Thyroid Sample
Scott Patton

Diagnosis
Follicular thyroid cancer

Accession No.
5259

xT

Date of Birth
1958-01-08

Sex
Male

Physician
Dr. Melissa Cooper

Institution
Miller, Schwartz and Watkins

Tumor specimen:
source Thyroid
CollectedDate 2023-11-19
ReceivedDate 2023-11-19
TumorPercentage 22%

Normal specimen:
source Blood
CollectedDate 2023-11-26
ReceivedDate 2023-11-26

GENOMIC VARIANTS

Somatic - Potentially Actionable		variant allele fraction
APC	c.3920T>A p.I1307K Spliceregionvariant-LOF	23.13%
KLF4	c.1225A>C p.K409Q Spliceregionvariant-GOF	23.52%

Somatic - Biologically Relevant		
IKZF1	c.3113A>G p.K409Q Nonsense-GOF	27.29%
MYO1G	c.145G>A p.N159Y Spliceregionvariant-LOF	3.93%
CSF3R	c.3113A>G p.G751A Nonsense-GOF	12.36%
ALK	c.3185A>T p.V49M Nonsense-GOF	11.14%
TEK	c.1354A>G p.F1174C Missensevariant(exon2)-GOF	9.03%

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

44 m/Mb 80%

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
CALR	c.1154_1155insTTGTC p.K385fs*47 Missensevariant(exon2)-GOF NM_001011645	12.36%
GNAS	c.602G>A p.R160C Frameshift-GOF NM_001011645	15.94%
SMO	c.3113A>G p.A374E Spliceregionvariant-LOF NM_001011645	5.84%
MAP2K2	c.383C>T p.P128L Frameshift-GOF NM_001011645	5.07%
STAG2	c.3113A>G p.R1012X Spliceregionvariant-LOF NM_001011645	3.67%
PRKCA	c.1387G>C p.D463H Missensevariant(exon2)-GOF NM_001011645	8.96%
KRAS	c.35_36delinsAA p.G12N Spliceregionvariant-LOF NM_001011645	9.53%
CSF3R	c.3113A>G p.G751A Frameshift-GOF NM_001011645	5.99%
ARHGAP45	c.416G>A p.R139H Nonsense-GOF NM_001011645	7.51%
NCSTN	c.3113A>G p.A572G Frameshift-LOF NM_001011645	3.44%
KLF1	c.115A>C p.A298P Frameshift-GOF NM_001011645	1.92%
DNMT3A	c.2711C>T p.P904L Spliceregionvariant-LOF NM_001011645	1.1%

LOW COVERAGE REGIONS

PAX5 BRCA2

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

APC c.3920T>A p.I1307K Spliceregionvariant-LOF VAF: 23.13%

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.

KLF4 c.1225A>C p.K409Q Spliceregionvariant-GOF VAF: 23.52%

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

IKZF1 c.3113A>G p.K409Q Nonsense-GOF VAF: 27.29%

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.N159Y Spliceregionvariant-LOF VAF: 3.93%

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.

CSF3R c.3113A>G p.G751A Nonsense-GOF VAF: 12.36%

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.

ALK c.3185A>T p.V49M Nonsense-GOF VAF: 11.14%

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.

TEK c.1354A>G p.F1174C Missensevariant(exon2)-GOF VAF: 9.03%

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.

CLINICAL HISTORY

Diagnosed on

2023-11-16