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### COVID-19 vaccination: possible short-term exacerbations of oral mucosal diseases

Dear Editor,

The coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, has become a global pandemic burden with extreme health, social, and economic implications.<sup>1</sup> With the rapid development and release of vaccinations against the virus, questions have been raised in regard to unforeseen effects, which may have impacted patients' willingness to receive the vaccine.<sup>2</sup>

There are currently three vaccines authorized by the United States Food and Drug Administration (FDA) for emergency use and recommended to prevent severe illness: Pfizer/BioNTech (BNT162b2), Moderna (mRNA-1273), and Johnson & Johnson (JNJ-78436735).<sup>1</sup> The Pfizer/BioNTech and Moderna vaccines are mRNA vaccines, while the Johnson & Johnson vaccine is a viral vector vaccine. Both mRNA and viral vector vaccines are shown to upregulate T-cell-mediated immunity.<sup>3</sup> In clinical trials, it was noted that the Pfizer/BioNTech vaccine elicited a robust CD8<sup>+</sup> and T helper type 1 (Th1) CD4<sup>+</sup> cell response, with higher serum levels of IL-2, TNF- $\alpha$ , and IFN- $\gamma$ .<sup>4</sup> Studies from animal models investigating the Moderna vaccine revealed benefits of using the mRNA-based vaccine, including T-cell responses characterized by increasing levels of IFN- $\gamma$ .<sup>3</sup> Consequently, administration of vaccines could lead to a surge in conditions mediated by similar processes and inflammatory markers.<sup>5</sup>

Patients with a diagnosis of oral lichen planus may experience a flare in their condition after the administration of the vaccine. As oral lichen planus is a T-cell-mediated chronic inflammatory condition of unknown etiology, the inflammatory markers involved with immune response to the administration of the vaccine mirror those involved in the disease process itself.<sup>4</sup> Patients with other autoimmune or immune-mediated conditions, such as mucous membrane pemphigoid, bullous pemphigoid, pemphigus vulgaris, chronic ulcerative stomatitis, and lichen planus pemphigoides, among others, may experience an increase in their clinical manifestations and symptoms.

Many of our patients reported an increase in their oral mucosal disease symptoms shortly after vaccination, which may or may not have been directly related to the administration of the vaccine. The symptoms quickly resolved within 2–4 weeks, and the patient returned to their baseline disease expression. A 65-year-old female patient with multifocal lichen planus was asymptomatic and did not endorse any active skin or oral lesions. Past medical history was significant for hyperlipidemia. Medications included rosuvastatin and vitamin D supplementation. The patient had routine surveillance appointments with no disease expression noted on follow-up. Immediately following the administration of the COVID-19 vaccination, the patient experienced a flare-up of her oral lichen planus symptoms with increased soreness and inflammation in her left buccal mucosa. Approximately 3 weeks after her flare-up, her disease expression regressed to baseline, and she no longer endorsed any symptoms.

Although the vaccine may exacerbate symptoms of existing conditions in the short term, these can be managed appropriately and should not deter patients from receiving the first available vaccine, as vaccination reduces COVID-19-related morbidity and mortality.<sup>5</sup> At this time, there is no definitive evidence of long-term adverse effects against chronic mucosal diseases, but as healthcare professionals, we should be aware of this possibility and counsel our patients accordingly.

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### COVID-19-related consequences on melanoma diagnoses from a local Italian registry in Genoa, Italy

