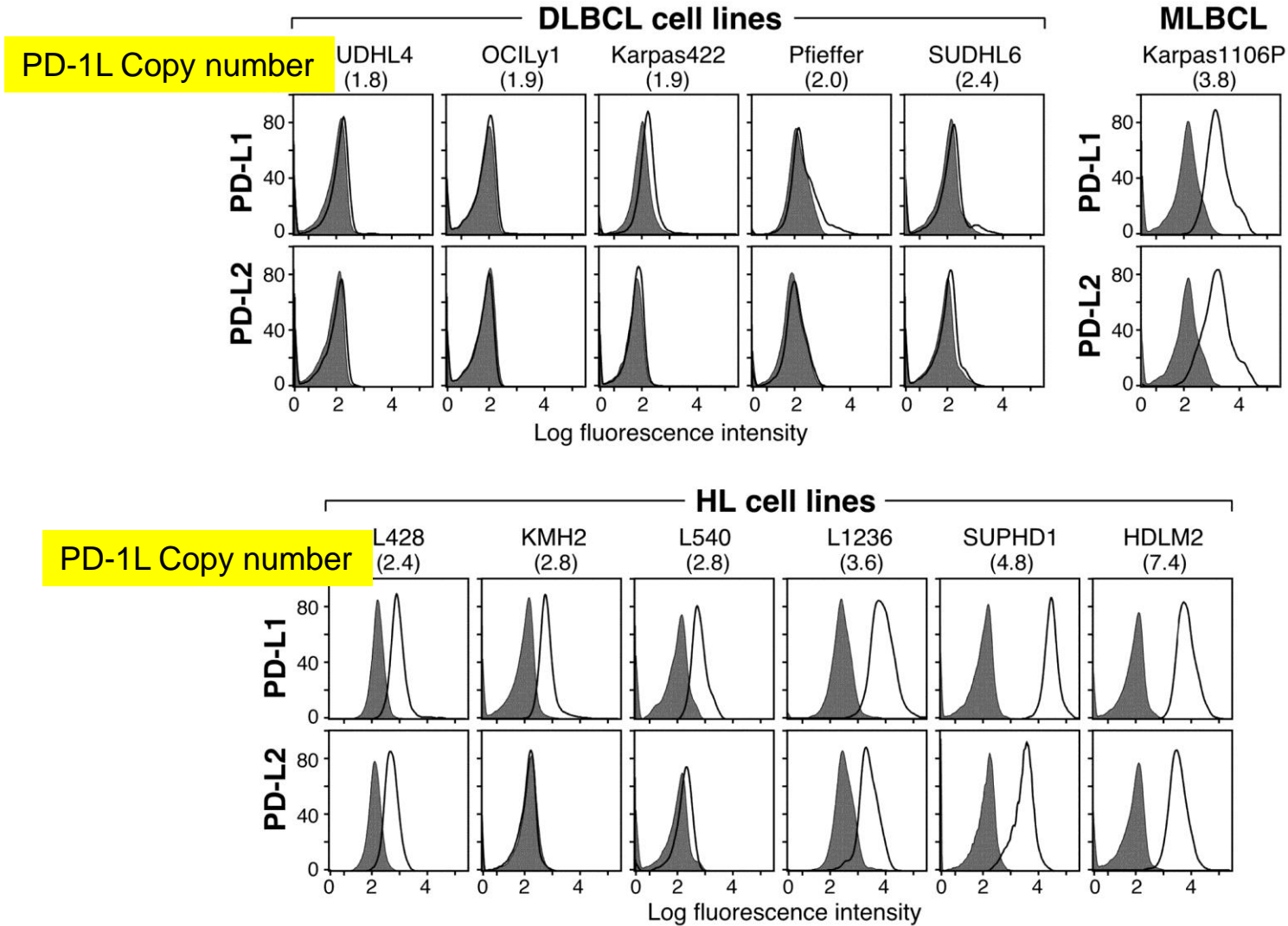
Expression of PDL1/PDL2 in HL cell lines

