Depletion in the rate of keratinocyte cancers and pre-cancerous lesions during PD-1 inhibition for advanced melanoma, with recrudescence on discontinuation.

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Background:

Immune checkpoint inhibition has revolutionised the treatment of many cancer subtypes. PD-1 inhibition typically results in T-cell activation via immune activation rather than by directly targeting tumour cells1-3. We present 3 patients treated with pembrolizumab for advanced melanoma, noted to have a significant depletion in the rate of development of keratinocyte cancers, pre-cancerous lesions and improvement in field carcinisation during PD-1 inhibition; 1 patient demonstrated a significant recrudescence on discontinuation of therapy.

Case 2:

The second patient, a 66-year-old female with stage IV malignant melanoma commenced pembrolizumab and during the first 8 weeks of treatment developed widespread inflamed scaly erythroderma on the chest, forehead and forearms, at sites of previous actinic keratoses (Figure 4). These settled spontaneously with complete resolution; clinically comparable to a topical 5-fluorouracil reaction. In addition, a superficial pyogenic granuloma on the right leg had resolved on review at her scheduled photodynamic therapy appointment.

Figure 4: Patient 2; 5-fluorouracil like reaction during treatment with pembrolizumab

Discussion:

The FDA has approved cemiplimab as well as pembrolizumab for treatment of locally advanced and metastatic cutaneous SCC. In Europe, approval only exists for cemiplimab4,5. Deinlein et al report 12 case reports outlining the response of cutaneous SCC with locally advanced disease to pembrolizumab with more cases are reported since6-7,8,9,10. Response of keratinocyte cancers to pembrolizumab is reported in patients with xeroderma pigmentosum11,12,13.

Typical cutaneous adverse events associated with PD-1 blockade in metastatic melanoma are lichenoid reactions, eczema and vitiligo14.

Orlaff et al report an 86-year-old female patient treated for metastatic melanoma with two doses of ipilimumab and pembrolizumab with complete resolution of field actinic keratosis, similar to our experience.

Additionally, 3 patients treated with nivolumab had complete resolution of several keratinocyte cancers thereafter. Conversely Freites-Martinez et al report eruptive keratoacanthomas in 3 patients receiving pembrolizumab, hypothesising that enhanced immune response with PD-1 inhibition in the setting of pre-existing mutations, could induce epithelial proliferation.

Conclusions:

We have observed resolution of precancerous skin lesions and field carcinisation as well as a reduction in keratinocyte cancers during treatment with pembrolizumab for advanced melanoma in 3 patients. This may be an additive benefit of treatment of patients with immunotherapy for advanced melanoma, which is worth further investigation.

References:


3. Pembrolizumab for Advanced Cutaneous Squamous Cell Carcinoma: What Do the Currently Know in 2020? in the right cheek during treatment with pembrolizumab on the right cheek during treatment with pembrolizumab. Figure 2&3: Patient 1 before (top) and during (bottom) treatment with pembrolizumab.

4. Case 1:

An 82-year-old female with stage IV malignant melanoma commenced immunotherapy with single-agent pembrolizumab. She had a history of multiple keratinocyte cancers and widespread field carcinisation. A 7x6mm clinical basal cell carcinoma (BCC) right cheek, planned for excision, reduced to 4x4mm at 1 month, and had fully resolved after 2 months on therapy. In addition, significant improvement in field carcinisation is shown and chest was noted (Figures 1, 2 & 3).

Pembrolizumab was discontinued after 8 months due to hepatotoxicity. During the 8 months of pembrolizumab therapy, she had no new invasive skin cancers. In the 16 months since treatment was discontinued, she has developed 6 invasive squamous cell carcinomas (SCCs); including high risk tumours, and her field carcinisation has deteriorated.

Figure 1: Patient 1; widespread field carcinisation of breast at baseline.

Case 3:

The final patient was a 79-year-old female with a history of multiple nodular BCCs and clinical stage III melanoma for which she underwent immunotherapy post surgical resection. She had complete resolution of multiple areas of superficial BCC on the lower limbs and SCC in situ on the right cheek during treatment with pembrolizumab.

Figure 2: Patient 1 before (top) and during (bottom) treatment with pembrolizumab.

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