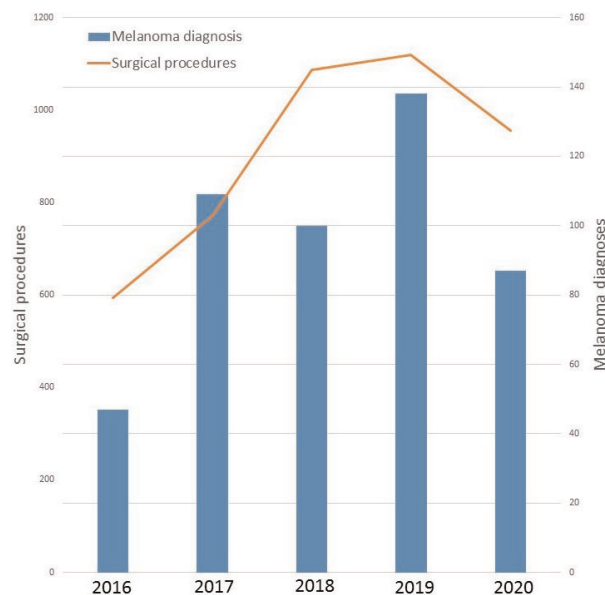
Dear Editor,

We read with interest the article of Valenti *et al.*<sup>1</sup> about the impact on skin cancer progression and prognosis due to the COVID-19 pandemic. The study reported a mean of approximately 6.2 months delay between the last follow-up visit. The excised tumor rate was higher between May 18 and November 18 in 2020 compared with the same period in 2019 (54 advanced skin cancers vs. 22, respectively). The number of surgical excisions was 280 (in 2020) versus 265 (from the same period in 2019) with eight advanced melanomas (in 2020) and four melanomas (in 2019).

We would like to focus on the impact of lockdown in Italy (from March 9, 2020, to May 18, 2020) and the COVID-19 emergency on melanoma prevention and diagnosis in 2020. Data from our institution (local referral center for skin cancers) comparing the period of time from January 1, 2019, to December 31, 2019, versus January 1, 2020, to December 31, 2020, showed an overall reduction of outpatients visits (20,384 vs. 11,374; –44%) and follow-up visits of melanoma patients with digital dermoscopy (956 vs. 619; –35%); therefore, a reduction of surgical procedures for skin cancers (1,120 vs. 956; –14%) and last melanoma diagnoses (138 vs. 87; –37%). Regarding melanoma thickness, the reduction was observed in both melanomas with <0.8 mm Breslow thickness (97 vs. 64; –33%) and T1b or with >0.8 mm Breslow index (41 vs. 23; –43%) and consequently of sentinel lymph node biopsies (SLNB; 36 vs. 18; –50%). From 2016 to 2019, we observed an increase in melanoma diagnoses and surgical procedures with subsequent pause in the trend in 2020 (Fig. 1).

A recent survey by IMI (Italian Melanoma Intergroup) reported that dermatological visits in 2020 underwent a significant reduction (–53%) from 7,732 (January 1, 2019–December 31, 2019) to 3,645 (January 1, 2020–December 31, 2020).

During the lockdown period in Italy, only dermatological first aid or follow-up visits under biologic treatment and urgent dermato-surgical procedures were guaranteed. Therefore, in most of the dermatology centers in Northern Italy, a significant reduction in surgical procedures and in the diagnosis of melanoma was observed (Table 1).<sup>2,3</sup> Barruscotti *et al.*<sup>2</sup> reported



**Figure 1** Melanoma diagnosis and surgical procedures from 2016 to 2020 in Galliera Hospital, Genoa, Italy

163 surgical excisions during the lockdown period in 2020 in comparison to 246 and 221 during the same period in 2019 and 2018, respectively. The total number of melanoma diagnoses was 6/163 in 2020 versus 24/246 in 2019. A similar situation has been reported by Longo *et al.*<sup>4</sup> with a reduction of new melanoma diagnoses from January 1, 2019, to May 9, 2019, (141 in Rome and 115 in Reggio Emilia) and the same timeframe in 2020 (62 in Rome and 28 in Reggio Emilia).<sup>4</sup> Filoni *et al.* observed a decrease of dermatological follow-up visits during the lockdown period (–30.2%) but with a total number of melanoma diagnoses almost unchanged (64 cases in 2020 and 66 in 2019; –3%).<sup>5</sup>

As a logical consequence of the reduced melanoma diagnosis, also SLNB in 2020 decreased in some institutions, as observed by Filoni *et al.* and in our department.<sup>5</sup> In contrast, data reported by IMI show a slight increase in SLNB but are referred only to February–April 2020, not to all of 2020.

In conclusion, the COVID-19 pandemic had a severe impact on melanoma patients. Restriction imposed by the pandemic with limitations to access to dermatological departments forced patients to postpone visits with consequent delay in diagnosis. Particularly, the reduction observed in SLNB shows that high-risk melanoma patients were significantly affected.

The COVID-19 pandemic must become a lesson for healthcare providers and politicians, and future pandemics must be better managed. Teledermatology and teledermoscopy represent a valid alternative to face-to-face visits but still have to be implemented in routine work in Italy.