Poster number: A-290

Efficacy and safety of RP1 plus nivolumab in patients with non-melanoma skin cancer

Dirk Schadendorf[1], Michael K. Wong[2], Georgia M. Beasley[3], Anna C. Pavlick[4], Kevin J. Harrington[5], Bartosz Chmielowski[6], Jiaxin Niu[7], Ari M. VanderWalde[8], Tawnya Lynn Bowles[9], Katy K. Tsai[10], Evan T. Hall[11], Trisha M. Wise-Draper[12], Judith Michels[13], Ana Arance[14], Mona Amini-Adle[15], Junhong Zhu[16], Marcus Viana[16], Jeannie W. Hou[16], Mohammed M. Milhem[17]

[1]Department of Dermatology, West German Cancer Center, University Hospital Essen & National Center for Tumor Diseases (NCT-West), Campus Essen & University Alliance Ruhr, Research Alliance Ruhr, Research Center One Health, University Duisburg-Essen, Campus Essen, Essen, Germany; [2]Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; [3]Duke Cancer Institute, Duke University, Durham, NC, USA; [4]Weill Cornell Medical College, New York, NY, USA; [5]The Institute of Cancer Research/Royal Marsden NIHR Biomedical Research Centre, London, UK; [6]Jonsson Comprehensive Cancer Center, University of California Los Angeles, Los Angeles, CA, USA; [7]Banner MD Anderson Cancer Center, Gilbert, AZ, USA; [8]West Cancer Center and Research Institute, Germantown, TN, USA; [9]Intermountain Medical Center, Murray, UT, USA; [10]Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA, USA; [11]Fred Hutchinson Cancer Center, University of Washington School of Medicine, Seattle, WA, USA; [12]University of Cincinnati Cancer Center, University of Cincinnati, Cincinnati, OH, USA; [13]Département de Médecine Oncologique, Gustave Roussy, Villejuif, France; [14]Medical Oncology Department, Hospital Clinic, Translational Genomics and Targeted Therapies in Solid Tumors, IDIBAPS, Barcelona, Spain; [15]Centre Léon Bérard, Lyon, France; [16]Replimune, Inc., Woburn, MA, USA; [17]Holden Comprehensive Cancer Center, University of Iowa, Iowa City, IA, USA

Background

- Non-melanoma skin cancer (NMSC) is a common group of malignancies that includes basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (CSCC), as well as less common cancers, such as Merkel cell carcinoma (MCC) and angiosarcoma[1,2]
- Although easily treatable in early stages, some NMSCs recur or metastasize and require systemic treatments such as immune checkpoint inhibitors.[3] Furthermore, patients with advanced NMSC that progressed on an anti–programmed cell death protein 1 (PD-1)- or anti–programmed death-ligand 1 (PD-L1)-containing therapy have poor clinical outcomes and limited treatment options[4-7]
  - There is currently no standard of care for NMSC that has progressed on anti–PD-1/PD-L1 therapy[3-7]
- RP1 (vusolimogene oderparepvec) is a replication-selective herpes simplex virus type 1–based oncolytic immunotherapy that expresses human granulocyte-macrophage colony-stimulating factor and a fusogenic glycoprotein (GALV-GP-R$^-$), which substantially increases the degree and immunogenicity of tumor cell death[8]
- In the phase 1/2 IGNYTE trial (NCT03767348), RP1 combined with nivolumab showed clinically meaningful and durable efficacy (objective response rate of 33.6% and duration of response of 24.8 months by Response Evaluation Criteria in Solid Tumors version 1.1) in 140 patients with advanced anti–PD-1–failed melanoma (data cutoff: October 15, 2024)[9]
- The IGNYTE trial also evaluated the safety and efficacy of RP1 alone or combined with nivolumab in cohorts of other patients with advanced tumors, including a cohort of patients with NMSC

Objective

To report the efficacy and safety of RP1 plus nivolumab in the NMSC cohort from the IGNYTE trial