LMP1 and LMP2A enhanced the transcriptional activity of PDL1/PDL2

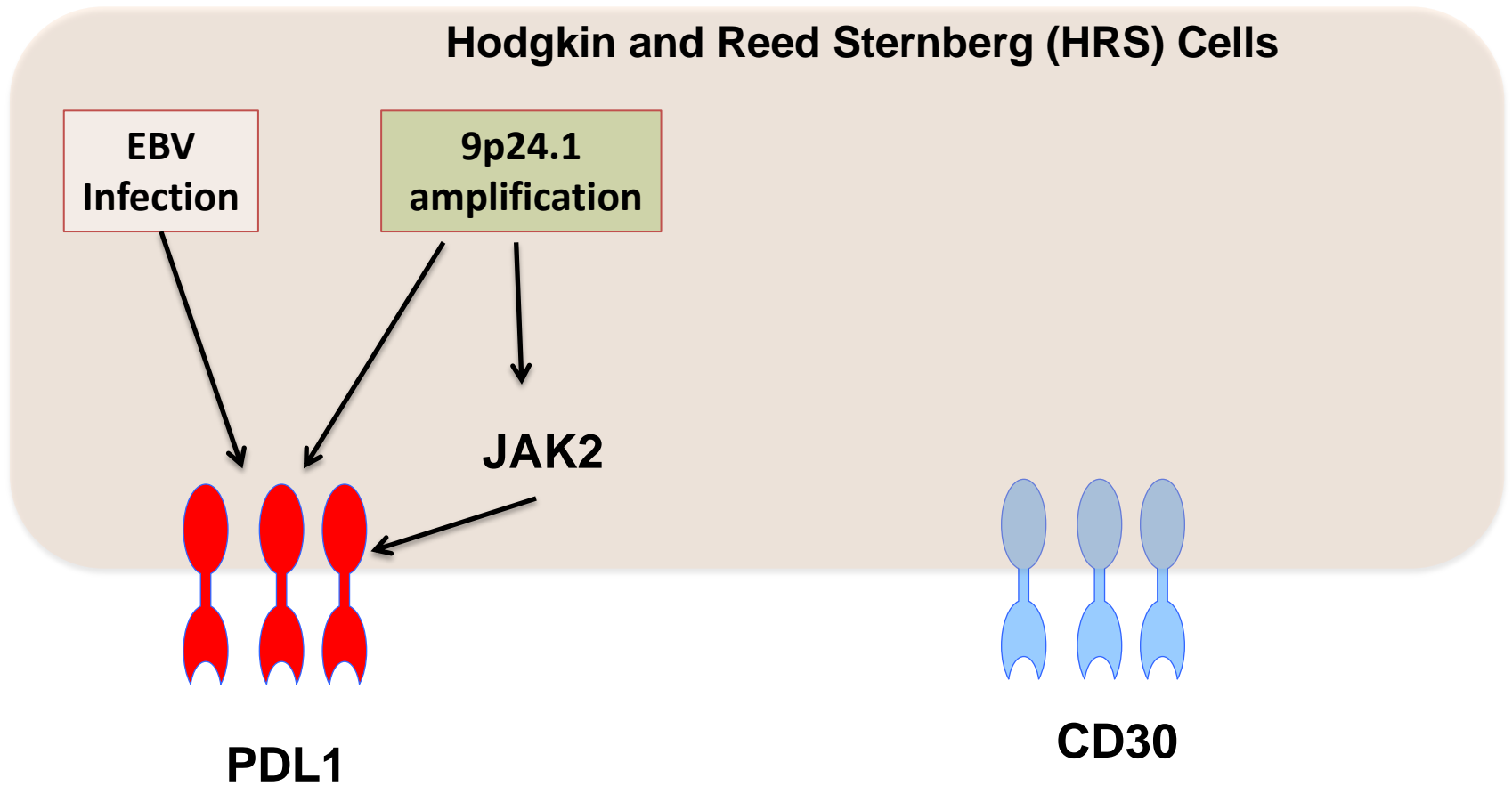


PDL1/PDL2 Expression in EBV+ and EBV- cHL

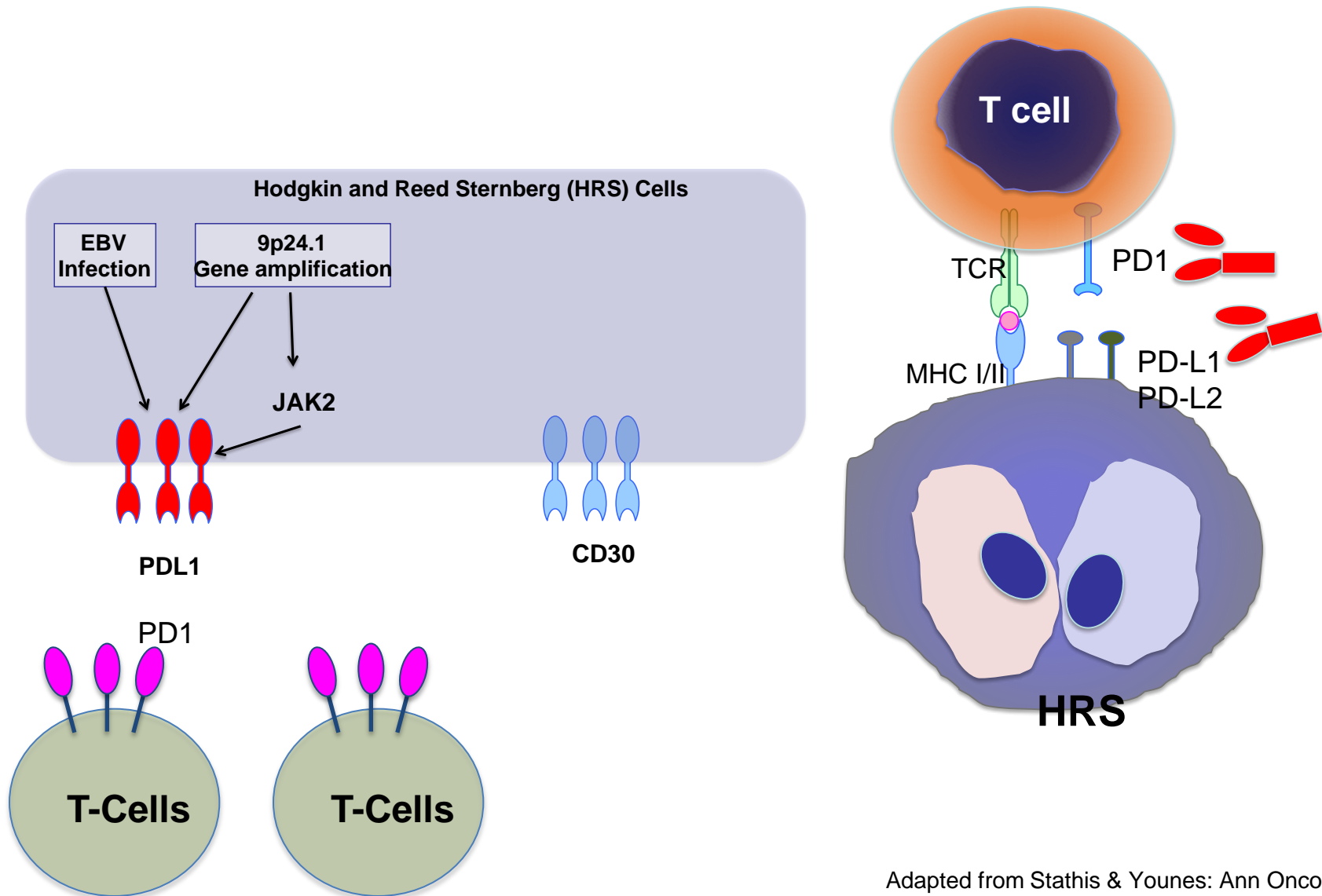
9p24.1 amplification and PD-1L cell-surface expression in HL and MLBCL cell lines.



