2026 ASCO® ANNUAL MEETING

A 3-YEAR LANDMARK OVERALL SURVIVAL ANALYSIS OF RP1 PLUS NIVOLUMAB IN PATIENTS WITH ANTI–PD-1–FAILED MELANOMA FROM THE IGNYTE CLINICAL TRIAL

Michael K. Wong, Joseph J. Sacco, Gino K. In, Eva Muñoz Couselo, Dirk Schadendorf, Jiaxin Niu, Georgia M. Beasley, Trisha M. Wise-Draper, Bartosz Chmielowski, Judith Michels, Mohammed M. Milhem, Tawnya Lynn Bowles, Katy K. Tsai, Céleste Lebbé, Caroline Gaudy-Marqueste, Adel Samson, George Kong, Praveen K. Bommareddy, Jeannie W. Hou, Caroline Robert

Dr Michael K. Wong, MD, PhD, FRCPC
Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA

Key Takeaway Points

RP1 + NIVOLUMAB IN ANTI–PD-1–FAILED MELANOMA

1

- **Deep** and **durable responses**
- **Long-term clinical benefit**

2

- **mOS: 32.9 months**
- **3-year OS: 47.8% (83.5% among responders)**
- Consistent benefit across clinically relevant patient subgroups

3

RP1 + nivolumab continues to demonstrate:

- **Favorable safety profile**
- **No new safety signals**

mOS, median OS; OS, overall survival; PD-1, programmed cell death protein 1.

Background

- While advanced melanoma has a high mortality rate, survival for patients treated with anti–PD-1 therapy typically plateaus at 3 to 4 years[1,2]
  - Patients alive at **3 years** are therefore likely to have **prolonged benefit**[2]
- **RP1** (vusolimogene oderparepvec) is an HSV-1–based oncolytic immunotherapy expressing **GM-CSF** and a fusogenic glycoprotein (**GALV-GP-R$^-$**)[3]
- The IGNYTE trial evaluated RP1 + nivolumab for the treatment of patients with advanced melanoma that had confirmed progression on anti–PD-1 therapy[4,5]
  - As of the October 15, 2024, data cutoff, the **ORR**[a] by RECIST 1.1 was **33.6%** (**16.4% CR**) and the median **DOR** was **24.8 months**[5]

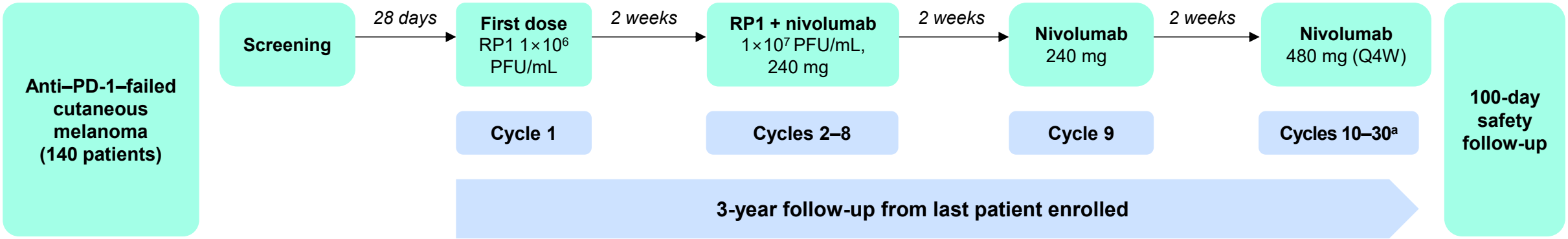
Objective: Present 3-year survival analysis of patients treated with RP1 + nivolumab from IGNYTE

[a]ORR per RECIST 1.1 by blinded independent central review.

CR, complete response; DOR, duration of response; GALV-GP-R$^-$, gibbon ape leukemia virus glycoprotein with the R sequence deleted; GM-CSF, granulocyte-macrophage colony-stimulating factor; HSV-1, herpes simplex virus type 1; ORR, objective response rate; PD-1, programmed cell death protein 1; RECIST 1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

1. Robertson BM, et al. *Nat Cancer*. 2024;5(7):964-82. 2. Michielin O, et al. *J Immunother Cancer*. 2020;8(2):e000948. 3. Thomas S, et al. *J Immunother Cancer*. 2019;7(1):214. 4. Wong MK, et al. *J Clin Oncol*. 2025;43(33):2589-99. 5. Wise-Draper TM, et al. *J ImmunoTher Cancer*. 2025;13(suppl 3):1327.

