undergoing immunosuppressive therapy did seroconvert. Our findings reported here do not provide evidence to warrant holding or altering immunotherapy regimens before vaccination with a messenger RNA—based vaccine or other vaccine strategies that preclude the potential for viral replication, although additional studies are necessary to investigate vaccination strategies in immunosuppressed patients.

Jeffrey S. Smith, MD, PhD, a,b,c,d,e Jordan T. Said, BA, a,e Scott A. Elman, MD, a,b,c,d,e Claire E. P. Smith, MD, and Joseph F. Merola, MD, MMSca,e

From the Departments of Dermatology at Brigham and Women's Hospital, <sup>a</sup> Massachussetts General Hospital, <sup>b</sup> and Beth Israel Deaconess Medical Center, <sup>c</sup> the Dermatology Program at Boston Children's Hospital, <sup>d</sup> Harvard Medical School, <sup>e</sup> and the Division of Hematology and Oncology, <sup>f</sup> Boston Medical Center, Boston, Massachusetts.

Authors Smith and Said contributed equally to this article.

Funding sources: None.

IRB approval status: Approved by the Massachusetts General Brigham IRB (protocol 2020P003006).

Reprint requests: Joseph F. Merola, MD, MMSc, Brigham and Women's Hospital, 41 Avenue Louis Pasteur, Rm 319, Boston, MA 02115

E-mail: jfmerola@bwb.harvard.edu

### Conflicts of interest

Dr Merola is a consultant or investigator for Merck, Abbvie, Dermavant, Eli Lilly, Novartis, Janssen, UCB, Celgene, Sanofi, Regeneron, Arena, Sun Pharma, Biogen, Pfizer, EMD Sorono, Avotres, and Leo Pharma.

#### REFERENCES

- Freites Nunez DD, Leon L, Mucientes A, et al. Risk factors for hospital admissions related to COVID-19 in patients with autoimmune inflammatory rheumatic diseases. *Ann Rheum Dis*. 2020;79:1393-1399.
- Zahedi Niaki O, Anadkat MJ, Chen ST, et al. Navigating immunosuppression in a pandemic: a guide for the dermatologist from the COVID task force of the Medical Dermatology Society and Society of Dermatology Hospitalists. J Am Acad Dermatol. 2020;83:1150-1159.
- Kimby E. Tolerability and safety of rituximab (MabThera). Cancer Treat Rev. 2005;31:456-473.
- Long QX, Liu BZ, Deng HJ, et al. Antibody responses to SARS-CoV-2 in patients with COVID-19. Nat Med. 2020;26: 845-848.
- Wolfel R, Corman VM, Guggemos W, et al. Virological assessment of hospitalized patients with COVID-2019. *Nature*. 2020;581:465-469.

## COVID-19 in melanoma patients: Results of the Spanish Melanoma Group Registry, GRAVID study



To the Editor: The COVID-19 pandemic, which has produced devastating effects on the health care system, has also affected the care of melanoma patients. During the first months of the pandemic, several studies from China pointed out that cancer patients infected with SARS-CoV-2 had a higher risk of complications.<sup>1,2</sup> In particular, there were concerns as to whether anti-cancer drugs might increase the aggressiveness of the infection. Conversely, some recent studies from western countries have found no association between mortality and cancer treatment.<sup>3,4</sup> Although an increased risk of death in patients with a cancer diagnosis is suggested, it is not fully confirmed.<sup>3-5</sup> Most studies have included a limited number of melanoma patients (Supplemental Table I available via Mendeley at 10.17632/5b8h5hszdg.1).<sup>3-5</sup>

The Spanish Melanoma Group (GEM) started a national registry of melanoma patients infected with SARS-CoV-2 in Spain (Supplemental Fig 4). Here, we present data from the first 70 patients entered between April 1 and June 8, 2020. Thirty-nine (56%) patients had stage IV melanoma, 8 (11%) had stage III, 10 (14%) had stage II, and 14 (20%) had stage I. Thirty-six (51%) patients were undergoing active anti-cancer treatment, including 22 (31%) patients treated with anti-PD-1 antibodies and 14 (20%) with BRAF plus MEK inhibitors. Thirty-eight (54%) patients had no evidence of active tumor (no macroscopic disease). According to the Response Evaluation Criteria in Solid Tumors (RECIST) guideline, version 1.1, there were 20 (29%) patients with stable disease or tumor response and 12 (17%) with tumor progression as their best radiological response. In terms of the clinical severity of the infection, 20 (29%) patients were asymptomatic or had mild symptoms, 12 (17%) had moderate symptoms, 18 (26%) developed severe symptoms, and 20 (28%) had critical complications (Table I, Supplemental Fig 5).