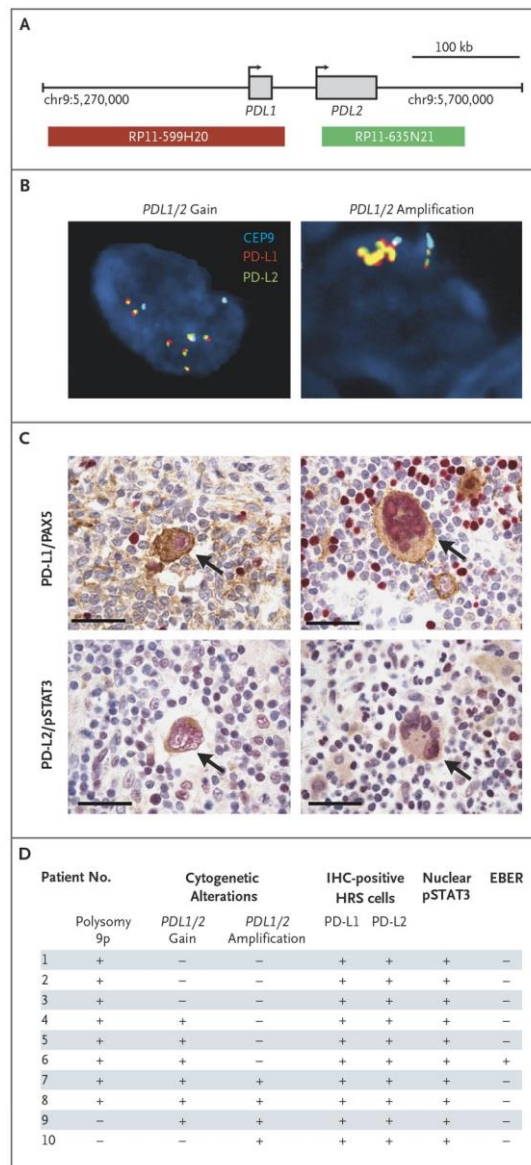
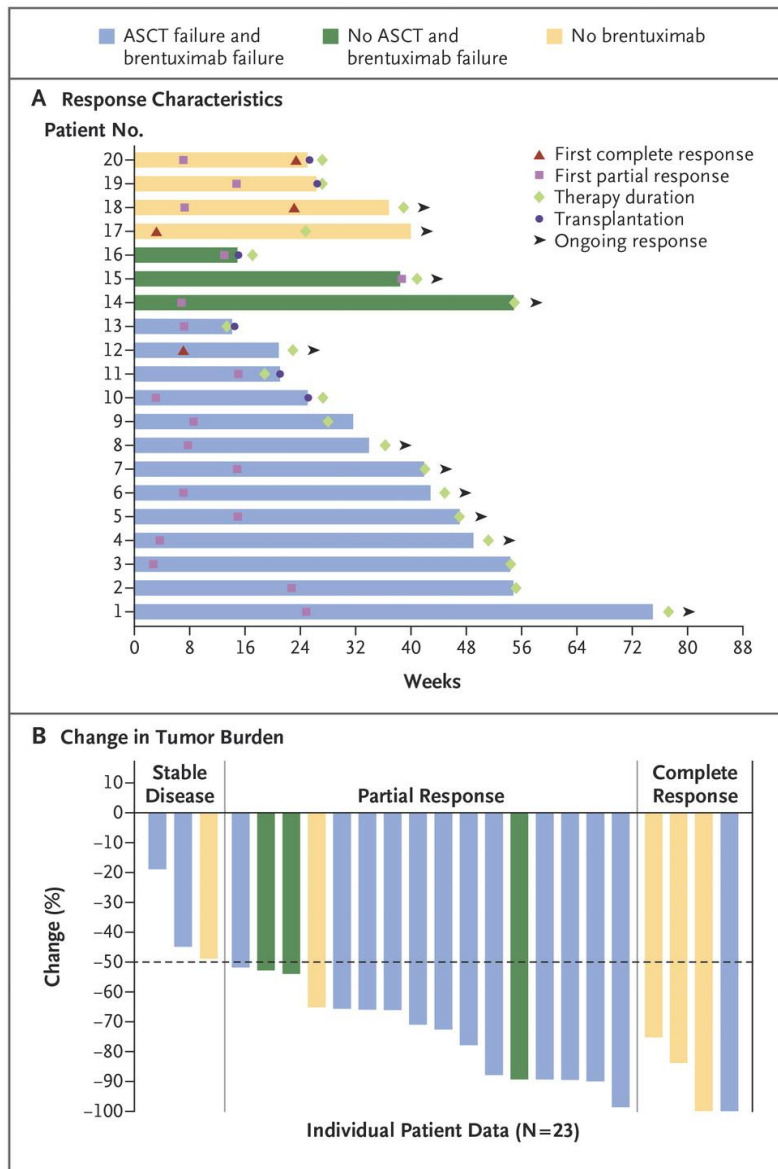
HRS Cells Express High Levels of PDL-1



