Monitoring response to treatment utilizing liquid biopsy among African American men with advanced prostate cancer: Real-world experience in a safety net hospital oncology clinic

Tamer Khashab[1,2], Salma Kaochar[2,4], Alexander Le[3], Samantha B. Cohen[3], Attiya Batool Noor[1], Heidi Dowst[2,4], Neda Zarrin-Khameh[1,2,4], Michael Austin Brooks[1,2,4], Guilherme Godoy[1,2,4], Maria A. Berezina[3], Anna E. Schwarzbach[3], Michael Scheurer[2,4], Martha Mims[1,2,4], Nicholas Mitsiades[1,2,4]

[1]Harris Health/Ben Taub Hospital (Houston, TX); [2]Baylor College of Medicine (Houston, TX); [3]Tempus Labs (Chicago, IL); [4]Dan L. Duncan Comprehensive Cancer Center (Houston, TX)

INTRODUCTION

African American (AA) men with prostate cancer (PC) have higher incidence and mortality rates, relative to non-AA men, primarily due to healthcare access and other socio-economic factors. While next generation sequencing (NGS) is becoming a more prevalent technique for supporting cancer treatment decisions, minority and uninsured patients have been under-represented in prior NGS studies and biomarker-driven precision oncology clinical trials.

Ben Taub Hospital (BTH) is a safety net hospital that serves a racially/ethnically diverse patient population (91% of patients are minorities). In this study, we compare the genomic features of PC patients from the BTH cohort with a nationwide cohort gathered from the genomic database at Tempus Labs, Inc. Patients from the BTH cohort are defined as AA or White (including White Hispanic), while those from the Tempus cohort are defined as AA or non-AA. We also demonstrate the clinical utility of monitoring treatment response in AA PC patients using longitudinal NGS liquid biopsy assessment (Tempus|xF).

METHODS

We retrospectively analyzed de-identified NGS data obtained via the Tempus|xT solid tumor assay (DNA sequencing of 648 genes in tumor tissue at 500x depth) and/or the Tempus|xF liquid biopsy assay (circulating tumor DNA [ctDNA] sequencing of 105 genes in peripheral blood samples at 5,000x depth). We analyzed germline and/or somatic mutations detected in 61 AA and 56 White (including White Hispanic) BTH patients receiving treatment for locally advanced, biochemically recurrent or metastatic PC (mPC). We also analyzed de-identified NGS data from a nationwide dataset of 1765 metastatic PC patients (307 AA) previously sequenced with xT and/or xF assays (Tempus Labs, Chicago, IL). Genomic data analysis was conducted using the Tempus LENS analytical tool.

RESULTS

Figure 1: Mutation frequencies in AA vs non-AA PC patients within the BTH or Tempus datasets

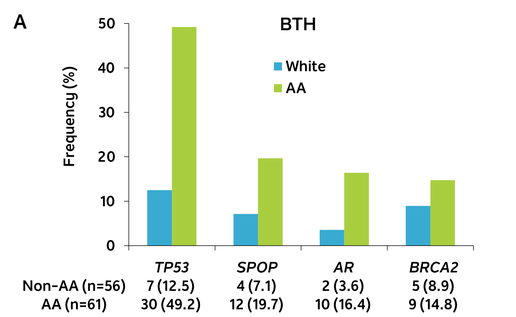

Figure 1. A) Prevalence of molecular alterations in *TP53*, *SPOP*, *AR*, and *BRCA2* compared between AA (n=61) and White (n=56, including White Hispanic) PC patients treated at BTH. **B)** Prevalence of molecular alterations in *TP53*, *SPOP*, *AR* and mutations identified in homologous recombination repair (HRR) genes (*BRCA1, BRCA2, ATM, BRIP1, BARD1, CDK12, CHEK1, CHEK2, FANCL, PALB2, PPP2R2A, RAD51B, RAD51C, RAD51D, RAD54L*) compared between AA (n=307) and non-AA (n=1548) PC patient data within the Tempus database. Our data show high mutation frequency in key PC drivers in AA patients at our safety net hospital (BTH).

Figure 2: Longitudinal liquid biopsy monitoring of two AA PC patients treated with hormonal therapy

