Thyroid Sample
Monica Nichols

Diagnosis
Follicular thyroid cancer

Accession No.
4528

xT

Date of Birth
1958-05-25

Sex
Male

Physician
Dr. David Williams

Institution
Hughes Group

Tumor specimen:
source Thyroid
CollectedDate 2024-04-09
ReceivedDate 2024-04-10
TumorPercentage 53%

Normal specimen:
source Blood
CollectedDate 2024-04-11
ReceivedDate 2024-04-11

GENOMIC VARIANTS

Somatic - Potentially Actionable		variant allele fraction
PRKCA	c.1387G>C p.D463H Frameshift-LOF	1.91%
AKT1	c.49G>A p.E17K Stopgain-LOF	19.48%
ARID2	c.798G>A p.W266* Nonsense-LOF	25.86%

Somatic - Biologically Relevant		
SMO	c.3113A>G p.W266* Nonsense-GOF	19.68%
FLT3	c.2028C>A p.D835X Spliceregionvariant-LOF	18.03%
HSD3B1	c.1100C>A p.T367N Nonsense-GOF	10.09%

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

27 m/Mb 43%

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
FBXW7	c.1394G>A p.R465H Nonsense-LOF NM_001011645	4.36%
CSF3R	c.3113A>G p.G751A Frameshift-LOF NM_001011645	3.51%
KRAS	c.39C>A p.G12L Stopgain-LOF NM_001011645	5.6%
XPC	c.3113A>G p.S346P Spliceregionvariant-GOF NM_001011645	8.22%
SDHD	c.34G>A p.G12S Nonsense-LOF NM_001011645	5.63%
IDH1	c.394C>A p.R119Q Nonsense-GOF NM_001011645	3.29%
DNMT3A	c.2711C>T p.P904L Nonsense-GOF NM_001011645	9.76%
CDKN2A	c.151G>A p.V51D Frameshift-GOF NM_001011645	1.27%
H3.3	c.3113A>G p.G35L Missensevariant(exon2)-GOF NM_001011645	9.68%
XPC	c.3113A>G p.S346P Nonsense-LOF NM_001011645	4.39%
MAPK1	c.964G>A p.E322K Nonsense-LOF NM_001011645	6.4%

LOW COVERAGE REGIONS

PTCH1

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

PRKCA c.1387G>C p.D463H Frameshift-LOF VAF: 1.91%

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.

AKT1 c.49G>A p.E17K Stopgain-LOF VAF: 19.48%

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.

ARID2 c.798G>A p.W266* Nonsense-LOF VAF: 25.86%

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.

SOMATIC VARIANT DETAILS - BIOLOGICALLY RELEVANT

SMO c.3113A>G p.W266* Nonsense-GOF VAF: 19.68%

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.

FLT3 c.2028C>A p.D835X Spliceregionvariant-LOF VAF: 18.03%

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.

HSD3B1 c.1100C>A p.T367N Nonsense-GOF VAF: 10.09%

PTEN encodes a phosphatase that acts as a tumor suppressor by negatively regulating the PI3K-AKT-mTOR pathway. Loss of function mutations, copy number loss, and underexpression of PTEN are associated with cancer progression.

CLINICAL HISTORY

Diagnosed on

2024-04-06