47 BASELINE BLOOD DNA METHYLATION-BASED IMMUNE PROFILES AND TUMOR MUTATIONAL BURDEN PREDICT SURVIVAL OUTCOMES IN ANTI-PD-1 TREATED HEAD AND NECK CANCER PATIENT

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Background Immune checkpoint inhibitors (ICIs) are approved to treat patients with recurrent/metastatic head and neck squamous cell carcinoma (HNSCC). However, currently approved biomarkers are limited due to the heterogeneity and availability of tumor samples. The development of peripheral biomarkers offers an alternative noninvasive approach to assess immunotherapy response. DNA methylation-based immune cell deconvolution provides opportunities for developing blood-based biomarkers to predict immunotherapy response outcomes in HNSCC.

Methods Our study is an ongoing prospective multi-center study aimed at identifying blood DNA methylation biomarkers of therapy response in patients with HNSCC undergoing standard-of-care, FDA-approved ICIs. Blood was drawn prior to immunotherapy initiation. DNA isolated from these samples underwent methylation profiling using the Illumina EPIC microarray. Peripheral blood immune profiles were generated using cellular deconvolution.[1] 69 HNSCC patients with anti-PD-1 monotherapy were included (figure 1). 47 patients' tumor samples were sequenced to evaluate tumor mutational burden (TMB) (figure 2). We investigated 48 immune variables and TMB for relation with progression-free survival (PFS) and overall survival (OS) using Cox proportional-hazard models adjusted for age, sex, and a marker for corticosteroid exposure.[2] 12 primary immune cell proportions and TMB were investigated for interaction. A p-value < 0.05 was used as the cut-off for statistical significance.

Results In 69 patients with HNSCC who received anti-PD-1 therapy, neutrophil proportion, monocyte count, and total B cell count were associated with worse PFS outcomes while CD4T memory cell count and total T cell count were associated with better PFS outcomes (figure 3). Regarding OS, NLR, neutrophil proportion, total naïve lymphocyte proportion, monocyte count, CD4T naïve percentage, CD4T naïve to memory ratio, and T regulatory cell percentage were found to be associated with poorer survival while total CD4 T cell count, total CD4 T cell proportion, CD4 T memory cell proportion, total T cell count, lymphocyte to monocyte ratio, and total lymphocyte proportion were found to be associated with better outcomes (figure 4). Higher TMB was found to be associated with better survival outcomes. TMB exhibits significant interaction with peripheral monocyte proportion. TMB is a better predictor of survival in individuals with a lower level of monocyte proportion (figure 5).

Conclusions DNA methylation-based immune profiling in peripheral blood at baseline identifies clinically relevant biomarkers of benefit from ICIs. Our results demonstrate the potential of new blood DNA methylation-based biomarkers to predict immunotherapy response prior to the initial treatment, and connected peripheral immune profile with TMB through their interactive impact on survival outcomes.

