

A Phase 2 Study of Retifanlimab in Patients With Advanced or Metastatic Merkel Cell Carcinoma (POD1UM-201)

Giovanni Grignani,¹ Piotr Rutkowski,² Céleste Lebbé,³ Natalie Prinzi,⁴ Jean Jacques Grob,⁵ Enrica Teresa Tanda,⁶ Michele Guida,⁷ Melissa Burgess,⁸ Jennifer Pulini,⁹ Mark Cornfeld,⁹ Chuan Tian,⁹ Shailender Bhatia¹⁰

Introduction

- Merkel cell carcinoma (MCC) is a rare but aggressive neuroendocrine skin cancer, with rapidly rising incidence rate especially in adults ≥65 years of age¹
- Programmed cell death protein 1 (PD-1) and programmed death ligand 1 (PD-L1) inhibitors for the treatment of patients with advanced/metastatic MCC have shown promising results in phase 2 clinical trials and are now the treatment of choice
 - Avelumab,² nivolumab,³ and pembrolizumab⁴ are recommended in guidelines for MCC⁵ based on durable responses^{6,7}
- Response rates of up to 70% for first-line chemotherapy and 9–20% for second-line chemotherapy or later have been reported⁵
- Duration of response to chemotherapy is short, with high rates of fatal toxicities especially in elderly patients. PD-1–directed therapies have become the treatment of choice in the first-line setting
- Retifanlimab (INCMGA00012) is an investigational humanized IgG4 monoclonal antibody targeting human PD-1 that is being evaluated in phase 2 and 3 studies in patients with solid tumors
 - Retifanlimab is well characterized, representative of the class, and has demonstrated activity in a variety of solid tumors^{8–16}
- POD1UM-201 (NCT03599713) is a phase 2 trial assessing efficacy and safety of retifanlimab in patients with chemotherapy-naïve advanced/metastatic MCC
 - Preliminary efficacy of retifanlimab in advanced/metastatic MCC has been previously reported¹⁵
 - Here, we report the primary efficacy results in a cohort of chemotherapy-naïve patients

Objectives

Primary

- To evaluate the objective response rate (ORR) of retifanlimab in chemotherapy-naïve patients with recurrent locally advanced or metastatic MCC

Secondary

- To evaluate duration of response (DOR), disease control rate, progression-free survival (PFS), and overall survival
- To evaluate the safety of retifanlimab in MCC
- To determine the pharmacokinetics of retifanlimab

Exploratory

- Biomarkers, immunogenicity, efficacy per immune-related response criteria, and health-related quality of life

Methods

Study Design and Treatment

- Phase 2, open-label, single-arm, multicenter study
- Per protocol amendment 5 (April 09, 2020), enrollment was limited to chemotherapy-naïve patients (Table 1)

Table 1. Key Eligibility Criteria

Inclusion	• Male and female patients ≥18 years of age with distant metastatic disease or recurrent, advanced locoregional disease not amenable to surgery or radiation, measurable per RECIST v1.1
	• Eastern Cooperative Oncology Group performance status 0 or 1
Exclusion	• Available tumor tissue (fresh or archival) for central pathology review
	• HIV-positive patients are eligible if CD4 cell count is ≥300 cells/μL, have undetectable viral load, and are receiving highly active antiretroviral therapy
Inclusion	• Previous systemic treatment for MCC, including chemotherapy and any anti–PD-L1 or anti–PD-L1 therapy
	• Treatment with anticancer drugs or participation in another interventional clinical trial ≤21 days before first study dose
Exclusion	• Radiation therapy ≤2 weeks before first dose or radiation therapy to the thoracic region >30 Gy ≤6 months before first dose
	• Known central nervous system metastases and/or carcinomatous meningitis
Inclusion	• Interstitial lung disease or active, noninfectious pneumonitis
	• Active autoimmune disease requiring systemic immunosuppression beyond maintenance treatment with corticosteroids, or chronic or current active infections requiring systemic antibiotics, antifungal, or antiviral treatment

HIV, human immunodeficiency virus; MCC, Merkel cell carcinoma; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1; RECIST, Response Evaluation Criteria in Solid Tumors.

