Thyroid Sample
Mary West

Diagnosis
Medullary thyroid cancer

Accession No.
5371

xT

Date of Birth
1999-01-23

Sex
Female

Physician
Dr. Katie Brown

Institution
Wilson and Sons

Tumor specimen:
source Thyroid
CollectedDate 2024-04-18
ReceivedDate 2024-04-21
TumorPercentage 6%

Normal specimen:
source Blood
CollectedDate 2024-04-19
ReceivedDate 2024-04-19

GENOMIC VARIANTS

Somatic - Potentially Actionable

		variant allele fraction
ALDH2	c.1510G>A p.E504K Missensevariant(exon2)-GOF	20.85%
MYO1G	c.145G>A p.V49M Missensevariant(exon2)-GOF	25.75%
BRCA1	c.68_69delAG p.E23Vfs*17 Nonsense-GOF	15.62%
NT5C2	c.1100G>A p.R367Q Frameshift-GOF	24.27%

Somatic - Biologically Relevant

BTK	c.3113A>G p.C481X Frameshift-GOF	13.58%
CHEK2	c.1283C>T p.S428F Nonsense-GOF	5.12%
CSF3R	c.3113A>G p.R367Q Spliceregionvariant-GOF	6.82%

Germline - Pathogenic

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

Pertinent Negatives

RNF43

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

41 m/Mb 61%

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
KRAS	c.34_36delinsTGG p.A146T Spliceregionvariant-LOF NM_001011645	6.02%
MUTYH	c.1014G>C p.Q338H Missensevariant(exon2)-GOF NM_001011645	3.23%
CALR	c.1092_1143del52 p.L367fs*46 Nonsense-GOF NM_001011645	10.1%
BRAF	c.1799_1800delinsAA p.L597R Nonsense-GOF NM_001011645	6.8%
MUTYH	c.1014G>C p.Q338H Frameshift-LOF NM_001011645	4.11%
CSF3R	c.3113A>G p.G751A Frameshift-LOF NM_001011645	6.45%
MPL	c.1544G>T p.W515K Nonsense-LOF NM_001011645	9.55%
CALR	c.1092_1143del52 p.L367fs*46 Spliceregionvariant-LOF NM_001011645	1.37%
SDHD	c.34G>A p.G12S Frameshift-GOF NM_001011645	4.9%
TLR8	c.3113A>G p.N515H Nonsense-GOF NM_001011645	2.55%

LOW COVERAGE REGIONS

CSF1R DDR2 CD74

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

ALDH2 c.1510G>A p.E504K Missensevariant(exon2)-GOF VAF: 20.85%

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.

MYO1G c.145G>A p.V49M Missensevariant(exon2)-GOF VAF: 25.75%

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BRCA1 c.68_69delAG p.E23Vfs*17 Nonsense-GOF VAF: 15.62%

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.

NT5C2 c.1100G>A p.R367Q Frameshift-GOF VAF: 24.27%

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

BTK c.3113A>G p.C481X Frameshift-GOF VAF: 13.58%

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.

CHEK2 c.1283C>T p.S428F Nonsense-GOF VAF: 5.12%

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.

CSF3R c.3113A>G p.R367Q Spliceregionvariant-GOF VAF: 6.82%

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

2024-04-17