Pembrolizumab

Robert Chen, MD
Associate Professor of Medicine
Co-Leader of Lymphoma Disease Team
Associate Director of Toni Stephenson Lymphoma Center
City of Hope National Medical Center

Disclosures

- Research Funding to Institution
  - Seattle Genetics, BMS
- Consultancy/Advisory Board
  - Seattle Genetics, BMS, Merck
- Speaker Bureau:
  - Seattle Genetics, Merck

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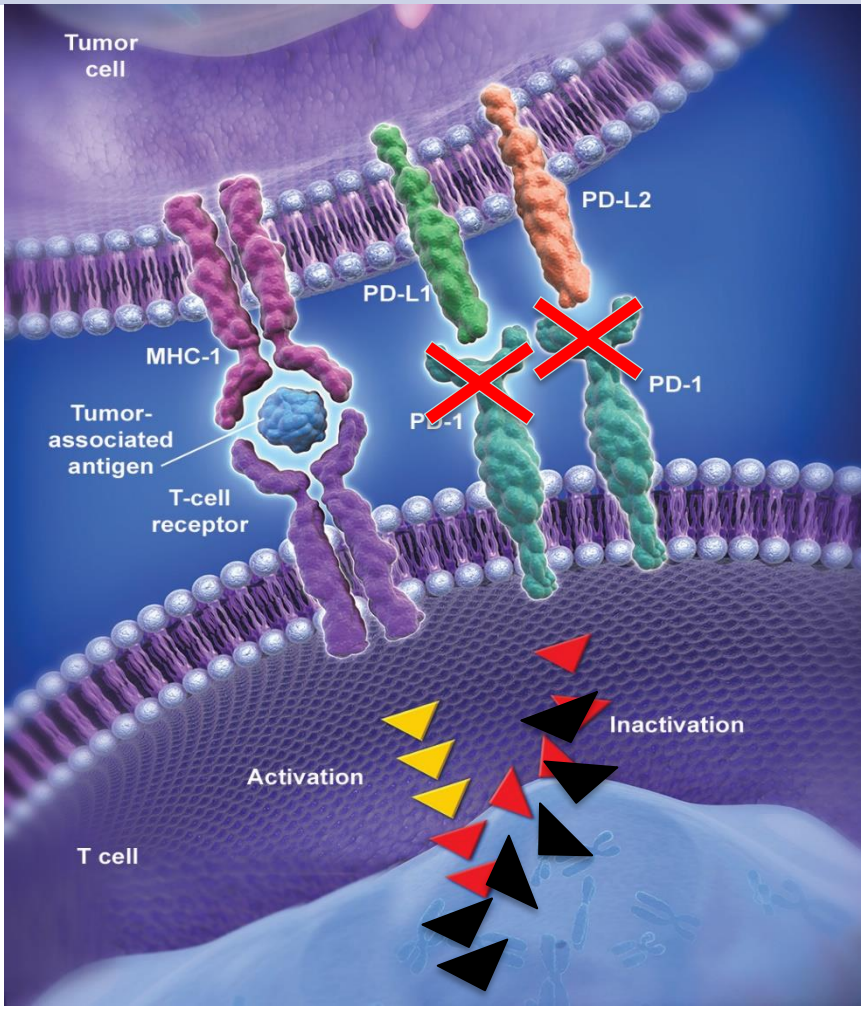
The PD-1 and PD-L1/L2 Pathway

- PD-1 is an immune checkpoint receptor
- Binding of PD-1 to PD-L1 or PD-L2 leads to downregulation of T-cell function
- This mechanism is usurped by many tumors
- PD-1 blockade through mAb therapy can restore effective anti-tumor immunity



Topalian et al. *N Engl J Med*. 2012.
Garon et al. *N Engl J Med*. 2015.
Robert et al. *Lancet.* 2014.

