Thyroid Sample
Gregory Griffin

Diagnosis
Medullary thyroid cancer

Accession No.
5410

xT

Date of Birth
1987-01-05

Sex
Female

Physician
Dr. Bryan Snyder

Institution
Merritt, Gonzalez and Ramos

Tumor specimen:
source Thyroid
CollectedDate 2024-02-02
ReceivedDate 2024-02-03
TumorPercentage 59%

Normal specimen:
source Blood
CollectedDate 2024-02-08
ReceivedDate 2024-02-11

GENOMIC VARIANTS

Somatic - Potentially Actionable		variant allele fraction
SF3B1	c.3113A>G p.D781X Spliceregionvariant-LOF	27.06%

Somatic - Biologically Relevant		
ERCC2	c.3113A>G p.D781X Missensevariant(exon2)-GOF	32.56%
KLF1	c.115A>C p.N626X Nonsense-GOF	3.7%
ALDH2	c.1510G>A p.G740X Spliceregionvariant-GOF	6.72%

Germline - Pathogenic

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

Pertinent Negatives

DNMT3A SDHD TOP2A

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

10 m/Mb 83%

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**
NCSTN	c.3113A>G p.A572G Spliceregionvariant-GOF NM_001011645	17.94%
PKLR	c.1436G>A p.R479H Nonsense-GOF NM_001011645	13.68%
MYOD1	c.365T>G p.L122R Spliceregionvariant-LOF NM_001011645	9.76%
NCSTN	c.3113A>G p.A572G Spliceregionvariant-LOF NM_001011645	9.74%
SDHB	c.487T>C p.S163P Nonsense-GOF NM_001011645	1.76%
CHD6	c.4800C>G p.I1600M Missensevariant(exon2)-GOF NM_001011645	3.37%
PKLR	c.1436G>A p.R479H Nonsense-LOF NM_001011645	4.14%
Germline	**Mutation effect**	**Condition**
EZH2	c.1937A>G p.Y646D Spliceregionvariant-LOF NM_001011645	score
IKZF1	c.3113A>G p.N159Y Spliceregionvariant-GOF NM_001011645	energy

LOW COVERAGE REGIONS

B2M APC PHF6

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

SF3B1 c.3113A>G p.D781X Spliceregionvariant-LOF VAF: 27.06%

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.

SOMATIC VARIANT DETAILS - BIOLOGICALLY RELEVANT

ERCC2 c.3113A>G p.D781X Missensevariant(exon2)-GOF VAF: 32.56%

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.

KLF1 c.115A>C p.N626X Nonsense-GOF VAF: 3.7%

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.

ALDH2 c.1510G>A p.G740X Spliceregionvariant-GOF VAF: 6.72%

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

2024-01-27

Electronically signed by	CLIA number	Date Signed/Reported	Laboratory Medical Director	ID #	Pipeline version
Bryan Snyder	14D2114007	2024-02-10	Dr. Whitney Hernandez	5410	3.2.0