Study Design



***Tumor response assessment**: Radiographic imaging at baseline, every 8 weeks from first dose, and every 12 weeks after confirmation of response*

Key eligibility
- Anti–PD-1–failed advanced melanoma; measurable disease; adequate organ function; no prior oncolytic therapy; ECOG performance status 0–1

Primary objective
- Safety and efficacy using mRECIST[b] by independent central review (also assessed by RECIST 1.1)

Secondary objectives
- ORR by investigator assessment (mRECIST[b])
- DOR, CR rate, and PFS by central and investigator assessment, 1-year and 2-year OS

Criteria for prior anti–PD-1 failure
- ***Confirmed progression while being treated with at least 8 weeks of anti–PD-1 therapy, alone or in combination; anti–PD-1 must be the last prior therapy***
- Patients on prior adjuvant therapy must have confirmed progression while being treated with adjuvant treatment (PD can be confirmed by biopsy)

Primary analysis conducted when all patients had ≥12 months of follow-up

[a]RP1 can be reinitiated beyond 8 cycles if protocol-specified criteria are met. [b]For mRECIST, PD must be confirmed by further progression at least 4 weeks after initial PD to better allow for pseudoprogression compared with RECIST 1.1.
CR, complete response; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; mRECIST, modified RECIST 1.1; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-1, programmed cell death protein 1; PFS, progression-free survival; PFU, plaque-forming units; Q4W, every 4 weeks; RECIST 1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Baseline Clinical Characteristics

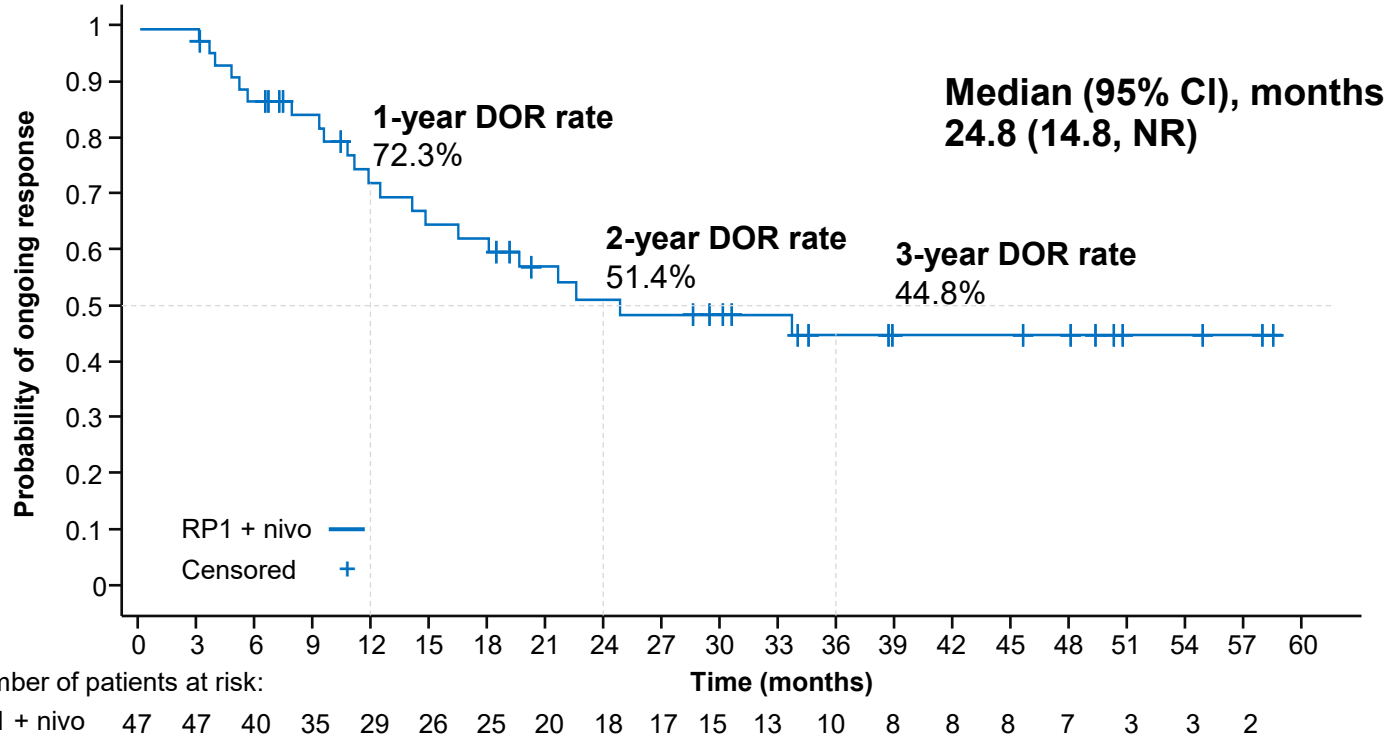
Patients, n (%)	N = 140
Age, median (range), y	62 (21–91)
Sex	
Female	45 (32.1)
Male	95 (67.9)
Stage[a]	
IIIB/IIIC/IVM1a	71 (50.7)
IVM1b/c/d	69 (49.3)
***BRAF* status**[a]	
Wild-type	89 (63.6)
Mutant	51 (36.4)
LDH level	
LDH ≤ULN	92 (65.7)
LDH >ULN	47 (33.6)
Unknown	1 (0.7)

