Abstracts

306 PREDICTORS OF IMMUNOTHERAPY BENEFIT IN MERKEL CELL CARCINOMA

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Background Merkel cell carcinoma is a rare cancer for which the standard-of-care is immune checkpoint blockade in the recurrent/metastatic setting. However, immunotherapy is not effective in all patients. A greater understanding of molecular mechanisms and potential predictive biomarkers are unmet needs for clinicians and researchers.

Methods We undertook a retrospective analysis of 45 patients treated at our institution from 2013 to 2020 to understand the clinical and genomic correlates of clinical benefit from immunotherapy. We gathered data from the electronic health record, including provider notes and results from our institutional next-generation sequencing panel of actionable genomic alterations.

Results Our cohort predominantly included individuals with stage III disease at diagnosis and stage IV disease at the time of diagnosis of recurrent/metastatic disease. Most patients received immunotherapy in the first line. 43% of patients experienced an objective response to immunotherapy (median duration of response 24.2 months, 95% confidence interval 8.8–not reached) and median overall survival was 15.5 months (95% confidence interval 9.0–28.7) (median follow-up 25.2 months). Lower stage at diagnosis of primary disease and shorter disease-free interval between completion of initial treatment and recurrence were each associated with greater odds of response (odds ratio of 0.06, p=0.04 for stage; odds ratio 0.75, p=0.05 for disease-free interval). The most common single-nucleotide variants among the sequenced cohort were those in TP53 (59%) and RB1 (51%). Single-nucleotide variants in the ARID2 and NTRK1 genes were associated with response without Bonferroni correction (p=0.05), while none of Merkel cell polyomavirus status, total mutational burden, ultraviolet mutational signatures, and copy-number alterations predicted outcomes (figure 1).

Conclusions Patients with shorter disease-free interval after definitive treatment may be particularly suitable candidates for immunotherapy. Our molecular findings point to ARID2 and NTRK1 as potential predictive markers and/or therapeutic targets (e.g., with Trk inhibitors), although this association needs to be confirmed in a larger sample.

Acknowledgements AJK receives research funding from the American Society of Hematology and from the Pritzker School of Medicine.

Ethics Approval The study was approved by the Dana-Farber institutional review board, protocol numbers 11-104 and 17-000.

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0306

Abstract 306 Figure 1 Mutation landscape by immune checkpoint inhibitor response. 

307 ATEZOLIZUMAB PLUS VEMURAFENIB AND COBIMETINIB PROVIDES FAVORABLE SURVIVAL OUTCOMES IN PATIENTS WITH HIGH TUMOR MUTATION BURDEN AND PROINFLAMMATORY GENE SIGNATURE IN THE PHASE 3 IMSPIRE150 STUDY


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Background The phase 3 IMspire150 study (NCT02908672) showed that first-line atezolizumab (A) combined with vemurafenib (V) + cobimetinib (C) improved progression-free survival (PFS) vs placebo (P) + V + C in patients with BRAFV600 mutation-positive advanced melanoma (15.1 vs 10.6 months; hazard ratio [HR] 0.78; 95% CI 0.63–0.97; P=0.0249). Insights into the clinical benefit of the A+V+C triple combination in prognostic molecular subgroups of patients can inform treatment selection and future clinical research.

Methods 514 patients were randomized 1:1 to A+V+C (n=256) or P+V+C (n=258). The efficacy endpoints analyzed included PFS and duration of response (DOR) estimated using the Kaplan-Meier method. Outcomes were based on investigator-assessed best overall response per Response Evaluation Criteria in Solid Tumors v1.1. Patients were primarily categorized into binary subgroups defined by tumor mutation burden (TMB; low or high: <10 or ≥10 mutations/Mb, respectively) or by the < or ≥ median values.