At the time of data cutoff, the infection had resolved in 37 (63%) patients, 8 (13%) had died due to melanoma, and 14 (24%) had died due to COVID-19. There were no significant differences in the clinical severity of the infection according to melanoma therapy. Severe or critical symptoms developed in 58% of patients who were in treatment with immunotherapy, 57% of patients who were in treatment with antitumoral BRAF plus MEK inhibitors, and 53% of patients who were not

Table I. Baseline characteristics of COVID-19 infected melanoma patients according to melanoma treatment

Characteristics	Total (N = 70)	Anti-PD-1 (N = 22) (31%)	BRAF/MEKi (N = 14) (20%)	No treatment* (N = 34) (49%)
Age, y				
Median (range)	68 (6-95)	68 (50-95)	56 (6-91)	71 (48-85)
Sex, n (%)				
Male	47 (67)	13 (59)	8 (57)	26 (76)
Melanoma stage, n (%)				
I	14 (20)	0	0	14 (41)
II	10 (14)	1 (4)	0	9 (26)
III	7 (10)	3 (14)	2 (12)	2 (6)
IV	39 (56)	18 (82)	12 (86)	9 (26)
Clinical management, n (%)				
Outpatient	21 (30)	5 (23)	4 (28)	12 (35)
Hospitalized	49 (70)	17 (77)	10 (71)	22 (65)
ICU	4 (6)	3 (14)	1 (7)	0 (0)
COVID-19 severity, n (%)				
Asymptomatic/Mild	20 (28)	5 (23)	6 (43)	9 (26)
Moderate	12 (17)	5 (23)	0 (0)	7 (21)
Severe	18 (26)	6 (28)	5 (36)	7 (21)
Critical	20 (29)	6 (28)	3 (21)	11 (32)
COVID-19 evolution, n (%)	59 <sup>†</sup> (100)	18	12	29
Resolved	37 (63)	10 (56)	8 (66)	19 (65)
Exitus by COVID-19	14 (21)	4 (22)	2 (17)	8 (28)
Exitus by melanoma	8 (13)	4 (22)	2 (17)	2 (7)

Anti-PD-1, Therapeutic anti-PD-1 antibody; BRAF/MEKi, BRAF inhibitors combined with MEK inhibitors drugs; ICU, intensive care unit; N, number of patients.

receiving any active antitumoral therapy (P=.427) (Table I). The COVID-19 mortality rate was 22%, 17%, and 27% for patients with immunotherapy, targeted drug treatment, and no systemic cancer treatment, respectively (P=.787) (Table I, Supplemental Fig 1, and Supplemental Tables II and III).

Univariate analysis showed that age over 60 years and previous cardiovascular disorders increased the probability of developing severe or critical infection (odds ratio [OR] 4.25, 95% confidence interval [CI], 1.50-12.07, and OR 4.46, 95% CI, 1.13-17.58, respectively) and death (OR 11.37, 95% CI, 1.37-94.41, and OR 4.87, 95% CI, 1.25-19.06, respectively). The effect of tumor stage, melanoma treatment, and cancer control were not significant factors for the risk of developing a critical or severe COVID-19 infection or death (Fig 1 and Supplemental Figs 2 and 3). Although this analysis included a low number of cases and we cannot exclude an unintended selection bias, in our data analyses, tumor stage, active tumor, and melanoma therapies did not have a relevant impact on COVID-19 evolution.

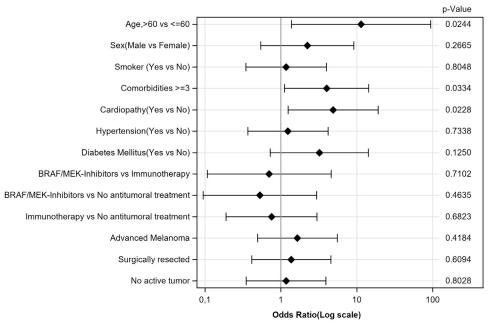
The authors thank Stephanie Davis for writing assistance.

