Leukemia Sample
Jennifer Delacruz

Diagnosis
Chronic myeloid leukemia (CML)

Accession No.
7519

xT

Date of Birth
1939-09-25

Sex
Male

Physician
Dr. Michelle White

Institution
Hernandez Ltd

Tumor specimen:
source Leukemia
CollectedDate 2023-10-10
ReceivedDate 2023-10-10
TumorPercentage 58%

Normal specimen:
source Blood
CollectedDate 2023-10-16
ReceivedDate 2023-10-22

GENOMIC VARIANTS

Somatic - Potentially Actionable		variant allele fraction
CSF1R	c.1085A>G p.N648S Nonsense-GOF	4.29%
XPC	c.3113A>G p.S346P Spliceregionvariant-LOF	32.81%
MUTYH	c.1014G>C p.Q338H Spliceregionvariant-LOF	3.95%
BRCA2	c.5946delT p.S1982Rfs*22 Frameshift-LOF	14.54%
Somatic - Biologically Relevant		
MTOR	c.5664C>A p.G1954R Stopgain-LOF	16.86%
ARID2	c.798G>A p.F1888L Frameshift-GOF	8.99%

Germline - Pathogenic

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

Pertinent Negatives

FLT3 BTK IKZF1

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

13 m/Mb 24%

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
H3.3	c.3113A>G p.G35R Missensevariant(exon2)-GOF NM_001011645	15.75%
SF3B1	c.3113A>G p.D781X Nonsense-GOF NM_001011645	2.12%
ERBB2	c.1976_1977delinsAG p.T733I Frameshift-GOF NM_001011645	11.53%
MUTYH	c.1014G>C p.Q338H Frameshift-GOF NM_001011645	9.8%
FGFR4	c.1162G>A p.G388R Nonsense-GOF NM_001011645	7.89%
MYOD1	c.365T>G p.L122R Nonsense-LOF NM_001011645	5.49%
FOXL2	c.402C>G p.C134W Spliceregionvariant-LOF NM_001011645	4.71%
EGFR	c.2375T>A p.S768_V769insVAS Spliceregionvariant-LOF NM_001011645	6.99%
RNF43	c.461C>T p.D140E Missensevariant(exon2)-GOF NM_001011645	3.16%
TLR8	c.3113A>G p.N515H Spliceregionvariant-LOF NM_001011645	6.38%
CSF3R	c.3113A>G p.G751A Nonsense-LOF NM_001011645	5.88%
ZEB2	c.3113A>G p.H1038R Frameshift-GOF NM_001011645	6.18%

LOW COVERAGE REGIONS

BRAF

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

CSF1R c.1085A>G p.N648S Nonsense-GOF VAF: 4.29%

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.

XPC c.3113A>G p.S346P Spliceregionvariant-LOF VAF: 32.81%

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.

MUTYH c.1014G>C p.Q338H Spliceregionvariant-LOF VAF: 3.95%

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.

BRCA2 c.5946delT p.S1982Rfs*22 Frameshift-LOF VAF: 14.54%

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.

SOMATIC VARIANT DETAILS - BIOLOGICALLY RELEVANT

MTOR c.5664C>A p.G1954R Stopgain-LOF VAF: 16.86%

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.

ARID2 c.798G>A p.F1888L Frameshift-GOF VAF: 8.99%

ARID2 encodes a protein that is a subunit of the SWI/SNF chromatin remodeling complex SWI/SNF-B or PBAF. This complex functions in ligand-dependent transcriptional activation. Loss of function mutations and copy number loss of ARID2 are associated with cancer progression.

CLINICAL HISTORY

Diagnosed on

2023-10-09