

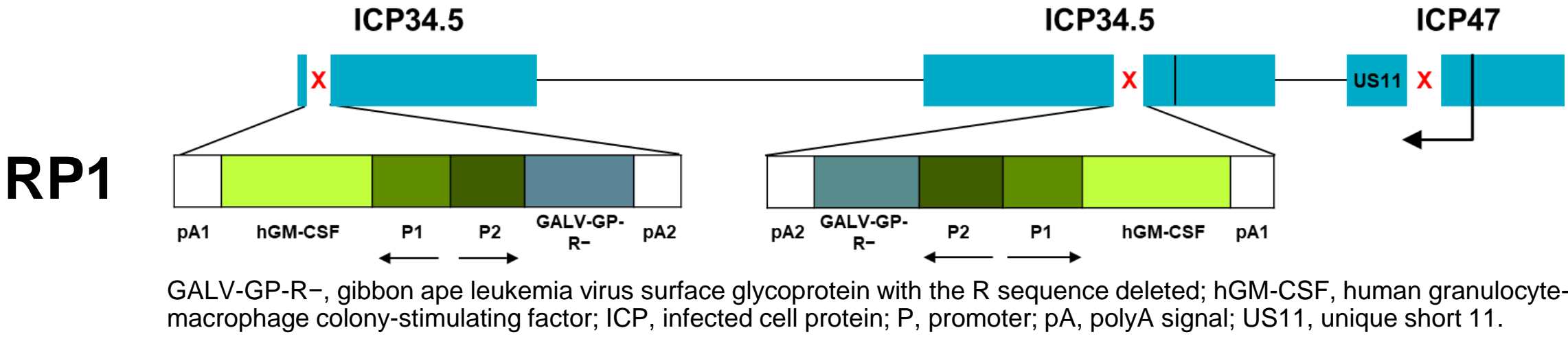
Updated data from the ongoing phase 1/2 clinical trial of RP1 combined with nivolumab (IGNYTE) in patients with melanoma

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Background

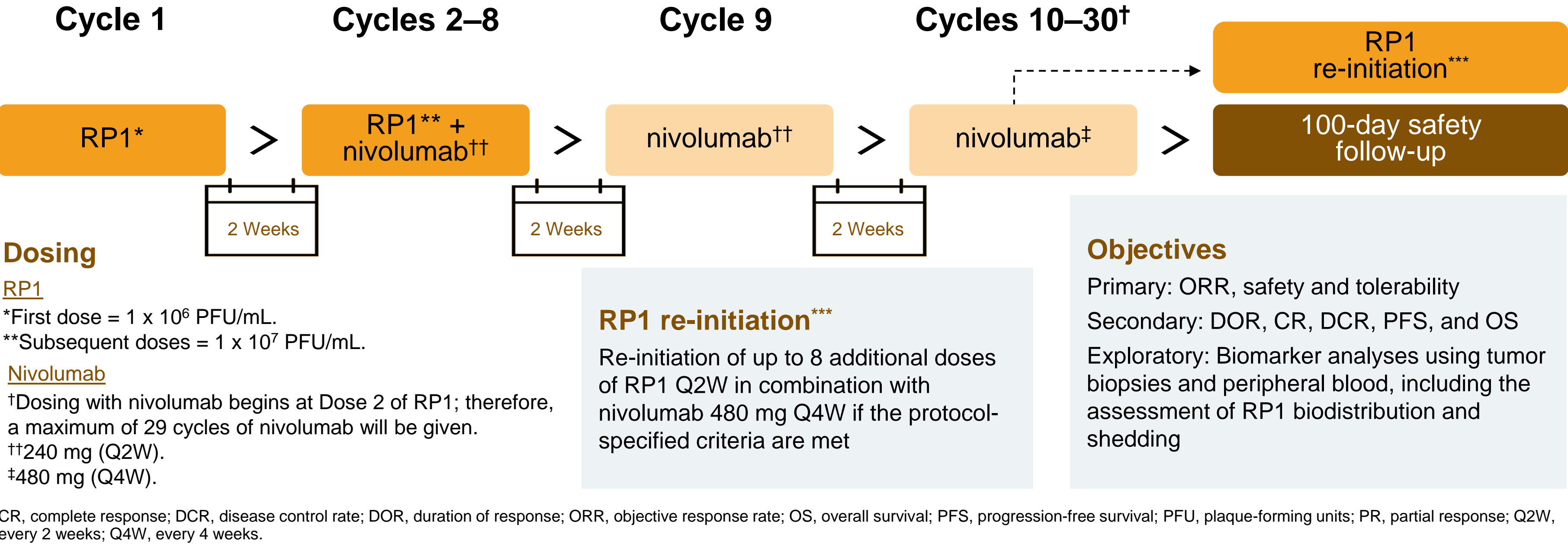
- RP1 is an enhanced potency oncolytic version of herpes simplex virus type 1 that expresses human granulocyte macrophage colony stimulating factor and the fusogenic protein GALV-GP-R- [1]
- IGNYTE is a phase 1/2 open-label, multicenter, dose escalation and expansion trial (NCT03767348) evaluating the safety and efficacy of RP1 in combination with the anti-programmed cell death protein 1 (PD-1) inhibitor nivolumab in a range of tumor types [2]
- Here, we present updated results from the melanoma and anti-PD-1-naïve non-melanoma skin cancer (NMSC) cohorts with RP1 combined with nivolumab



