Breast Sample
Richard Nguyen

Diagnosis
Lobular carcinoma in situ (LCIS)

Accession No.
3006

xT

Date of Birth
1933-09-30

Sex
Male

Physician
Dr. Kimberly Jenkins

Institution
Payne PLC

Tumor specimen:
source Breast
CollectedDate 2023-07-24
ReceivedDate 2023-07-27
TumorPercentage 17%

Normal specimen:
source Blood
CollectedDate 2023-07-31
ReceivedDate 2023-07-31

GENOMIC VARIANTS

Somatic - Potentially Actionable		variant allele fraction
PDGFRB	c.3113A>G p.T681I Frameshift-GOF	15.31%
XPC	c.3113A>G p.S346P Nonsense-GOF	26.74%
GNAS	c.680A>T p.Q227L Nonsense-GOF	12.4%
JAK3	c.3113A>G p.L857P Frameshift-GOF	22.42%

Somatic - Biologically Relevant

JAK2	c.1849G>T p.L857P Stopgain-LOF	11.56%

Germline - Pathogenic

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

Pertinent Negatives

SIX1 MSH2

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

15 m/Mb 27%

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 Stopgain-LOF NM_001011645	9.99%
BRAF	c.1405_1407delinsAGC p.V600X Spliceregionvariant-GOF NM_001011645	8.65%
FLT3	c.1992G>T p.Y842X Missensevariant(exon2)-GOF NM_001011645	6.5%
NF1	c.4394A>G p.N1465S Spliceregionvariant-GOF NM_001011645	7.56%
NCSTN	c.3113A>G p.A572G Nonsense-GOF NM_001011645	3.79%
BRAF	c.1789_1790delinsTC p.G469E Missensevariant(exon2)-GOF NM_001011645	4.65%
MET	c.3749T>C p.V1092I Nonsense-LOF NM_001011645	9.13%
NOTCH1	c.7507C>T p.S2467Rfs*13 Missensevariant(exon2)-GOF NM_001011645	7.71%
GNAS	c.374A>G p.Q227L Spliceregionvariant-GOF NM_001011645	4.38%
HSP90B1	c.3113A>G p.I66T Frameshift-LOF NM_001011645	2.32%
MET	c.1510G>C p.Y1003X Nonsense-LOF NM_001011645	5.87%

LOW COVERAGE REGIONS

FGFR1 JAK2

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

PDGFRB c.3113A>G p.T681I Frameshift-GOF VAF: 15.31%

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.

XPC c.3113A>G p.S346P Nonsense-GOF VAF: 26.74%

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.

GNAS c.680A>T p.Q227L Nonsense-GOF VAF: 12.4%

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.

JAK3 c.3113A>G p.L857P Frameshift-GOF VAF: 22.42%

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.

SOMATIC VARIANT DETAILS - BIOLOGICALLY RELEVANT

JAK2 c.1849G>T p.L857P Stopgain-LOF VAF: 11.56%

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.

CLINICAL HISTORY

Diagnosed on

2023-07-23