**eMethods**

**Data sources**

Data on baseline patient demographics, tumour characteristics, treatment regimens, and timing of infusions were collected through chart review via the electronic medical record system.

**Variable definitions**

Timing of infusion was defined by the median infusion time for each individual treatment.

Overall survival was defined as death from any cause and indexed from date of first infusion of ICI). Patients lost to follow up were censored at the time of last known contact.

Objective response rate was defined as per RECIST v1.1 criteria.1 The standard of care at our institution was to do restaging CT scans every four cycles to assess for disease response.

Immune related adverse events severity was defined by the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.2

**Statistical analysis**

Patient characteristics were summarized using descriptive statistics (median (interquartile ranges) for continuous variables (as data not normally distributed) and proportions and frequencies for categorical measures). The primary and secondary outcomes were analyzed with the Pearson chi-square test or Fisher’s Exact test, as appropriate, and the Mann-Whitney U. Kaplan–Meier curves were used to estimate median OS and PFS between patients with early versus late timing of infusions. Multivariable logistic regression was applied to estimate hazard ratios (HR) and 95% CI for the associations of timing of infusion with overall survival.

Final stage multivariable models were adjusted for ECOG performance status, baseline prednisone, single versus dual immune checkpoint inhibitor regimen, presence of brain metastases prior to immune checkpoint inhibitor therapy, and gender.

Exploratory analyses on the association between time-of-day for the first infusion only, all treatments received, and season of first infusion, were also conducted for OS and PFS.

Statistically significant outcomes were defined by two-sided p<0.05. Statistical analysis was conducted in IBM SPSS version 27 for Windows (Armonk, New York, 2020).

**References**

1. Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer.* 2009;45(2):228-247.

2. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. U.S. Department of Health and Human Services, National Institutes of Health. <https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf>. Published 2017. Accessed February 7, 2021.