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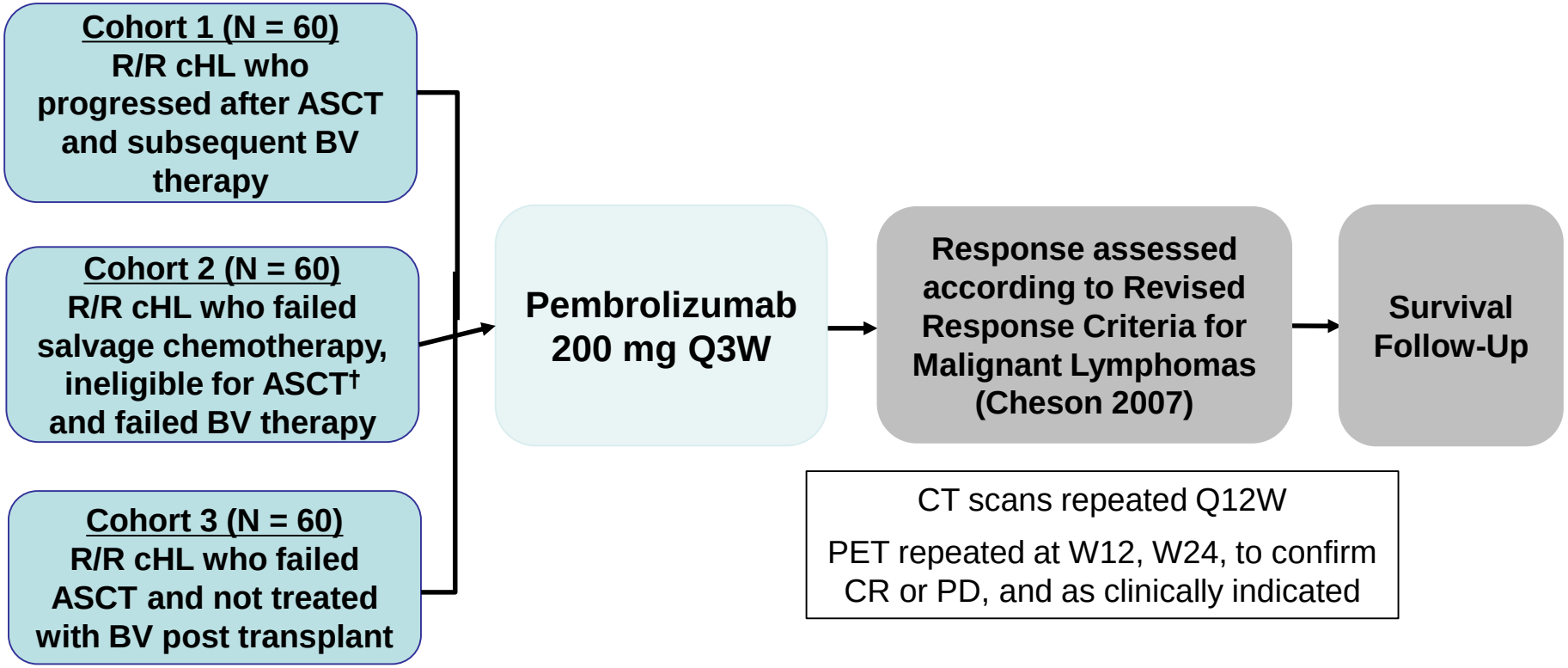
KEYNOTE-087: Study Design



- **Primary end point:** ORR (central review)
- **Secondary end points:** ORR (investigator review), PFS, OS
- Prespecified interim analysis, based on investigator-assessed response, performed after 30 patients in all 3 cohorts reached first response assessment

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Baseline Characteristics

	Cohort 1 Progressed after ASCT and subsequent BV therapy N = 69 n (%)	Cohort 2 Failed salvage chemotherapy, ineligible for ASCT and failed BV therapy N = 81 n (%)	Cohort 3 Failed ASCT and not treated with BV after transplantation N = 60 n (%)
Age, median (range), years	34 (19-64)	40 (20-76)	32 (18-73)
Previous lines of therapy **≥3** **<3**	 68 (99) 1 (1)	 78 (96) 3 (4)	 36 (60) 24 (40)
Previous lines of therapy, median (range)	4 (2-12)	4 (1-11)	3 (2-10)
Refractory or relapsed after 3 or more lines	69 (100)	81 (100)	60 (100)
Previous brentuximab vedotin use	69 (100)	81 (100)	25 (42)
Previous radiation	31 (45)	21 (26)	24 (40)

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Overall Response Rate

	By Blinded Independent Central Review (BCIR) All Patients N = 210		By Investigator Review All Patients N = 210	
	n (%)	95% CI†	n (%)	95% CI†
ORR	**145 (69.0)**	**62.3-75.2**	143 (68.1)	61.3-74.3
Complete remission‡	47 (22.4)	16.9-28.6	63 (30.0)	23.9-36.7
Partial remission	98 (46.7)	39.8-53.7	80 (38.1)	31.5-45.0
Stable disease	31 (14.8)	10.3-20.3	40 (19.0)	14.0-25.0
Progressive disease	30 (14.3)	9.9-19.8	23 (11.0)	7.1-16.0
Unable to determine	4 (1.9)	0.5-4.8	4 (1.9)	0.5-4.8

