Introduction: Immune checkpoint inhibitors (ICI) have proven to be efficacious in several oncologic disease states, however, the response rates can be variable and immune related adverse events (IRAE) remain significant. Identification and monitoring of prognostic indicators for efficacy and safety may be beneficial when making treatment decisions. Prior literature of ICIs as monotherapy suggest higher absolute lymphocyte count (ALC) both lengthens progression free survival (PFS) and increases IRAE-incidence.

Objective: This study aims to evaluate whether the same direct relationship between ALC , PFS and IRAE-incidence exists when ICIs are used in combination therapies as opposed to monotherapy.

Methods: This is a single-center, retrospective analysis of patients with metastatic renal cell carcinoma, melanoma, or neuroendocrine tumors who initiated treatment between 06/30/2015-06/30/2020 with ipilimumab/nivolumab, pembrolizumab/axitinib, or carboplatin/etoposide/atezolizumab. ALC was collected at baseline, the first, and third months of treatment. Patients were assessed until death or last known contact date for PFS and IRAE-incidence.

Results: A total of 120 patients met inclusion criteria. Lymphopenia (ALC < 900 cell/mcL) at baseline ALC was significantly associated with worse PFS, HR (95%CI),p-value: 0.54 (0.32 - 0.93), p=0.026. Median PFS (95% CI)of patients with ALC < 900 was 264 (193 - 484) days. If ALC ≥ 900, then median PFS (95% CI) was 456 (367 - 1434) days. Similarly significant results were seen if ALC > 800 cell/mcL after three months of therapy. ALC as a continuous variable was not significantly associated with PFS, OS, or IRAE. Trends to significance were seen with IRAE as the ALC rose from 1st to 3rd month of treatment.

Conclusion: A baseline ALC of greater than 900 cell/mcL may be prognostic of at least a 6-month PFS-benefit in patients with combination immunotherapy. Monitoring for IRAE could be considered in patients whose ALC rises from the 1st to 3rd month of treatment. Future prospective studies assessing the impact of lymphopenia on ICI efficacy could select ALC < 900 cell/mcL to define lymphopenia.