HHS Public Access

Author manuscript

Br J Dermatol. Author manuscript; available in PMC 2019 May 01.

Published in final edited form as:

Br J Dermatol. 2018 May ; 178(5): 1009. doi:10.1111/bjd.16525.

Pembrolizumab treatment of a patient with xeroderma pigmentosum with disseminated melanoma and multiple nonmelanoma skin cancers

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Xeroderma pigmentosum (XP) is a rare genodermatosis with a 10 000-fold increased risk of skin cancer because of an inability to repair ultraviolet radiation-induced DNA damage. Patients with untreated XP have developed skin cancer at a median age of 9 years.[1] Traditional management for the prevention of skin cancer includes rigorous sun protection,[2] topical field treatment with 5-fluorouracil or imiquimod, or oral retinoids. Cancer treatment approaches include cryotherapy, surgical excision and Mohs surgery.[3] X-radiation may be used for unresectable lesions. When the cancers have deeply invaded adjacent structures or have metastasized, standard treatments can be ineffective, resulting in early mortality.

In this issue of the *British Journal of Dermatology*, Salomon *et al*.[4] report treatment of a 17-year-old patient with XP with metastatic melanoma and multiple nonmelanoma skin cancers (NMSC) using the programmed death-ligand 1 (PD-L1) inhibitor, pembrolizumab. Hauschild *et al*.[5] previously reported the use of pembrolizumab in another patient with XP with metastatic melanoma and multiple NMSC. Treatment with pembrolizumab over several months resulted in partial regression of the melanoma and in clearance of most NMSC in both patients.

Pembrolizumab, an anti-PD-L1 monoclonal antibody that functions as a checkpoint inhibitor, is a new agent for the treatment of metastatic melanomas and other tumours expressing the PD-L1 receptor.[6] The most severe side-effect seen in the reported patients with XP was a cutaneous inflammatory response in the areas of heavy photodamage and a vitiligo-like skin response in the areas of the NMSC. However, pembrolizumab can have severe and fatal side-effects including immune-mediated pneumonitis, colitis, hepatitis, nephritis and hypophysitis, thyroid abnormalities, diabetes, Stevens–Johnson syndrome and toxic epidermal necrolysis.

The PD-L1 checkpoint inhibitor class of drugs may prove to be an effective treatment for patients with XP with advanced skin cancers, but should be used with caution until more patients are treated and the long-term effects are understood.

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Conflicts of interest

None to declare.

Acknowledgments

We thank Dr John J. Digiovanna for reviewing this manuscript. This research was supported by the Intramural Research Program of the NIH, National Cancer Institute, Center for Cancer Research.

Funding sources

No external funding.

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