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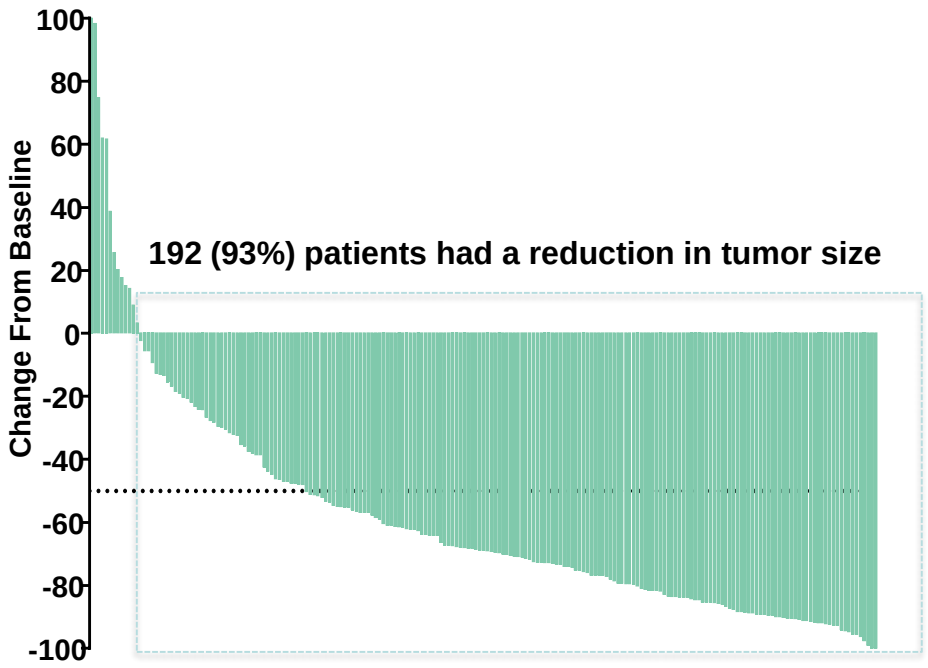
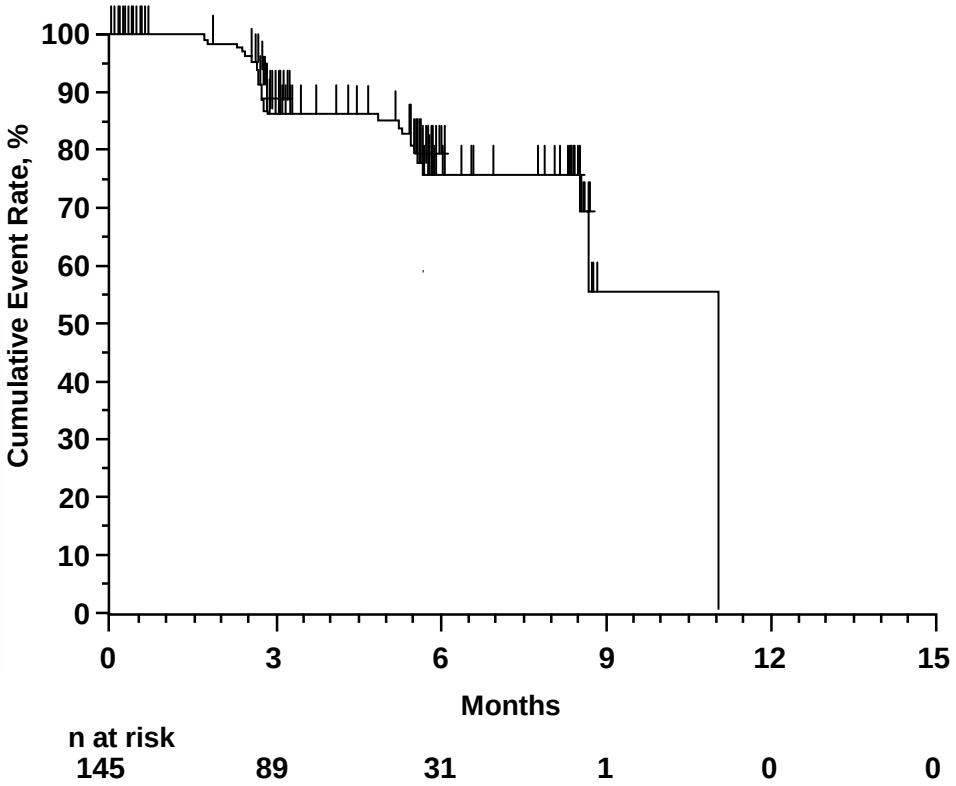
Change From Baseline in Tumor Size and Duration of Response (BICR): All Patients





- **Median number of treatment cycles:** 13 (range,1-21)
- Treatment is ongoing in 120 (57%) patients
- **Median follow-up**: 10.1 (1.0-15.0) months

- **Median (range) time to response:**
  - 2.8 (2.1-8.8) months
- **Response duration ≥6 months:** 75.6%†

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ORR by Cohort (BICR)

	Cohort 1 Progressed after ASCT and subsequent BV therapy N=69		Cohort 2 Failed salvage chemotherapy, ineligible for ASCT and failed BV therapy N = 81		Cohort 3 Failed ASCT and not treated with BV post transplant N = 60	
	n (%)	95% CI†	n (%)	95% CI†	n (%)	95% CI†
ORR	**51 (73.9)**	**61.9-83.7**	**52 (64.2)**	**52.8-74.6**	**42 (70.0)**	**56.8-81.2**
Complete remission*	15 (21.7)	12.7-33.3	20 (24.7)	15.8-35.5	12 (20.0)	10.8-32.3
Partial remission	36 (52.2)	39.8-64.4	32 (39.5)	28.8-51.0	30 (50.0)	36.8-63.2
Stable disease	11 (15.9)	8.2-26.7	10 (12.3)	6.1-21.5	10 (16.7)	8.3-28.5
Progressive disease	5 (7.2)	2.4-16.1	17 (21.0)	12.7-31.5	8 (13.3)	5.9-24.6
Unable to determine	2 (2.9)	0.4-10.1	2 (2.5)	0.3-8.6	0 (0)	–

