Breast Sample
Brandi Thomas

Diagnosis
Triple-negative breast cancer

Accession No.
8347

xT

Date of Birth
1976-07-21

Sex
Female

Physician
Dr. Timothy Johnson

Institution
Yates, Farley and Roberts

Tumor specimen:
source Breast
CollectedDate 2023-04-30
ReceivedDate 2023-05-04
TumorPercentage 52%

Normal specimen:
source Blood
CollectedDate 2023-05-05
ReceivedDate 2023-05-05

GENOMIC VARIANTS

Somatic - Potentially Actionable		variant allele fraction
CCND3	c.766_776del11 p.R256fs*64 Frameshift-GOF	30.18%
ZEB2	c.3113A>G p.H1038R Missensevariant(exon2)-GOF	31.52%
GNAS	c.601C>T p.Q125R Nonsense-GOF	2.26%

Somatic - Biologically Relevant		
DICER1	c.5428G>C p.W1831* Spliceregionvariant-GOF	16.85%
CDC73	c.1A>G p.E1813G Stopgain-LOF	10.25%
EGFR	c.1474A>C p.P772_H773insNPH Stopgain-LOF	8.07%

Germline - Pathogenic

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

Pertinent Negatives

KLF4 MAPK1 FGFR1

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

46 m/Mb 95%

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**
SMO	c.3113A>G p.A374E Missensevariant(exon2)-GOF NM_001011645	9.67%
RB1	c.3113A>G p.F650S Spliceregionvariant-LOF NM_001011645	9.37%
IDH1	c.394C>G p.R132X Stopgain-LOF NM_001011645	8.63%
DICER1	c.5439G>T p.E1813K Spliceregionvariant-LOF NM_001011645	7.0%
SF3B1	c.3113A>G p.K741X Nonsense-GOF NM_001011645	5.19%
SMO	c.3113A>G p.A374E Nonsense-LOF NM_001011645	9.61%

Germline	**Mutation effect**	**Condition**
CDC73	c.1A>G p.M1V Spliceregionvariant-LOF NM_001011645	her
PHF6	c.3113A>G p.R225X Nonsense-LOF NM_001011645	trial

LOW COVERAGE REGIONS

FLT3 MTOR HDAC2

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

CCND3 c.766_776del11 p.R256fs*64 Frameshift-GOF VAF: 30.18%

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.

ZEB2 c.3113A>G p.H1038R Missensevariant(exon2)-GOF VAF: 31.52%

FAT1 encodes a transmembrane protein involved in tumor suppressor signaling. FAT1 protein can regulate transcriptional activity by sequestering beta-catenin, thereby preventing it from entering the nucleus. Loss of function mutations and copy number loss of FAT1 are associated with cancer progression.

GNAS c.601C>T p.Q125R Nonsense-GOF VAF: 2.26%

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.

SOMATIC VARIANT DETAILS - BIOLOGICALLY RELEVANT

DICER1 c.5428G>C p.W1831* Spliceregionvariant-GOF VAF: 16.85%

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.

CDC73 c.1A>G p.E1813G Stopgain-LOF VAF: 10.25%

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.

EGFR c.1474A>C p.P772_H773insNPH Stopgain-LOF VAF: 8.07%

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.

CLINICAL HISTORY

Diagnosed on

2023-04-28