Lung Sample
Marilyn Mcbride

Diagnosis
Large cell carcinoma

Accession No.
5191

xT

Date of Birth
2000-04-16

Sex
Male

Physician
Dr. Jennifer Johnson

Institution
Gutierrez Group

Tumor specimen:
source Lung
CollectedDate 2023-12-29
ReceivedDate 2023-12-29
TumorPercentage 72%

Normal specimen:
source Blood
CollectedDate 2024-01-02
ReceivedDate 2024-01-07

GENOMIC VARIANTS

Somatic - Potentially Actionable — **variant allele fraction**

NF1	c.4394A>G p.S2309Cfs*10 Frameshift-LOF	3.51%

Somatic - Biologically Relevant

IKZF1	c.3113A>G p.N1465S Missensevariant(exon2)-GOF	18.76%
MPL	c.1543_1545delinsAAA p.W515K Spliceregionvariant-GOF	21.92%

Germline - Pathogenic

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

Pertinent Negatives

CSF1R HBB ERCC2 IDH1

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

18 m/Mb 89%

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

Electronically signed by	CLIA number	Date Signed/Reported	Laboratory Medical Director	ID #	Pipeline version
Jennifer Johnson	14D2114007	2024-01-05	Dr. Tammy Farley	5191	3.2.0

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**
DICER1	c.5492G>A p.E1705V Frameshift-GOF NM_001011645	10.63%
HBB	c.364G>A p.E27K Spliceregionvariant-GOF NM_001011645	18.81%
MYO1G	c.145G>A p.V49M Nonsense-GOF NM_001011645	3.43%
TLR8	c.3113A>G p.N515H Missensevariant(exon2)-GOF NM_001011645	2.28%
PHF6	c.3113A>G p.R225X Spliceregionvariant-GOF NM_001011645	3.88%
BRCA2	c.5946delT p.S1982Rfs*22 Nonsense-GOF NM_001011645	8.32%
PHF6	c.3113A>G p.R225X Spliceregionvariant-GOF NM_001011645	3.86%

Germline	**Mutation effect**	**Condition**
SDHB	c.487T>C p.S163P Nonsense-LOF NM_001011645	recent

LOW COVERAGE REGIONS

MAPK1 PIK3CA

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

NF1 c.4394A>G p.S2309Cfs*10 Frameshift-LOF VAF: 3.51%

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

IKZF1 c.3113A>G p.N1465S Missensevariant(exon2)-GOF VAF: 18.76%

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.

MPL c.1543_1545delinsAAA p.W515K Spliceregionvariant-GOF VAF: 21.92%

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

2023-12-27