Pembrolizumab in Relapsed/Refractory Classical Hodgkin Lymphoma: Phase 2 KEYNOTE-087 Study

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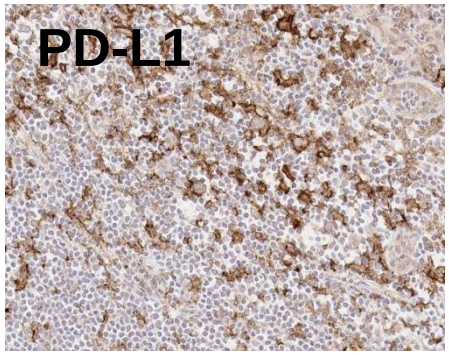
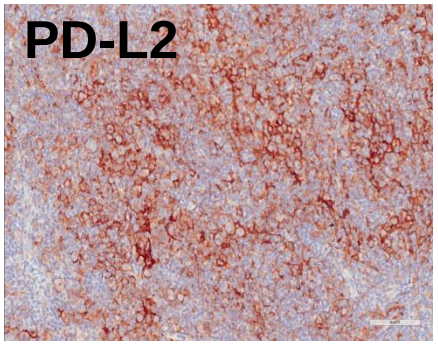
Pembrolizumab in Hodgkin Lymphoma

- Pembrolizumab is a humanized anti–PD-1 monoclonal antibody which effectively restores antitumor immunity against multiple malignancies[1,2]
- Overexpression of PD-L1 and PD-L2 due to genetic alterations is common in cHL[3-5]
  - HL may have a genetically driven vulnerability to PD-1 blockade





- Pembrolizumab 10 mg/kg demonstrated an ORR of 65% in R/R cHL[6]
- Exposure-response relationship for efficacy and safety is flat between 2 mg/kg to 10 mg/kg across clinical studies[7]
  - Based on population PK models, exposure for the 200 mg Q3W fixed-dose regimen is within this range and close to the 2 mg/kg Q3W exposure

1. Garon et al. *N Engl J Med*. 2015; 2. Robert et al. *Lancet.* 2014 3. Green MR et al. *Blood 2010*; 4. Chen BJ et al*. Clin Cancer Res*. 2013; 5. Roemer MGM et al. *Clin Oncol.* 2016; 6. Armand P et al. *J. Clin Oncol*. 2016; pii: JCO673467; 7.Freshwater T et al. Presented at the 6th American Conference on Pharmacometrics; October 4-7, 2015; Crystal City, VA. Abstract M-011.

