# Breast Sample
# Susan Barton

Diagnosis
**Invasive ductal carcinoma**

Accession No.
**4835**

xT

Date of Birth
**1934-06-10**

Sex
**Male**

Physician
**Dr. Elizabeth Wolfe**

Institution
**Ellis Inc**

Tumor specimen:
source Breast
CollectedDate 2024-03-28
ReceivedDate 2024-03-28
TumorPercentage 77%

Normal specimen:
source Blood
CollectedDate 2024-03-29
ReceivedDate 2024-03-30

## GENOMIC VARIANTS

| Somatic - Potentially Actionable | | variant allele fraction |
|---|---|---|
| MET | c.3209T>G p.I639L Frameshift-LOF | 4.03% |
| MAP2K2 | c.383C>T p.P128L Stopgain-LOF | 13.41% |
| PAX5 | c.239C>G p.A322T Frameshift-LOF | 8.64% |
| SDHB | c.487T>C p.S163P Nonsense-GOF | 20.88% |

**Somatic - Biologically Relevant**

| | | |
|---|---|---|
| SIX1 | c.530A>G p.S163P Nonsense-LOF | 6.19% |
| SDHA | c.1660C>T p.S163P Missensevariant(exon2)-GOF | 11.74% |

**Germline - Pathogenic**

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

**Pertinent Negatives**

MSH2 FGFR2

## IMMUNOTHERAPY MARKERS

**Tumor Mutational Burden**

27 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<br>MSK OncoKB, Level 1<br>KRASp.G12C G12C-GOF |

## FDA-APPROVED THERAPIES, Other Indications

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

## ADDITIONAL INDICATORS

| | |
|---|---|
| **Unfavorable Prognosis** | NCCN, Consensus, Non-Small Cell Lung Cancer<br>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**<br>City, state - x mi<br>**KRAS mutation** |
| A Phase 1/2 Study of MRTX849 in Patients With Cancer Having a KRAS G12C Mutation KRYSTAL-1 | **Phase 1/2**<br>City, state - x mi<br>**KRAS mutation**<br>**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**<br>City, state - x mi<br>**NFE2L2 mutation**<br>**STK11 mutation** |

## VARIANTS OF UNKNOWN SIGNIFICANCE

| Somatic | Mutation effect | Variant allele fraction |
|---|---|---|
| NTRK1 | c.1792C>T p.G607V Spliceregionvariant-LOF<br>NM_001011645 | 7.48% |
| FGFR3 | c.746C>G p.K650E Nonsense-LOF<br>NM_001011645 | 12.77% |
| TEK | c.1354A>G p.N452D Spliceregionvariant-LOF<br>NM_001011645 | 12.68% |
| PAX5 | c.547G>A p.A322T Missensevariant(exon2)-GOF<br>NM_001011645 | 8.76% |
| BRCA1 | c.5265_5266insC p.E23Vfs*17 Missensevariant(exon2)-GOF<br>NM_001011645 | 2.29% |
| BLM | c.2207_2212delinsTAGATTC p.Y736fs*4 Stopgain-LOF<br>NM_001011645 | 8.0% |
| HBA2 | c.427T>C p.*143Qext*31 Missensevariant(exon2)-GOF<br>NM_001011645 | 2.92% |
| STAG2 | c.3113A>G p.R1012X Frameshift-LOF<br>NM_001011645 | 6.99% |
| CTNNB1 | c.110C>T p.S45F Nonsense-GOF<br>NM_001011645 | 2.83% |
| CDKN2A | c.151G>A p.H83Y Frameshift-GOF<br>NM_001011645 | 6.99% |
| KLF1 | c.892G>C p.M39L Missensevariant(exon2)-GOF<br>NM_001011645 | 3.39% |
| ERBB2 | c.2089G>T p.I655V Frameshift-GOF<br>NM_001011645 | 3.46% |

## LOW COVERAGE REGIONS

NRAS JAK3

## SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

**MET** c.3209T>G p.I639L Frameshift-LOF VAF: 4.03%

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.

**MAP2K2** c.383C>T p.P128L Stopgain-LOF VAF: 13.41%

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.

**PAX5** c.239C>G p.A322T Frameshift-LOF VAF: 8.64%

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.

**SDHB** c.487T>C p.S163P Nonsense-GOF VAF: 20.88%

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.

## SOMATIC VARIANT DETAILS - BIOLOGICALLY RELEVANT

**SIX1** c.530A>G p.S163P Nonsense-LOF VAF: 6.19%

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.

**SDHA** c.1660C>T p.S163P Missensevariant(exon2)-GOF VAF: 11.74%

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

2024-03-28