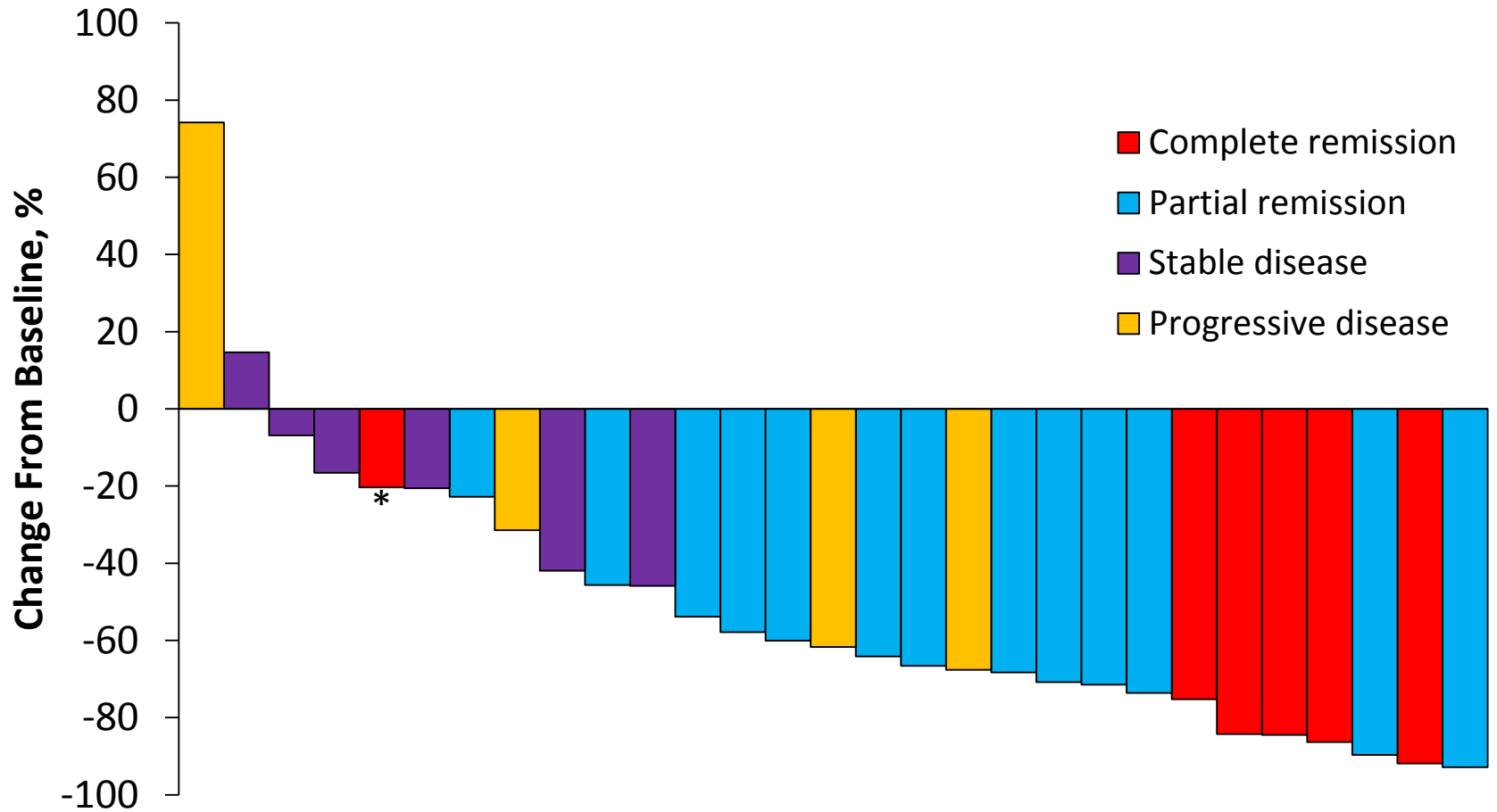
HRS Cells Express High Levels of PDL-1



Nivolumab in Relapsed Hodgkin Lymphoma



Pembrolizumab (MK-3475) in Patients With Relapsed Classical Hodgkin Lymphoma



**Nivolumab in Patients (Pts) With Relapsed or Refractory Classical
Hodgkin Lymphoma
Clinical Outcomes From Extended Follow-up of a Phase 1 Study
(CA209-039)**