Patients, n (%)	N = 140
PD-L1 tumor expression[a]	
Positive (≥1%)	45 (32.1)
Negative (<1%)	78 (55.7)
Undetermined or missing	17 (12.1)
Prior therapy	
Anti–PD-1	
Anti–PD-1 only as adjuvant therapy	36 (25.7)
Anti–PD-1 as advanced/metastatic therapy	104 (74.3)
Anti–CTLA-4	
Anti–PD-1 combined with anti–CTLA-4	61 (43.6)
Anti–PD-1 treated with anti–CTLA-4 sequentially	4 (2.9)
BRAF/MEK therapy	17 (12.1)
Anti–PD-1 resistance category[a]	
Primary resistance[b]	91 (65.0)
Secondary resistance[c,d]	49 (35.0)

- Due to the requirement that patients must have confirmed PD on an immediate prior anti–PD-1–based therapy, most patients had 1 or 2 prior lines of therapy; **96% received the prior course of anti–PD-1 for ≥12 weeks**
- The median (95% CI) follow-up per reverse KM at the time of this analysis was 39.0 months (37.2, 41.6)

Data cutoff: March 8, 2026. [a]Denotes a patient(s) was recategorized at extended follow up. [b]Primary resistance: progressed within 6 months of starting the immediate prior course of anti–PD-1 therapy. [c]Secondary resistance: progressed after 6 months of treatment on the immediate prior course of anti–PD-1 therapy. [d]Includes 1 patient with unknown resistance status.
CI, confidence interval; CTLA-4, cytotoxic T-lymphocyte antigen 4; LDH, lactate dehydrogenase; KM, Kaplan Meier; PD, progressive disease; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; ULN, upper limit of normal.