REFERENCES

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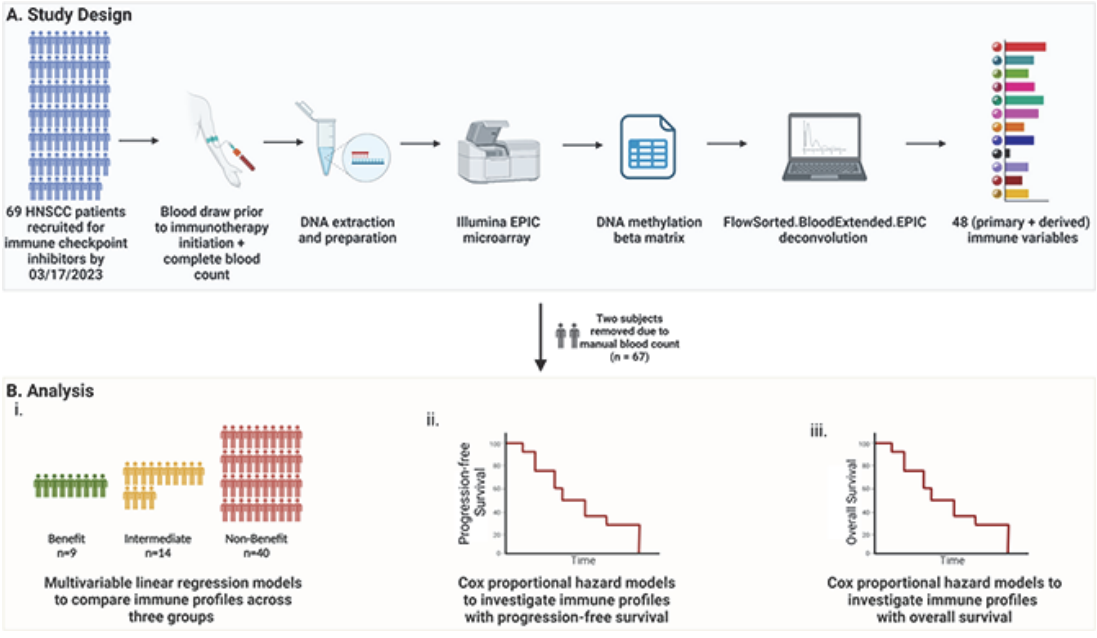
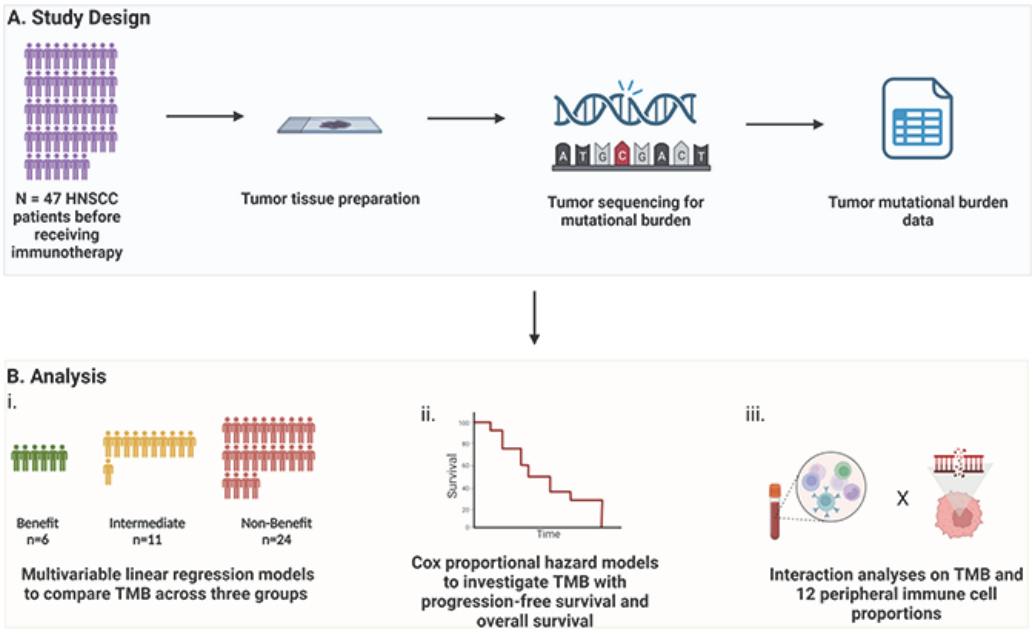
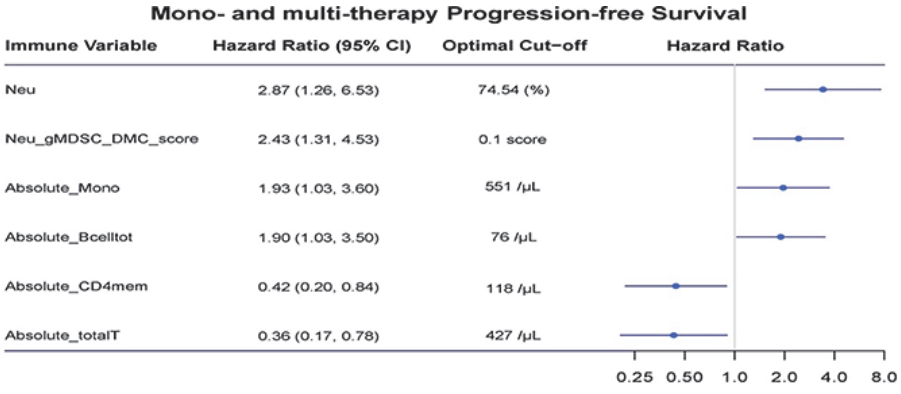
Ethics Approval The study is approved by Dartmouth Cancer Center IRB (STUDY02001227), Brown University IRB (1901002321), and Dana-Farber Cancer Institute IRB (18–548).