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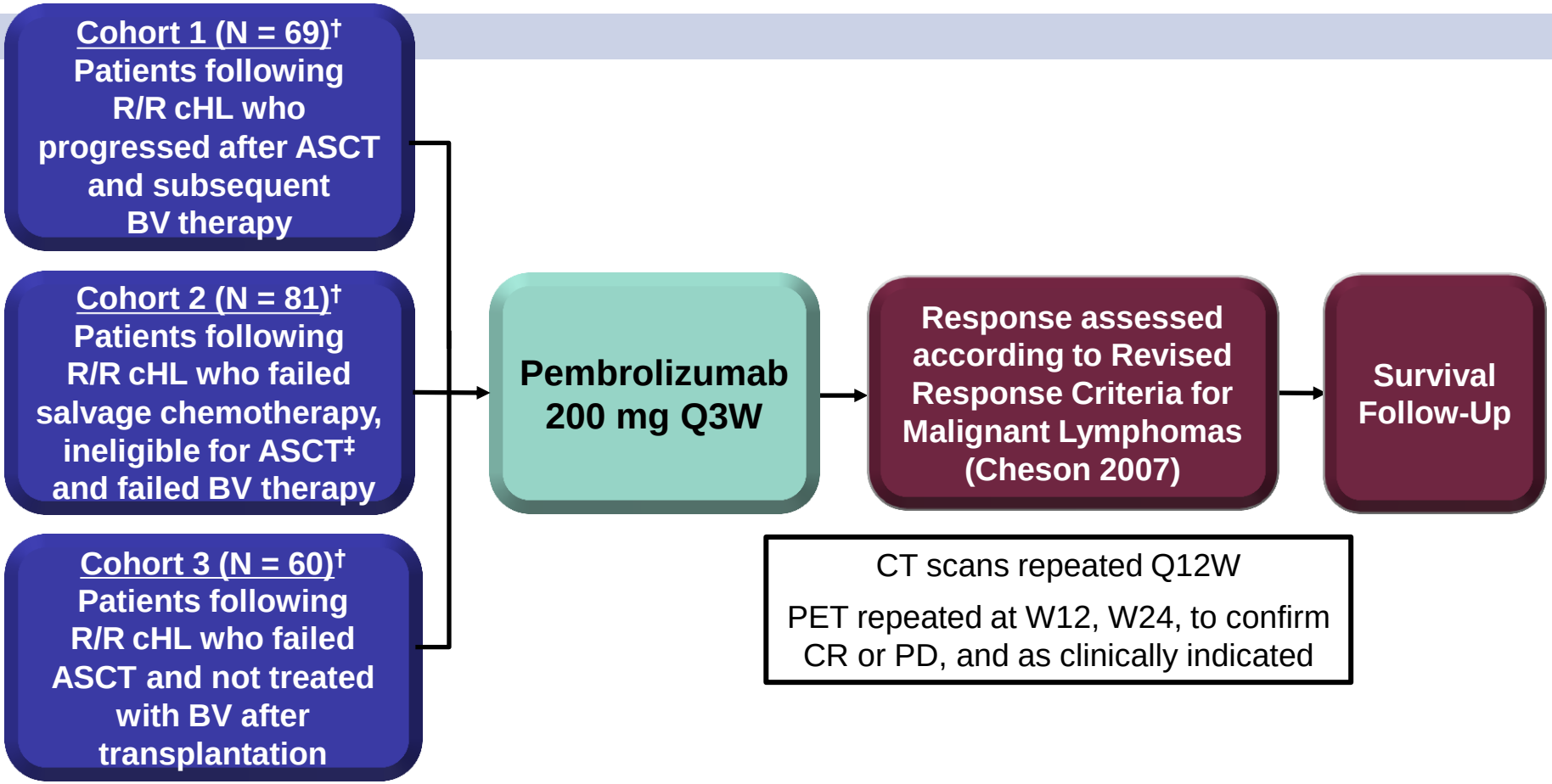
KEYNOTE-087: Study Design



- **Primary end point:** Overall response rate (ORR; blinded independent central review)
- **Secondary end points:** ORR (investigator review), DOR, PFS, OS

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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