Maria Gonzalez-Cao, MD, PbD, a Cristina Carrera, MD, b Juan Francisco Rodriguez Moreno, MD, c Rodríguez-Jiménez, MD, d Mónica Antonanzas Basa, MD, Rosa Feltes Ochoa, MD, Teresa Puertolas, MD, Eva Muñoz-Couselo, MD, b,i José Luis Manzano, MD, Ivan Marauez-Rodas, MD, luan Martin-Liberal, MD, lainara Soria, MD, <sup>m</sup> Pilar Lopez Criado, MD, <sup>n</sup> Almudena Garcia-Castaño, MD, Aram Boada, MD, Pablo Ayala de Miguel,  $MD_{,}^{q}$  Susana Puig,  $MD_{,}^{b}$ Guillermo Crespo, MD, Pablo Luna Fra, MD, S Cristina Aguayo Zamora, MD, Marta Feito Rodríguez, MD, Lara Valles, MD, Ana Drozdowskyj, PhD, a Cayetana Maldonado-Seral, MD, <sup>v</sup> Jesús Gardeazabal, MD, <sup>w</sup> Laura Villalobos, MD, Rafael Rosell, MD, Luis Antonio Fernandez-Morales, MD, Alberto Rodrigo, MD, aa Santiago Viteri, MD, Mariano Provencio, MD, bb and Alfonso Berrocal, MD<sup>cc</sup> for the Spanish Melanoma Group (GEM)

From the Translational Cancer Research Unit, Instituto Oncologico Dr Rosell, Dexeus University Hospital, Barcelona, Spain, Dermatology Department, Melanoma Group IDIBAPS, Hospital Clinic, University of Barcelona, Centro de Investigación Biomédica en Red de

<sup>\*</sup>No treatment, patients who were not in active antitumoral treatment defined as time from the last antitumor treatment at least 8 weeks. <sup>†</sup>Covid-19 evolution is reported from 59 patients, indicating that COVID-19 either was resolved or those patients died.

## Risk of death due to COVID19



## Odds Ratios with 95% Wald Confidence Limits

Fig 1. OR Plot showing effect on COVID-19 mortality. OR plot showing effect on COVID-19 mortality. Age over 60 years old and previous cardiovascular disorders increased risk of death due to COVID-19 (OR 11.37, 95% CI 1.37-94.41, P = .024 and OR 4.87, 95% CI 1.25-19.06, P = .022, respectively). Patients with 3 or more co-morbidities had higher risk of death due to COVID-19 (OR 4.00, 95% CI 1.12-14.35, P = .033). Previous diagnose of hypertension or diabetes mellitus did not increased the risk of death (OR 1.24, 95% CI 0.37-4.18, P = .734 and OR 3.20, 95% CI 0.72-14.15, P = .125, respectively). The effect of sex and smoking status were not significant factor for the risk of death due to COVID-19 (OR 2.23, 95% CI 0.54-9.13, P = .266and OR 1.17, 95% CI 0.34-3.96, P = .805, respectively). BRAF plus MEK inhibitors combination did not increase the mortality risk by COVID-19 (OR 0.53, 95% CI 0.09-2.94, P = .463). Immunotherapy treatment did not increase the risk of death by COVID-19 (OR 0.75, 95% CI 0.19-2.97, P = .682). The effect of advanced stage was not a significant factor for the risk of death by COVID-19 (OR 0.61, 95% CI 0.18-2.03, P = .4184). The effect of a previous melanoma complete surgical resection was not a significant factor for the risk of death due to COVID-19 infection (OR 1.37, 95% CI 0.41-4.56, P = .609). ORs with 95% Wald confidence limits. CI, Confidence interval; OR, odds ratio.

Enfermedades Raras (CIBERER) Spain, b Medical Oncology Department, Centro Integral Oncologico HM Clara Campal, Madrid, Spain, c Dermatology Department, Hospital Universitario La Princesa, Madrid, Spain, d Medical Oncology Department, Hospital Clinico San Carlos, Madrid, Spain, e Hospital Universitario La Paz, Madrid, Spain, Medical Oncology Department, Hospital Universitario Miguel Servet, Zaragoza, Spain,<sup>g</sup> Medical Oncology Department, Hospital Universitari Vall d'Hebron, Barcelona, Spain, b Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain, Catalonian Institute of Oncology (ICO-Badalona), Medical Oncology Department, Germans Trias i Pujol Research Institute and Hospital (IGTP), Badalona,

Barcelona, Spain, Medical Oncology Department, Hospital General Universitario Gregorio Marañon and CIBERONC, Madrid, Spain, k Medical Oncology Department, Catalan Institute of Oncology (ICO) Hospitalet, Barcelona, Spain, Medical Oncology Department, Hospital Ramon y Cajal, Madrid, Spain,<sup>m</sup> Medical Oncology Department, Hospital MD Anderson, Madrid, Spain, Medical Oncology Department, Hospital Marqués de Valdecilla, Santander, Spain,º Dermatology Department, Hospital Germans Trias i Pujol Research Institute and Hospital (IGTP), Badalona, Barcelona, Spain, Medical Oncology Department, Hospital San Pedro de Alcántara, Cáceres, Spain, Medical Oncology Department, Hospital Universitario de Burgos,

