Thyroid Sample
Sarah Jackson

Diagnosis
Medullary thyroid cancer

Accession No.
4014

xT

Date of Birth
1983-07-18

Sex
Female

Physician
Dr. Stacy Rodriguez

Institution
Dunlap PLC

Tumor specimen:
source Thyroid
CollectedDate 2023-11-01
ReceivedDate 2023-11-01
TumorPercentage 96%

Normal specimen:
source Blood
CollectedDate 2023-11-02
ReceivedDate 2023-11-03

GENOMIC VARIANTS

Somatic - Potentially Actionable		variant allele fraction
MUTYH	c.1014G>C p.Q338H Spliceregionvariant-GOF	6.1%
ALK	c.3735C>A p.F1174V Spliceregionvariant-LOF	5.34%
SRSF2	c.3113A>G p.P95X Frameshift-LOF	21.07%

Somatic - Biologically Relevant		
CSF1R	c.1085A>G p.N648S Missensevariant(exon2)-GOF	3.81%
SDHA	c.1660C>T p.H362R Frameshift-LOF	6.16%

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

26 m/Mb 38%

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
NF1	c.4394A>G p.N1465S Nonsense-LOF NM_001011645	2.37%
SDHA	c.1660C>T p.R554W Frameshift-LOF NM_001011645	19.27%
RB1	c.3113A>G p.F650S Frameshift-LOF NM_001011645	1.17%
FGFR3	c.1138G>A p.S249C Frameshift-GOF NM_001011645	5.27%
B2M	c.2T>G p.M1R Missensevariant(exon2)-GOF NM_001011645	9.97%
JAK3	c.3113A>G p.L857P Frameshift-GOF NM_001011645	6.86%
FLT3	c.2028C>G p.V592G Missensevariant(exon2)-GOF NM_001011645	8.89%
KLF1	c.892G>C p.M39L Nonsense-GOF NM_001011645	9.67%
SDHD	c.34G>A p.G12S Stopgain-LOF NM_001011645	7.45%
RB1	c.3113A>G p.F650S Nonsense-GOF NM_001011645	1.01%
HSD3B1	c.1100= p.T367= Frameshift-GOF NM_001011645	1.94%

LOW COVERAGE REGIONS

TLR8 SF3B1 BRCA1

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

MUTYH c.1014G>C p.Q338H Spliceregionvariant-GOF VAF: 6.1%

TP53 encodes a protein that is a transcription factor that regulates the expression of genes involved in cell cycle arrest, apoptosis, and DNA repair. TP53 is a tumor suppressor gene that is mutated in many cancers. Mutations in TP53 are associated with cancer progression.

ALK c.3735C>A p.F1174V Spliceregionvariant-LOF VAF: 5.34%

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.

SRSF2 c.3113A>G p.P95X Frameshift-LOF VAF: 21.07%

TP53 encodes a protein that is a transcription factor that regulates the expression of genes involved in cell cycle arrest, apoptosis, and DNA repair. TP53 is a tumor suppressor gene that is mutated in many cancers. Mutations in TP53 are associated with cancer progression.

SOMATIC VARIANT DETAILS - BIOLOGICALLY RELEVANT

CSF1R c.1085A>G p.N648S Missensevariant(exon2)-GOF VAF: 3.81%

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.

SDHA c.1660C>T p.H362R Frameshift-LOF VAF: 6.16%

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.

CLINICAL HISTORY

Diagnosed on

2023-10-31