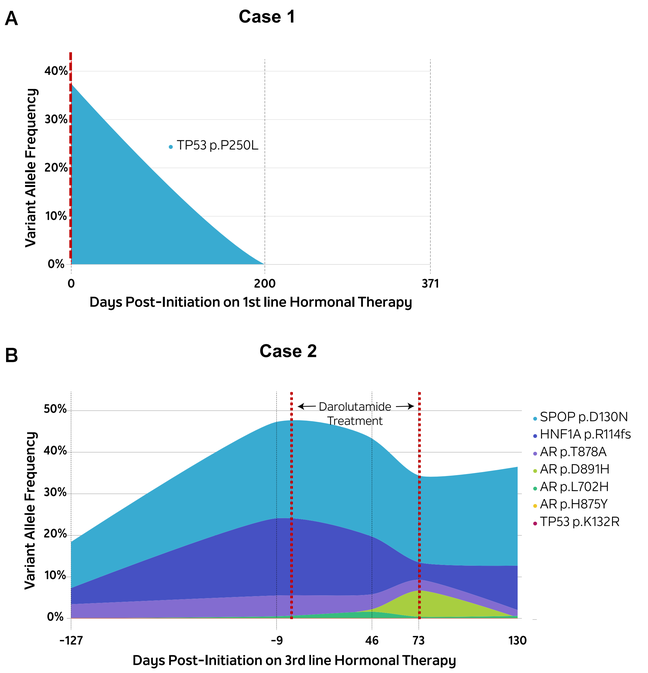

Figure 2. A) Variant allele frequency (VAF) for a *TP53* alteration detected in ctDNA in a 57-year-old AA metastatic PC patient treated with 1st line hormonal therapy, which involved a short course of bicalutamide, followed by androgen deprivation therapy (ADT) and abiraterone acetate (together with prednisone). Vertical dashed red line indicates start of treatment. Reduction in VAF corresponded with similar reduction in prostate-specific antigen (PSA) levels and overall treatment response (not shown). **B)** VAFs for gene alterations (*SPOP, HNF1A, AR,* and *TP53*) detected in ctDNA in a 59-year-old AA metastatic castration-resistant PC patient treated with 3rd line hormonal therapy, including darolutamide. VAFs remained high and were associated with persistently elevated PSA levels and lack of clinical response to therapy (not shown). Vertical dotted red lines indicate darolutamide treatment window.

Figure 3: Longitudinal liquid biopsy monitoring and corresponding PSA levels of two MSI-H AA PC patients treated with pembrolizumab

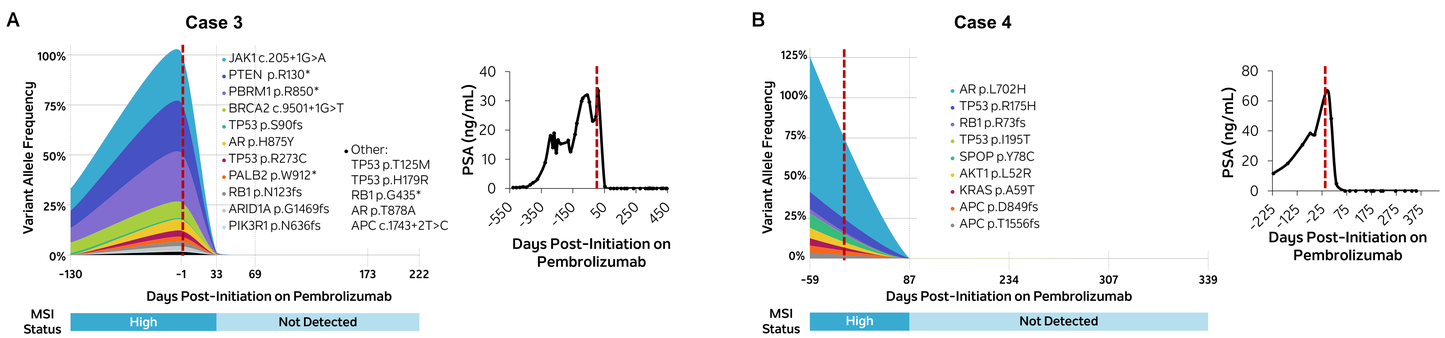

Figure 3. Longitudinal liquid biopsy was used to assess VAFs for genetic alterations and microsatellite instability (MSI) status in metastatic castration-resistant PC (mCRPC) AA patients treated with the immune checkpoint inhibitor, pembrolizumab. **A)** VAFs for alterations in *JAK1, PTEN, PBRM1, BRCA2, TP53, AR, PALB2, RB1, ARID1A, PIK3R1,* and *APC,* in a 72-year-old AA mCRPC patient and corresponding PSA levels. **B)** VAFs for alterations in *AR, TP53, RB1, SPOP, AKT1, KRAS* and *APC,* in a 64-year-old AA mCRPC patient and corresponding PSA levels. Vertical dashed red lines indicate start of treatment. In both cases, treatment with pembrolizumab reduced VAFs and MSI-high status, and the reduction in VAFs corresponded with similar a reduction in blood PSA levels.

CONCLUSIONS

- The high mutation frequency in key PC drivers in AA pts at our safety net hospital can be attributed to underlying disease biology or the more advanced disease at presentation in AA pts with socioeconomic factors delaying access to healthcare.
- Liquid biopsy (Tempus|xF) is a minimally invasive tool that allows longitudinal monitoring of response (or lack thereof) to treatment.
- Longitudinal liquid biopsy assessment revealed durable response to therapy in MSI-H PC patients treated with immune checkpoint inhibition.
- Use of comprehensive tissue and liquid biopsy NGS testing has the potential to expand treatment options for AA PC patients to include targeted therapies as well as allow participation in biomarker-based precision oncology clinical trials.

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