Pathogenic *BRAF* mutations in prostate cancer: frequency and distribution

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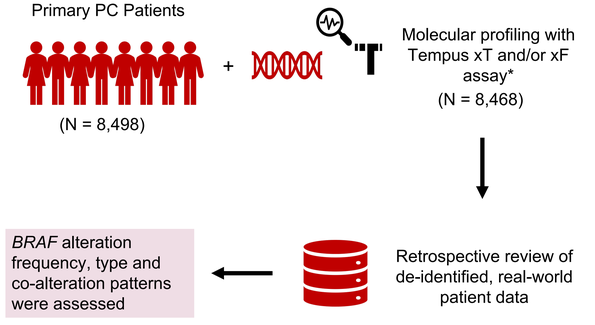
INTRODUCTION

- In prostate cancer, *BRAF* mutations are a rare but clinically significant finding.
- *BRAF* activating mutations may affect tumor growth and could be exploited as a therapeutic target.
- *BRAF* p. V600E is the most common and well described hot spot mutation, however, other activating *BRAF* mutations are less well studied.
- In the current study, we evaluate the landscape of *BRAF* pathogenic/likely pathogenic (P/LP) variations from real-world data of prostate cancer patients via tissue and ctDNA assays.

METHODS



***Tempus xT assay** - Tissue panel that detects single-nucleotide variants (SNVs), insertions and/or deletions (indels), and copy number variants (CNVs) in 648 genes, as well as chromosomal rearrangements in 22 genes (500× coverage, full transcriptome RNAseq)

***Tempus xF assay** - liquid biopsy panel that identifies SNVs and indels in 105 genes, CNVs in six genes, and chromosomal rearrangements in seven genes.

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SUMMARY

- This study presents the **first large-scale genomic characterization of *BRAF* mutations** in patients with prostate cancer using both tissue and ctDNA NGS analysis.
- Among 8,468 patients from prostate cancer patients, **K601E was the most frequently altered *BRAF* mutation** followed by G4669A, v600E, L597R, D594N and D594G.
- This finding could have implications for anti-BRAF therapeutic development.

RESULTS

Table 1. *Cohort Characteristics*

	Overall Cohort, N = 8,468[1]
Age at Diagnosis	65 (60, 72)
Unknown	1,567
Race	
White	3,746 (74%)
Black or African American	945 (19%)
Other	209 (4.1%)
Asian	148 (2.9%)
Unknown	3,420
Ethnicity	
Not Hispanic or Latino	2,442 (88%)
Hispanic or Latino	345 (12%)
Unknown	5,681
Sample Testing Type	
Received xF testing	4,177 (49%)
BRAF P/LP* by xF	50 (1.2%)
Received xT testing	5,902 (70%)
BRAF P/LP* by xT	85 (1.4%)

[1] Median (IQR); n (%)
*P/LP = pathogenic/likely pathogenic

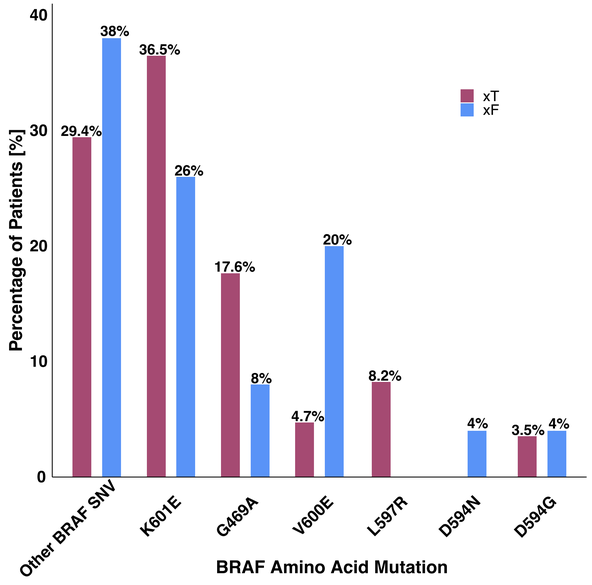

Figure 1. Prevalence of amino acid mutations among prostate cancer patients with a P/LP *BRAF* SNV.

Testing type			
Tissue, xT N = 5,902		ctDNA, xF N = 4,177	
BRAF Mutation	N = 85	*BRAF* Mutation	N = 50
Lys601Glu	31 (36%)	Lys601Glu	13 (26%)
Gly469Ala	15 (18%)	Val600Glu	10 (20%)
Leu597Arg	7 (8%)	Gly469Ala	4 (8.0%)
Val600Glu	4 (4.7%)	Asp594Asn	2 (4.0%)
Asp594Gly	3 (3.5%)	Asp594Gly	2 (4.0%)

Table 2. Most frequently altered mutations.

Of these 85 patients, the most prevalent *BRAF* mutation identified within tissue samples was *BRAF* K601E (Lys601Glu) (36%), Gly469Ala (18%) and Leu597Arg (8%). Similarly, the most prevalent *BRAF* mutation identified within ctDNA was *BRAF* K601E (26%).