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Margaret A. Shipp, MD,² M. Brigid Bradley Garelick, MD,⁴ Lili Zhu, MS,⁵
Alexander M. Lesokhin, MD⁶

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³Jonsson Comprehensive Cancer Center, University of California, Los Angeles, CA, USA;
⁴Bristol-Myers Squibb, Wallingford, CT, USA; ⁵Bristol-Myers Squibb, Princeton, NJ, USA;
⁶Memorial Sloan Kettering Cancer Center, New York, NY, USA

HL Baseline Characteristics

Characteristic	cHL (n = 23)
Age, median (range)	35 (20–54)
Histology, n	
Nodular sclerosing	22
Mixed cellularity	1
Prior autotransplant, n (%)	18 (78)
Prior brentuximab vedotin, n (%)	18 (78)
Number of prior therapies, median (range)	5 (2–15)

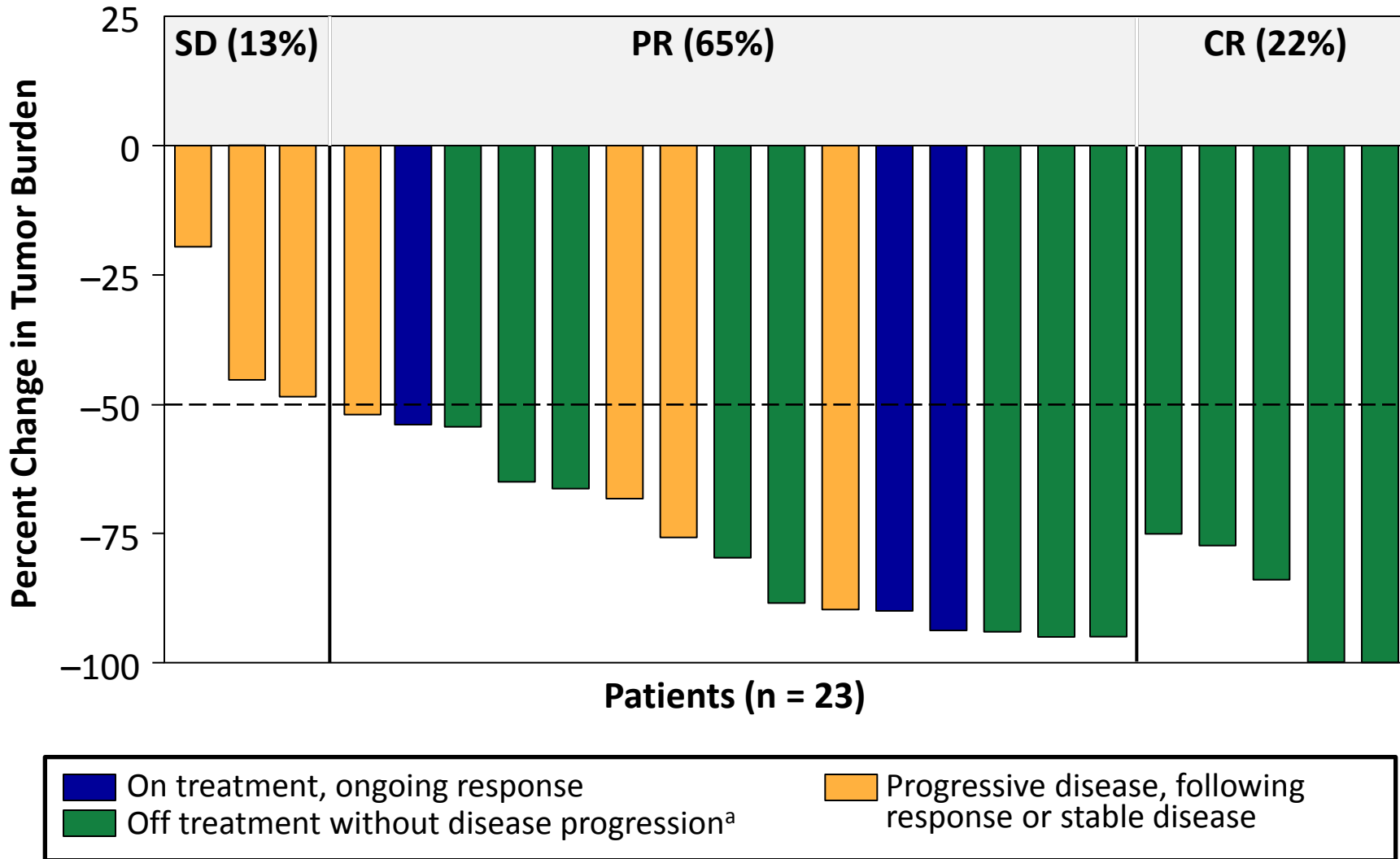
Select Treatment-Related Adverse Events

