Breast Sample
James Hayes

Diagnosis
Invasive ductal carcinoma

Accession No.
6354

xT

Date of Birth
1957-03-17

Sex
Male

Physician
Dr. Terri Francis

Institution
Ho-Jackson

Tumor specimen:
source Breast
CollectedDate 2024-04-16
ReceivedDate 2024-04-16
TumorPercentage 85%

Normal specimen:
source Blood
CollectedDate 2024-04-17
ReceivedDate 2024-04-19

GENOMIC VARIANTS

Somatic - Potentially Actionable		variant allele fraction
KIT	c.2464A>T p.K818Q Frameshift-LOF	3.21%
PHF6	c.3113A>G p.R225X Stopgain-LOF	7.95%

Somatic - Biologically Relevant		
SDHD	c.34G>A p.G12S Stopgain-LOF	1.69%
SIX1	c.530A>G p.G12S Frameshift-GOF	17.8%
FGFR2	c.1144T>C p.C382R Nonsense-GOF	8.51%

Germline - Pathogenic

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

Pertinent Negatives

PKLR FGFR3 PRKCA HDAC1

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

28 m/Mb 81%

Microsatellite Instability Status

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**
MET	c.1510G>C p.S1236R Frameshift-LOF NM_001011645	1.71%
HBA2	c.427T>C p.*143Qext*31 Nonsense-GOF NM_001011645	16.91%
XPC	c.3113A>G p.S346P Missensevariant(exon2)-GOF NM_001011645	7.8%
FOXL2	c.402C>G p.C134W Spliceregionvariant-LOF NM_001011645	8.76%
FOXL2	c.402C>G p.C134W Spliceregionvariant-LOF NM_001011645	1.86%
PDGFRB	c.3113A>G p.T681I Frameshift-LOF NM_001011645	8.15%
PAX5	c.239C>G p.A322T Stopgain-LOF NM_001011645	7.15%
HBA2	c.427T>C p.*143Qext*31 Nonsense-LOF NM_001011645	8.7%

Germline	**Mutation effect**	**Condition**
PRKCA	c.1387G>C p.D463H Nonsense-GOF NM_001011645	leg
STAG2	c.3113A>G p.R1012X Frameshift-LOF NM_001011645	cell

LOW COVERAGE REGIONS

RNF43 AKT1

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

KIT c.2464A>T p.K818Q Frameshift-LOF VAF: 3.21%

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.

PHF6 c.3113A>G p.R225X Stopgain-LOF VAF: 7.95%

PTEN encodes a phosphatase that acts as a tumor suppressor by negatively regulating the PI3K-AKT-mTOR pathway. Loss of function mutations, copy number loss, and underexpression of PTEN are associated with cancer progression.

SOMATIC VARIANT DETAILS - BIOLOGICALLY RELEVANT

SDHD c.34G>A p.G12S Stopgain-LOF VAF: 1.69%

KRAS is a GDP/GTP binding protein that acts as an intracellular signal transducer. KRAS is involved in several pathways involved in cellular proliferation and survival, including the PI3K-AKT-mTOR pathway and the Ras-Raf-MEK-ERK pathway. Activating mutations, copy number gains, and overexpression of KRAS are associated with cancer progression.

SIX1 c.530A>G p.G12S Frameshift-GOF VAF: 17.8%

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.

FGFR2 c.1144T>C p.C382R Nonsense-GOF VAF: 8.51%

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.

CLINICAL HISTORY

Diagnosed on

2024-04-14