Methods

Cohorts	Target N
Melanoma ^a	30
Non-melanoma skin cancer anti-PD-1/PD-L1-failed and -naïve ^b	60
Cutaneous melanoma anti-PD-1-failed ^c	125
Non-small cell lung cancer anti-PD-1/PD-L1-failed	30
Microsatellite instability-high and deficient mismatch repair anti-PD-1/PD-L1-failed	30

^aMelanoma (N = 30) is fully enrolled and not recruiting.
^bAnti-PD-1/PD-L1-naïve is fully enrolled and not recruiting; anti-PD-1/ PD-L1-failed (N = 30).
^cRegistration-directed cohort.
PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1.



Results

Melanoma

Table 1. Demographics

	All	Cutaneous	Mucosal	Uveal
Patients, N	36	24	6	6
Age range, years	28–95	28–95	40–78	44–85
Prior Tx				
Prior anti-PD-1 (alone or combined), n	25	24 ^a	5	4
Prior single agent anti-PD-1, n	9	7	1	1
Prior anti-PD-1/anti-CTLA-4, n	16	9	4	3
Prior anti-PD-1, %	69	67	83	75
Disease Characteristics				
Stage IIIC, n	2	2	0	0
Stage IV M1a, n	7	3	4	0
Stage IV M1b, n	11	10	1	0
Stage IV M1c, n	16	9	1	6
Stage IV M1b/c, %	75	79	33	100

^a87.5% of anti-PD-1-failed patients had stage IV M1b/c (visceral) disease.
CTLA-4, cytotoxic T-lymphocyte antigen 4; PD-1, programmed cell death protein 1; Tx, treatment.

- 36 patients with melanoma were enrolled: 24 had cutaneous, 6 mucosal, and 6 uveal melanoma (enrollment complete in January 2020; **Table 1**)