Adverse Event	cHL (n = 23)	
	Any Grade, n (%)	Resolved, %
Gastrointestinal	4 (17)	
Diarrhea	3 (13)	100
Colitis	1 (4)	100
Hepatic	2 (9)	
ALT increased	1 (4)	100
AST increased	1 (4)	100
Blood alkaline phosphatase increased	1 (4)	0
Pulmonary	1 (4)	
Pneumonitis	1 (4)	100
Skin	5 (22)	
Rash	4 (17)	100
Pruritus	3 (13)	100
Pruritic rash	1 (4)	100
Skin hypopigmentation	1 (4)	0
Endocrine disorders		
Hyperthyroidism	4 (17)	75
Hypersensitivity/infusion reaction	2 (9)	
Bronchospasm	1 (4)	100
Infusion-related reaction	1 (4)	100

- All AEs were Grade 1/2 except colitis and pneumonitis which were Grade 3
- There were no Grade 4 or Grade 5 AEs and no treatment-related deaths

Nivolumab in Patients With Relapsed or Refractory Classical Hodgkin Lymphoma

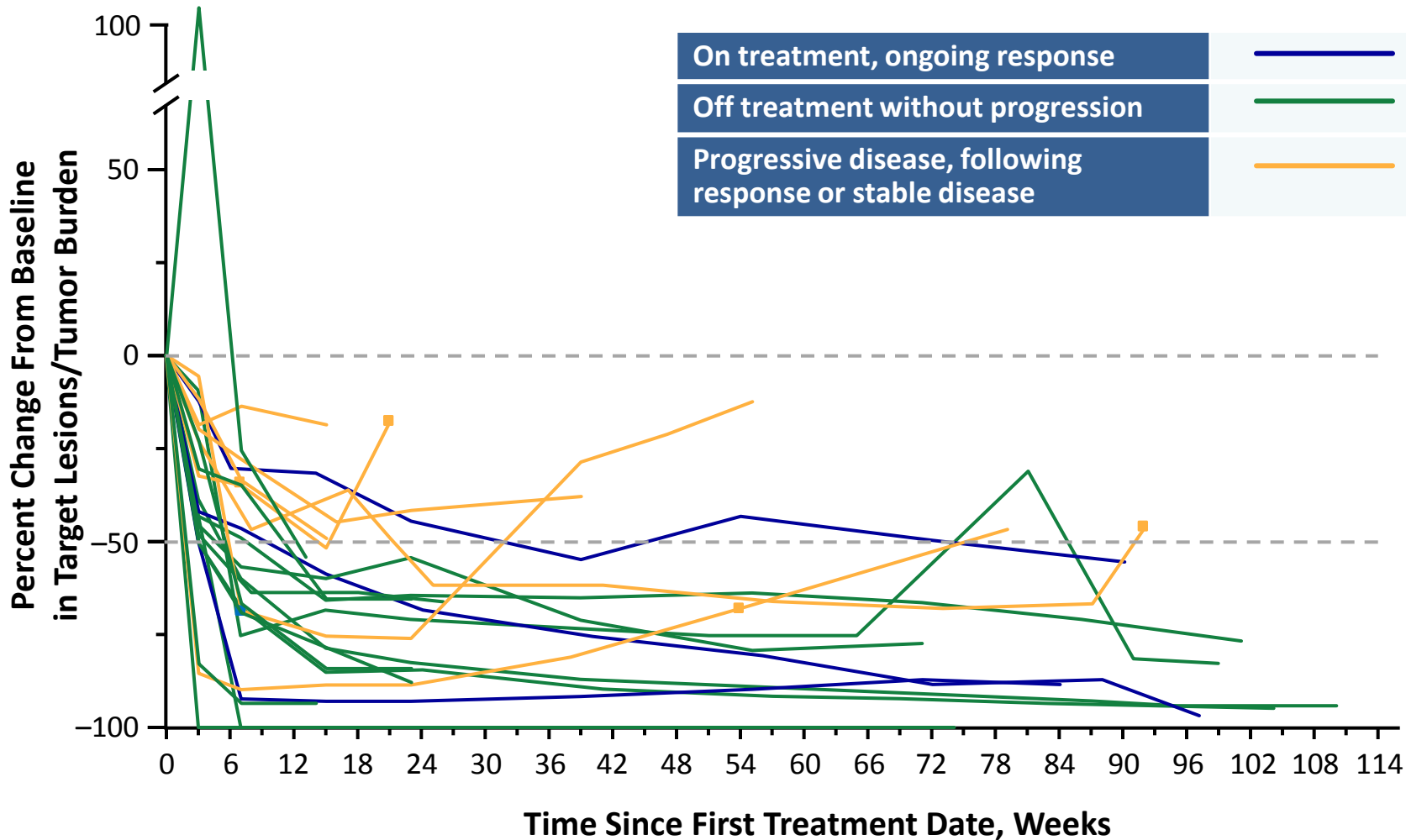
Best Response (PR + CR = 87%)



