553 INCREASED EFFICACY OF CETUXIMAB AFTER PEMBROLIZUMAB FAILURE IN CUTANEOUS SQUAMOUS CELL CARCINOMA

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Background Chemotherapy and anti-epidermal growth factor receptor (EGFR) therapy, such as cetuximab have had limited success in treating advanced cutaneous squamous cell carcinoma (cSCC) due to a short duration of durable response.[1] Focus has now turned to programmed cell death protein 1 (PD-1) inhibitors as first-line therapy.[1] Unfortunately, up to half of patients with advanced metastatic cSCC experience no benefit from immunotherapy, often exhibiting disease progression.[2] Interestingly, it has been observed that the efficacy of cetuximab immediately after pembrolizumab failure is higher compared to its use before immunotherapy.[1] Cutaneous SCC has the capacity to upregulate the expression of immune checkpoint regulators such as PD ligand 1 (PD-L1) which promote T-cell exhaustion.[3] Cetuximab's anti-tumor activity is achieved through several types of immune-based mechanisms such as the activation of natural killer (NK) cells via CD 16 to initiate antibody-dependent cellular cytotoxicity (ADCC) as well as the induction of tumor cell death via cytotoxic T cell priming.[4 5] PD-1 inhibitors such as Pembrolizumab promote T-cell activation via PD-1 blockade leading to the rejuvenation of tumor-specific cytotoxic T cells in the tumor microenvironment (TME) to exert an anti-tumor effect.[2 3 6] We report three metastatic cSCC cases that exhibited significant clinical response after progressing on Pembrolizumab monotherapy.

Methods A retrospective chart review of three cases at a single academic center was conducted. Cases were confirmed to have started on Cetuximab after progressing on Pembrolizumab monotherapy.

Results All three cases achieved clinical response (two partial, one complete) after the addition of cetuximab following progression on pembrolizumab monotherapy. Treatment was well-tolerated and, remarkably, had significant responses within 3–7 months of treatment.

Conclusions While the benefit of cetuximab and immunotherapy in HNSCC has growing evidence, information on this relationship in cSCC remains limited. In addition to the case series by Acevedo (detailed above), a separate report observed clinical remission of auricular cSCC with combinatory Nivolumab and cetuximab.[7] This benefit has also been observed in other anti-EGFR inhibitors - several metastatic cSCC patients refractory to immunotherapy achieved durable complete responses after the addition of Panitumumab.[8] This present study is especially unique as it adds three cases to the under-reported body evidence on treating advanced cSCC with cetuximab after immunotherapy. Additionally, whereas prior studies primarily used Nivolumab, in the present study Pembrolizumab was the primary immunotherapy agent.

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Ethics Approval The present study did not require ethics approval in accordance with Washington University School of Medicine's HRPO protocol as it is a case series and did not involve patient interaction leading to a research question; it did not directly compare or contrast with other cases (e.g., not a comparative study); it did not involve data collection more extensive than under normal clinical practice; and our intention is not to publish an analytical report. All participants provided consent for the study

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