Efficacy: Duration of Response Among Responders by BICR RECIST 1.1

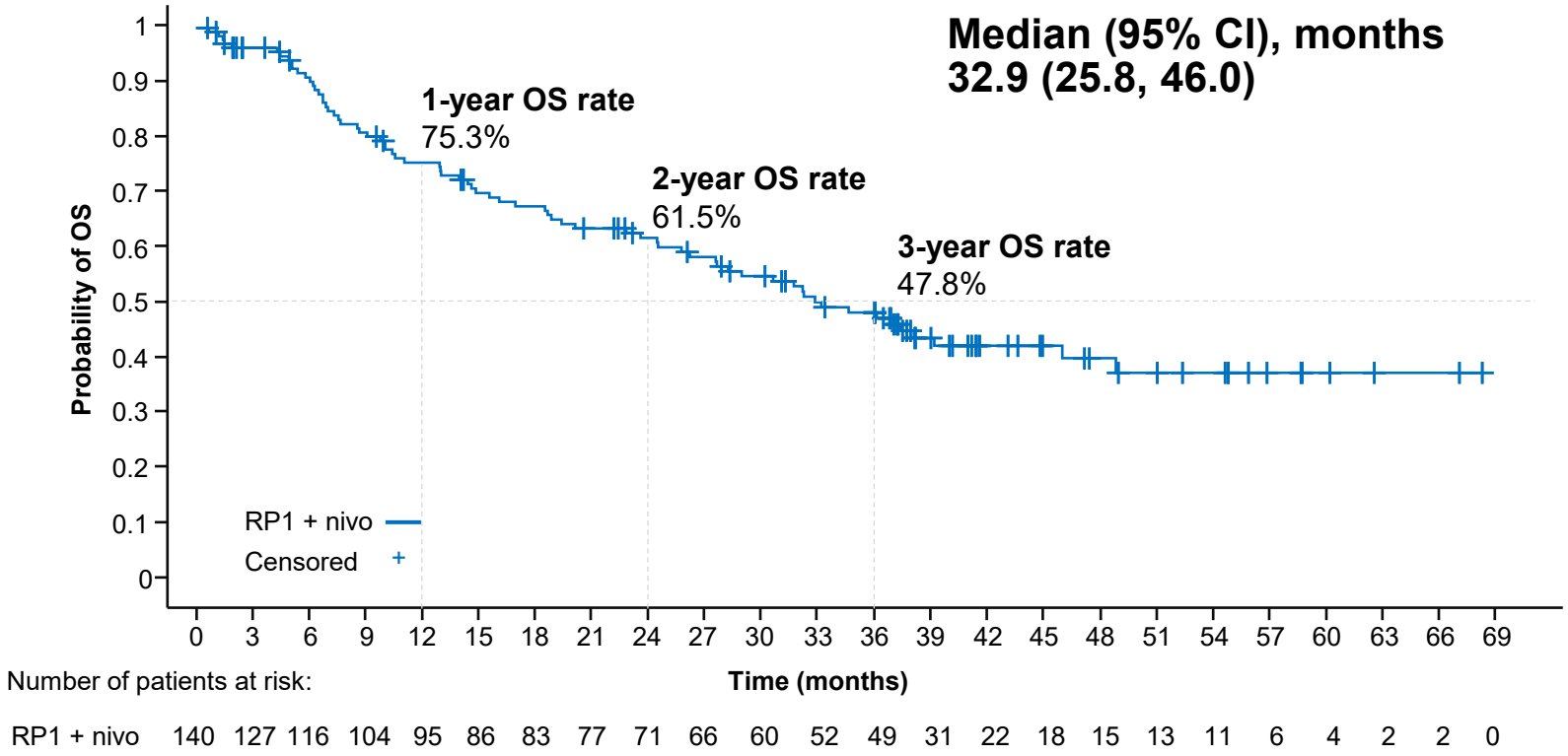


- **ORR** (95% CI) was **33.6%** (25.8%, 42.0%), and the median **DOR** (95% CI) was **24.8 months** (14.8, NR)
- The overall median **PFS** (95% CI) was **3.6 months** (2.0, 5.0); **34.9 months** (22.0, NR) for responders

Data cutoff: March 8, 2026.

BICR, blinded independent central review; CI, confidence interval; DOR, duration of response; nivo, nivolumab; NR, not reached; ORR, objective response rate; PFS, progression-free survival; RECIST 1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