^aMaximum clinical benefit, transplant, or toxicity

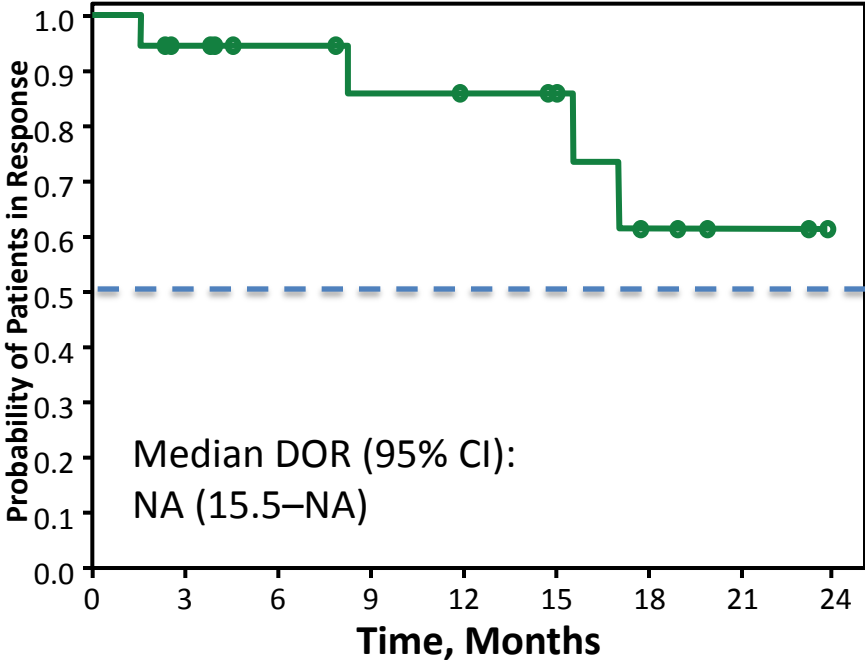
Nivolumab in Patients With Relapsed or Refractory Classical Hodgkin Lymphoma

Durability of Response

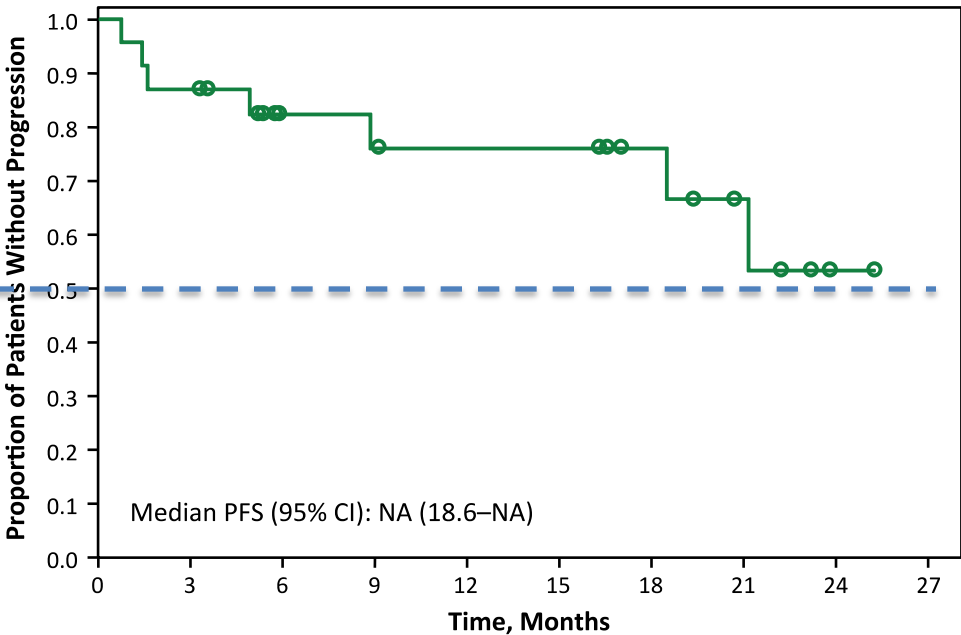


Nivolumab in Patients With Relapsed or Refractory Classical Hodgkin Lymphoma

Duration of Response



PFS



Nivolumab for classical Hodgkin lymphoma after autologous stem-cell transplantation and brentuximab vedotin failure: A phase 2 study

Anas Younes, MD¹, Armando Santoro, MD², Margaret Shipp, MD³, Pier Luigi Zinzani, MD⁴, John M Timmerman, MD⁵, Stephen Ansell, MD⁶, Philippe Armand, MD³, Michelle Fanale, MD⁷, Voravit Ratanatharathorn, MD⁸, John Kuruvilla, MD⁹, Jonathon Cohen, MD¹⁰, Graham Collins, MD¹¹, Kerry J Savage, MD¹², Marek Trneny, MD¹³, Kazunobu Kato, MD¹⁴, Benedetto Farsaci, MD¹⁴, Susan M Parker, PhD¹⁴, Scott Rodig, MD¹⁵, Margaretha GM Roemer, MS³, Azra H Ligon, PhD¹⁵, Andreas Engert, MD¹⁶