- Retifanlimab was administered at a flat dose of 500 mg intravenously over 60 minutes every 4 weeks (Q4W; on day 1 of each 28-day cycle)
 - Premedication was not required
- Treatment could continue up to 2 years in the absence of disease progression, intolerable toxicity, death, withdrawal of consent, loss to follow-up, or premature discontinuation for any other reason
- Primary efficacy analysis is based on chemotherapy-naïve patients with at least 6 months of tumor assessment following first confirmed response, at data cutoff of June 16, 2021 (N = 65)
- Safety analysis is based on all patients who received at least 1 dose of retifanlimab (N = 105)

Assessments

- Objective responses were assessed per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 every 8 weeks for the first 12 months, and then every 12 weeks thereafter
 - Modified version of RECIST v1.1 for immune-based therapeutics was also used to evaluate patient responses and guide treatment decisions
- Adverse events, graded by Common Terminology Criteria for Adverse Events version 5.0, were monitored until ≥90 days after the last dose of study drug or until the start of new anticancer therapy, whichever occurred first
- Tumor tissue was collected during screening to measure PD-L1 expression levels and Merkel cell polyomavirus large T-antigen, as well as for biomarker and translational analyses

Results

Patients

- As of the June 16, 2021 data cutoff, 105 patients (chemotherapy-naïve, n = 99; chemotherapy-refractory, n = 6) were enrolled and received ≥1 dose of retifanlimab (safety evaluable population)
 - Of these patients, the first 65 chemotherapy-naïve patients enrolled (full analysis set) were included in the primary efficacy analysis (response by independent central review [ICR])
 - Six chemotherapy-refractory patients were treated under a previous version of the protocol
 - Median (range) duration of follow-up for the full analysis set was 7.5 (1.1–16.6) months
- Patient demographics and disease characteristics are presented in Table 2
- At the data cutoff, 60 patients (57.1%) were still ongoing treatment (chemotherapy-naïve, n = 57 [57.6%]; chemotherapy-refractory, n = 3 [50.0%])

Table 2. Baseline Demographics and Disease Characteristics (Safety Evaluable Population)

Variable	Chemotherapy-Naïve (n = 99)	Chemotherapy-Refractory (n = 6)
Age, median (range), years	71.0 (38–90)	65.5 (49–78)
Sex, n (%)		
Women	33 (33.3)	1 (16.7)
Men	66 (66.7)	5 (83.3)
Race, n (%)		
White	77 (77.8)	6 (100.0)
Other or Unknown	22 (22.2)*	0
ECOG PS, n (%)		
0	72 (72.7)	3 (50.0)
1	27 (27.3)	3 (50.0)
Time since initial MCC diagnosis, median (range), months	4.7 (0.2–64.0)	15.4 (2.3–37.1)
Stage at current diagnosis, n (%)		
3	10 (10.1)	0
4	89 (89.9)	6 (100.0)
Visceral metastasis, n (%)	36 (36.4)	3 (50.0)
Liver metastasis, n (%)	8 (8.1)	2 (33.3)
Prior systemic therapy, n (%)	0	6 (100.0)
Prior radiotherapy, n (%)	36 (36.4)	3 (50.0)
Prior surgery, n (%)	67 (67.7)	5 (83.3)

*1 patient was of Asian race; 21 patients were of unknown race due to local reporting requirements; ECOG PS, Eastern Cooperative Oncology Group performance status; MCC, Merkel cell carcinoma.

Drug Exposure

- Median (range) number of retifanlimab 500 mg Q4W infusions was 6.0 (1–26)
- Median (range) duration of treatment was 169.0 (1–708) days

Antitumor Activity

- Primary efficacy results based on the full analysis set (chemotherapy-naïve patients with median 12 months of survival follow-up at data cutoff; N = 65) are summarized in Table 3
- The best percentage change from baseline in target lesion size among patients assessable for response is shown in Figure 1 and representative patient images in Figure 2

Table 3. Summary of Overall Response by ICR per RECIST v1.1 (Full Analysis Set)

Variable	Chemotherapy-Naïve (N = 65)
Objective response rate (95% CI), %	50.8 (38.1–63.4)
Best overall response, n (%)	
Complete response	11 (16.9)
Partial response	22 (33.8)
Stable disease	13 (20.0)
Progressive disease	13 (20.0)
Not evaluable*	6 (9.2)
Disease control rate, [†] n (%)	39 (60.0)
Median progression-free survival (95% CI), months	13.8 (7.4–NE)
Median overall survival (95% CI), months	NR (NE–NE)
Median duration of response [‡] (95% CI), months	NR (9.2–NE)

