816 SELECTIVE IMMUNE SUPPRESSION USING INTERLEUKIN-6 BLOCKADE IN IMMUNE RELATED ADVERSE EVENTS

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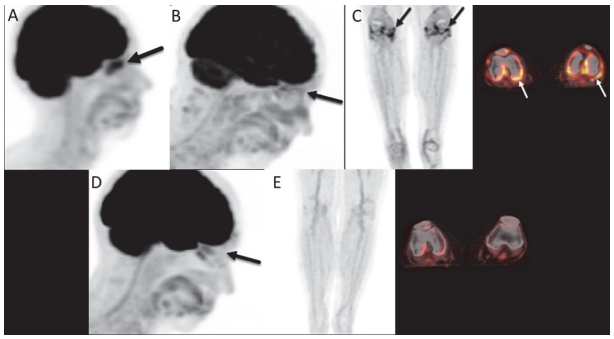
Background Managing immune-related adverse events (irAEs) has become a critical challenge with the increasing implementation of immune-checkpoint inhibitors (ICIs) in cancer treatment. IrAEs may cause treatment interruption or discontinuation, the rate of which is higher with multi-agent ICI regimen needed to overcome resistant tumor microenvironment. Herein, we describe our clinical experience using interleukin-6 receptor antagonists (IL-6RA) to manage irAEs in cancer patients receiving ICIs.

Methods We conducted a retrospective, multi-center study to evaluate the safety and efficacy of IL-6RA for irAE management. Eligible patients were identified from the institutional databases (pharmacy records, tumor registries, oncology and specialty clinic records for diagnosis and management of irAEs). The primary objective was assessing changes in irAE symptoms. The secondary objective was assessing overall response rate (ORR) before and after IL-6RA treatment.

Results A total of 81 patients received an IL-6RA (tocilizumab or sarilumab); median age was 66 years, 41% were females, 70% received single-agent anti-PD-1 and 23% received nivolumab plus ipilimumab. Cancer types were primarily melanoma (44%), genitourinary cancer (37%), and lung cancer (8.6%). Indications for using IL-6RA were inflammatory arthritis (74%), polymyalgia rheumatica (6%), myositis/myocarditis/myasthenia gravis (5%) encephalitis (5%), and 1% each with pneumonitis, colitis, hepatitis, central nervous system vasculitis, oral mucositis, and flare of pre-existing myasthenia gravis, psoriasis, and Crohn's disease. Notably, 83 % of patients received corticosteroids as first-line therapy, and 29% received disease-modifying antirheumatic drugs, without improvement. After initiation of IL-6RA, improvement of irAEs was observed in 78% after a median of 2.1 months. Of evaluable patients with inflammatory arthritis, the median clinical disease activity index (CDAI) at IL-6RA initiation was 28, indicating high disease activity, and dropped to 6 after treatment, indicating low disease activity. The median CRP level at IL-6RA initiation was 59.5 mg/L and dropped to 1.5 mg/L within 10 weeks of treatment. Seventy-two patients tolerated IL-6RA, and nine stopped treatment due to side effects. Thirty-eight patients were evaluated for tumor response by RECIST 1.1 criteria; the ORR was 58% prior to IL-6RA and 66% after treatment. Of 21 evaluable melanoma patients, the ORR was 62% prior to IL-6RA compared to 71% after treatment (figure 1).

Conclusions Our study demonstrated that targeting IL-6R could be an effective approach to mitigate autoimmunity while maintaining and possibly boosting tumor immunity. Clinical trials are currently evaluating the safety and efficacy of tocilizumab in combination with ICIs in patients with melanoma, non-small cell lung cancer, and urothelial carcinoma (NCT04940299, NCT03999749).

Ethics Approval The study was approved by The University of Texas MD Anderson Cancer Center intuition's Ethics Board, approval number PA19-0089



Abstract 816 Figure 1 A patient with sinonasal malignant melanoma involving the ethmoid air cells. (A) Baseline maximum intensity projection (MIP) PET image at 1 month before initiation of ICI (ipilimumab and nivolumab) shows avid FDG uptake of the tumor at the ethmoid air cells (arrow). (B) MIP PET image at 7 months after ICI initiation shows resolution of the FDG uptake at the site of the tumor, consistent with complete response. (C) Concurrent MIP PET and corresponding fused PET-CT images 7 months after initiation of ICI show avid radiotracer uptake at the knee joints, suggestive of arthritis. (D) MIP PET image at 10 months after concomitant therapy with IL6R antagonist and nivolumab shows persistent absence of hypermetabolic radiotracer activity at the paranasal sinuses, consistent with complete response. (E) Concurrent MIP PET and corresponding fused PET-CT images show physiologic radiotracer uptake at the knee joints, consistent with resolving arthritis.

http://dx.doi.org/10.1136/jitc-2021-SITC2021.816