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Data cutoff: September 25, 2016

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 after transplantation 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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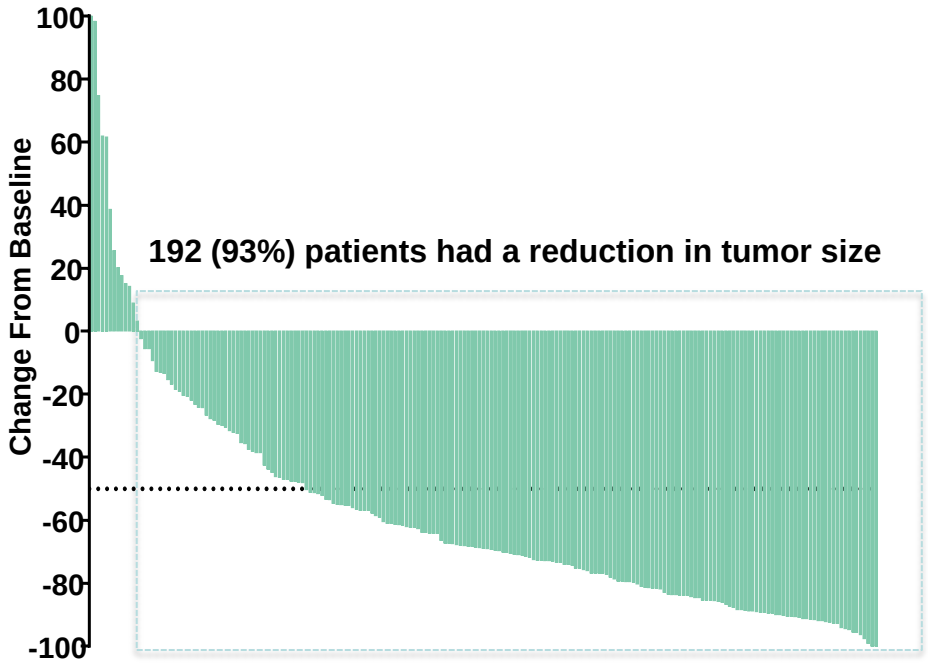
Change From Baseline in Tumor Size and Duration of Response