*Includes “Not assessed,” “Not evaluable,” and “Missing.” [†]Proportion of patients with a confirmed response or SD lasting ≥6 months. [‡]Median (range) duration of follow-up 7.5 (1.1–16.6) months. CI, confidence interval; ICR, independent central review; NE, not estimable; NR, not reached; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

Figure 1. Best Percentage Change From Baseline in Target Lesion Size (Sum of Diameters) for Individual Patients by ICR* (Full Analysis Set, N = 65)

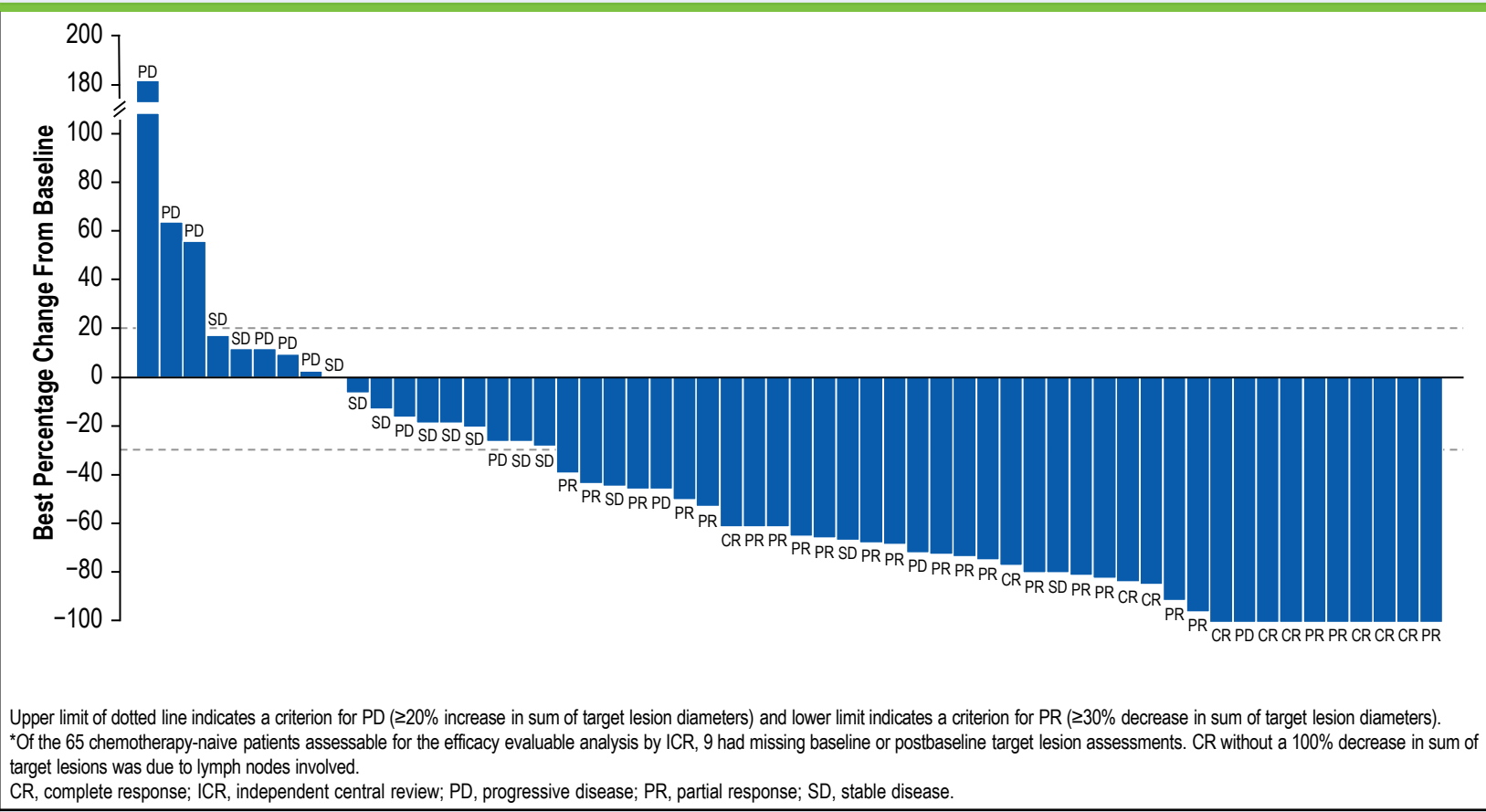


Figure 2. Response to Retifanlimab Was Rapid and Sustained in Both Skin and Visceral Tumors

Patient 1

- Prior resections and radiotherapy to primary tumor on left forearm
- PR achieved at 8-week scan following initiation of retifanlimab therapy
- Continues to respond as of DCO with DOR of 13.8 months

Baseline **Week 8** **Week 68**

Patient 2

- Target lesion in pelvis shown
- PR achieved at 8-week scan following initiation of retifanlimab therapy
- Continues to respond as of DCO with DOR of 13.0 months

Baseline **Week 8** **Week 64**

DCO, data cutoff; DOR, duration of response; PR, partial response.

