Prostate Sample
Michael Bennett

Diagnosis
Adenocarcinoma

Accession No.
5903

xT

Date of Birth
1966-07-03

Sex
Female

Physician
Dr. Michelle Wilson

Institution
Jones, Obrien and Williams

Tumor specimen:
source Prostate
CollectedDate 2023-12-23
ReceivedDate 2023-12-23
TumorPercentage 78%

Normal specimen:
source Blood
CollectedDate 2023-12-24
ReceivedDate 2023-12-24

GENOMIC VARIANTS

Somatic - Potentially Actionable		variant allele fraction
CTNNB1	c.101G>T p.T41I Stopgain-LOF	20.35%

Somatic - Biologically Relevant		
IDH1	c.395G>T p.S45P Missensevariant(exon2)-GOF	7.96%
JAK2	c.1848_1849delinsCT p.S37C Spliceregionvariant-LOF	12.16%
NOTCH1	c.3587G>A p.R132L Spliceregionvariant-LOF	17.91%
MPL	c.1544G>T p.T875N Missensevariant(exon2)-GOF	8.17%

Germline - Pathogenic

No Germline - Pathogenic variants were found in the limited set of genes on which we report.

Pertinent Negatives

No Pertinent Negatives variants were found in the limited set of genes on which we report.

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden		Microsatellite Instability Status
33 m/Mb	8%	Stable / Equivocal / **High**

FDA-APPROVED THERAPIES, Current Diagnosis

KRAS G12C Inhibitors	**Sotorasib**	NCCN, Consensus, Non-Small Cell Lung Cancer MSK OncoKB, Level 1 KRASp.G12C G12C-GOF

FDA-APPROVED THERAPIES, Other Indications

KRAS G12C Inhibitors	**Sotorasib**	NCCN, Consensus, Non-Small Cell Lung Cancer MSK OncoKB, Level 1 KRASp.G12C G12C-GOF

ADDITIONAL INDICATORS

Unfavorable Prognosis	NCCN, Consensus, Non-Small Cell Lung Cancer KRASp.G12C Gain-of-function

CLINICAL TRIALS

A Study of VS-6766 v. VS-6766 + Defactinib in Recurrent G12V, Other KRAS and BRAF Non-Small Cell Lung Cancer	**Phase 2** City, state - x mi **KRAS mutation**
A Phase 1/2 Study of MRTX849 in Patients With Cancer Having a KRAS G12C Mutation KRYSTAL-1	**Phase 1/2** City, state - x mi **KRAS mutation** **STK11 mutation**
First-in-human Study of DRP-104 (Sirpiglenastat) as Single Agent and in Combination With Atezolizumab in Patients With Advanced Solid Tumors. (NCT04471415)	**Phase 1/2** City, state - x mi **NFE2L2 mutation** **STK11 mutation**

VARIANTS OF UNKNOWN SIGNIFICANCE

Somatic	**Mutation effect**	**Variant allele fraction**
ABL1	c.3113A>G p.A34V Stopgain-LOF NM_001011645	22.82%
HRAS	c.35_36delinsTA p.G12D Frameshift-LOF NM_001011645	8.7%
EZH2	c.1936T>G p.Y646F Frameshift-LOF NM_001011645	8.8%
PDGFRB	c.3113A>G p.T681I Frameshift-LOF NM_001011645	1.01%
JAK3	c.3113A>G p.L857P Frameshift-GOF NM_001011645	9.76%
DNMT3A	c.2711C>T p.P904L Stopgain-LOF NM_001011645	2.83%
MSH2	c.1906G>C p.A636P Spliceregionvariant-GOF NM_001011645	8.24%

Germline	**Mutation effect**	**Condition**
BTK	c.3113A>G p.C481X Frameshift-GOF NM_001011645	agent

LOW COVERAGE REGIONS

ARHGAP45 PAX5

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

CTNNB1 c.101G>T p.T41I Stopgain-LOF VAF: 20.35%

NFE2L2 acts as a transcription factor for proteins that contain an antioxidant response element (ARE) within their promoter sequence. Genes that contain ARE are involved in injury and inflammation response. Activating mutations and overexpression of NFE2L2 are associated with cancer progression.

SOMATIC VARIANT DETAILS - BIOLOGICALLY RELEVANT

IDH1 c.395G>T p.S45P Missensevariant(exon2)-GOF VAF: 7.96%

BCL11B encodes a C2H2-type zinc finger protein that functions as a transcriptional repressor and plays a role in T-cell development and survival. Loss of function mutations, copy number loss, and fusions resulting in the underexpression of BCL11B are associated with cancer progression.

JAK2 c.1848_1849delinsCT p.S37C Spliceregionvariant-LOF VAF: 12.16%

RBM10 encodes a protein that contains a RNA-binding motif and interacts with RNA homopolymers, and is thought to function in regulating alternative splicing. Loss of function mutations and copy number loss of RBM10 are associated with cancer progression.

NOTCH1 c.3587G>A p.R132L Spliceregionvariant-LOF VAF: 17.91%

STK11 (LKB1) encodes an enzyme in the serine/threonine kinase family that is responsible for maintaining energy metabolism and cellular polarization through the activation of AMP-activated protein kinase and other members of the AMPK family. The enzyme also acts as a tumor suppressor by regulating cell growth. Loss of function mutations, copy number loss, epigenetic variation, and underexpression of STK11 are associated with cancer progression.

MPL c.1544G>T p.T875N Missensevariant(exon2)-GOF VAF: 8.17%

TP53 encodes a protein that is a transcription factor that regulates the expression of genes involved in cell cycle arrest, apoptosis, and DNA repair. TP53 is a tumor suppressor gene that is mutated in many cancers. Mutations in TP53 are associated with cancer progression.

CLINICAL HISTORY

Diagnosed on

2023-12-18