

P3.335: Evaluating T-cell infiltration and antigen presentation status as predictive biomarkers for immunotherapy response in small cell lung cancer

Jiyeon Kim^{1,2}, Hyemin Kim³, Jinyong Kim², Sehhoon Park², Hyun Ae Jung², Jong-Mu Sun², Jin Seok Ahn², Yoon-La Choi², Se-Hoon Lee^{1,2,*}

¹Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, ³Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Correspondence: shlee119@skku.edu

INTRODUCTION

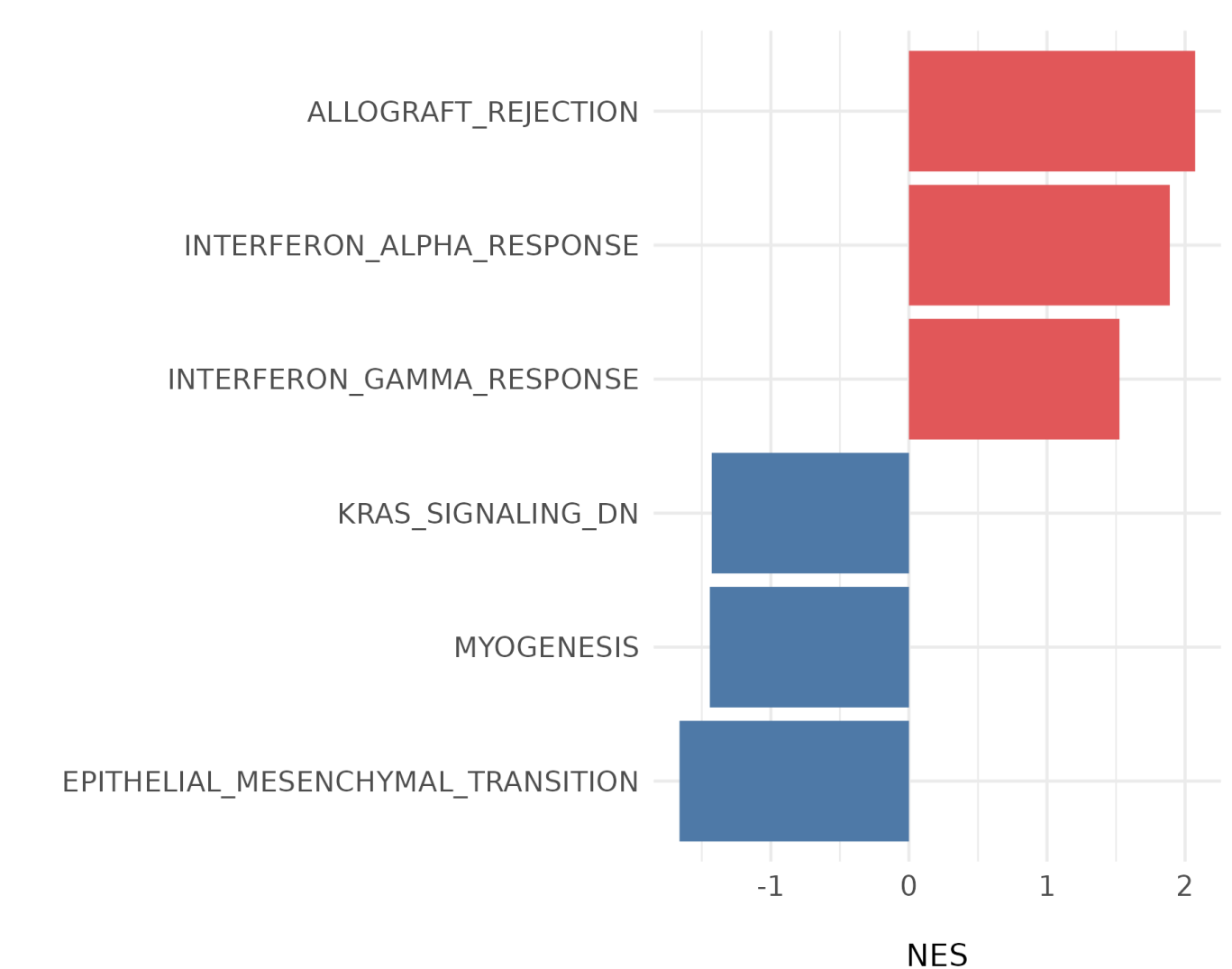
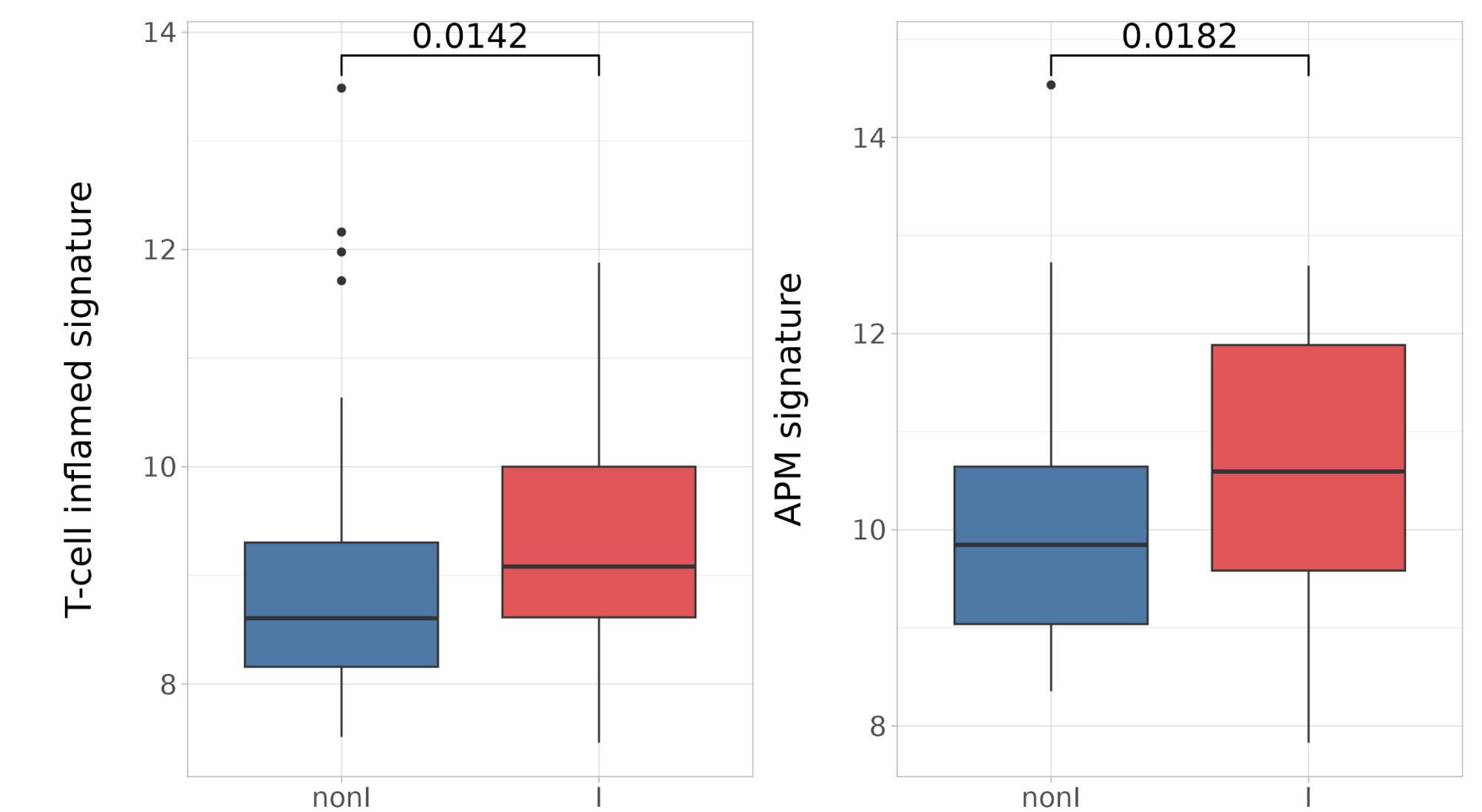
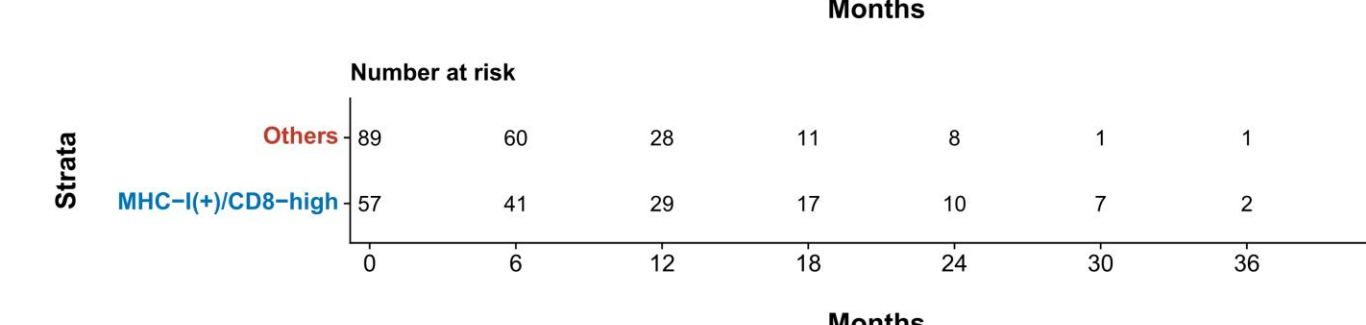
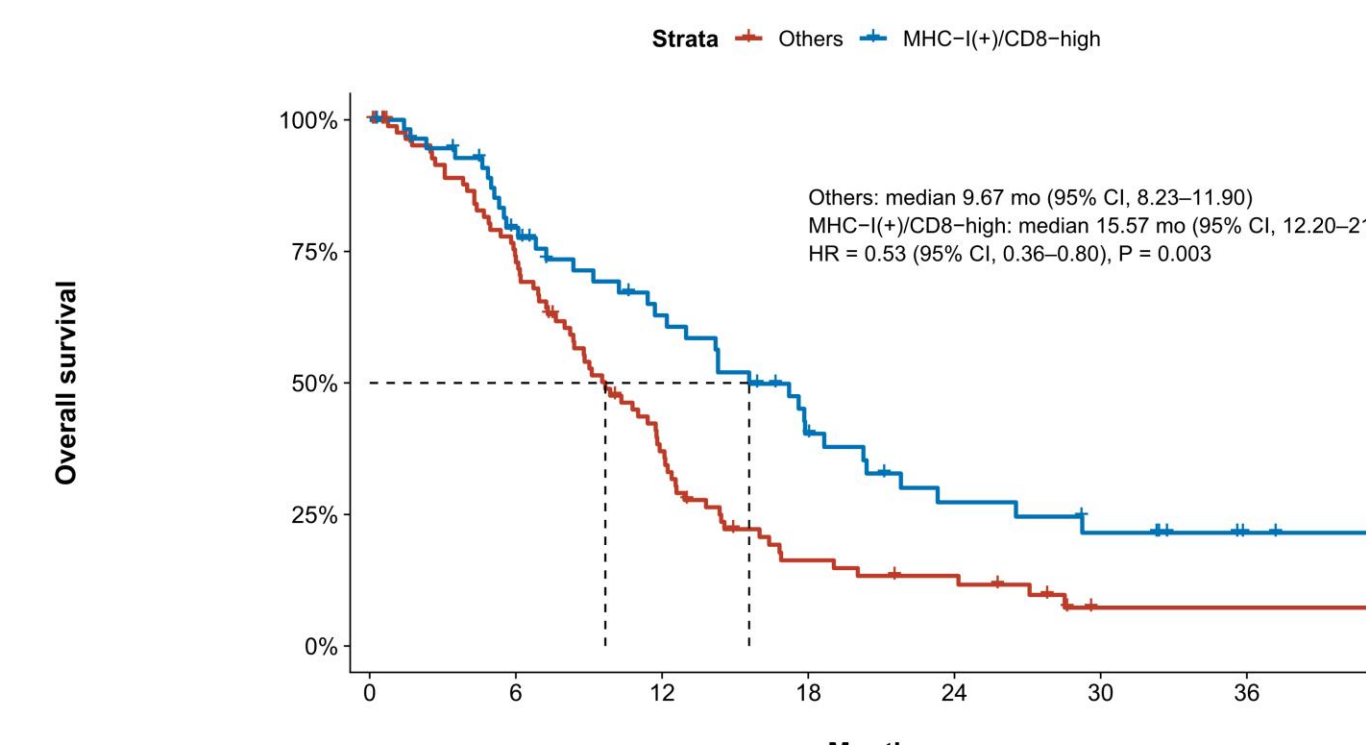
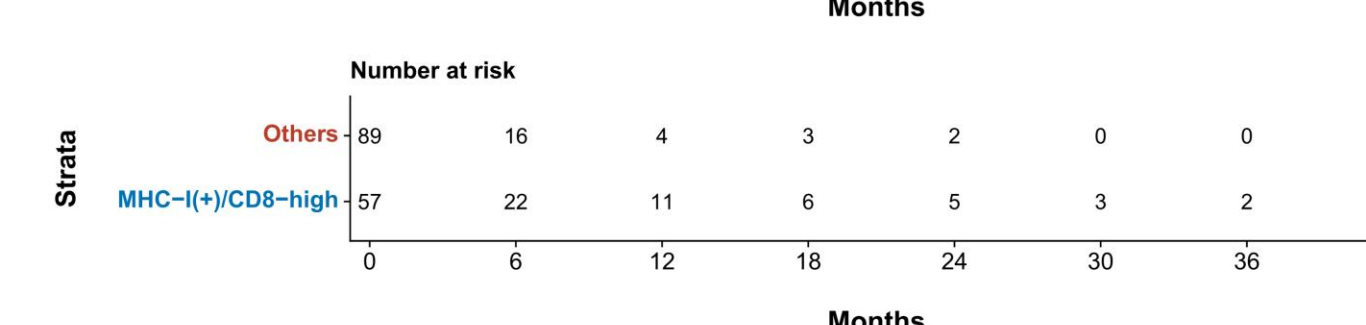
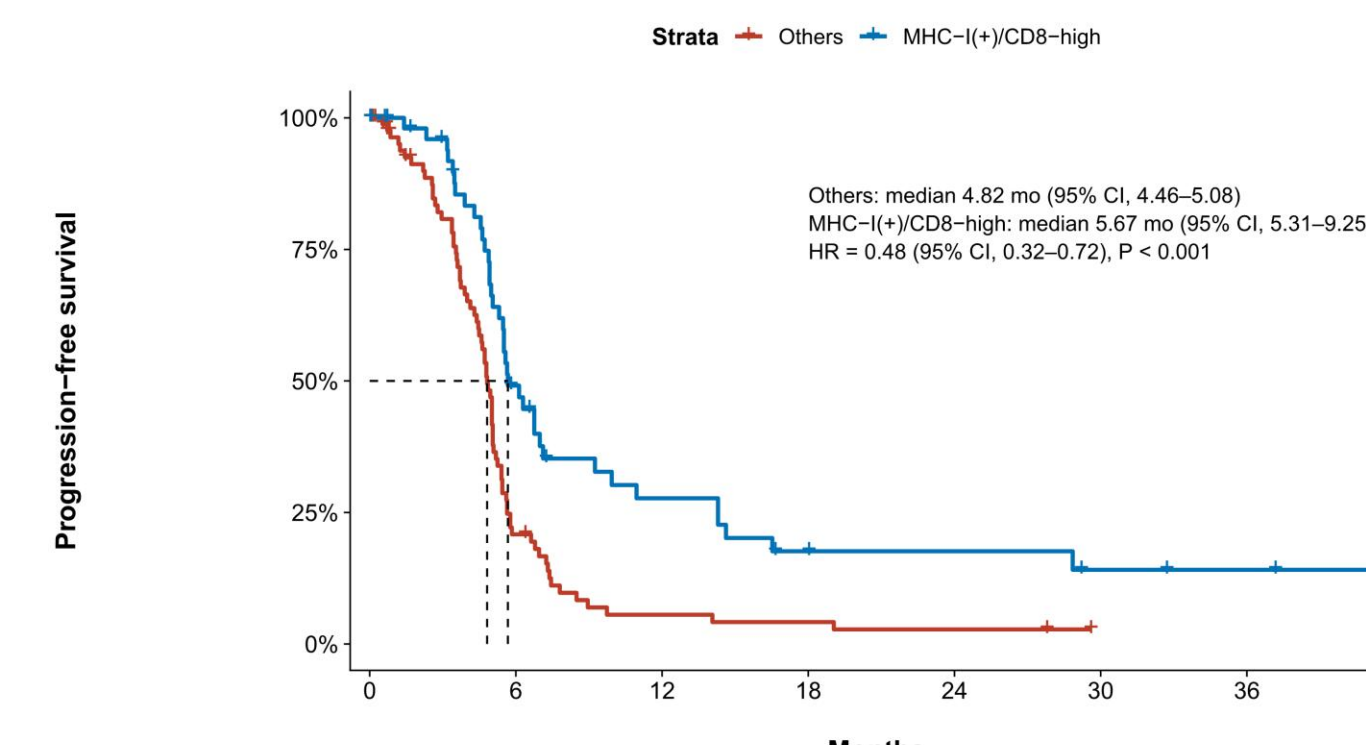
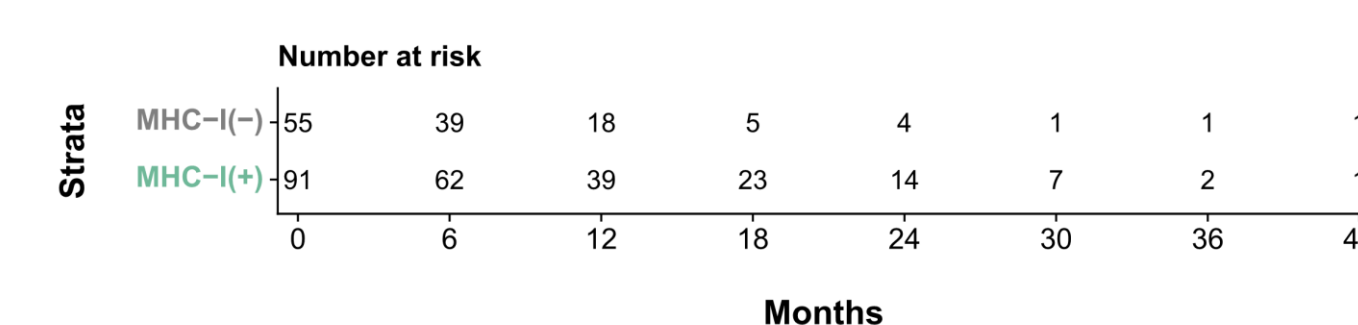
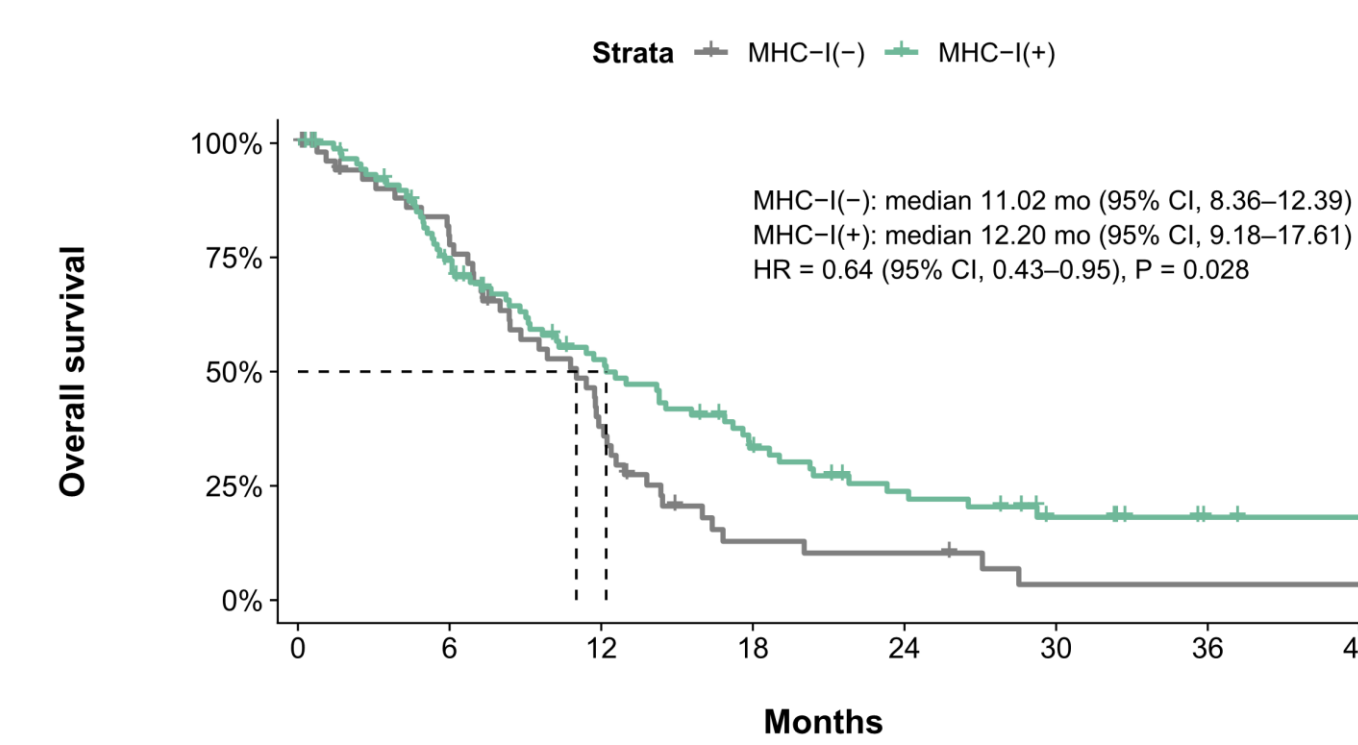
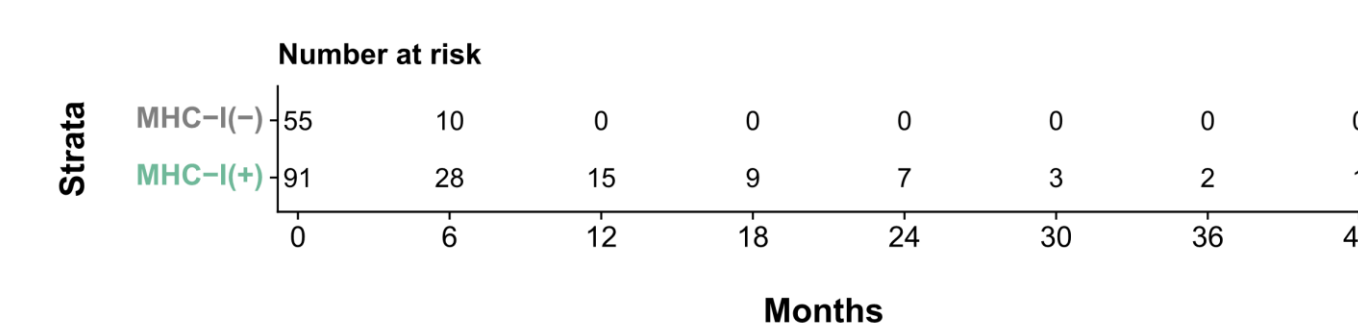