- The duration of treatment and time point response of individual chemotherapy-naïve patients assessable for response are shown in Figure 3
- Median PFS was 13.8 (95% confidence interval, 7.4–not estimable) months (Figure 4); median DOR has not been reached

Figure 3. Duration of Treatment and Best Objective Responses by ICR* (Full Analysis Set; N = 65)

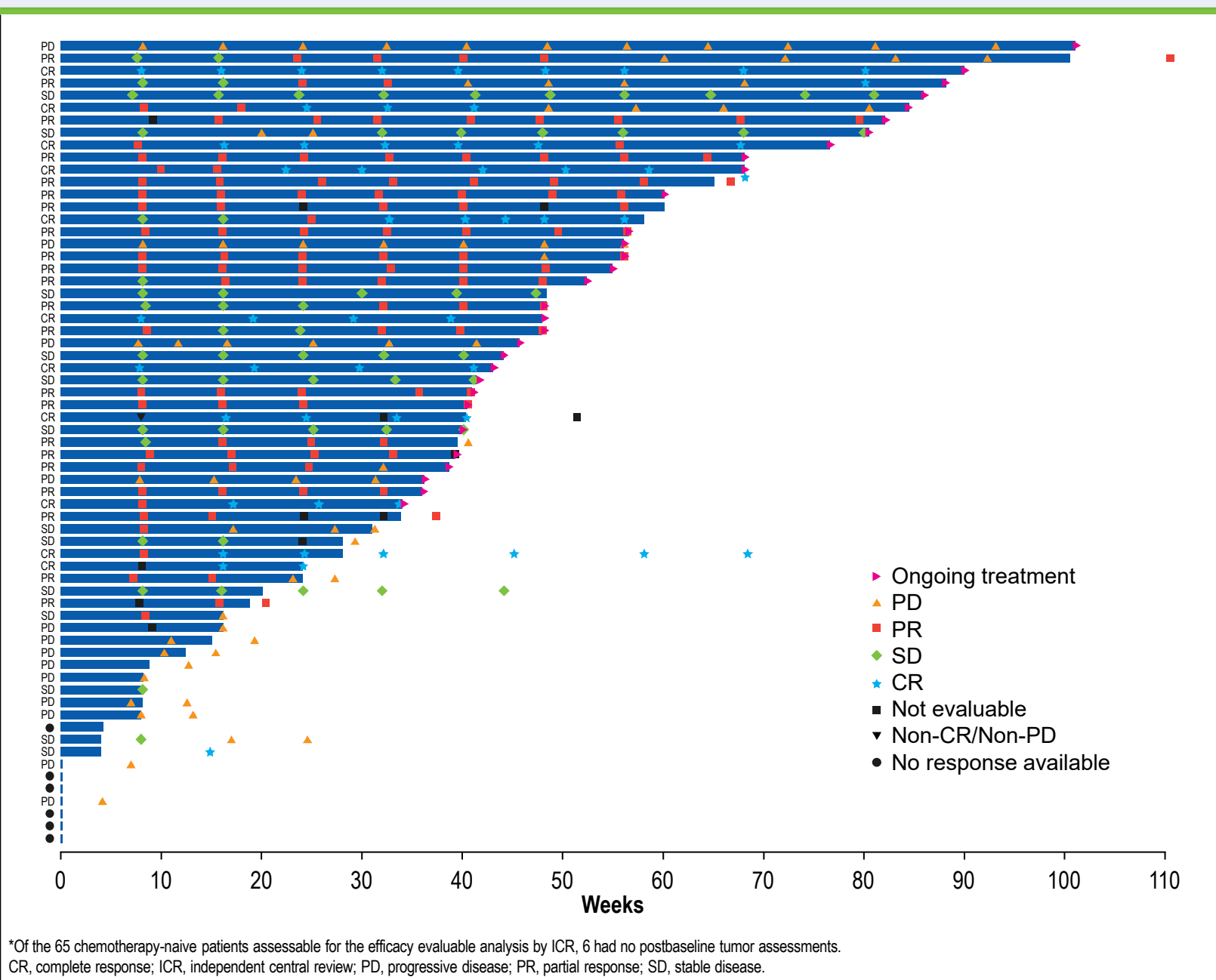
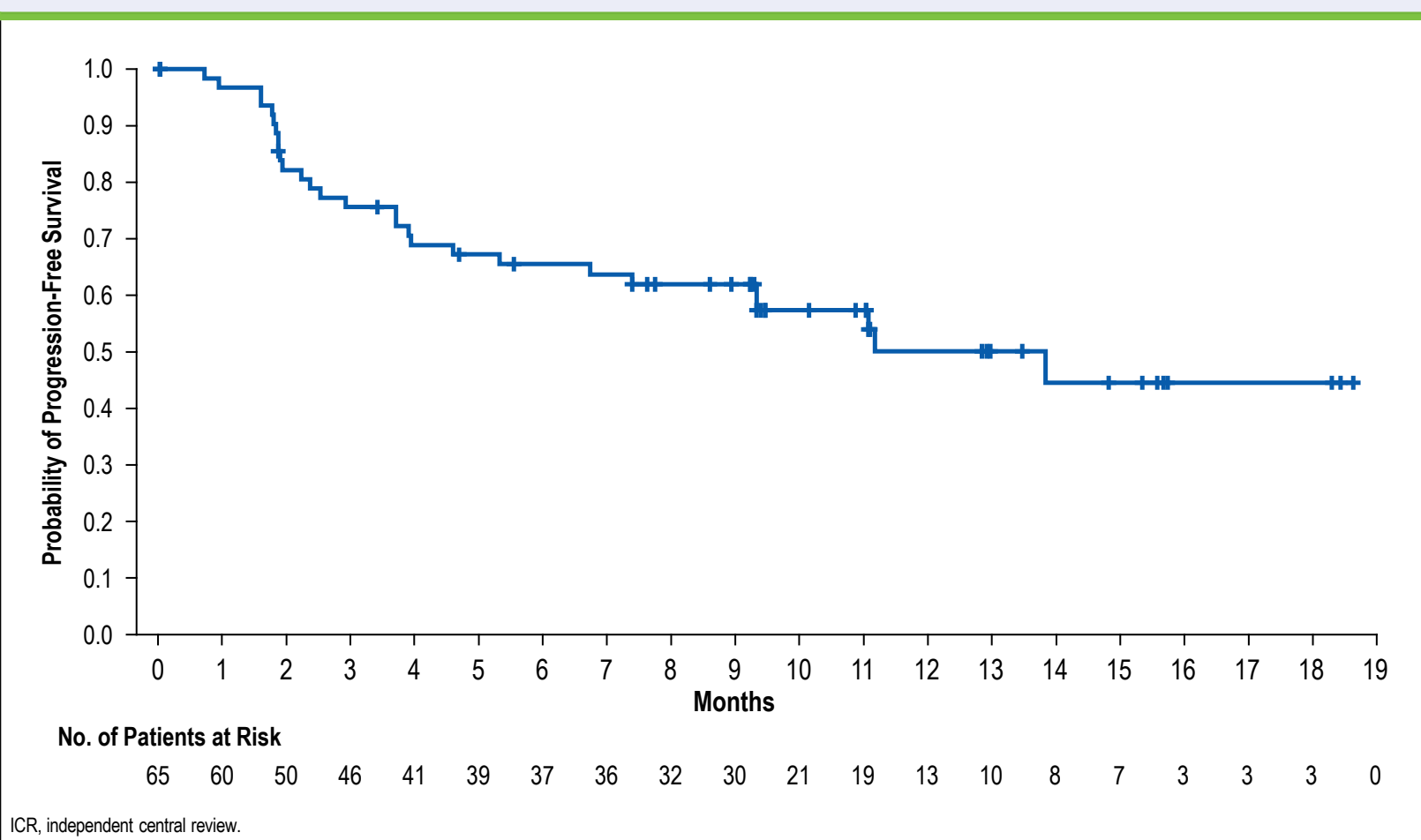


Figure 4. Kaplan-Meier Estimates of Progression-Free Survival by ICR (Full Analysis Set; N = 65)



