DETERMAIO (IO SCORE) IS ASSOCIATED WITH EFFICACY OF ICI MONOTHERAPY IN ADVANCED NSCLC PATIENTS WITH ECOG 2

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Background Immune checkpoint inhibitor (ICI) therapy is an attractive option for aNSCLC patients with poor performance status (ECOG 2) but several studies have failed to demonstrate benefit. DetermaIO (IO score) is a 27-gene RT-qPCR immuno-oncology tumor immune microenvironment (TIME) RNA expression classifier that has been previously shown to be associated with clinical response to ICI therapy in multiple tumor types. This study was performed to explore the possibility that the IO score (IO+/IO-) could identify responders in patients with ECOG 2 whose overall poor outcome might otherwise obscure detecting a significant clinical benefit.

Methods Available FFPE specimens with ECOG 2 from two studies of advanced NSCLC patients treated with ICI monotherapy were analyzed independently. The first, composed of 46 patients from BC Cancer (BCCA), was split into two cohorts due to the differences in treatment and PD-L1 status: Cohort 1 was composed of patients with PD-L1/C21 ≥ 50% who received 1st line ICI monotherapy (n=26). Cohort 2 was composed of mostly PD-L1 negative or 1–49% patients who received ICI monotherapy in the 2nd+ line (n=20). Cohort 3 was comprised of thirteen patients of mixed PD-L1 phenotype and mixed line of therapy from an independent center, West Cancer Center (WCC). In total, 59 patients treated with ICI monotherapy from the three cohorts were analyzed separately for association with PFS using Cox proportional hazards.

Results Overall, 35 of 59 patients were IO+ (cohort 1 = 18/26, cohort 2 = 10/20 cohort 3 = 7/13). Median PFS improved for IO+ versus IO- in each of the three cohorts (cohort 1 IO- = 67, IO+ = 357; cohort 2 IO- = 100, IO+ =189; cohort 3 IO- = 127, IO+ = 404). The Cox proportional hazard for cohort 1 was 0.27 (95%CI 0.10 to 0.72, p=0.0095), cohort 2 was 0.51 (95%CI 0.20 to 1.32, p=0.17), and cohort 3 was 0.14 (95%CI 0.027 to 0.76, p=0.023).

Conclusions DetermaIO has identified significant benefit for PFS from two cohorts of ECOG 2 patients and trended towards significance in a 3rd cohort treated in the 2nd+ line. While each cohort alone is modestly powered, the consistent results in three independent cohorts, separated for analysis to control for other confounding prognostic variables, suggests that DetermaIO is worthy of further study as a biomarker to better identify ECOG 2 patients likely to benefit from ICI therapy.

Ethics Approval This study was approved by the Research Ethics Board (REB) of University of British Columbia (H20–02635). Individual consent for this retrospective analysis and the use of tumor samples for the IO score assay was required for live patients. Consent was waived by the REB for deceased patients.