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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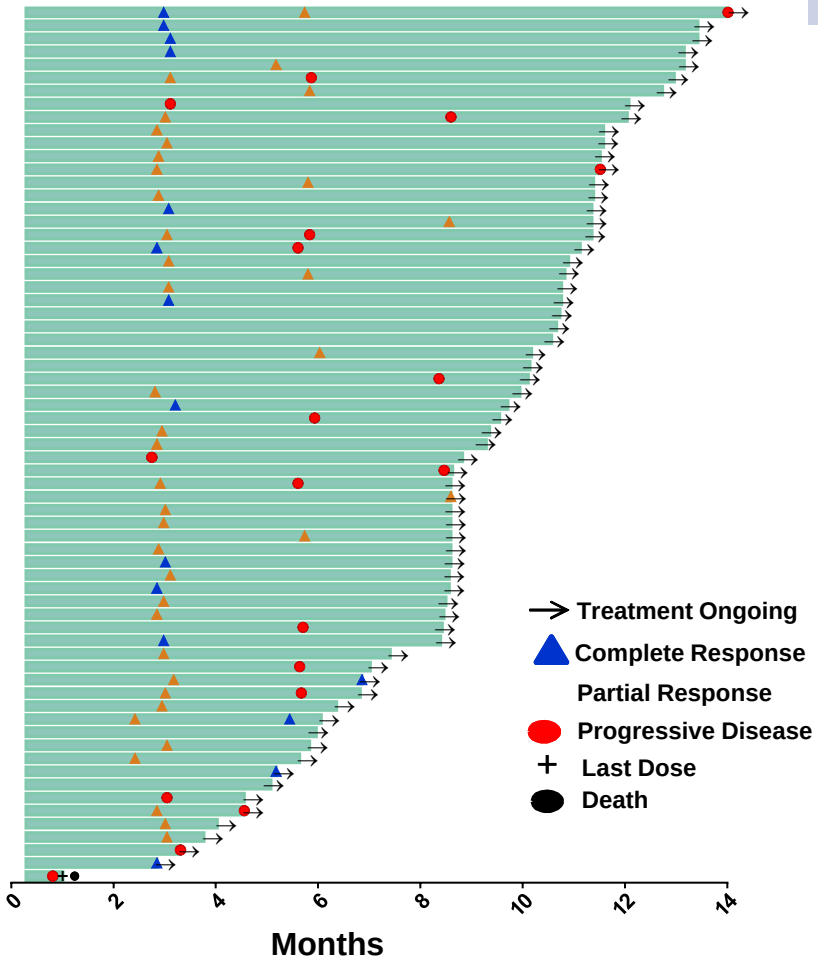
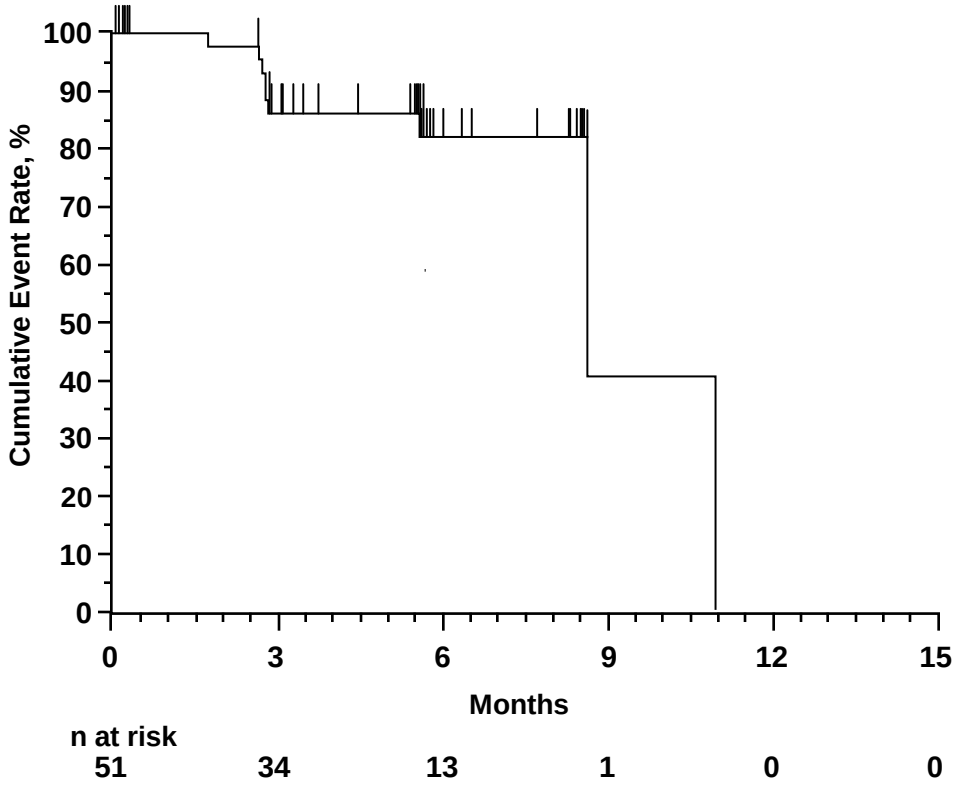
Treatment Exposure and Response Duration: Cohort 1