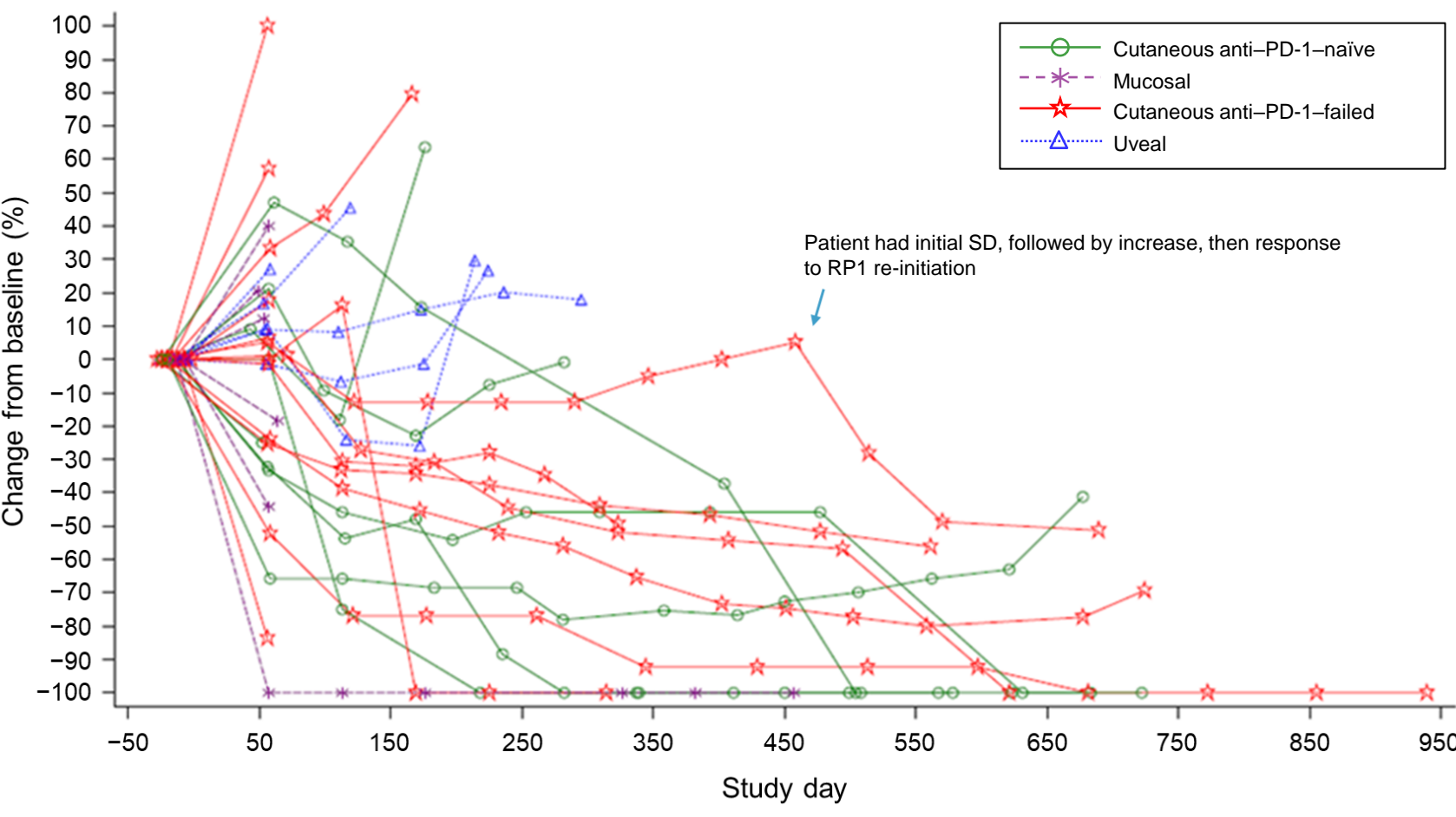
Table 2. Melanoma: Efficacy

	Cutaneous: Anti-PD-1-naïve	Cutaneous: Anti-PD-1-failed	Mucosal: Anti-PD-1-naïve	Mucosal: Anti-PD-1-failed	Uveal: Anti-PD-1-naïve	Uveal: Anti-PD-1-failed
Patients, N	8	16	1	5	3	3
Best overall response, n (%)						
CR	3 (37.5)	2 (12.5)	1 (100.0)	1 (20.0)	0	0
PR	2 (25.0)	4 (25.0) ^a	0	0	0	0
SD	2 (25.0)	1 (6.3) ^b	0	0	1 (33.3)	3 (100.0)
PD	1 (12.5)	8 (50.0)	0	4 (80.0)	2 (66.7)	0
ORR	5 (62.5)	6 (37.5)	1 (100.0)	1 (20.0)	0	0
CR+PR	5 (62.5)	6 (37.5)	1 (100.0)	1 (20.0)	0	0
CR+PR+SD	7 (87.5)	7 (43.8)	1 (100.0)	1 (20.0)	1 (33.3)	3 (100.0)