Burgos, Spain, Medical Oncology Department, Hospital Son Espases, Mallorca, Spain, Medical Oncology Department, Hospital Universitario Infanta Sofia, Madrid, Spain, Medical Oncology Department, Hospital General de Villalba, Madrid, Spain, <sup>u</sup> Medical Oncology Department, Hospital Universitario Central de Asturias, Oviedo, Spain, Medical Oncology Department, Hospital de Cruces, Bizkaya, Spain, W Medical Oncology Department, Hospital Principe de Asturias, Alcala de Henares, Spain, \* Germans Trias i Pujol Research Institute and Hospital (IGTP), Badalona, Spain, Medical Oncology Department, Hospital Parc Tauli, Sabadell, Spain, Medical Oncology Department, Hospital Arnau de Vilanova, Lleida, Spain, aa Medical Oncology Department, Hospital Puerta de Hierro, Madrid, Spain, bb and Medical Oncology Department, Hospital Universitario General de Valencia, Valencia, Spain.cc

Funding sources: This study has been funded by Spanish Melanoma Group. It has not been sponsored by any pharmaceutical company.

IRB approval status: Reviewed and approved by the Ethics Committee of the Hospital Puerta del Hierro, Madrid (Exp. 6/2020).

Reprints not available from the authors.

Correspondence to: Maria Gonzalez-Cao, MD, PhD, Translational Cancer Research Unit, Instituto Oncologico Dr Rosell, Dexeus University Hospital, C/Sabino Arana, 5, 080028 Barcelona, Spain

E-mail: mgonzalezcao@oncorosell.com

#### Conflicts of interest

None disclosed.

#### REFERENCES

- Zhang L, Zhu F, Xie L, et al. Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China. Ann Oncol. 2020;31(7): 894-901.
- Dai M, Liu D, Liu M, et al. Patients with cancer appear more vulnerable to SARS-CoV-2: a multicenter study during the COVID-19 outbreak. *Cancer Discov.* 2020;10(6):783-791.
- Lee LYW, Cazier JB, Angelis V, et al. COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. *Lancet*. 2020; 395(10241):1919-1926.
- **4.** Kuderer NM, Choueiri TK, Shah DP, et al. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. *Lancet*. 2020;395(10241):1907-1918.
- Mehta V, Goel S, Kabarriti R, et al. Case fatality rate of cancer patients with COVID-19 in a New York Hospital System. Cancer Discov. 2020;10(7):935-941.

# Fitzpatrick phototype disparities in identification of cutaneous malignancies by Google Reverse Image



To the Editor: Many US adults seek health information online, with a high volume of searches for cutaneous malignancies. Because many dermatologic conditions are visually apparent, patients may use image-based search tools, such as Google Reverse Image (GRI), to augment text searches, potentially affecting use of health care services or patient-physician relationships. We previously found that GRI showed moderate diagnostic frequency but limited accuracy for cutaneous neoplasms. However, such modalities may be even less efficacious in skin of color. We thus studied the effects of skin color on GRI accuracy in the identification of cutaneous neoplasms.

Basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and melanoma images from published dermatology textbooks (Table I) were categorized by 2 investigators as Fitzpatrick phototype (FP) I to III or IV to VI, with FP IV to VI representing skin of color. Equal numbers of BCC, SCC, and melanoma subtypes between FP groups were selected. Images with poor quality, absent subtype information, or discordant FP classifications were excluded. Twenty-five images per neoplasm and FP group were entered into GRI with the text prompt "skin" or "nail" to improve accuracy and relevance.<sup>3</sup> Diagnostic frequency was calculated as the percentage of images with at least 1 accurate diagnosis in the top 10 search results. Diagnostic accuracy and melanoma false positive rates were calculated as the proportion of the top 10 visually similar image results with the correct diagnosis or misdiagnosis as melanoma, respectively. Statistical significance was calculated using t tests in SAS, version 9.4 (SAS Institute, Cary, NC).

The diagnostic frequencies for BCC and SCC were significantly lower for FP IV to VI compared to FP I to III (Table II). Diagnostic accuracy was significantly lower, and melanoma false positive rates were significantly higher, in FP IV to VI for all neoplasms. BCC had the largest difference in accuracy (0.072 vs 0.232; P < .001) and melanoma false positive rate (0.268 vs 0.112; P = .004) between FP groups.

Our findings support the hypothesis that GRI performs more poorly for dermatologic queries in skin of color. This discrepancy may reflect insufficient availability of FP IV to VI images in GRI's database, leading to misinterpretation of features unique to this group by GRI's classification