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Ixekizumab for the treatment of erythrodermic psoriasis triggered by durvalumab-tremelimumab in a cancer patient

Tremelimumab and durvalumab are monoclonal antibodies that stimulate the immune system to detect and destroy cancer cells. Tremelimumab acts against cytotoxic T-lymphocyte associated protein 4 (CTLA-4) and durvalumab targets programmed death-ligand 1 (PDL1) [1]. We present a 55-year-old man with advanced medullary thyroid carcinoma (pT3, pN1, RET mutation) who developed erythrodermic psoriasis following treatment with durvalumab and tremelimumab, treated successfully with ixekizumab. The patient had a long history of mild psoriasis. In April 2019, 10 days after having started durvalumab-tremelimumab, he developed mild generalized erythema and desquamation. Three months later, the immunotherapy was discontinued because of progression of the medullary carcinoma. Despite this, the skin symptoms worsened, coinciding with the tapered withdrawal of an oral corticosteroid regimen that was initially prescribed by the oncologist to control the skin eruption. At this time, the patient presented with erythematous desquamative plaques with elevated edges and onychodystrophy of all nails. Histology revealed focal epidermal parakeratosis, marked interphase damage, and isolated necrotic keratinocytes.

Two months later, within a setting of continued neoplastic progression, the patient was referred to the oncology department for a third line of therapy. Physical examination revealed erythematous-desquamative and hyperkeratotic plaques, covering 70% of the body surface, palmoplantar involvement, nail dystrophy with oil drop discolouration, mild subungual hyperkeratosis and scalp desquamation. This was compatible with a clinical picture of psoriasis (Psoriasis Area and Severity Index score [PASI] of 30.6 and Body Surface Area [BSA] of 68) (*figure 1*) that precluded the resumption of immunotherapy. Treatment with ixekizumab was proposed because the patient's skin condition had previously failed to respond to conventional therapies (corticosteroids and acitretin) and there was a need for a rapid response. After three months of treatment using the regular induction dose, the patient achieved complete remission (PASI 0, BSA 0). Examination of the skin revealed generalized confluent achromic macules distributed predominantly on the trunk. Histology demonstrated an absence of melanocytes, a finding consistent with immune-mediated vitiligo. Resolution of the skin lesions

Figure 1. **A)** Physical examination before starting ixekizumab showing psoriasis-like erythroderma: erythematous-desquamative and hyperkeratotic plaques cover 70% of body surface, leaving small patches of unaffected skin. **B)** Control after three months of ixekizumab: the patient shows complete remission of psoriasis-like lesions (PASI 0), but there are new achromic macules with a confetti-like distribution all over the trunk.

allowed the patient to follow a new experimental treatment for his underlying cancer, which is currently in remission. Ixekizumab was discontinued once the psoriasis cleared, and nine months later, the patient was still free of lesions. Cutaneous manifestations are common in patients treated with anti-PDL1, anti-PD1 and anti-CTLA4 drugs [2, 3]. Of note, among these are erythematous macular eruptions and generalized pruritus; vitiligo is also a frequent effect, presenting with a generalized distribution favouring the trunk [3]. While some cases have been described in the literature, psoriasis (whether *de novo* or occurring on previous psoriasis) is an uncommon adverse effect [4-8]. Histological

findings may, as in the present case, indicate a combination of traits indicative of psoriasis and toxicoderma [7, 8]. In most of these patients, the lesions can be controlled with topical therapy [4-6, 8]. In the present case, however, the skin condition not only worsened when the anticancer therapy was stopped (perhaps because cessation coincided with the withdrawal of oral corticosteroids) but also prevented the use of alternative therapies to halt tumour progression. Ixekizumab is an anti-IL-17A drug approved for the treatment of moderate-to-severe plaque psoriasis. It is highly effective and produces a rapid clinical response, achieving a 75-90% reduction in PASI score in 70-90% of patients at 12 weeks [9]. A case of pembrolizumab-induced psoriasis treated with secukinumab is documented in the literature [10]. However, there are no previous reports of ixekizumab use for psoriasis triggered by tremelimumab and durvalumab. In the present case, given the urgent need to obtain clinical remission, ixekizumab was administered, achieving complete resolution of the skin condition within a few weeks. Biologic therapy may be a rapid and effective therapeutic option in patients with severe psoriasis triggered by immunotherapy, although more information is needed on long-term outcome and safety in these patients. ■

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The impact of COVID-19 on the new diagnoses of melanoma

The COVID-19 pandemic has had serious impact on general and dermatology health care in terms of diagnosis, treatment and follow-up [1]. In Belgium, there were two lockdown periods. During the first period (18/3/2020-11/05/2020), access to routine medical and dermatology care was prohibited (access to a dermatologist or a hospital was granted only for urgent cases). Following a progressive re-installation of visits, during the first six weeks, one patient per 30 minutes was permitted in order to respect the recommended disinfection measures. During the second lockdown (since October 2020), dermatology consultations were maintained but the huge backlog of cancelled appointments severely impacted the return to the usual workflow. Our working hypothesis was that the strict lockdown measures could have an impact on the total number of new diagnoses and the mean Breslow measurements of cutaneous melanomas (CM). We therefore compared the number and Breslow thickness of CM diagnosed per month during the COVID-19 period (15/03/2020-31/12/2020) with the same periods in 2018 and 2019. Data were retrieved from the University Dermatopathology Laboratory, servicing the University Dermatology Department and several local-regional private and hospital dermatologists.

During the COVID-19 period, 140 invasive versus 21 *in situ* CM were diagnosed. In the 2018 and 2019 periods, the respective figures were 169 versus 56, and 161 versus 45. The proportion of invasive CM was similar for the three periods ($p=0.24$) (Chi-square test for equal proportions). The mean ($\pm$ SD) and median (IQR) invasive CM thickness was 1.13 ± 1.55 and 0.58 ($0.35-1.15$), 1.27 ± 2.24 and 0.70 ($0.38-1.47$), and 1.24 ± 1.59 and 0.50 ($0.35-1.50$) for 2018, 2019 and 2020, respectively ($p=0.75$ and $p=0.38$). The number of new invasive CM per month for all the observation periods is illustrated in *figure 1*.

There was a statistically non-significant decrease in the total number of new cases during the COVID-19 period. This is in line with an American group who observed 102 new cases in 2020 versus 106 during the 2015-2019 period. However, they observed a significant increase in melanoma thickness and ulceration [2]. Another Spanish group reported 18 new cases in the period April-August in 2020 versus 48 cases in the same period in 2019 [3], with four melanomas >2 mm thick (compared to seven cases during the COVID-19 period). Another American dermatopathology laboratory evaluated 172 versus 153 melanoma patients in the pre-COVID-19 and COVID-19 periods, respectively. The Breslow thickness was 0.81 mm versus 1.4 mm, respectively [4]. An Italian group also reported a significantly increased number of advanced basal and squamous cell carcinomas [5].