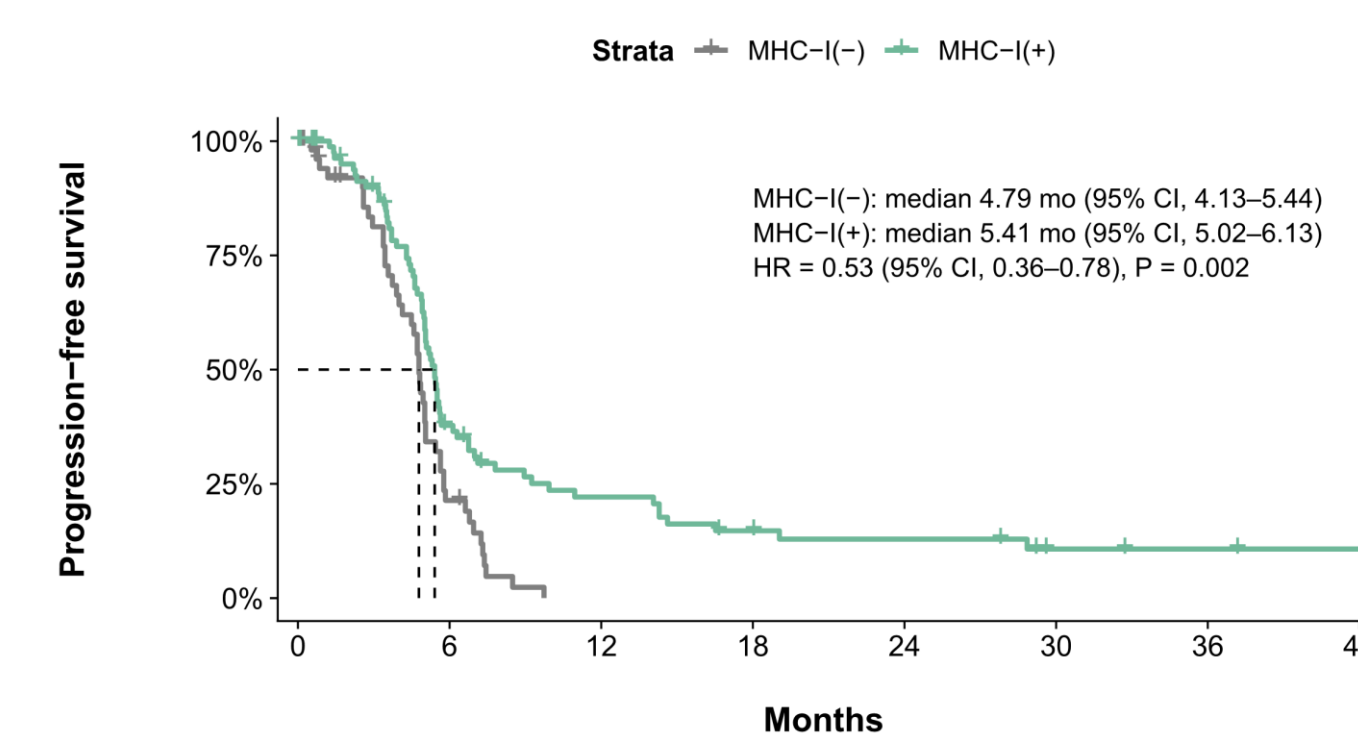
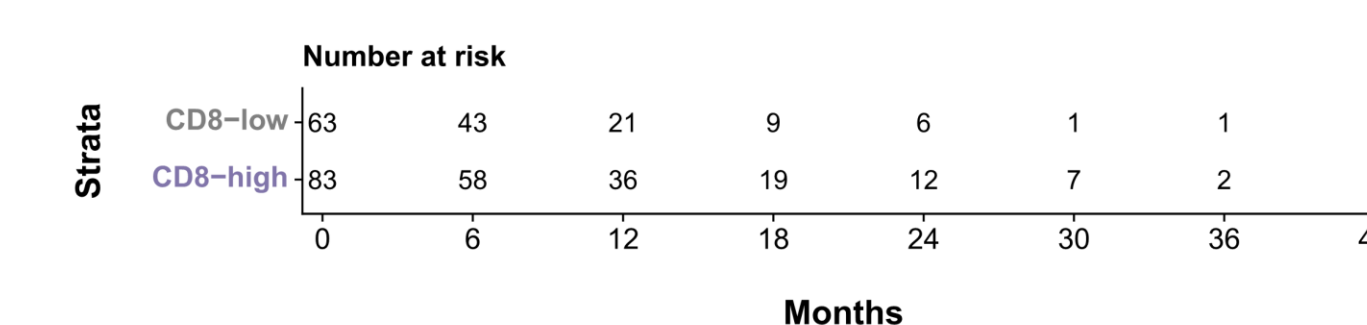
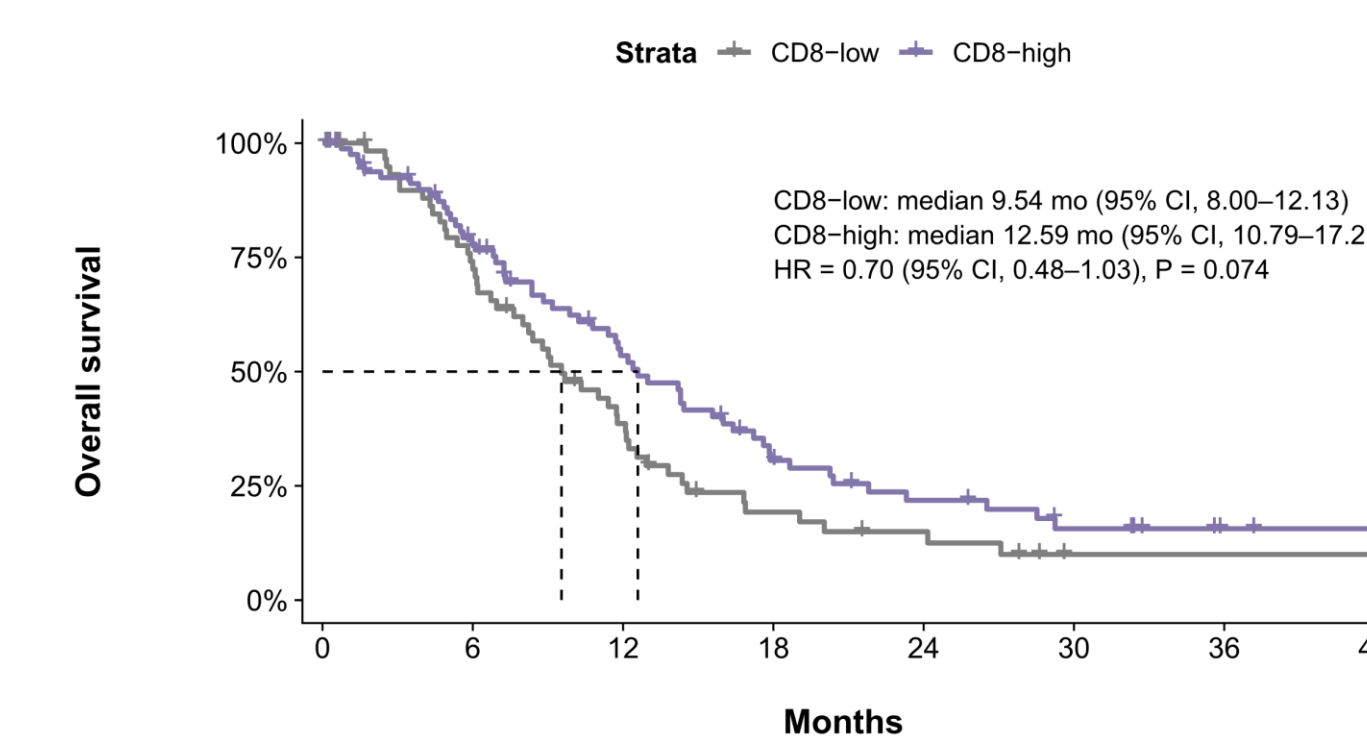
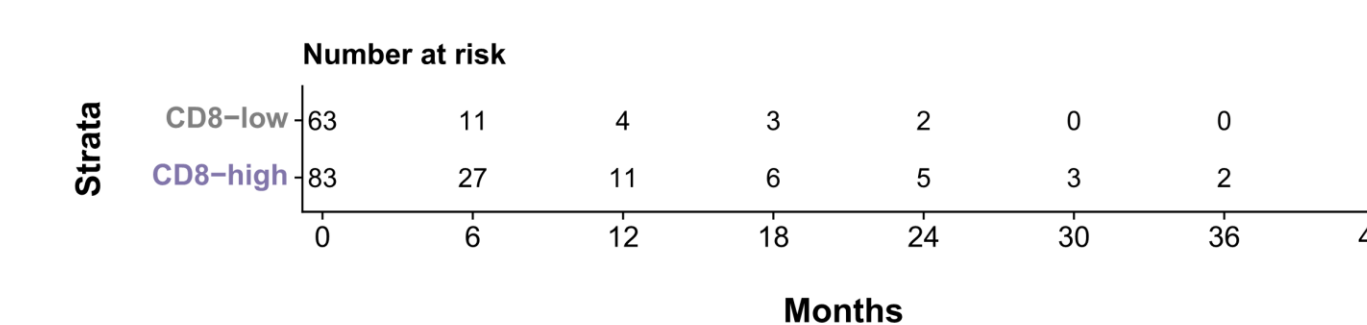
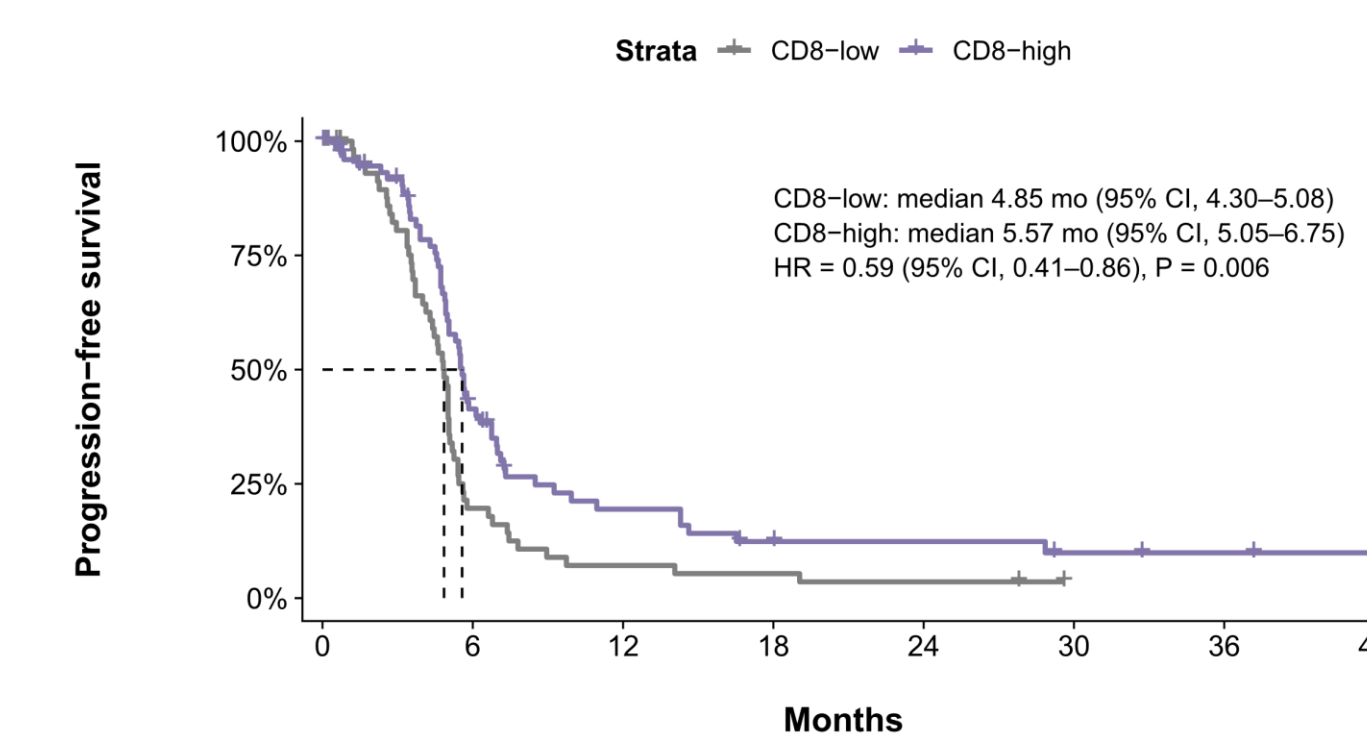
Small cell lung cancer (SCLC) is typically characterized by limited T-cell infiltration and frequent loss of MHC-I expression, contributing to an immune-excluded tumor microenvironment (TME) that