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)
- **Response duration ≥6 months:** 82.2%

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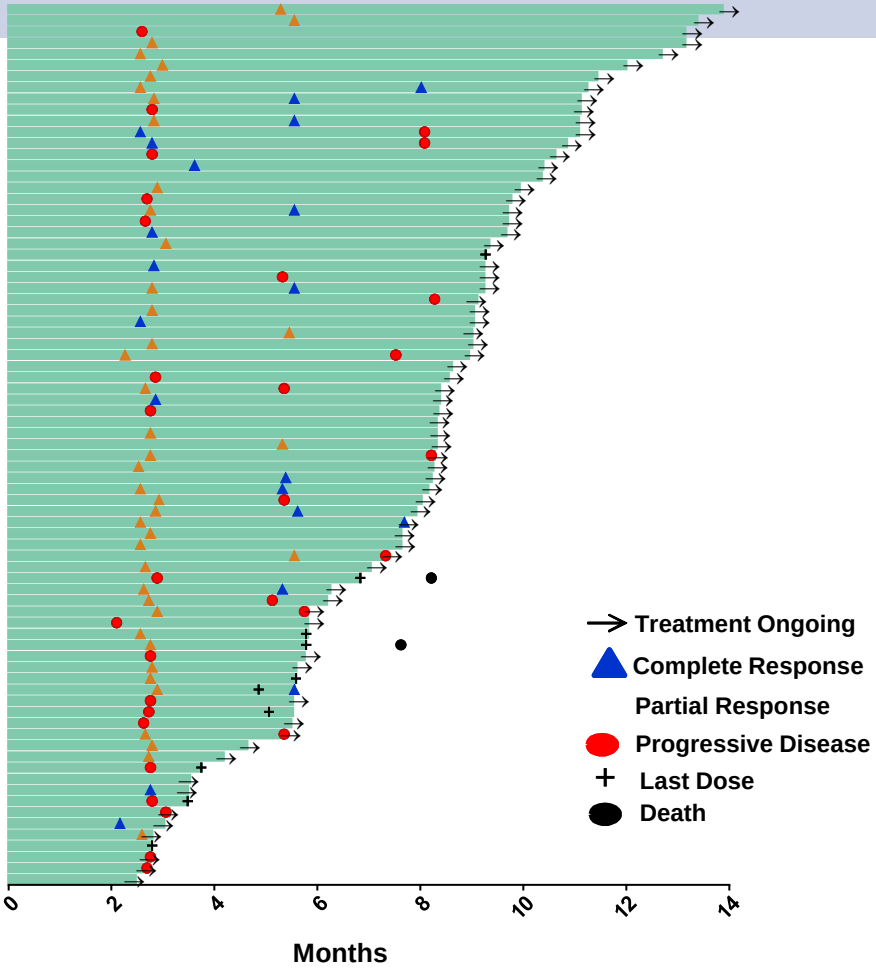
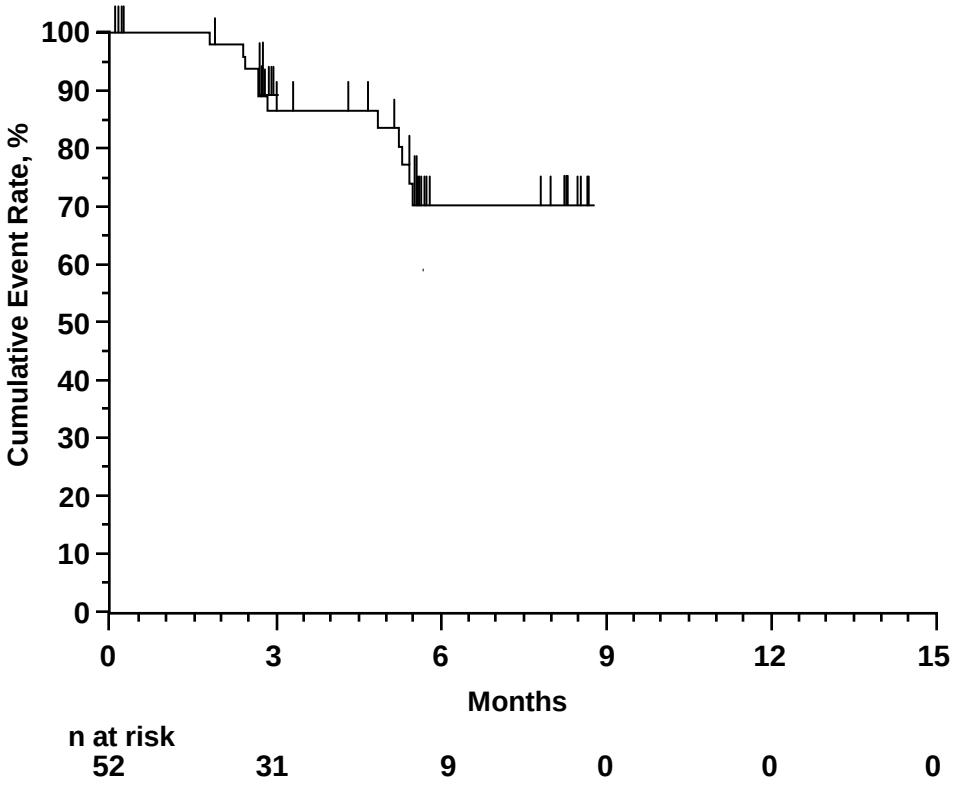
Treatment Exposure and Response Duration: Cohort 2

Failed salvage chemotherapy, ineligible for ASCT and failed BV therapy



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



- **Median (range) time to response**
  - 2.8 (2.2-5.6) months
- **Response duration ≥6 months:** 70%