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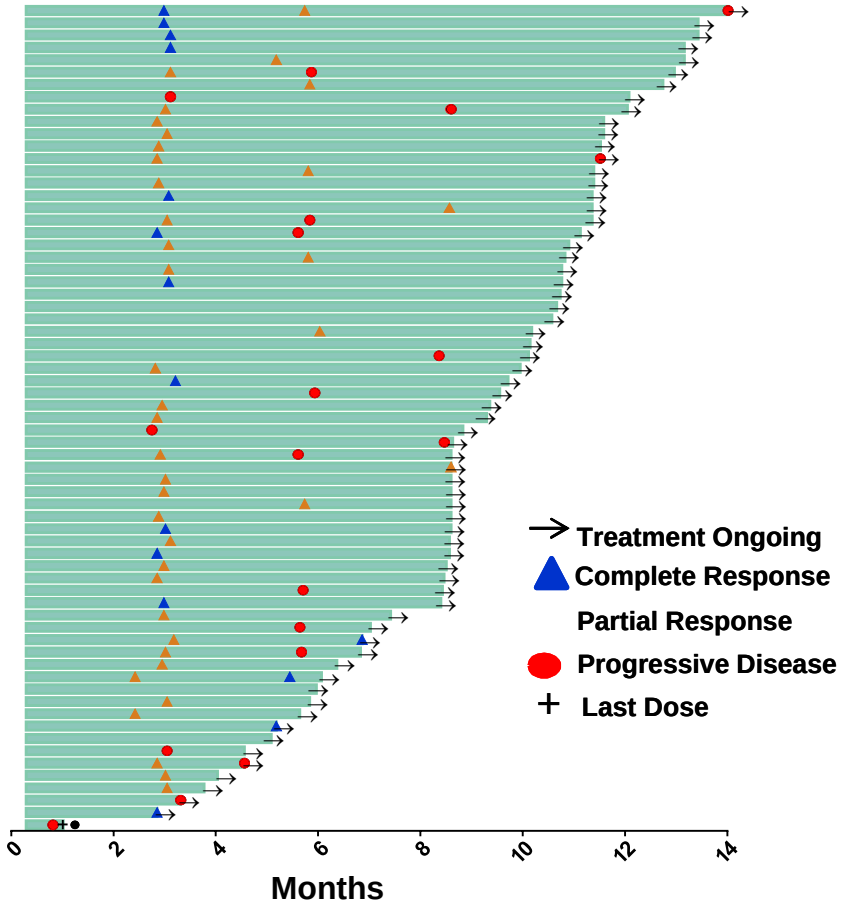
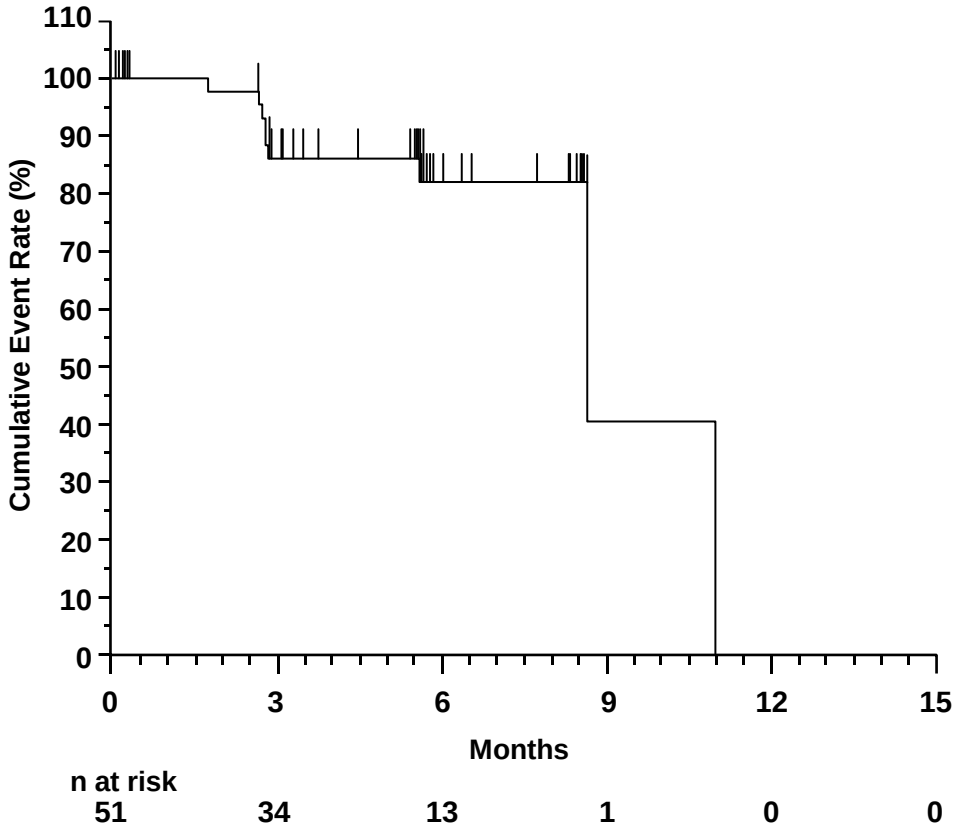
Treatment Exposure and Response Duration: Cohort 1

Progressed after ASCT and subsequent BV therapy





- **Median number of treatment cycles:** 13 (range, 1-21)

Median (range) time to response

- 2.7 months (2.1-8.3)