constrains immunotherapy efficacy. We investigated whether CD8 and MHC-I expression could serve as predictive biomarkers for clinical benefit from atezolizumab-based combination therapy, similar to the Impower133 trial.

METHODS

From 357 SCLC patients treated with first-line atezolizumab plus platinum-etoposide, 146 with evaluable tissue underwent immunohistochemistry (IHC) for CD8 (Ventana, 790-4460; manual counting, 10x objective) and MHC-I (Abcam, ab70328; H-score). Differential gene expression and pathway enrichment analysis were performed using whole transcriptome sequencing data from 89 samples. A separate chemo-only cohort receiving platinum-based chemotherapy without immunotherapy was included, with 58 patients evaluable for CD8 and MHC-I IHC.

RESULTS

CD8 IHC was assessable in 154 and MHC-I in 149 samples, with 146 evaluable for both markers. The CD8-high group (median cut-off 20) demonstrated improved PFS (HR 0.59, P=0.01) and a trend toward prolonged OS (HR 0.70, P=0.07). MHC-I H-score of 0 was observed in 39% (58/149), and MHC-I-positive patients showed superior PFS (HR 0.53, P<0.01) and OS (HR 0.64, P=0.03). The combined MHC-I-positive/CD8-high group achieved the greatest benefit in both PFS (HR 0.48, P<0.01) and OS (HR 0.53, P<0.01), while all other subgroups had shorter median PFS and OS than the overall cohort. Transcriptomic analysis demonstrated enrichment of the interferon-gamma response pathway in the MHC-I-positive/CD8-high group and epithelial-mesenchymal transition pathway in the remaining other group. In the chemo-only cohort (N=58), no significant survival differences were observed between the MHC-I-positive/CD8-high group and the other in PFS (HR 1.43, P=0.23) and OS (HR 1.14, P=0.66).



DISCUSSION AND CONCLUSION

Combined CD8 and MHC-I expression serves as a specific predictive biomarker for clinical outcomes in extensive-stage SCLC patients treated with atezolizumab combination therapy, effectively reflecting an inflamed tumor microenvironment essential for immunotherapy response.