^aOne anti-PD-1-naïve PR patient is being treated with re-initiated RP1 with the aim of achieving a CR; one anti-PD-1-failed PR patient is a CR by PET scan (no metabolic activity seen) and PET scans are being scheduled for two others suspected to be NED at 18 and 23 months.
^bOne SD patient has the potential for response following ongoing RP1 re-initiation; the second SD patient is a surgical CR (residual tumor removed at 4 months, ongoing at 18 months).
CR, complete response; NED, no evidence of disease; ORR, objective response rate; PD, progressive disease; PD-1, programmed cell death protein 1; PET, positron emission tomography; PR, partial response; SD, stable disease.

- The objective response rate (ORR) and complete response (CR) rate for the anti-PD-1-failed cutaneous melanoma cohort increased from 31.3% to 37.5% and from 6.3% to 12.5%, respectively
- Disease control (CR+ partial response [PR] + stable disease [SD]) was achieved in 87.5% and 43.8% of patients in the anti-PD-1-naïve and anti-PD-1-failed cutaneous melanoma, respectively

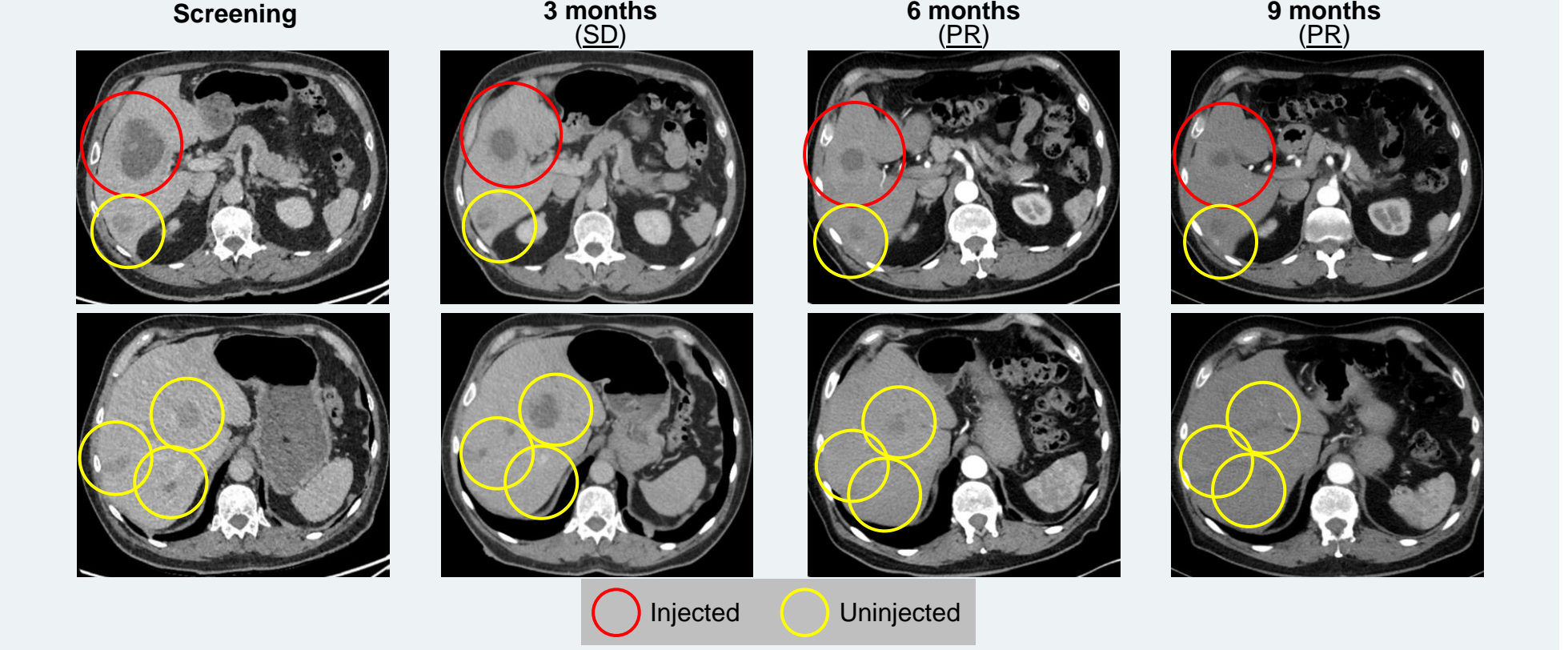
Figure 1. Melanoma: Change in sum of tumor diameters