Median (range) duration of response

- 8.7 (0.0+-11.1)
- Response duration ≥6 months: 82.2%

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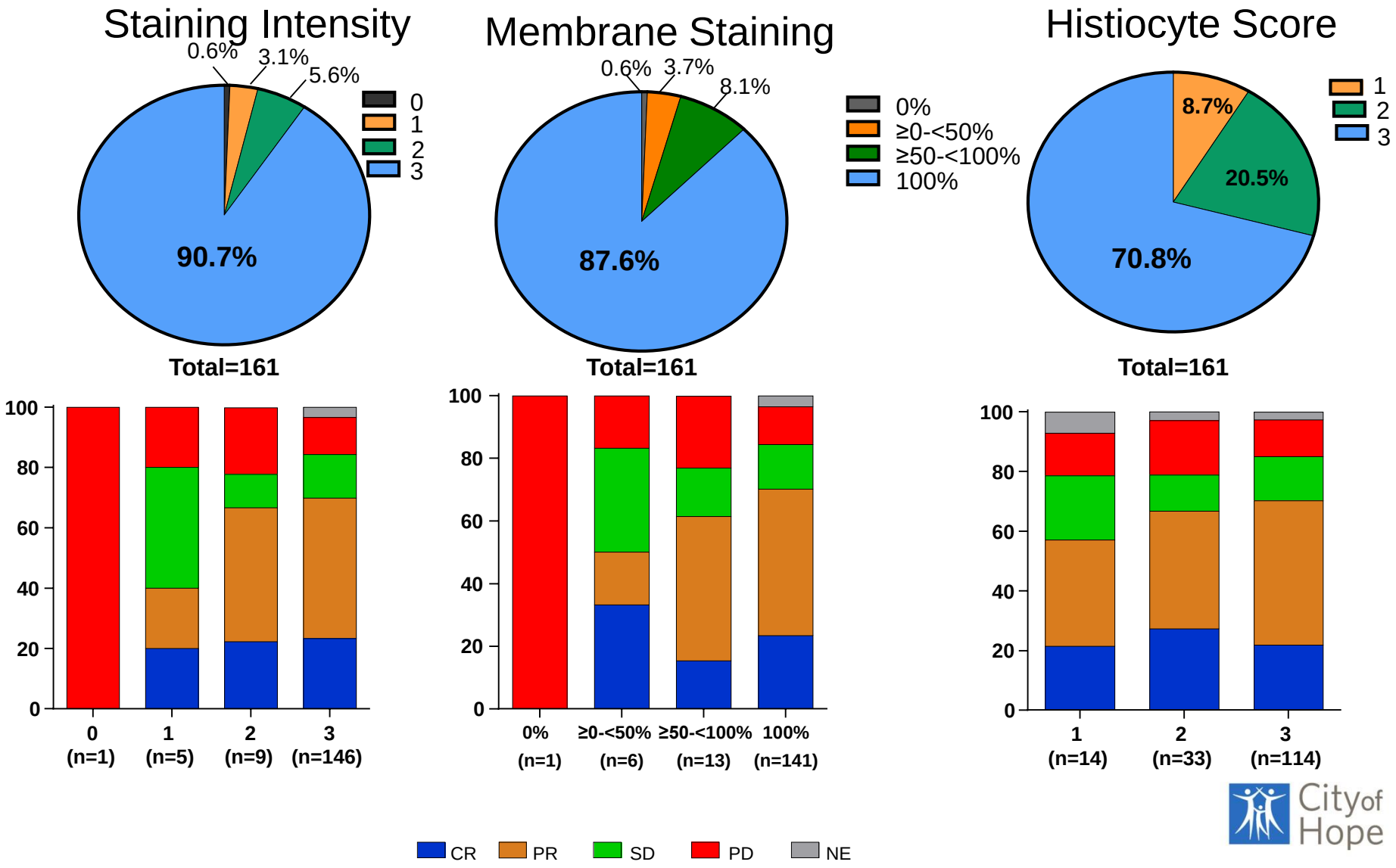
Distribution of PD-L1 Expression Scores and Response to Pembrolizumab



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Treatment-Related Adverse Events

Any-Grade AEs ≥5% of patients	Total Population N = 210 n (%)
Hypothyroidism	26 (12.4)
Pyrexia	22 (10.5)
Fatigue	19 (9.0)
Rash	16 (7.6)
Diarrhea	15 (7.1)
Headache	13 (6.2)
Nausea	12 (5.7)
Cough	12 (5.7)
Neutropenia	11 (5.2)

Grade 3/4 AEs	Total Population N = 210 n (%)
Any grade 3/4 AE	23 (11)
AEs in ≥2 patients	
Neutropenia, grade 3	5 (2.4)
Diarrhea, grade 3	2 (1.0)
Dyspnea, grade 3	2 (1.0)

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Immune Related AEs

AEs of interest in ≥2 patients	Total Population N = 210 n (%)
Infusion-related reactions, grades 1 and 2	10 (4.8)
Pneumonitis, all grade 2	6 (2.9)
Hyperthyroidism, grades 1 and 2	6 (2.9)
Colitis, grades 2 and 3	2 (1.0)
Myositis, grades 2 and 3	2 (1.0)