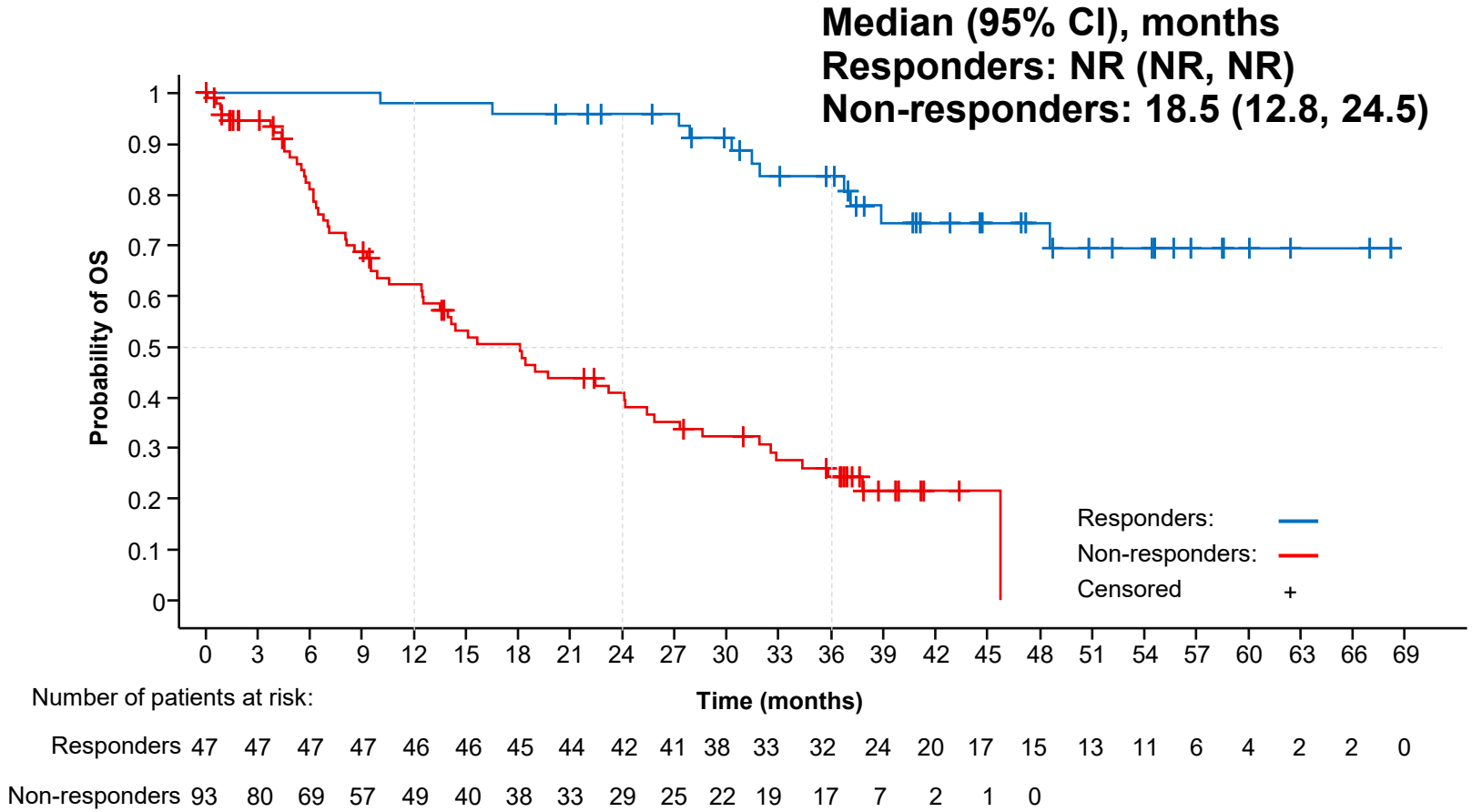
Efficacy: Overall Survival Among All Patients



	OS rates, % (95% CI)
1-year	**75.3** (66.9, 81.9)
2-year	**61.5** (52.4, 69.4)
3-year	**47.8** (38.6, 56.5)

Data cutoff: March 8, 2026.
CI, confidence interval; nivo, nivolumab; OS, overall survival.

Efficacy: Overall Survival Among Responders vs Non-Responders



	OS rates, % (95% CI)	
	Responder	Non-responder
1-year	**97.9** (85.8, 99.7)	**62.4** (51.0, 71.9)
2-year	**95.7** (84.0, 98.9)	**41.2** (30.2, 51.8)
3-year	**83.5** (68.5, 91.8)	**26.4** (16.9, 36.9)

Data cutoff: March 8, 2026.
CI, confidence interval; NR, not reached; OS, overall survival.

Efficacy: Benefit in Overall Survival Across Subgroups

	Overall (N = 140)	Stage		PD-L1 Status		Anti–CTLA-4		Resistance	
		IIIB/IIIC/IVM1a (n = 71)	IVM1b/c/d (n = 69)	PD-L1 positive (n = 45)	PD-L1 negative (n = 78)	No prior anti–CTLA-4 (n = 75)	Prior anti–CTLA-4 (n = 65)	Primary (n = 91)	Secondary (n = 49)
Median OS, months (95% CI)	32.9 (25.8, 46.0)	39.2 (27.6, NR)	27.6 (12.9, 37.4)	NR (32.2, NR)	25.8 (18.6, 36.1)	46.0 (28.9, NR)	18.6 (12.9, 37.1)	32.9 (22.8, 48.9)	34.7 (20.1, NR)

Data cutoff: March 8, 2026.
CI, confidence interval; CTLA-4, cytotoxic T-lymphocyte antigen 4; NR, not reached; OS, overall survival; PD-L1, programmed death-ligand 1.