Methods

Study design and treatment

- The trial enrolled patients with anti–PD-1–naïve and –failed NMSC, including MCC, BCC, angiosarcoma, and CSCC
- RP1 was administered intratumorally into superficial and/or deep/visceral tumors at 1 × 10^6 plaque-forming units (PFU)/mL initially, then at 1 × 10^7 PFU/mL once every 2 weeks for up to 7 doses (≤10 mL per cycle) with intravenous nivolumab (240 mg); nivolumab was then given alone (240 mg every 2 weeks or 480 mg every 4 weeks) for up to 2 years, with further RP1 allowed if indicated according to protocol-defined criteria
- The data cutoff date for this study was June 11, 2025

Results

Baseline demographics and clinical characteristics

- Among 118 patients with NMSC, 86 (72.9%) patients had disease progression on prior anti–PD-1 therapy (**Table 1**)

Table 1. Baseline demographics and clinical characteristics of patients with NMSC

Characteristic	MCC (n = 33)		BCC (n = 14)		Angiosarcoma (n = 16)		CSCC (n = 55)	
	Anti–PD-1 naïve (n = 6)	Anti–PD-1 failed (n = 27)	Anti–PD-1 naïve (n = 4)	Anti–PD-1 failed (n = 10)	Anti–PD-1 naïve (n = 6)	Anti–PD-1 failed (n = 10)	Anti–PD-1 naïve (n = 16)	Anti–PD-1 failed (n = 39)
Age, median (range), y	72.5 (46.0–90.0)	73.0 (48.0–89.0)	70.0 (44.0–83.0)	62.5 (44.0–78.0)	74.0 (43.0–97.0)	72.5 (60.0–88.0)	67.5 (47.0–87.0)	69.0 (38.0–93.0)
Sex, n (%)								
Male	5 (83.3)	22 (81.5)	2 (50.0)	9 (90.0)	5 (83.3)	3 (30.0)	12 (75.0)	30 (76.9)
Female	1 (16.7)	5 (18.5)	2 (50.0)	1 (10.0)	1 (16.7)	7 (70.0)	4 (25.0)	9 (23.1)
Stage, n (%)								
M0	2 (33.3)	10 (37.0)	2 (50.0)	2 (20.0)	2 (33.3)	7 (70.0)	5 (31.3)	10 (25.6)
M1	4 (66.7)	17 (63.0)	2 (50.0)	8 (80.0)	4 (66.7)	3 (30.0)	11 (68.8)	29 (74.4)
ECOG performance status, n (%)								
0	5 (83.3)	10 (37.0)	0	10 (100.0)	1 (16.7)	4 (40.0)	5 (31.3)	19 (48.7)
1	1 (16.7)	17 (63.0)	4 (100.0)	0	5 (83.3)	6 (60.0)	11 (68.8)	20 (51.3)
PD-L1 tumor expression, n (%)								
Positive (≥1%)	0	5 (18.5)	1 (25.0)	2 (20.0)	3 (50.0)	2 (20.0)	9 (56.3)	17 (43.6)
Negative (<1%)	4 (66.7)	13 (48.1)	3 (75.0)	7 (70.0)	2 (33.3)	5 (50.0)	4 (25.0)	11 (28.2)
Undetermined or missing	2 (33.3)	9 (33.3)	0	1 (10.0)	1 (16.7)	3 (30.0)	3 (18.8)	11 (28.2)

BCC, basal cell carcinoma; CSCC, cutaneous squamous cell carcinoma; ECOG, Eastern Cooperative Oncology Group; MCC, Merkel cell carcinoma; NMSC, non-melanoma skin cancer; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1.