Disclosures

Grignani: Honoraria – Bayer, Eisai, Eli Lilly and Company, Merck, Novartis, Pfizer, PharmaMar; Consulting or advisory role – Bayer, Eisai, Eli Lilly & Company, Novartis, Pfizer, PharmaMar; Research funding – Bayer, Novartis, PharmaMar. **Rutkowski:** Honoraria for lectures and advisory boards – Blueprint Medicines, Bristol Myers Squibb, Merck Serono, MSD, Novartis, Pierre Fabre, Sanofi; Institutional support – Pfizer. **Lebbé:** Honoraria – Bristol Myers Squibb, Merck Serono, MSD, Novartis, Pierre Fabre, Roche, Sanofi; Institutional support – Bristol Myers Squibb, MSD, Novartis, Pierre Fabre, Roche, Travel grants – Bristol Myers Squibb, Roche, Prinzi; Consultancies – Merck. **Grob:** Advisory board – Amgen, Bristol Myers Squibb, Merck, MSD, Novartis, Pfizer, Philogen, Pierre Fabre, Roche, Sanofi. **Tanda:** Nothing to disclose. **Guida:** Advisory role – Bristol Myers Squibb, MSD, Novartis, Pierre Fabre. **Burgess:** Research funding – Merck; Advisory board member – EMD Serono, Immune Design. **Pulini, Cornfeld, Tian:** Employment and stock ownership – Incyte Corporation. **Bhatia:** Advisory board/consultant (with honorarium) – Bristol Myers Squibb, Castle Biosciences, EMD Serono, Excure, Genentech, Sanofi-Genzyme; Research grants (to institution) – 4SC, Amphivena Therapeutics, Bristol Myers Squibb, Checkmate, EMD Serono, Excure, Immune Design, Incyte, Merck, NantKwest, Nektar, Novartis, OncoSec, Xenocr. Stock/equity – Moderna.

Acknowledgments

The authors wish to thank the patients and their families, the investigators, and the site personnel who participated in this study, and Xiaohan Xu and Sadhna Shankar (Incyte Corporation, Wilmington, DE) for their contribution to the study. This study was sponsored by Incyte Corporation. Medical writing assistance was provided by Matthew Bidgood, PhD, of Envision Pharma Group (Philadelphia, PA) and funded by Incyte Corporation.

¹Candiolo Cancer Institute, FPO-IRCCS, Candiolo (TO), Italy; ²Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; ³Université de Paris, Department of Dermatology and CIC, AP-HP Hôpital Saint-Louis, Paris, France; ⁴Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; ⁵Aix-Marseille University, AP-HM Timone, Marseille, France; ⁶IRCCS Ospedale Policlinico San Martino, Skin Cancer Unit, Genoa, Italy; ⁷Unit Melanoma and Rare Tumors, IRCCS Istituto Tumori Giovanni Paolo II, Bari, Italy; ⁸UPMC Hillman Cancer Center, Pittsburgh, PA, USA; ⁹Incyte Corporation, Wilmington, DE, USA; ¹⁰University of Washington, Seattle, WA, USA

Safety and Tolerability

- Grade ≥3 treatment-related TEAEs were reported in a total of 13 patients (12.4%)

Table 4. Summary of Adverse Events (Safety Evaluable Population)

Adverse Event, n (%)	Chemotherapy-Naïve (n = 99)	Chemotherapy-Refractory (n = 6)	Total (N = 105)
TEAEs (all grade, treatment-related and -unrelated)	77 (77.8)	4 (66.7)	81 (77.1)
Treatment-related TEAEs	55 (55.6)	4 (66.7)	59 (56.2)
Grade ≥3 TEAEs (treatment-related and -unrelated)	27 (27.3)	2 (33.3)	29 (27.6)
Grade ≥3 treatment-related TEAEs	12 (12.1)	1 (16.7)	13 (12.4)
Serious TEAEs (all grade, treatment-related and -unrelated)	21 (21.2)	2 (33.3)	23 (21.9)
Serious treatment-related TEAEs	8 (8.1)	1 (16.7)	9 (8.6)
TEAEs leading to discontinuation	10 (10.1) [†]	1 (16.7) [‡]	11 (10.5)
TEAEs leading to death	3 (3.0) [§]	0	3 (2.9)
Immune-related TEAEs*	25 (25.3)	2 (33.3)	27 (25.7)
Grade ≥3 immune-related TEAEs	8 (8.1)	1 (16.7)	9 (8.6)
Infusion reaction TEAEs*	4 (4.0)	0	4 (3.8)
Grade ≥3 infusion reaction TEAEs	1 (1.0)	0	1 (1.0)

