Breast Sample
Kristin Sanders

Diagnosis
Lobular carcinoma in situ (LCIS)

Accession No.
5011

xT

Date of Birth
2004-03-09

Sex
Male

Physician
Dr. Beth Lopez

Institution
Lopez, Walters and Wilson

Tumor specimen:
source Breast
CollectedDate 2023-06-30
ReceivedDate 2023-07-05
TumorPercentage 31%

Normal specimen:
source Blood
CollectedDate 2023-07-05
ReceivedDate 2023-07-07

GENOMIC VARIANTS

Somatic - Potentially Actionable		variant allele fraction
SDHA	c.1660C>T p.R554W Missensevariant(exon2)-GOF	28.8%
IDH2	c.516G>C p.R140L Frameshift-GOF	6.47%

Somatic - Biologically Relevant		
MSH2	c.1906G>C p.R140Q Nonsense-LOF	15.91%
HSP90B1	c.3113A>G p.R172M Spliceregionvariant-LOF	14.55%
KRAS	c.38_39delinsAA p.Q61P Missensevariant(exon2)-GOF	4.16%
RNF43	c.461C>T p.Q61E Stopgain-LOF	9.0%

Germline - Pathogenic

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

Pertinent Negatives

SMO TP53

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

32 m/Mb 90%

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
MYO1G	c.145G>A p.V49M Frameshift-LOF NM_001011645	18.3%
PTEN	c.389G>C p.R130G Nonsense-LOF NM_001011645	11.67%
NT5C2	c.1100G>A p.R367Q Stopgain-LOF NM_001011645	14.59%
FLT3	c.1992G>C p.F594Y Nonsense-GOF NM_001011645	8.8%
SDHD	c.34G>A p.G12S Frameshift-LOF NM_001011645	7.36%
KLF4	c.1225A>C p.K409Q Nonsense-GOF NM_001011645	8.16%
GNAS	c.602G>A p.R201S Frameshift-GOF NM_001011645	3.09%
TP53	c.742C>T p.P250L Frameshift-LOF NM_001011645	3.22%
MPL	c.1544G>T p.W515L Spliceregionvariant-LOF NM_001011645	9.97%
PDGFRB	c.3113A>G p.T681I Frameshift-LOF NM_001011645	8.81%
FGFR2	c.1144T>C p.P253R Spliceregionvariant-GOF NM_001011645	1.65%
TLR8	c.3113A>G p.N515H Nonsense-LOF NM_001011645	9.81%

LOW COVERAGE REGIONS

ABL1

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

SDHA c.1660C>T p.R554W Missensevariant(exon2)-GOF VAF: 28.8%

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.

IDH2 c.516G>C p.R140L Frameshift-GOF VAF: 6.47%

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.

SOMATIC VARIANT DETAILS - BIOLOGICALLY RELEVANT

MSH2 c.1906G>C p.R140Q Nonsense-LOF VAF: 15.91%

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.

HSP90B1 c.3113A>G p.R172M Spliceregionvariant-LOF VAF: 14.55%

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.

KRAS c.38_39delinsAA p.Q61P Missensevariant(exon2)-GOF VAF: 4.16%

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.

RNF43 c.461C>T p.Q61E Stopgain-LOF VAF: 9.0%

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.

CLINICAL HISTORY

Diagnosed on

2023-06-29