- 2 deaths occurred
  - No treatment-related deaths
- 9 patients discontinued because of treatment-related Aes
  - 1 myocarditis, grade 4
  - 1 myelitis, grade 3
  - 1 myositis, grade 2
  - 4 pneumonitis, grade 2
  - 1 infusion-related reaction, grade 2, 1 cytokine release syndrome, grade 3
  - 1 infusion-related reaction, grade 2
  - Pts with prior autoimmune disease were excluded from trial

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Pembrolizumab Monotherapy in Patients With Primary Refractory Classical Hodgkin Lymphoma: Subgroup Analysis of the Phase 2 KEYNOTE-087 Study

P.L. Zinzani[1]; M.A. Fanale[2]; R. Chen[3]; P. Armand[4]; N. Johnson[5]; P. Brice[6]; J. Radford[7]; V. Ribrag[8]; D. Molin[9]; T. P. Vassilakopoulos[10]; A. Tomita[11]; B. von Tresckow[12]; M.A. Shipp[4]; J. Lin[13]; A. Balakumaran[13]; C.H. Moskowitz[14]

[1]Institute of Hematology "L. e A. Seràgnoli," University of Bologna, Bologna, Italy; [2]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]City of Hope National Medical Center, Duarte, CA, USA; [4]Dana-Farber Cancer Institute, Boston, MA , USA; [5]Jewish General Hospital, Montreal, QC, Canada; [6]Hôpital Saint-Louis, Paris, France; [7]The University of Manchester and the Christie NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK; [8]Institut Gustave Roussy, Villejuif, France; [9]Uppsala University, Uppsala, Sweden; [10]National and Kapodistrian University of Athens, Laikon General Hospital, Athens, Greece; [11]Nagoya University Graduate School of Medicine, Nagoya, Japan, *Current affiliation: Fujita Health University School of Medicine, Toyoake, Japan; [12]University Hospital Cologne, Cologne, Germany; [13]Merck & Co., Inc., Kenilworth, NJ, USA; [14]Memorial Sloan Kettering Cancer Center, New York, NY , USA

Baseline Characteristics:

Characteristic	Pembrolizumab n = 73
Age, median (range), y	31.0 (18.0-73.0)
Male, n (%)	37 (50.7)
Race, n (%)	
White	66 (90.4)
Asian	2 (2.7)
Black/African American	2 (2.7)
Multiracial	1 (1.4)
American Indian/Alaska Native	1 (1.4)
Missing	1 (1.4)
ECOG PS, n (%)	
0	41 (56.2)
1	32 (43.8)
Bulky lymphadenopathy, n (%)	10 (13.7)
Baseline B symptoms, n (%)	21 (28.8)

Prior therapy (tx)	Pembrolizumab n = 73
≥3 prior lines of tx, n (%)	65 (89.0)
Median (range) prior lines of tx	3.0 (1.0-12.0)
Median (range) time of relapse since SCT failure, months	5.0 (0.5-102.5)
Prior brentuximab vedotin use, n (%)	63 (86.3)
Prior radiation, n (%)	17 (23.3)

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Best Overall Response by Central Review

	Primary refractory cHL (n = 73)[1]		Other patients (n = 137)	
	n	% (95% CI[a])	n	% (95% CI[a])
ORR	**58**	**79.5% (68.4-88.0)**	**87**	**63.5% (54.9-71.6)**
CR	17	23.3% (14.2-34.6)	30	21.9% (15.3-29.8)
PR	41	56.2% (44.1-67.8)	57	41.6% (33.3-50.3)
SD	4	5.5% (1.5-13.4)	27	19.7% (13.4-27.4)
PD	8	11.0% (4.9-20.5)	22	16.1% (10.3-23.3)
NA	3	4.1% (0.9-11.5)	1	0.7% (0-4.0)

[a]Based on binomial exact confidence interval.

1. Chen R et al. *J Clin Oncol*. 2017. doi: 10.1200/JCO.2016.72.1316.

Data cutoff: September 25, 2016.

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Prior Lines of Therapy

	<3 Prior lines of therapy (n = 8)		≥3 Prior lines of therapy (n = 65)	
	n	% (95% CI[a])	n	% (95% CI[a])
ORR	**8**	**100.0% (63.1-100.0)**	**50**	**76.9% (64.8-86.5)**
CR	2	25.0% (3.2-65.1)	15	23.1% (13.5-35.2)
PR	6	75.0% (34.9-96.8)	35	53.8% (41.0-66.3)
SD	0	0% (0-36.9)	4	6.2% (1.7-15.0)
PD	0	0% (0-36.9)	8	12.3% (5.5-22.8)
NA	0	0% (0-36.9)	3	4.6% (1.0-12.9)

[a]Based on binomial exact confidence interval.
Data cutoff: September 25, 2016.

