1263 CHARACTERIZING STEROID-REFRACTORY IMMUNOTHERAPY TOXICITIES AND EFFECT OF SECOND-LINE IMMUNOSUPPRESSION ON CLINICAL OUTCOMES

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Background Immune-related adverse events (irAEs) are major factors limiting optimal application of immune checkpoint inhibitors (ICIs). Up to 30% of irAEs are steroid-refractory, necessitating addition of second-line immunosuppression (2nd-line IS).[1] Unfortunately, there is a paucity of clinical studies describing factors that may predict steroid-refractory irAEs or their characteristics. Furthermore, it is unclear whether patients requiring additional immunosuppression beyond steroids have similar clinical outcomes as those requiring only steroids for irAE control.

Methods We performed a retrospective cohort study to elucidate clinical characteristics that may be associated with development of steroid-refractory irAEs and examine the effect of additional 2nd-line IS use on clinical outcomes of patients receiving ICIs. An electronic database search was performed for patients who received anti-PD-(L)1 and/or anti-CTLA-4 therapies for stage III-IV immunogenic (skin, GU, lung, GI) malignancies from 2013–2020 at Duke-affiliated hospitals; of these patients, those who were hospitalized and received IV methylprednisolone for treatment of severe irAEs were included in the study.

Results Overall, a total of 214 patients were included in the study, with 64 (30%) requiring 2nd-line IS. The most common steroid-refractory irAEs were enterocolitis (51.6%), pneumonitis (12.5%), and hepatitis (9.38%). The most common 2nd-line IS treatments required were infliximab (72%), IVIG (19%), and mycophenolate (9%). There was no significant difference in gender or age at ICI start, but there was a significant difference in race composition between the two groups. Surprisingly, patients who required 2nd-line IS had lower ECOG PS at ICI initiation compared to patients who did not require 2nd-line IS (0.53 vs. 0.86, $p = 0.0025$) and also had a lower Charlson comorbidity index at ICI start (7.53 vs 8.75, $p < 0.0001$). Those requiring 2nd-line IS had similar numbers of total severe irAEs requiring hospitalization than those not requiring 2nd-line IS (1.14 vs 1.23, $p = 0.25$). Those requiring 2nd-line IS had significantly longer durations of hospitalization (13.34 days vs 6.69 days, $p < 0.0001$),were significantly less likely to have their ICI re-introduced after admission ($p = 0.03$), and had higher rates of irAE-related mortality ($p = 0.049$)than those who did not.

Conclusions Need for 2nd-line IS for irAE control may increase duration of hospitalization, lead to fewer ICI re-introductions, and increase irAE-specific mortality, highlighting the importance of recognition, prediction, and prevention of steroid-refractory irAEs. Higher ECOG PS and comorbidity burden may be associated with need for 2nd-line IS. Further studies on effect of 2nd-line IS on survival outcomes are ongoing.

REFERENCE

1. Horvat TZ, Adel NG, Dang TO, *et al*. Immune-related adverse events, need for systemic immunosuppression, and effects on survival and time to treatment failure in patients with melanoma treated with ipilimumab at Memorial Sloan Kettering Cancer Center. *J Clin Oncol*. 2015;**33**(28):3193–3198. doi:10.1200/JCO.2015.60.8448

Ethics Approval This study was approved under IRB Pro00110199. As this study was a retrospective chart review of hospital visits that have already occurred using pre-existing clinical data in the electronic medical record, a waiver of informed consent was obtained.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.1263