# Prostate Sample
# Kimberly Berry

Diagnosis
**Small cell carcinoma**

Accession No.
**1616**

xT

Date of Birth
**1945-08-15**

Sex
**Male**

Physician
**Dr. Linda Phillips**

Institution
**Montgomery, Lynn and Stone**

Tumor specimen:
source Prostate
CollectedDate 2024-04-05
ReceivedDate 2024-04-07
TumorPercentage 59%

Normal specimen:
source Blood
CollectedDate 2024-04-10
ReceivedDate 2024-04-11

## GENOMIC VARIANTS

| Somatic - Potentially Actionable | | variant allele fraction |
|---|---|---|
| SDHB | c.487T>C p.S163P Nonsense-LOF | 7.0% |
| DICER1 | c.5437G>A p.E1813K Nonsense-LOF | 30.62% |

| Somatic - Biologically Relevant | | |
|---|---|---|
| MUTYH | c.1014G>C p.Y1225X Spliceregionvariant-LOF | 4.74% |
| IDH1 | c.394C>T p.E1813K Frameshift-LOF | 21.76% |
| CHD6 | c.4800C>G p.I1600M Stopgain-LOF | 2.66% |

**Germline - Pathogenic**

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

**Pertinent Negatives**

MYCN TP53 ARID2 ALDH2 BRCA2

## IMMUNOTHERAPY MARKERS

**Tumor Mutational Burden**

42 m/Mb 14%

**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 |
|---|---|---|
| MAP2K2 | c.383C>T p.P128L Nonsense-GOF<br>NM_001011645 | 21.12% |
| MAP2K2 | c.383C>T p.P128L Spliceregionvariant-GOF<br>NM_001011645 | 10.92% |
| NTRK1 | c.1792C>T p.G607V Stopgain-LOF<br>NM_001011645 | 14.75% |
| CDKN2A | c.248A>C p.R80X Nonsense-GOF<br>NM_001011645 | 6.98% |
| PTPN11 | c.1508G>C p.G503A Frameshift-LOF<br>NM_001011645 | 9.14% |
| SDHA | c.1660C>T p.R554W Frameshift-GOF<br>NM_001011645 | 5.11% |
| PHF6 | c.3113A>G p.R225X Missensevariant(exon2)-GOF<br>NM_001011645 | 4.69% |
| SIX1 | c.530A>G p.Q177R Frameshift-GOF<br>NM_001011645 | 8.84% |
| PTCH1 | c.3583A>T p.T1195S Stopgain-LOF<br>NM_001011645 | 5.77% |

## LOW COVERAGE REGIONS

KLF4 PIK3CA SMO

## SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

**SDHB** c.487T>C p.S163P Nonsense-LOF VAF: 7.0%

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.

**DICER1** c.5437G>A p.E1813K Nonsense-LOF VAF: 30.62%

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.

## SOMATIC VARIANT DETAILS - BIOLOGICALLY RELEVANT

**MUTYH** c.1014G>C p.Y1225X Spliceregionvariant-LOF VAF: 4.74%

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.

**IDH1** c.394C>T p.E1813K Frameshift-LOF VAF: 21.76%

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.

**CHD6** c.4800C>G p.I1600M Stopgain-LOF VAF: 2.66%

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

2024-04-05