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Best Overall Response by Central Review by Cohort

	Cohort 1 (n = 14) After ASCT/BV		Cohort 2 (n = 33) Ineligible for ASCT and experienced treatment failure with BV		Cohort 3 (n = 26) No BV after ASCT	
	n	% (95% CI[a])	n	% (95% CI[a])	n	% (95% CI[a])
ORR	**11**	**78.6% (49.2-95.3)**	**23**	**69.7% (51.3-84.4)**	**24**	**92.3% (74.9-99.1)**
CR	3	21.4% (4.7-50.8)	9	27.3% (13.3-45.5)	5	19.2% (6.6-39.4)
PR	8	57.1% (28.9-82.3)	14	42.4% (25.5-60.8)	19	73.1% (52.2-88.4)
SD	2	14.3% (1.8-42.8)	2	6.1% (0.7-20.2)	0	0% (0-13.2)
PD	0	0% (0-23.2)	6	18.2% (7.0-35.5)	2	7.7% (0.9-25.1)
NA	1	7.1% (0.2-33.9)	2	6.1% (0.7-20.2)	0	0% (0-13.2)

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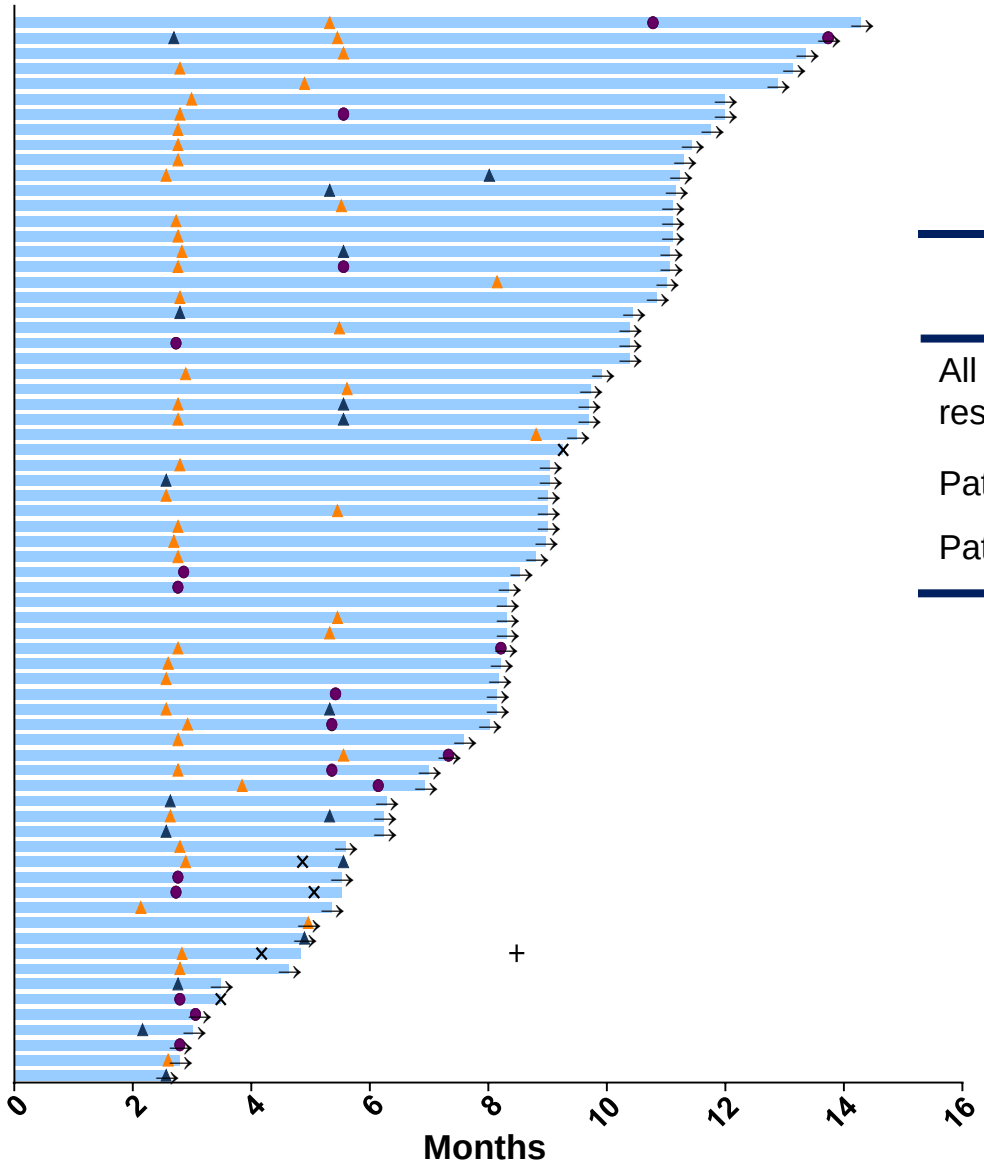
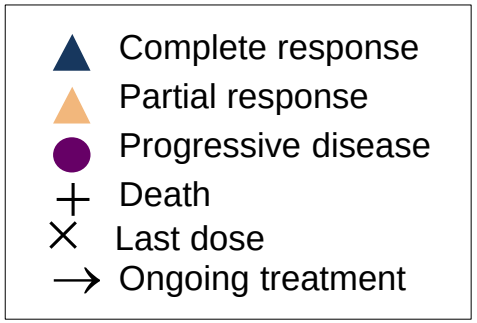
Response Characteristics



	Median time to response[b] (range), months
All primary refractory responders (n = 58)	2.8 (2.1-8.8)
Patients with CR (n = 17)	2.7 (2.2-5.3)
Patients with PR (n = 41)	2.8 (2.1-8.8)