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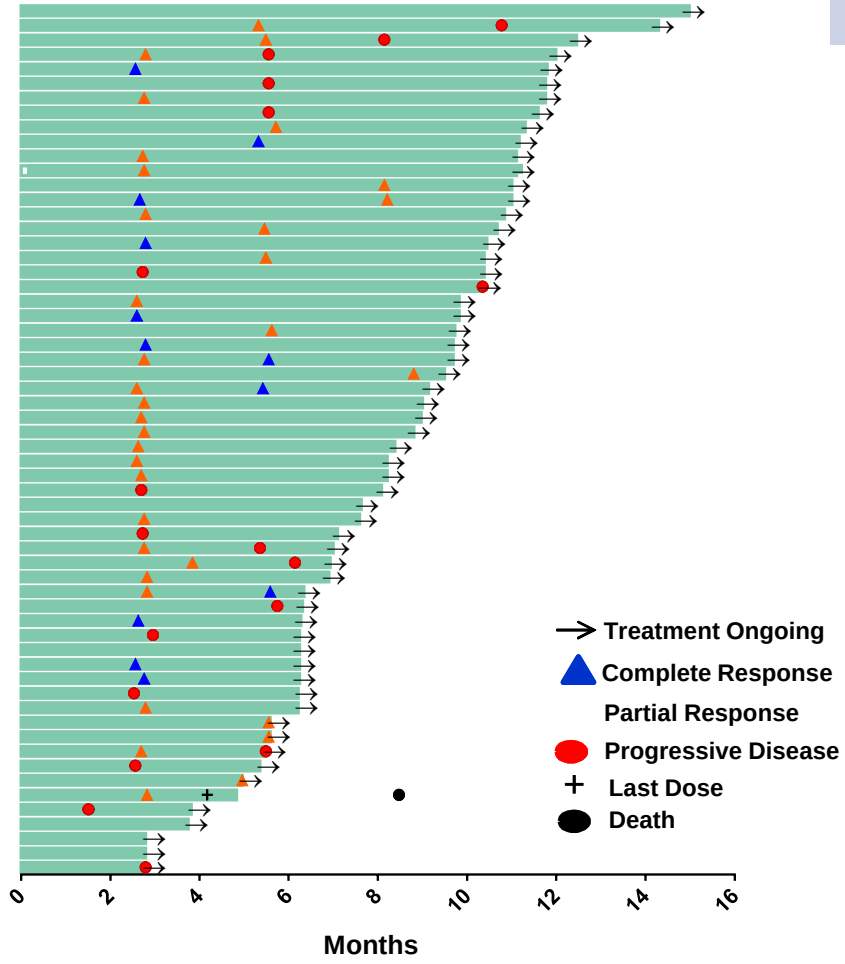
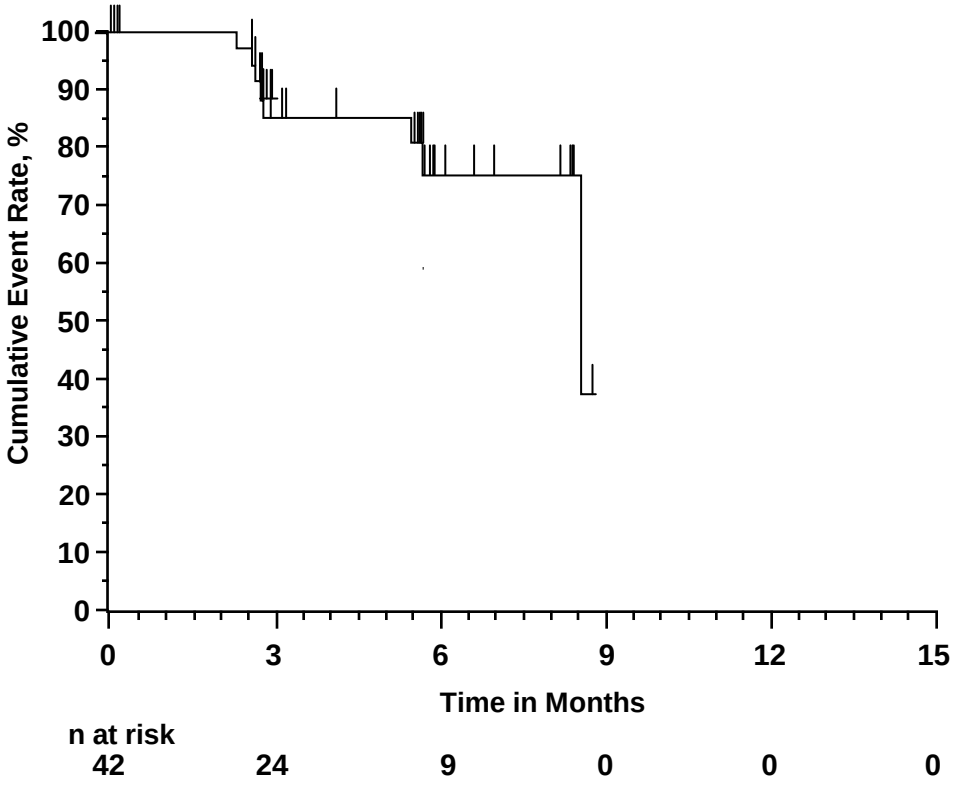
Treatment Exposure and Response Duration: Cohort 3

