# Lefter to the Editor

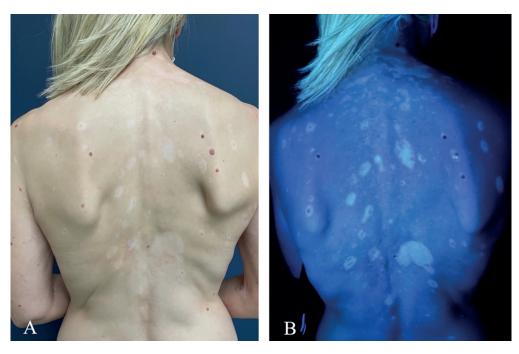
# The unexpected regression of melanocytic naevi

Dear Editor,

The advent of Immune Checkpoint Inhibitors (ICIs) as a standard of care for several cancers has changed the therapeutic approach to these conditions<sup>1</sup>. Within the class, Nivolumab is a human IgG<sup>4</sup> monoclonal antibody directed against the programmed cell death 1 (PD-1) receptor found on the surface of T cells<sup>2</sup>, that has been approved as monotherapy or in combination with other drugs in the treatment of patients with metastatic cutaneous melanoma, head and neck squamous cell carcinoma, renal cell carcinoma, lung cancer and other advance malignancies<sup>3-5</sup>.

Recently, a 52-year-old woman who had undergone resection of a stage III cutaneous melanoma of her back 10 years earlier, came to our department in November 2021 for regular follow-up. She was being treated with nivolumab since 2019 due to the extensive metastasizing in bilateral lung parenchyma, celiac trunk lymph nodes, bilateral ilo-mediastinal recesses and right cardiophrenic angle. After 2 years on nivolumab therapy, Positron Emission Tomography (PET) showed a stable remission of the disease.

During the treatment, the patient noticed fading and disappearance of cutaneous naevi of the trunk. Physical examination, supported by Wood's light, showed a marked depigmentation of almost all her benign melanocytic naevi associated with vitiligo-like areas and halo-like reactions (Figure 1A-B). Pre-existing familial and personal autoimmune disorders were excluded as well as history of vitiligo.



**Figure 1.** A, Vitiligo-like lesions with halo phenomenon of the trunk; **B,** Notable is the regression of multiple melanocytic naevi. Wood's light emphasizes vitiligo that surrounds the residual pigmented lesions.

ICIs-related skin toxicity is a well-established phenomenon, presenting with several conditions<sup>2,3</sup>. Among these, it is estimated that the risk of development of vitiligo is 10-fold higher in patients with melanoma, compared to general population. One of the main explanations is the immune activation against melanoma-associated antigens expressed by normal melanocytes because of a cross-reaction from melanoma cells that share the same antigens<sup>3,6,7</sup>. Given that PD-L1 can be expressed by melanocytes of benign melanocytic naevi, the blockade of this pathway could potentially affect the evolution of these lesions.

#### Conflict of Interest

The Authors declare that they have no conflict of interests.

#### **Ethics Approval**

All the investigators ensure that the study has been conducted according with the Declaration of Helsinki Guidelines. No local ethic committee approval was needed.

# **Informed Consent**

Written consent to image recording for academic purposes was obtained.

#### Availability of Data and Material

The study data are available at our University Hospital archive.

#### **Authors' Contributions**

Conceptualization, methodology and writing — original draft preparation (L.M.), data collection (A.M., R.T.), writing — review & editing and supervision (C.G.). All authors have read and agreed to the published version of the manuscript.

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