April 14, 2016: FDA Grants Nivolumab Priority Review in Hodgkin Lymphoma

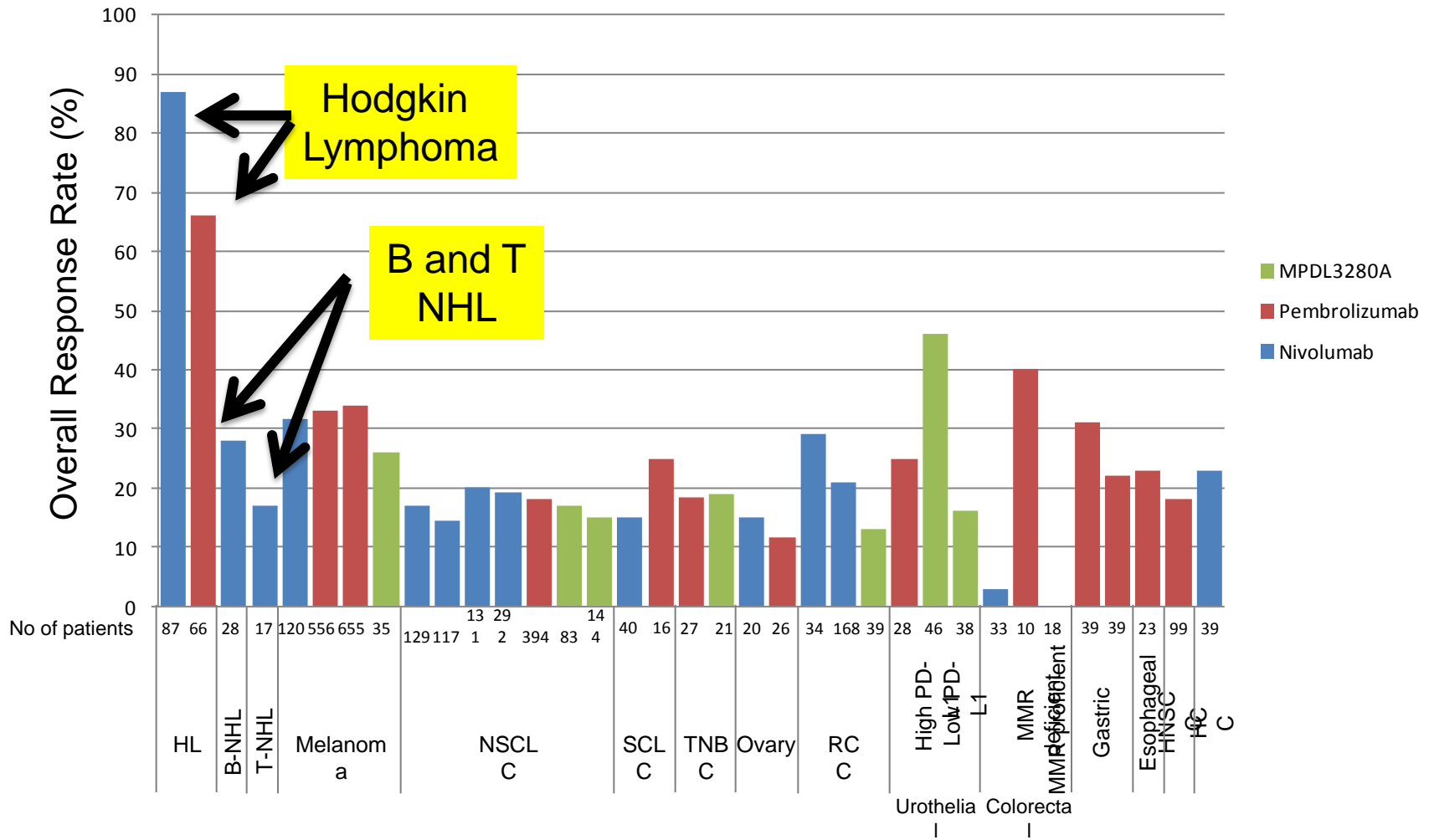
Results of PD1 Blocking Antibodies in Relapsed HL

Drug	Dose/Schedule	N	% ORR	% CR	ORR in BV treated HL	1 st Author
Pembrolizumab (humanized IgG4)	10 mg/kg IV Q 2wks	29	66%	21%	66% (n=19)	Moskowitz C
Nivolumab (Fully human IgG4)	3 mg/kg IV Q 2wks	23	87%	17%	70% (n=16)	Ansel SM

Single Agent Activity of PD1 Blocking Antibodies in Lymphoma

Drug	Antibody	1 st Author (s)	Hodgkin	Follicular	DLBCL	T-cell
Nivolumab	Fully human IgG4	Ansell Lesokin Timmerman	87% (20/23)	40% (4/10)	36% (4/11)	17% (4/23)
Pembrolizumab	Humanized IgG4	Moskowitz Armand	65% (20/31)			
Pidilizumab	Humanized IgG1	Armand			51% (18/38)	

Single agent activity of PD-1/PD-L1 axis blockade in relapsed/refractory Cancer



Single agent activity of novel agents in relapsed cHL