*Immune-related TEAEs and infusion reaction TEAEs were identified programmatically. [†]Atel fibrillation, pancreatitis, asthenia, concomitant disease progression, infusion-related reaction, transamiasis increased, eosinophilic fasciitis, polyarthritides, demyelinating polyneuropathy, lung disorder. [‡]Dyslipidopathy. [§]Asthma, concomitant disease progression (CLL), acute respiratory failure, CLL, chronic lymphocytic leukemia; TEAE, treatment-emergent adverse event.

Table 5. Potential Immune-Related Adverse Events Occurring in ≥2 Patients (Safety Evaluable Population)*

Adverse Event, n (%)	Total (N = 105)	
	Any Grade	Grade ≥3
Hypothyroidism	8 (7.6)	0
Skin reactions [†]	6 (5.7)	1 (1.0)
Hyperthyroidism	5 (4.8)	0
Pneumonitis [‡]	5 (4.8)	2 (1.9)
Adrenal insufficiency	2 (1.9)	1 (1.0)
Colitis	2 (1.9)	0

Patients were counted once under the highest grade.

*Immune-related adverse events occurring in ≥2 patients: autoimmune thyroiditis, demyelinating polyneuropathy, diabetic ketoacidosis, eosinophilic fasciitis, hypopharyngitis, pancreatitis, polyarthritides, rhabdomyopathy. [†]Skin reactions includes the following MedDRA terms (patients may have had more than 1 term reported): bullous dermatitis (n = 1), maculopurpuric rash (n = 2), pruritus (n = 3), and rash (n = 2). [‡]Pneumonitis includes the following MedDRA terms: interstitial lung disease (n = 1), organizing pneumonia (n = 1), and pneumonitis (n = 3). MedDRA, Medical Dictionary for Regulatory Activities.

Conclusions

- Retifanlimab shows promising efficacy in advanced or metastatic MCC
 - ORR was 50.8% and median DOR was not reached with median survival follow-up of 12 months
- Retifanlimab was generally well tolerated with a safety profile that is representative of the PD-1 inhibitor class
 - Safety profile is favorable compared with historical data for chemotherapy
 - Q4W treatment schedule without need for premedications is less burdensome for patients
- Correlation of efficacy endpoints with biomarker such as PD-L1 and viral status is ongoing
- Retifanlimab is a potential new treatment option for patients with MCC
- This study is ongoing to further describe the efficacy in a larger patient population with MCC

References

1. Paulson KG, et al. *J Am Acad Dermatol*. 2018;78:457–63.e2.
2. Bavencio® (avelumab) [prescribing information]. Rockland, MA: EMD Serono, Inc; November 2020.
3. Opdivo (nivolumab) [prescribing information]. Princeton, NJ: Bristol Myers Squibb Company; August 2021.
4. Keytruda® (pembrolizumab) [prescribing information]. Whitehouse Station, NJ: Merck & Co, Inc; August 2021.
5. NCCN clinical practice guidelines: Merkel cell carcinoma. Version 1.2021. February 18, 2021.
6. D'Angelo SP, et al. *J ImmunoTher Cancer*. 2021;9:e02646.
7. Nghiem PT, et al. *J ImmunoTher Cancer*. 2021;9:e02478.
8. Lakhani N, et al. *J ImmunoTher Cancer*. 2017;5:87. Abstract P249.
9. Mehner JM, et al. *J ImmunoTher Cancer*. 2018;6:115. Abstract P669.
10. Mehner JM, et al. *J ImmunoTher Cancer*. 2019;7:282. Abstract P394.
11. Chen X, et al. *Cancer Res*. 2019;79. Abstract LB268.
12. Condamine T, et al. *Cancer Res*. 2019;79. Abstract CT085.
13. Rao S, et al. *Ann Oncol*. 2020;31. Abstract LBA42.
14. Berton-Rigaud D, et al. *J ImmunoTher Cancer*. 2020;8. Abstract A268.
15. Grignani G, et al. *Ann Oncol*. 2020;31. Abstract 1089P.
16. Maio M, et al. *J Clin Oncol*. 2021;39. Abstract 2571.



Scan code to download a copy of this poster