Efficacy

- Responses to RP1 plus nivolumab occurred across the NMSC tumor types enrolled, with confirmed responses seen in patients with both anti–PD-1–naïve and –failed disease (**Table 2**)
- Response profiles for individual patients are shown in **Figure 1**

Table 2. Confirmed response by NMSC type (full analysis set)

BOR, n (%)	MCC		BCC		Angiosarcoma		CSCC	
	Anti–PD-1 naïve (n = 6)	Anti–PD-1 failed (n = 27)	Anti–PD-1 naïve (n = 4)	Anti–PD-1 failed (n = 10)	Anti–PD-1 naïve (n = 6)	Anti–PD-1 failed (n = 10)	Anti–PD-1 naïve (n = 16)	Anti–PD-1 failed (n = 39)
CR	4 (66.7)	5 (18.5)	1 (25.0)	0	2 (33.3)	2 (20.0)	6 (37.5)	4 (10.3)
PR	0	3 (11.1)	0	3 (30.0)	2 (33.3)	2 (20.0)	3 (18.8)	2 (5.1)
SD	0	4 (14.8)	1 (25.0)	4 (40.0)	2 (33.3)	3 (30.0)	3 (18.8)	14 (35.9)
PD	0	9 (33.3)	1 (25.0)	2 (20.0)	0	3 (30.0)	3 (18.8)	13 (33.3)
NE	2 (33.3)	6 (22.2)	1 (25.0)	1 (10.0)	0	0	1 (6.3)	6 (15.4)
ORR	4 (66.7)	8 (29.6)	1 (25.0)	3 (30.0)	4 (66.7)	4 (40.0)	9 (56.3)	6 (15.4)

ORR by investigator assessment using mRECIST. For mRECIST, PD must be confirmed by further progression at least 4 weeks after initial PD; this is intended to better allow for pseudoprogression than RECIST 1.1.
BCC, basal cell carcinoma; BOR, best overall response; CR, complete response; CSCC, cutaneous squamous cell carcinoma; MCC, Merkel cell carcinoma; mRECIST, modified Response Evaluation Criteria in Solid Tumors version 1.1; NE, not evaluable; 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.

Safety

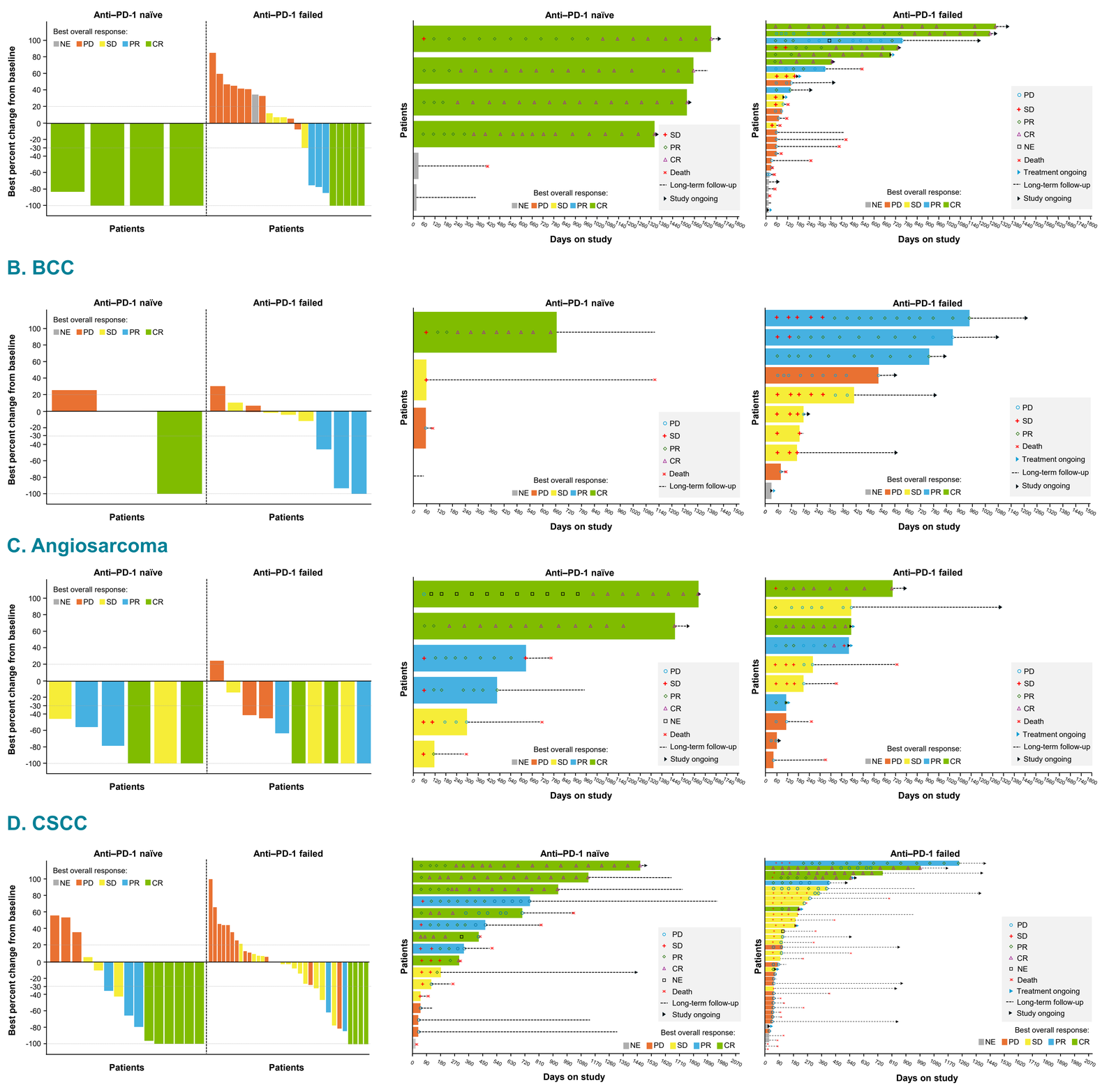
- RP1 plus nivolumab had a tolerable safety profile in patients with NMSC; most treatment-related adverse events (TRAEs) were grade 1/2 in severity (**Table 3**)
- The most common TRAEs among all patients (≥15%) were fatigue, chills, and pyrexia
- The most common grade ≥3 TRAEs (≥2 events in patients with anti–PD-1–naïve or –failed disease) were fatigue, rash maculo-papular, abdominal pain, diarrhea, mental status changes, and pyrexia. There were two RP1-related grade 5 AEs (disease hyperprogression and capillary leak syndrome)