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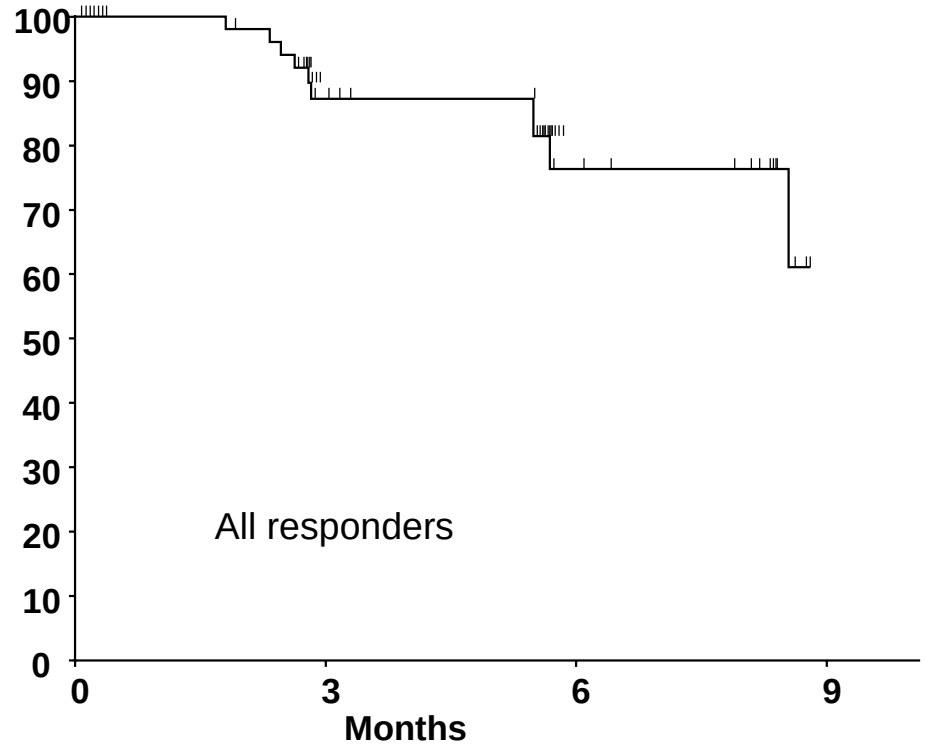
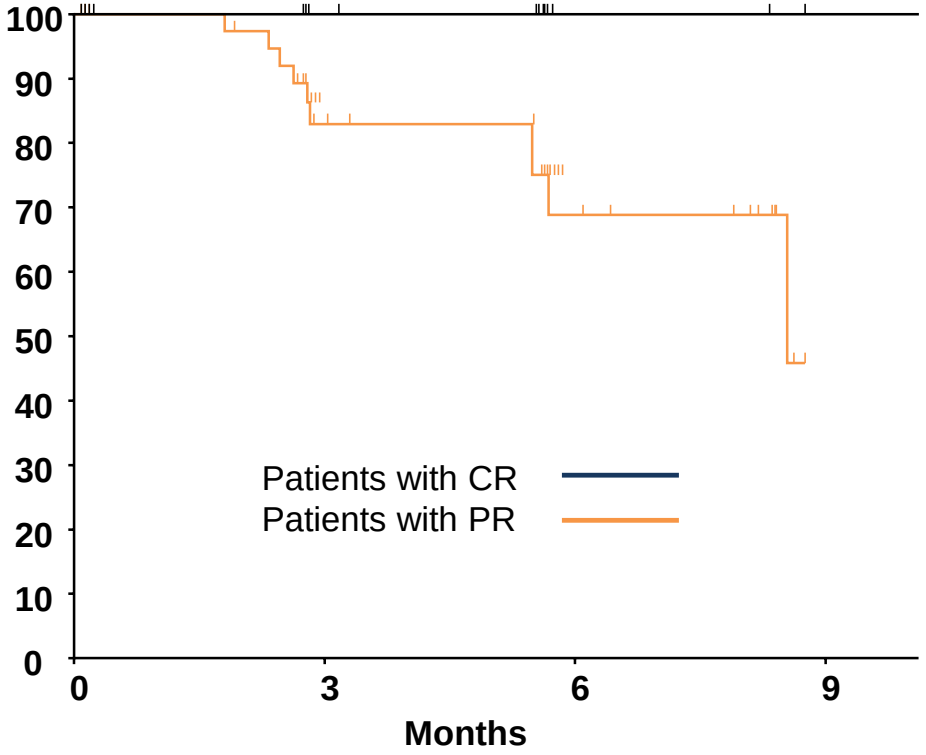
Duration of Response

- Median DOR was not reached in all groups





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Conclusions

- Pembrolizumab demonstrated a high response rate in the subgroup of patients with primary refractory cHL
  - Response was comparable with that in the overall study population of KEYNOTE-087
- Pembrolizumab demonstrated an acceptable safety profile in patients with primary refractory cHL
- Pembrolizumab may be an effective treatment option for patients who have primary refractory cHL and need new treatment options

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cHL Trials in Progress

- Pembrolizumab + AFM 13
- Pembrolizumab + Ibrutinib
- Pembrolizumab + Vorinostat
- Pembrolizumab + ICE
- Pembrolizumab + XRT
- Pembrolizumab vs. BV
- Pembrolizumab in untreated HL
- Pembrolizumab as consolidation post ASCT

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