Safety Profile: No New Safety Signals

TRAEs in ≥5% of patients (related to either RP1 or nivolumab)

Preferred term, n (%)	Patients (N = 141)	
	All grades	Grade 3–4
≥1 TRAE	**125 (88.7)**	**18 (12.8)**
Chills	45 (31.9)	0 (0.0)
Fatigue	45 (31.9)	1 (0.7)
Pyrexia	43 (30.5)	0 (0.0)
Nausea	32 (22.7)	0 (0.0)
Influenza-like illness	25 (17.7)	0 (0.0)
Injection-site pain	21 (14.9)	0 (0.0)
Diarrhea	20 (14.2)	1 (0.7)
Pruritus	19 (13.5)	0 (0.0)
Vomiting	19 (13.5)	0 (0.0)
Headache	18 (12.8)	0 (0.0)
Asthenia	14 (9.9)	1 (0.7)
Arthralgia	10 (7.1)	1 (0.7)
Myalgia	9 (6.4)	0 (0.0)
Cough	8 (5.7)	0 (0.0)
Decreased appetite	8 (5.7)	1 (0.7)
Rash	8 (5.7)	0 (0.0)
Hypothyroidism	7 (5.0)	0 (0.0)
Injection-site reaction	7 (5.0)	0 (0.0)
Vitiligo	7 (5.0)	0 (0.0)

RP1 combined with nivolumab continued to be **well tolerated over long-term follow-up**

- Predominantly grade 1 and 2 constitutional-type side effects
- Low incidence of grade 3 events (none occurring in >5% of patients); five grade 4 events in total
- No grade 5 events

Additional grade 3/4 TRAEs (grade 4 TRAEs are italicized):

- **Two events each (1.4%):** Hypophysitis and rash maculopapular
- **One event each (0.7%):** Abdominal pain, acute left ventricular failure, amylase increased, cancer pain, *cytokine release syndrome*, eczema, enterocolitis, extranodal marginal zone B-cell lymphoma (MALT type), *hepatic cytolysis*, hyponatremia, immune-mediated enterocolitis, infusion-related reaction, left ventricular dysfunction, *lipase increased*, memory impairment, meningitis aseptic, muscular weakness, *myocarditis*, palmar-plantar erythrodysesthesia syndrome, paresthesia, peripheral sensory neuropathy, radiculitis brachial, sinus arrhythmia, *splenic rupture*, tricuspid valve incompetence, tumor pain, and type 1 diabetes mellitus

Data cutoff: March 8, 2026.
AE, adverse event; MALT, mucosa-associated lymphoid tissue; TRAE, treatment-related AE.

Conclusions

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Dr Bartosz Chmielowski	University of California, Los Angeles
Dr John Fruehauf	University of California, Irvine
Dr Gino K In	USC Norris Comprehensive Cancer Center
Dr George M Beasley	Duke Cancer Institute
Dr Trisha M Wise-Draper	University of Cincinnati Cancer Center
Dr Robert McWilliams	Mayo Clinic - Minnesota
Dr Mahesh Seetharam	Mayo Clinic - Arizona
Dr Aleksandar Sekulic	Mayo Clinic - Arizona
Dr Issam Makhoul	CARTI Cancer Center
Dr Michael K Wong	Roswell Park Comprehensive Cancer Center
Dr Céleste Lebbé	Hôpital Saint Louis APHP
Dr Sophie Dalac-Rat	CHU Dijon-Bourgogne
Dr Caroline Gaudy-Marqueste	CHU de La Timone Aix-Marseille University
Dr Charlée Nardin	CHU Besancon – Hôpital Jean Minjoz
Dr Antoine Italiano	Institut Bergonié
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Additional information can be obtained by visiting ClinicalTrials.gov (NCT03767348)