Table 3. TRAEs in patients with NMSC (related to RP1 or nivolumab; any-grade TRAEs in ≥10% of patients with anti–PD-1–naïve or –failed disease)[a]

TRAEs, n (%)	Anti–PD-1–naïve NMSC (n = 32)		Anti–PD-1–failed NMSC (n = 96)	
	All grades	Grades ≥3	All grades	Grades ≥3
All TRAEs	29 (90.6)	13 (40.6)	77 (80.2)	21 (21.9)
Fatigue	12 (37.5)	2 (6.3)	26 (27.1)	1 (1.0)
Chills	5 (15.6)	0	27 (28.1)	0
Pyrexia	8 (25.0)	1 (3.1)	19 (19.8)	1 (1.0)
Nausea	10 (31.3)	0	7 (7.3)	0
Influenza-like illness	7 (21.9)	0	10 (10.4)	1 (1.0)
Diarrhea	7 (21.9)	2 (6.3)	10 (10.4)	0
Pruritus	9 (28.1)	1 (3.1)	6 (6.3)	0
Injection-site pain	2 (6.3)	0	10 (10.4)	0
Rash	5 (15.6)	0	4 (4.2)	0
Decreased appetite	4 (12.5)	1 (3.1)	3 (3.1)	0

[a]The safety population included additional patients with other NMSC subtypes (basosquamous carcinoma [n = 1], non-HIV–related Kaposi's sarcoma [n = 2], sebaceous gland carcinoma [n = 1], eccrine carcinomas [n = 6]).
HIV, human immunodeficiency virus; NMSC, non-melanoma skin cancer; PD-1, programmed cell death protein 1; TRAE, treatment-related adverse event.