PD-1, programmed cell death protein 1; SD, stable disease.

- Durability was maintained, with general deepening of response over time

Figure 2. Patient example: Systemic response in anti-PD-1 (nivolumab)/anti-CTLA-4 (ipilimumab)-failed cutaneous melanoma



Melanoma (Patient 1122-2007): PR. Ongoing at 19 months from first RP1 dose. All lesions show no evidence of metabolic activity by PET.
CTLA-4, cytotoxic T-lymphocyte antigen 4; PET, positron emission tomography; PD-1, programmed cell death protein 1; PR, partial response; SD, stable disease.

NMSC

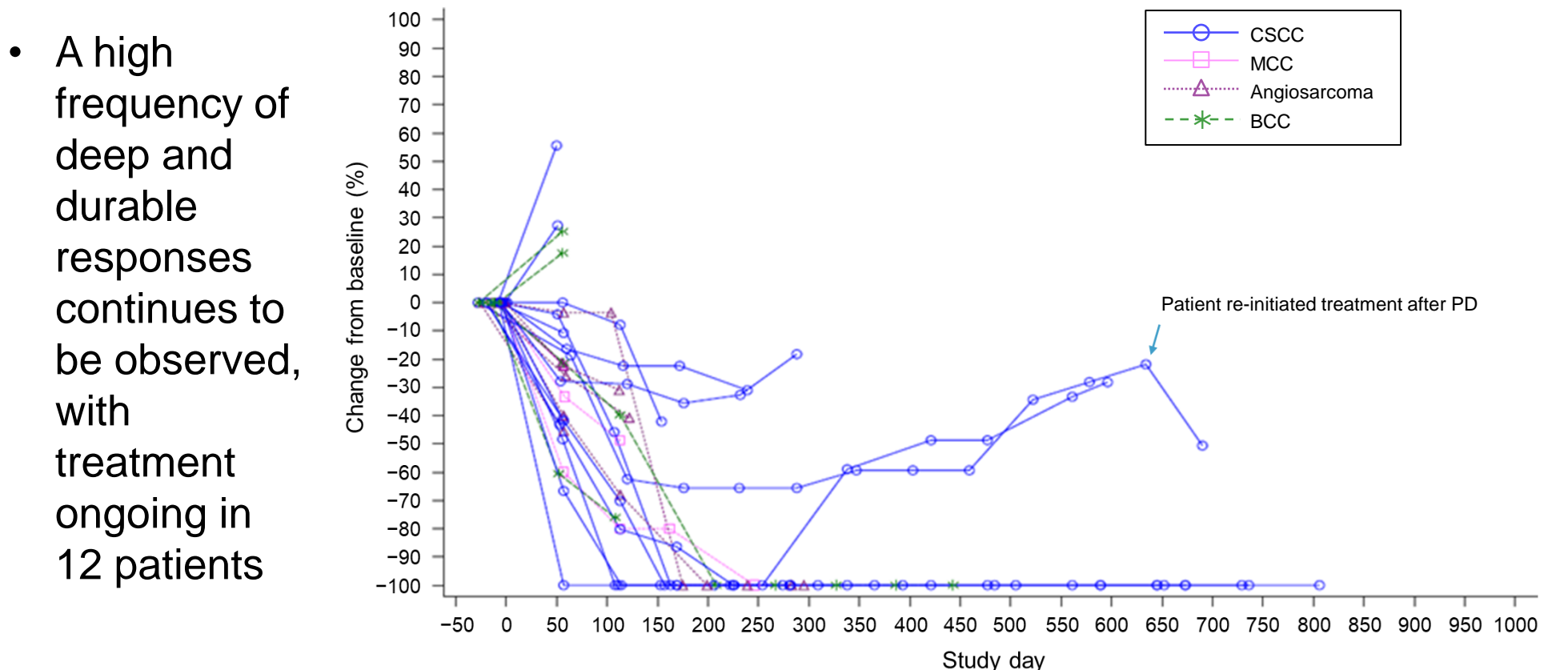
Table 3. Anti-PD-1-naïve NMSC: Efficacy

	CSCC	BCC	MCC	Angiosarcoma
Patients, N ^a	17	4	4	6
Best overall response, n (%)				
CR	8 (47.1)	1 (25.0)	2 (50.0)	1 (16.7)
PR	3 (17.6)	0	1 (25.0)	3 (50.0)
SD	1 (5.9)	2 (50.0)	0	1 (16.7)
PD	4 (23.5)	1 (25.0)	1 (25.0)	1 (16.7)
ORR (CR+PR)	11 (64.7)	1 (25.0)	3 (75.0)	4 (66.7)
CR+PR+SD	12 (70.6)	3 (75.0)	3 (75.0)	5 (83.3)

^aPatients with follow-up assessments (n = 31), on study with no follow-up currently for the other patient (MCC).
BCC, basal cell carcinoma; CR, complete response; CSCC, cutaneous squamous cell carcinoma; MCC, Merkel cell carcinoma; NMSC, non-melanoma skin cancer; ORR, objective response rate; PD, progressive disease; PD-1, programmed cell death protein 1; PR, partial response; SD, stable disease.

- The ORR for the cutaneous squamous cell carcinoma (CSCC) cohort increased from 60.0% (last data cut, March 2022) to 64.0%, with 47.1% of patients achieving a CR