Failed ASCT and not treated with BV





- **Median number of treatment cycles**
  - 12.5 (range, 3-21)

- **Median (range) time to response**
  - 2.8 (2.6-8.8) months
- **Response duration ≥6 months:** 75.6%

Data cutoff: September 25, 2016

ORR by Blinded Central Review: Subgroup Analyses

	Primary Refractory Disease (n = 73)		Relapsed After ≥3 Lines of Therapy (n = 146)	
	n (%)	95% CI‡	n (%)	95% CI‡
ORR	58 (79.5)	68.4-88.0	99 (67.8)	59.6-75.3
Complete remission	17 (23.3)	14.2-34.6	31 (21.2)	14.9-28.8
Partial remission	41 (56.2)	44.1-67.8	68 (46.6)	38.3-55.0
Stable disease	4 (5.5)	1.5-13.4	24 (16.4)	10.8-23.5
Progressive disease	8 (11.0)	4.9-20.5	20 (13.7)	8.6-20.4
Unable to determine	3 (4.1)	0.9-11.5	3 (2.1)	0.4-5.9

†These subgroups are not mutually exclusive
‡Based on binomial exact confidence interval method

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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)

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)

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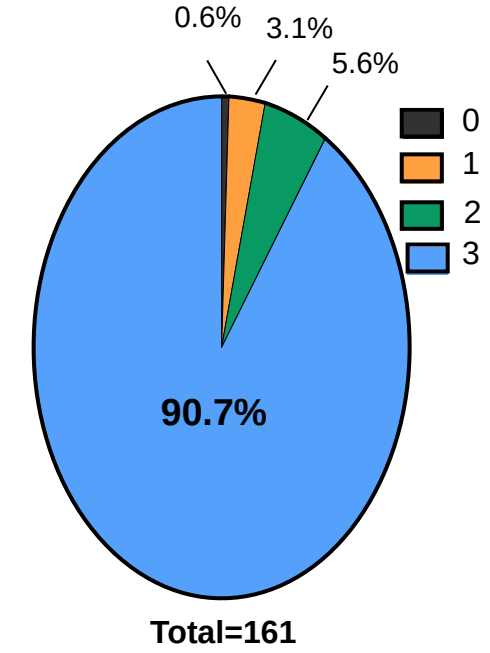
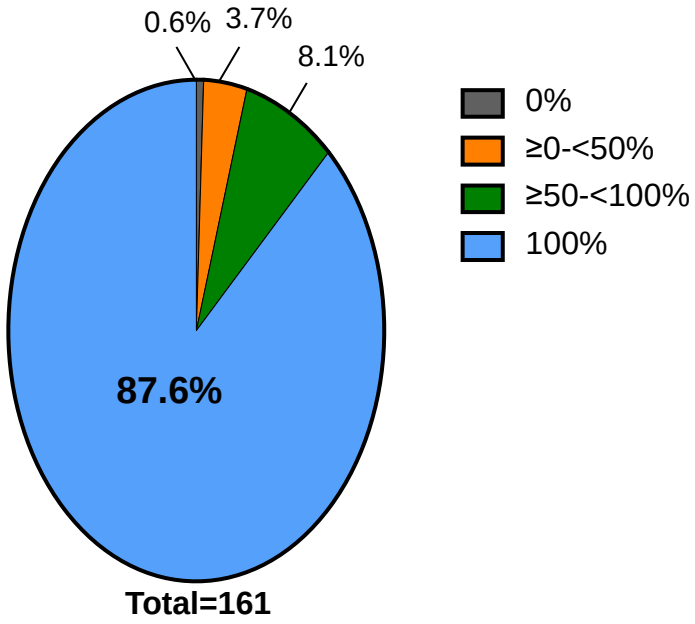
Distribution of PD-L1 Expression Scores