Figure 1. Response profile for individual patients with (A) MCC, (B) BCC, (C) angiosarcoma, and (D) CSCC



BCC, basal cell carcinoma; CR, complete response; CSCC, cutaneous squamous cell carcinoma; MCC, Merkel cell carcinoma; NE, not evaluable; PD, progressive disease; PD-1, programmed cell death protein 1; PR, partial response; SD, stable disease.

Conclusions

- RP1 plus nivolumab provided responses across multiple advanced NMSC tumor types, including in anti–PD-1–failed disease
- RP1 plus nivolumab represents a promising treatment option for patients with advanced NMSC for whom no other safe and effective treatments are available

Additional information can be obtained by visiting ClinicalTrials.gov (NCT03767348)

Presenter disclosure

DS received research funding from Amgen, Bristol Myers Squibb, Merck Sharpe & Dohme, and Novartis; received consulting fees from 4SC, AstraZeneca, BioAtla, BioNTech, Boehringer Ingelheim, Bristol Myers Squibb, Daiichi Sankyo, Erasca, Formycon, Immatics, Immunocore, InflaRx, IO BioTech, Iovance Therapeutics, Ipsen, Labcorp, Merck-Serono, Merck Sharpe & Dohme, NeraCare, Novartis, Pfizer, Philogen, Pierre Fabre, Regeneron, Replimune, Sanofi, Seagen, SkylineDx, and Sun Pharma; received honoraria from Bristol Myers Squibb, InflaRx, Merck Sharpe & Dohme, Novartis, Pfizer, Pierre Fabre, Regeneron, Sanofi, and Sun Pharma; received travel support from Bristol Myers Squibb, Merck Sharpe & Dohme, Novartis, Pierre Fabre, Regeneron, and Sanofi; served on advisory boards for 4SC, AstraZeneca, Bristol Myers Squibb, BioNTech, Daiichi Sankyo, Immatics, Immunocore, InflaRx, Iovance Therapeutics, Labcorp, Merck Sharpe & Dohme, NeraCare, Novartis, Pfizer, Philogen, Pierre Fabre, Regeneron, Replimune, Sanofi, SkylineDx, and Sun Pharma; and had a leadership role in Dermatologic Cooperative Oncology Group (DeCOG), Deutsche Hautkrebsstiftung/Hiege-Stiftung, EUMelaReg, and NVKH.

Acknowledgments

The authors would like to thank the patients and their families for their participation in the trial. Medical writing and editorial support were provided by Jane Kovalevich, PhD, of Red Nucleus, and were funded by Replimune, Inc.

References

1. Sendín-Martín M, et al. *Clin Transl Oncol*. 2026;28(1):302-19.
2. Deinlein T, et al. *J Dtsch Dermatol Ges*. 2016;14(2):144-51.
3. Ascierto PA, et al. *J Immunother Cancer*. 2022;10(12):e005082.
4. National Comprehensive Cancer Network. NCCN clinical practice guidelines® for basal cell skin cancer. Version 2.2025.
5. National Comprehensive Cancer Network. NCCN clinical practice guidelines® for squamous cell skin cancer. Version 1.2026.
6. National Comprehensive Cancer Network. NCCN clinical practice guidelines® for Merkel cell carcinoma. Version 2.2025.
7. Nghiem P, et al. *J Immunother Cancer*. 2021;9(4):e002478.
8. Thomas S, et al. *J Immunother Cancer*. 2019;7(1):214.
9. Wise-Draper TM, et al. *J Immunother Cancer*. 2025;13(suppl 3). doi:10.1136/jitc-2025-SITC2025.1327.

Study sponsor

This study is sponsored by Replimune, Inc. (Woburn, MA). Nivolumab was supplied by Bristol Myers Squibb.

Disclaimer

These data were previously presented in part at the 2025 European Society for Medical Oncology (ESMO) Annual Meeting, Dirk Schadendorf, et al. FPN (Final Publication Number): 1661P; *Annals of Oncology*, Volume 36, 2025 Supplement 2. Reused with permission.

Presented at the 22nd European Association of Dermato-Oncology (EADO) Congress; April 23–25, 2026; Prague, Czech Republic