- CR rates increased from 46.0% to 47.1% in CSCC, from 0% to 25.0% in basal cell carcinoma (BCC), to 50.0% in Merkel cell carcinoma (MCC), and to 16.7% in angiosarcoma
- Overall, disease control (CR+PR+SD) was achieved in >70.0% of patients in each subtype

Figure 3. Anti-PD-1-naïve NMSC: Change in sum of tumor diameters



BCC, basal cell carcinoma; CSCC, cutaneous squamous cell carcinoma; MCC, Merkel cell carcinoma; NMSC, non-melanoma skin cancer; PD, progressive disease; PD-1, programmed cell death protein 1.

Conclusions

- A high frequency of durable response continues to be seen in patients with skin cancers, including in anti-PD-1/anti-CTLA-4-failed melanoma, and in CSCC
 - Promising evidence of activity continues to also be observed in BCC, MCC, and angiosarcoma
- Systemic overall responses were seen irrespective of the sites of disease and the site of injection
- RP1 combined with nivolumab continued to be well tolerated, irrespective of injection route
- Based on these data, enrollment into a registration-directed cohort of patients who have anti-PD-1-failed cutaneous melanoma (N = 125) is currently ongoing

References:

- Thomas S, et al. *J Immunother Cancer*. 2019;7(1):214.
- Middleton M, et al. *J Clin Oncol*. 2020;38(15_suppl):e22050.

Study sponsor:

The study is sponsored by Replimune Inc., Woburn, MA, USA. Nivolumab was supplied by Bristol Myers Squibb.

