

## **Pembrolizumab for B-cell lymphomas relapsing after or refractory to CD19-directed CAR T-cell therapy**

Elise A. Chong, Cécile Alanio, Jakub Svoboda, Sunita D. Nasta, Daniel J. Landsburg, Simon F. Lacey, Marco Ruella, Siddharth Bhattacharyya, E. John Wherry, Stephen J. Schuster

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**Table S1. Peripheral blood sample time points for CAR qPCR**

ID	CART response	Response	Description	Days from pembrolizumab	Days from CART	Figure 2A
1	refractory	PD	Baseline	0	99	Yes
1	refractory	PD	Cycle 1, Day 1	1	100	Yes
1	refractory	PD	Cycle 1, Day 2	2	101	Yes
1	refractory	PD	Cycle 1, Day 7	7	106	Yes
1	refractory	PD	Cycle 1, Day 21	21	120	Yes
1	refractory	PD	Cycle 1, Day 22	22	121	Yes
2	refractory	PD	Baseline	0	92	Yes
2	refractory	PD	Cycle 1, Day 1	1	99	Yes
2	refractory	PD	Cycle 1, Day 2	2	100	Yes
2	refractory	PD	Cycle 1, Day 3	3	101	Yes
2	refractory	PD	Cycle 1, Day 7	7	105	Yes
2	refractory	PD	Cycle 1, Day 13	13	111	Yes
3	refractory	PD	Baseline	0	13	Yes
3	refractory	PD	Cycle 1, Day 1	1	14	Yes
3	refractory	PD	Cycle 1, Day 2	2	15	Yes
3	refractory	PD	Cycle 1, Day 5	5	18	Yes
3	refractory	PD	Cycle 1, Day 7	7	20	Yes
3	refractory	PD	Cycle 1, Day 12	12	25	Yes
4	refractory	CR	Baseline	0	100	Yes
4	refractory	CR	Cycle 1, Day 1	1	101	Yes
4	refractory	CR	Cycle 1, Day 4	4	104	Yes
4	refractory	CR	Cycle 1, Day 7	7	107	Yes
4	refractory	CR	Cycle 1, Day 14	14	114	Yes
4	refractory	CR	Cycle 2, D1	27	127	Yes
4	refractory	CR	Cycle 3, D1	53	153	Yes

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4	refractory	CR	Cycle 3, Day 21	74	174	Yes
4	refractory	CR	Cycle 3, Day 30	83	183	Yes
4	refractory	CR	Cycle 4, Day 1	104	204	Yes
5	refractory	PR	Baseline	0	113	Yes
5	refractory	PR	Cycle 1, Day 1 post-pembro	0.5	113.5	Yes
5	refractory	PR	Cycle 1, Day 2	2	115	Yes
5	refractory	PR	Cycle 1, Day 5	5	118	Yes
5	refractory	PR	Cycle 1, Day 20	19	132	Yes
5	refractory	PR	Cycle 1, Day 30	29	142	Yes
5	refractory	PR	Cycle 2, Day 1	41	154	Yes
5	refractory	PR	Cycle 1, Day 22	63	176	Yes
5	refractory	PR	Cycle 3, Day 18	86	199	Yes
6	refractory	PD	Baseline	0	28	Yes
6	refractory	PD	Cycle 1, Day 1	1	29	Yes
6	refractory	PD	Cycle 1, Day 2	2	30	Yes
6	refractory	PD	Cycle 1, Day 6	6	34	Yes
7	refractory	PD	Cycle 1, Day 1	0	24	Yes
7	refractory	PD	Cycle 1, Day 3	3	27	Yes
7	refractory	PD	Cycle 1, Day 6	6	30	Yes
7	refractory	PD	Cycle 1, Day 13	13	37	Yes
7	refractory	PD	Cycle 2, Day 1	20	44	Yes
7	refractory	PD	Cycle 2, Day 20	40	64	Yes
7	refractory	PD	Cycle 4, Day 1	62	86	Yes
7	refractory	PD	Cycle 4, Day 20	82	106	Yes
8	refractory	PD	Baseline	0	54	Yes
8	refractory	PD	Cycle 1, Day 2	2	56	Yes
8	refractory	PD	Cycle 1, Day 7	7	61	Yes
8	refractory	PD	Cycle 1, Day 17	17	71	Yes
10	relapsed	SD	Baseline	0	140	Yes

