Leukemia Sample
Alvin Trujillo

Diagnosis
Acute myeloid leukemia (AML)

Accession No.
5450

xT

Date of Birth
1969-12-12

Sex
Male

Physician
Dr. Benjamin Sullivan

Institution
Casey-Williams

Tumor specimen:
source Leukemia
CollectedDate 2023-07-19
ReceivedDate 2023-07-22
TumorPercentage 36%

Normal specimen:
source Blood
CollectedDate 2023-07-23
ReceivedDate 2023-07-23

GENOMIC VARIANTS

Somatic - Potentially Actionable		variant allele fraction
IKZF1	c.3113A>G p.N159Y Frameshift-LOF	15.21%

Somatic - Biologically Relevant		
KLF4	c.1225A>C p.K409Q Stopgain-LOF	22.76%
MUTYH	c.1014G>C p.N159Y Frameshift-LOF	3.78%
U2AF1	c.3113A>G p.K409Q Missensevariant(exon2)-GOF	6.14%
U2AF1	c.3113A>G p.Q338H Frameshift-LOF	19.67%

Germline - Pathogenic

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

Pertinent Negatives

CTNNB1 SDHA MSH2

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

39 m/Mb 33%

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
PDGFRA	c.2525A>T p.K385L Frameshift-GOF NM_001011645	20.33%
DPYD	c.1236G>A p.I560S Missensevariant(exon2)-GOF NM_001011645	8.29%
ALK	c.3733T>C p.T1087I Nonsense-GOF NM_001011645	12.7%
MTOR	c.5664C>G p.G1954R Spliceregionvariant-GOF NM_001011645	9.9%
TP53	c.523C>T p.R273S Spliceregionvariant-GOF NM_001011645	8.58%
PTCH1	c.3583A>T p.T1195S Nonsense-GOF NM_001011645	1.17%
AKT1	c.49G>A p.E17K Frameshift-LOF NM_001011645	5.53%
CCND3	c.766_776del11 p.R256fs*64 Spliceregionvariant-GOF NM_001011645	6.18%
JAK3	c.3113A>G p.L857P Frameshift-LOF NM_001011645	4.71%
ABL1	c.3113A>G p.A34V Spliceregionvariant-GOF NM_001011645	1.05%
CTNNB1	c.110C>G p.D32Y Spliceregionvariant-LOF NM_001011645	6.33%
NTRK1	c.1792C>T p.H598T Stopgain-LOF NM_001011645	5.84%

LOW COVERAGE REGIONS

MET U2AF1

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

IKZF1 c.3113A>G p.N159Y Frameshift-LOF VAF: 15.21%

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.

SOMATIC VARIANT DETAILS - BIOLOGICALLY RELEVANT

KLF4 c.1225A>C p.K409Q Stopgain-LOF VAF: 22.76%

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.

MUTYH c.1014G>C p.N159Y Frameshift-LOF VAF: 3.78%

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.

U2AF1 c.3113A>G p.K409Q Missensevariant(exon2)-GOF VAF: 6.14%

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.

U2AF1 c.3113A>G p.Q338H Frameshift-LOF VAF: 19.67%

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.

CLINICAL HISTORY

Diagnosed on

2023-07-18