Leukemia Sample
Terry Simmons

Diagnosis
Chronic lymphocytic leukemia (CLL)

Accession No.
8954

xT

Date of Birth
1966-10-29

Sex
Male

Physician
Dr. James Miller

Institution
Austin Inc

Tumor specimen:
source Leukemia
CollectedDate 2023-11-11
ReceivedDate 2023-11-18
TumorPercentage 1%

Normal specimen:
source Blood
CollectedDate 2023-11-13
ReceivedDate 2023-11-14

GENOMIC VARIANTS

Somatic - Potentially Actionable		variant allele fraction
PKLR	c.1436G>A p.R479H Spliceregionvariant-GOF	14.93%
XPC	c.3113A>G p.S346P Nonsense-LOF	29.57%
SDHB	c.487T>C p.S163P Frameshift-GOF	27.84%
CD74	c.3113A>G p.P98S Nonsense-LOF	2.72%

Somatic - Biologically Relevant

PAX5	c.964G>A p.G183S Spliceregionvariant-LOF	17.08%

Germline - Pathogenic

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

Pertinent Negatives

No Pertinent Negatives variants were found in the limited set of genes on which we report.

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

21 m/Mb 48%

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
EGFR	c.2310_2311ins9 p.L792Y Frameshift-LOF NM_001011645	13.59%
NTRK1	c.1792C>T p.G607V Spliceregionvariant-LOF NM_001011645	3.11%
HDAC2	c.3113A>G p.E455fs*7 Nonsense-GOF NM_001011645	3.47%
SDHD	c.34G>A p.G12S Frameshift-LOF NM_001011645	6.79%
HSP90B1	c.3113A>G p.I66T Missensevariant(exon2)-GOF NM_001011645	2.95%
ALDH2	c.1510G>A p.E504K Frameshift-LOF NM_001011645	4.9%
SDHD	c.34G>A p.G12S Nonsense-GOF NM_001011645	3.93%
FGFR4	c.1162G>A p.G388R Missensevariant(exon2)-GOF NM_001011645	7.38%
SDHD	c.34G>A p.G12S Spliceregionvariant-GOF NM_001011645	9.19%

LOW COVERAGE REGIONS

SRSF2 SDHD ZEB2

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

PKLR c.1436G>A p.R479H Spliceregionvariant-GOF VAF: 14.93%

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.

XPC c.3113A>G p.S346P Nonsense-LOF VAF: 29.57%

BCL11B encodes a C2H2-type zinc finger protein that functions as a transcriptional repressor and plays a role in T-cell development and survival. Loss of function mutations, copy number loss, and fusions resulting in the underexpression of BCL11B are associated with cancer progression.

SDHB c.487T>C p.S163P Frameshift-GOF VAF: 27.84%

BCL11B encodes a C2H2-type zinc finger protein that functions as a transcriptional repressor and plays a role in T-cell development and survival. Loss of function mutations, copy number loss, and fusions resulting in the underexpression of BCL11B are associated with cancer progression.

CD74 c.3113A>G p.P98S Nonsense-LOF VAF: 2.72%

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

PAX5 c.964G>A p.G183S Spliceregionvariant-LOF VAF: 17.08%

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.

CLINICAL HISTORY

Diagnosed on

2023-11-10