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10	relapsed	SD	Cycle 1, Day 1	1	141	Yes
10	relapsed	SD	Cycle 1, Day 3	3	143	Yes
10	relapsed	SD	Cycle 1, Day 7	6	146	Yes
10	relapsed	SD	Cycle 1, Day 14	13	153	Yes
10	relapsed	SD	Cycle 2, Day 1	20	160	Yes
10	relapsed	SD	Cycle 3, Day 1	41	181	Yes
10	relapsed	SD	Cycle 4, Day 1	65	205	Yes
10	relapsed	SD	Cycle 5, Day 14	100	240	Yes
10	relapsed	SD	Cycle 5, Day 39	125	265	Yes
11	relapsed	PD	Baseline	-12	813	Yes
11	relapsed	PD	Cycle 1, Day 1	0	825	Yes
11	relapsed	PD	Cycle 1, Day 1	1	826	Yes
11	relapsed	PD	Cycle 1, Day 2	2	827	Yes
11	relapsed	PD	Cycle 1, Day 3	3	828	Yes
11	relapsed	PD	Cycle 1, Day 7	7	832	Yes
11	relapsed	PD	Cycle 1, Day 14	14	839	Yes
11	relapsed	PD	Cycle 2, Day 1	30	855	Yes
11	relapsed	PD	Cycle 3, Day 1	52	877	Yes
11	relapsed	PD	Cycle 3, Day 29	80	905	Yes
12	relapsed	PD	Cycle 1, Day 1	0	1301	Yes
12	relapsed	PD	Cycle 1, Day 1	1	1302	Yes
12	relapsed	PD	Cycle 1, Day 2	2	1303	Yes
12	relapsed	PD	Cycle 1, Day 4	4	1305	Yes
12	relapsed	PD	Cycle 1, Day 8	8	1309	Yes
12	relapsed	PD	Cycle 1, Day 15	15	1316	Yes
13	relapsed	PR	Cycle 1, Day 0	Not depicted	Not depicted	No

**Table 2S. Peripheral blood sample time points for flow CyTOF studies**

Patient ID	CART response	Cycle	Days from first pembrolizumab dose	Days from most recent pembrolizumab dose	Time	Time point	Pembrolizumab Clinical Benefit	Figure 2D	Figure 3	Figure 4
1	refractory	1	7	7	CART qPCR peak 1	Post	Non Responders	Yes	Yes	Yes
2	refractory						Non Responders	No	No	No
3	refractory	1	0	0	Baseline	Pre	Non Responders	Yes	Yes	Yes
3	refractory	1	2	2	CART qPCR peak 1	Post	Non Responders	Yes	Yes	Yes
3	refractory	1	5	5	CART qPCR trough	Later	Non Responders	Yes	Yes	No
4	refractory	1	0	0	Baseline	Pre	Responders	Yes	Yes	Yes
4	refractory	1	4	4	CART qPCR peak 1	Post	Responders	Yes	Yes	Yes
4	refractory	2	27	27	CART qPCR peak 2	Later	Responders	Yes	Yes	No
4	refractory	3	74	21	CART qPCR peak 3	Later	Responders	Yes	Yes	No
4	refractory	9	235	11	last dose of pembro	Later	Responders	Yes	Yes	No
5	refractory	1	0	0	Baseline	Pre	Responders	Yes	Yes	Yes
5	refractory	1	2	2	CART qPCR peak 1	Post	Responders	Yes	Yes	Yes
5	refractory	2	41	41	CART qPCR peak 2	Later	Responders	Yes	Yes	No
5	refractory	2	63	22	CART trough	Later	Responders	Yes	Yes	No
6	refractory	1	0	0	Baseline	Pre	Non Responders	Yes	Yes	Yes
6	refractory	1	2	2	CART qPCR peak 1	Post	Non Responders	Yes	Yes	Yes
6	refractory	1	6	6	CART qPCR trough	Later	Non Responders	Yes	Yes	No
7	refractory	1	0	0	Baseline	Pre	Non Responders	Yes	Yes	Yes
7	refractory	1	13	13	CART qPCR peak 1	Post	Non Responders	Yes	Yes	Yes
7	refractory	4	82	20	CART qPCR trough	Later	Non Responders	Yes	Yes	No
8	refractory	1	0	0	Baseline	Pre	Non Responders	Yes	Yes	Yes
8	refractory	1	7	7	CART qPCR peak 1	Post	Non Responders	Yes	Yes	Yes
10	refractory	1	0	0	Baseline	Pre	Responders	Yes	Yes	Yes
10	refractory	1	13	13	CART qPCR peak 1	Post	Responders	Yes	Yes	Yes

