Abstract 3138

Paired Tumor/Normal Sequencing Reduces Apparent Racial Differences In Tumor Mutational Burden

Kenneth R. Carson, MD, PhD,[1,2] Ameen Salahudeen, MD, PhD,[1,3] Mary Jo J. Fidler, MD,[2] Kristiyana Kaneva, MD, MS,[1] Christopher W. Seder, MD,[4] Michael Liptay, MD,[4] Lawrence E. Feldman, MD,[3] Ryan Nguyen, DO,[3] Frank Weinberg, MD, PhD,[3] Mary Pasquinelli, DNP,[3] Karen Huelsman, MS, LGC,[5] Brooke Rhead, PhD,[1] Yannick Pouliot, PhD,[1] Francisco M. De La Vega, DSc,[1]

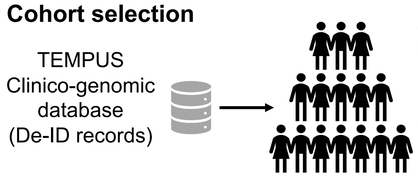
[1]Tempus Labs, Inc., Chicago, IL, [2]Department of Internal Medicine, Division of Hematology, Oncology, and Stem Cell Transplant, Rush University Medical Center, Chicago, IL, [3]Department of Internal Medicine, Division of Hematology/Oncology, University of Illinois, Chicago, IL, [4]Department of Cardiovascular and Thoracic Surgery, Rush University Medical Center, Chicago, IL, [5]Department of Precision Medicine, TriHealth Cancer Institute, Cincinnati, Ohio

INTRODUCTION

- TMB is routinely reported in cancer patients tested with broad-panel next generation sequencing and has become a predictive biomarker associated with response to checkpoint inhibitor (CPI) therapy.
- Sequencing of paired tumor and normal specimens allows correction of TMB estimates with patient-specific germline variants.
- When a paired normal specimen is unavailable, TMB estimates are corrected using annotations derived from population-scale germline variant surveys.
- **To evaluate TMB differences in paired sequencing (PS) and tumor-only sequencing (TOS), we compared TMB assessments—stratified by race — in three common malignancies.**

METHODS

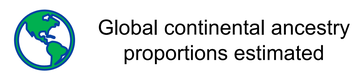
Cohort selection



Patient Characteristics:
- Cancer type - Lung, NSCLC, Breast, Colorectal
- Sequenced with Tempus xT NGS platform[1]

TMB values (mut/Mb), race/ethnicity labels and other metadata were obtained. Comparisons between tumor-only sequencing (TOS) vs. paired tumor/normal sequencing (PS) were performed.

Ancestry inference and race imputation



We have previously shown[2] that a heuristic method combining global ancestry proportions can impute race and ethnicity categories. This allowed us to include more patients in our analysis.

Statistical analysis

- The Kruskall-Wallis test was used to compare TMB distributions within sequencing modality groups.
- The Mann-Whitney test was used for pairwise comparisons between TOS and PS values for a given race/ethnicity and sequencing modality.

[1]Tempus xT NGS platform: DNA-seq of 595-648 genes at 500x coverage, whole exome capture RNA seq, [2]Hein *et al.,* J Natl Cancer Inst (2022) Feb 2; djac014. doi: 10.1093/jnci/djac014

SUMMARY

- **Paired tumor/normal sequencing reduces estimated TMB** compared to tumor-only sequencing across all racial groups with a pronounced difference in Black and Asian racial groups.
- Paired tumor/normal sequencing provides a **more accurate estimate of TMB** regardless of race and could **reduce the use of CPI in patients with a low likelihood of response**.

RESULTS

- TMB median values were studied for cohorts of patients with NSCLC, breast, and colorectal cancers.
- A statistically significant inflation of TMB median values is observed for all race/ethnicity categories studied.
- The inflation in TMB values is more extreme in Black and Asian patients, and less pronounced in White patients.

