Background SPICE is a phase 1 study of the oncolytic adenovirus enadenotucirev in combination with nivolumab in patients with advanced epithelial tumors (NCT02636036). Preliminary data has indicated a survival advantage in patients with mCRC resulting in a median OS of 14 months. To further understand this OS signal, a comparison to historical patient-level data from the placebo arm of the CORRECT study (NCT01103323) was performed using data obtained from Project Data Sphere.

Methods Individual patients from SPICE were matched with patients in the placebo arm of the CORRECT study in terms of covariates known to be associated with OS (ECOG, presence of liver mets, haemoglobin, albumin, LDH and platelet count). The OS outcomes were then compared between the matched SPICE and CORRECT patients to minimise any bias due to patient selection. The distribution of the covariates was broadly similar between studies with minor differences favouring the SPICE study.

Results The mOS in confirmed microsatellite stable mCRC patients (n=25) in the SPICE study was 15.4 months (95% CI; 11.8 m, 21.0 m) as compared to 5.0 months for patients in the placebo arm of the CORRECT study (n=231). Two different statistical analyses were performed to compare the outcomes between studies: (1) A comparison of OS matching each SPICE patient to a maximum of 10 (average of 5.5) placebo patients from CORRECT using M:1 variable nearest neighbour propensity score matching; (2) Multivariate analysis of SPICE vs CORRECT adjusting for all covariates in a Cox regression model. The Hazard Ratio (SPICE:CORRECT) from the regression model was 0.28 with an upper 2-sided 95% confidence limit of 0.48, which was consistent with results using propensity score matching. The upper 95% CL for the HR for method (2) was 0.61.

Conclusions The results appear promising, particularly in a population that has historically shown little response to PD-1 intervention and warrant further exploration in a randomised study. However, these analyses cannot be regarded as definitive, due to the possible presence of unmeasured confounders between a small phase 1 cohort and a large phase 3 control group.

Ethics Approval The study was approved by the Western Institutional Review Board, study approval number 1160755.

REFERENCE


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