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10	refractory	3	65	24	CART qPCR peak 2	Later	Responders	Yes	Yes	No
10	refractory	4	100	14	CART qPCR trough	Later	Responders	Yes	Yes	No
11	relapsed	1	0	0	Baseline	Pre	Non Responders	Yes	Yes	Yes
11	relapsed	1	3	3	CART qPCR peak 1	Post	Non Responders	Yes	Yes	Yes
12	relapsed	1	0	0	Baseline	Pre	Non Responders	Yes	Yes	Yes
12	relapsed	1	2	2	CART qPCR peak 1	Post	Non Responders	Yes	Yes	Yes
13	relapsed	1	0	0	Baseline	Pre	Responders	Yes	Yes	Yes
13	relapsed	1	3	3	CART qPCR peak 1	Post	Responders	Yes	Yes	Yes

**Table 3S. Cytokine release syndrome, corticosteroid and tocilizumab use after CAR T cells and pembrolizumab**

ID	CRS grade post CAR T cells	Corticosteroids post CAR T cells	Tocilizumab use post CAR T cells	Infusion related reaction post pembrolizumab	Fever or CRS grade post pembrolizumab	Corticosteroids post pembrolizumab**
1	1	No	No	No	No	No
2	--	No	No	No	No	No
3	1	No	No	No	Yes	No
4	--	No	No	No	No	No
5	1	No	No	Yes – Grade 2	Yes – Grade 2	Yes – once for IRR
6	1	No	No	No	No	No
7	--	No	No	No	Yes	No
8	1	No	No	No	No	No
10	2	No	No	No	No	No
11	2	No	No	No	No	No
12	2	No	No	No	No	Yes – for facial swelling
13	3	No	Yes – Day 4*	No	No	No

\*This patient received pembrolizumab 20.4 months after CAR T cell infusion

\*\*One patient received hydrocortisone 50mg X 1 dose for a grade 2 infusion-related reaction after the first dose of pembrolizumab. One patient received more than one dose of corticosteroids (beginning day 4, solumedrol 1mg/kg) to palliate facial swelling from tumor that was thought tumor flare/pseudoprogression versus progressive lymphoma; biopsy confirmed that facial swelling was due to progressive lymphoma, and the patient was withdrawn from study

**Table 4S. Duration of time between CAR T and pembrolizumab, CAR T expansion, and clinical response**

Subject ID	Months between CAR T infusion & pembrolizumab	CAR19 transgene peak copies / uL after pembrolizumab	Response to pembrolizumab <sup>1</sup>
-03	0.4	748.9	PD
-07	0.8	8511.1	PD
-06	0.9	18080.5	PD
-08	1.8	38.5	PD
-02	3.2	8.0	PD
-01	3.3	76.1	PD
-04	3.3	2068.5	CR
-05	3.7	200.9	PR
-10	4.6	277.8	SD
-11	20.2	25.1	PD
-12	27.1	23.1	PR
-13	42.8	41.9	PD

Abbreviations:

CR: complete response; PR: partial response; SD: stable disease; PD: progressive disease.

<sup>1</sup>Responses assessment was determined by 2007 Revised response criteria for malignant lymphoma<sup>28</sup>