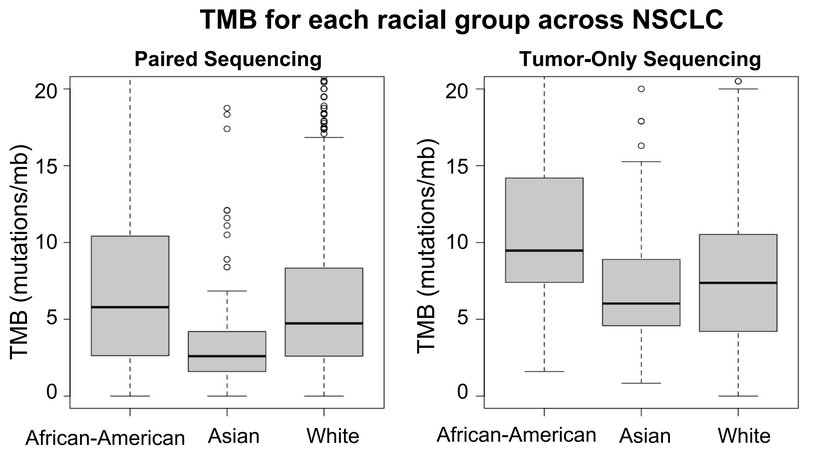


Figure 1. Among 4,817 NSCLC patients with available race information (13% Black (B), 5% Asian (A), 82% White (W), 3,052 had PS, and 1,765 had TOS performed. Median TMB for B, A, and W patients was 5.8, 2.6, and 4.7 (within group p<0.0001), respectively in patients with PS, and 9.5, 6, and 7.4 (within group p<0.0001), in patients with TOS. Comparisons across PS and TOS were highly significant (p<0.0001). The absolute difference in median TMB was 3.7, 3.4, and 2.5, respectively.

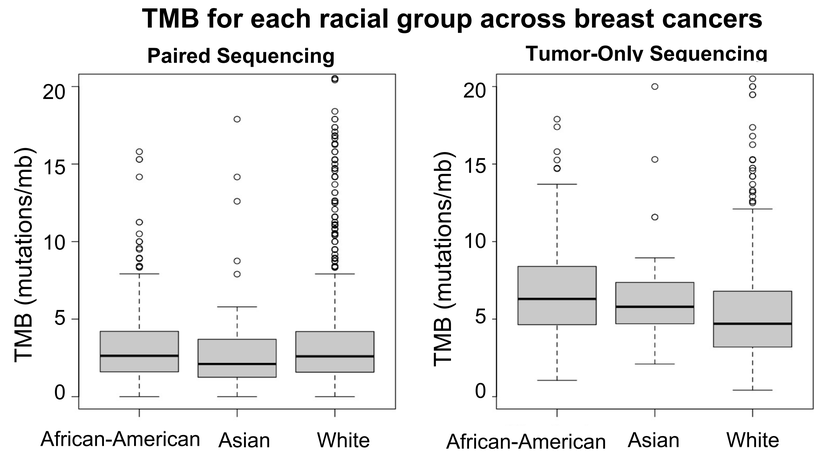


Figure 2. Among 3,191 patients with breast cancer with available race information (17% B, 4% A, 78% W), 2,220 had PS, and 971 had TOS. Median TMB for B, A, and W patients was 2.6, 2.1, and 2.6 (within group p=0.11), respectively, in patients with PS, and 6.3, 5.8, and 4.7 (within group p<0.0001) n patients with TOS. Comparisons across PS and TOS were highly significant (p<0.0001). The absolute difference in median TMB was 3.7, 3.7, and 2.1, respectively.

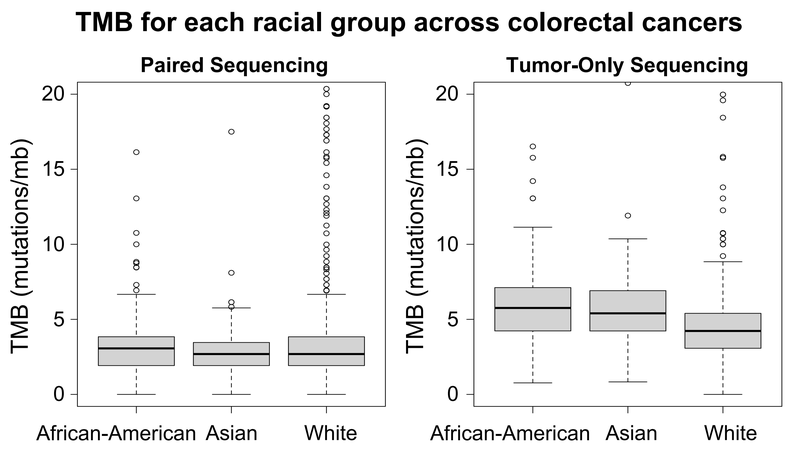


Figure 3. Among 4,857 patients with colorectal cancer with imputed race information (15% B, 6% A, 79% W), 2,820 had PS, and 2,037 had TOS. Median TMB for B, A, and W patients was 3.1, 2.7, and 2.7 (within group p=0.20), respectively, in patients with PS, and 5.8, 5.4, and 4.2 (within group p<0.0001) in patients with TOS. Comparisons across PS and TOS were highly significant (p<0.0001). The absolute difference in median TMB was 2.7, 2.7, and 1.5, respectively.

Correspondence:
Ken.Carson@tempus.com

Acknowledgements: We thank Amrita A. Iyer, PhD from Tempus Scientific Communications for visualization and poster review.