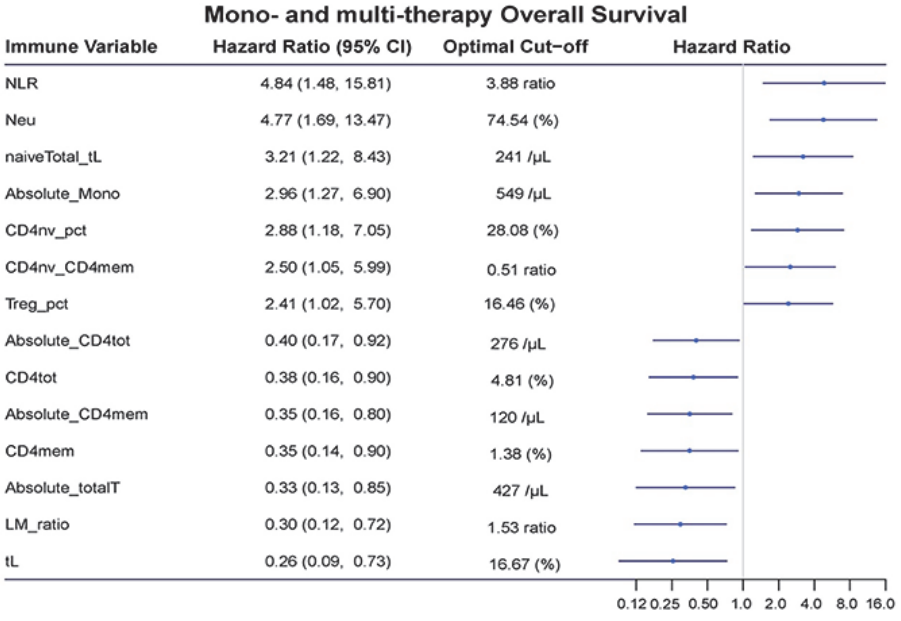
Abstract 47 Figure 1



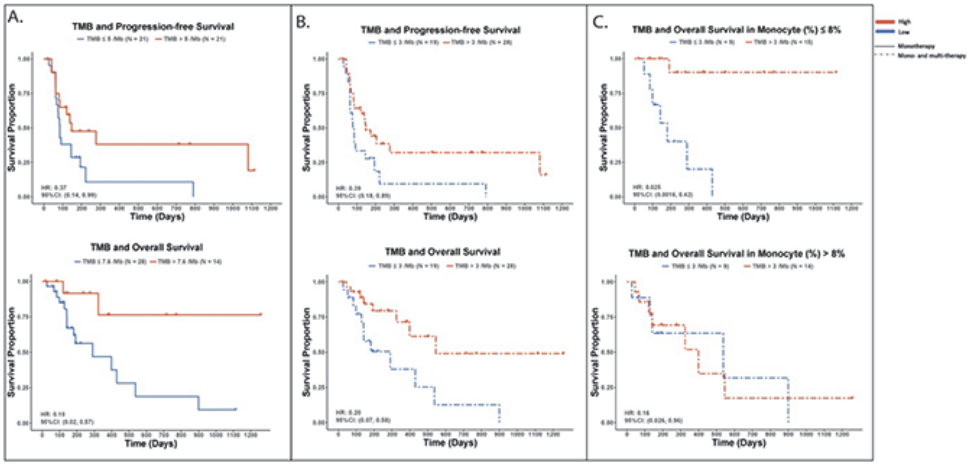
Abstract 47 Figure 2



Abstract 47 Figure 3



Abstract 47 Figure 4



Abstract 47 Figure 5

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