Staining Intensity



Membrane Staining



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Conclusions

- By blinded independent central review and investigator review the ORR was 69% and 68%, respectively. Median duration of response has not been reached
- In this study there were two unique patient populations:
  - Transplant ineligible cHL secondary to failure of salvage therapy and BV (81/210, 39%)
    - 64% ORR (25% CR)
  - Primary refractory cHL (73/210, 35%)
    - 80% ORR (23% CR)
- Most responses were observed at first disease assessment
- The fixed dose of 200 mg Q3W is associated with an acceptable safety profile
- Received accelerated FDA approval in the US
- Phase 3 study of pembrolizumab versus BV in patients with R/R cHL has been initiated (KEYNOTE-204 [NCT02684292])

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Future Plans

- Phase 3 study of pembrolizumab versus BV in patients with R/R cHL has been initiated (KEYNOTE-204 [NCT02684292])
- Phase II IST: Pembrolizumab + ICE as bridge to ASCT

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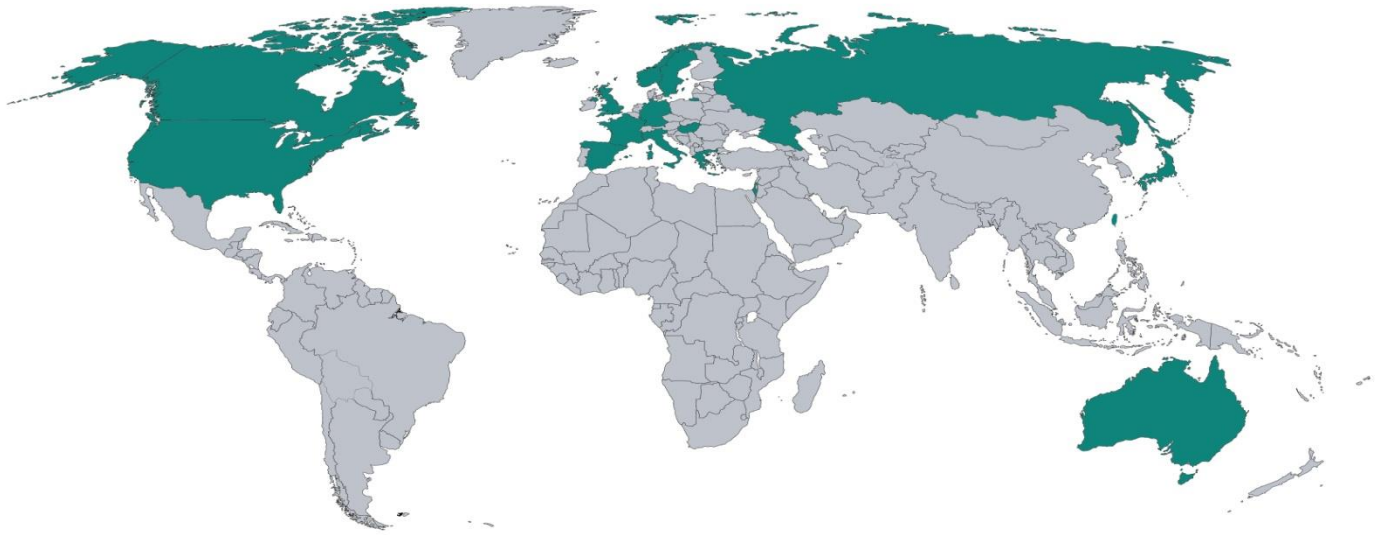
Acknowledgments

- **PATIENTS AND THEIR FAMILIES**
- **Investigators and personnel from 51 study sites**



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