Leukemia Sample
Jennifer Castillo

Diagnosis
Acute lymphocytic leukemia (ALL)

Accession No.
3523

xT

Date of Birth
1963-12-08

Sex
Female

Physician
Dr. William Martin

Institution
Young, Thomas and Watkins

Tumor specimen:
source Leukemia
CollectedDate 2024-03-26
ReceivedDate 2024-03-26
TumorPercentage 8%

Normal specimen:
source Blood
CollectedDate 2024-03-29
ReceivedDate 2024-03-31

GENOMIC VARIANTS

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

KIT	c.1669T>A p.V559D Stopgain-LOF	25.44%

Somatic - Biologically Relevant

BRAF	c.1397G>C p.K642E Frameshift-LOF	10.63%
BRCA2	c.5946delT p.V600K Missensevariant(exon2)-GOF	28.01%

Germline - Pathogenic

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

Pertinent Negatives

HRAS

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

9 m/Mb 43%

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
XPC	c.3113A>G p.S346P Spliceregionvariant-LOF NM_001011645	3.25%
ARHGAP45	c.416G>A p.R139H Nonsense-LOF NM_001011645	14.86%
GNAS	c.680A>G p.R201H Frameshift-LOF NM_001011645	5.1%
MYO1G	c.145G>A p.V49M Frameshift-GOF NM_001011645	4.24%
CSF1R	c.1085A>G p.H362R Frameshift-LOF NM_001011645	9.17%
SMO	c.3113A>G p.A374E Spliceregionvariant-GOF NM_001011645	1.1%
ERBB2	c.926G>A p.G776C Frameshift-GOF NM_001011645	4.82%
H3.3	c.3113A>G p.G35L Missensevariant(exon2)-GOF NM_001011645	7.72%
HBB	c.79G>A p.E7V Spliceregionvariant-GOF NM_001011645	7.18%
MET	c.3749T>C p.V1070G Missensevariant(exon2)-GOF NM_001011645	2.35%
PDGFRA	c.1154_1155delinsTA p.D842V Nonsense-LOF NM_001011645	5.15%
SIX1	c.530A>G p.Q177R Spliceregionvariant-LOF NM_001011645	8.91%

LOW COVERAGE REGIONS

KLF1 MAPK1

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

KIT c.1669T>A p.V559D Stopgain-LOF VAF: 25.44%

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

BRAF c.1397G>C p.K642E Frameshift-LOF VAF: 10.63%

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.

BRCA2 c.5946delT p.V600K Missensevariant(exon2)-GOF VAF: 28.01%

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.

CLINICAL HISTORY

Diagnosed on

2024-03-25