Thyroid Sample
Charles Turner

Diagnosis
Medullary thyroid cancer

Accession No.
6947

xT

Date of Birth
1972-09-21

Sex
Male

Physician
Dr. Rebecca Flynn

Institution
Fletcher PLC

Tumor specimen:
source Thyroid
CollectedDate 2023-04-28
ReceivedDate 2023-04-29
TumorPercentage 68%

Normal specimen:
source Blood
CollectedDate 2023-05-04
ReceivedDate 2023-05-06

GENOMIC VARIANTS

Somatic - Potentially Actionable		variant allele fraction
PDGFRB	c.3113A>G p.T681I Frameshift-GOF	22.86%
CCND3	c.766_776del11 p.R256fs*64 Nonsense-GOF	5.48%

Somatic - Biologically Relevant		
ERBB2	c.2584A>G p.R896C Spliceregionvariant-LOF	1.03%
MAPK1	c.964G>A p.L755P Nonsense-LOF	6.25%
CDC73	c.1A>G p.L755S Nonsense-GOF	10.39%
SDHA	c.1660C>T p.R256fs*64 Frameshift-GOF	13.38%
ABL1	c.3113A>G p.G660D Missensevariant(exon2)-GOF	7.63%
KRAS	c.36T>C p.G12C Nonsense-GOF	4.59%

Germline - Pathogenic

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

Pertinent Negatives

SRSF2 PAX5 CCND3 HDAC2 PDGFRA

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

40 m/Mb 97%

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
FGFR3	c.1138G>A p.R248C Stopgain-LOF NM_001011645	18.87%
IDH2	c.515G>A p.R140L Spliceregionvariant-LOF NM_001011645	7.92%
KLF4	c.1225A>C p.K409Q Nonsense-GOF NM_001011645	3.74%
NCSTN	c.3113A>G p.A572G Spliceregionvariant-GOF NM_001011645	8.64%
U2AF1	c.3113A>G p.Q157X Nonsense-GOF NM_001011645	1.22%
HSD3B1	c.1100= p.T367= Spliceregionvariant-GOF NM_001011645	6.81%
ARHGAP45	c.416G>A p.R139H Frameshift-LOF NM_001011645	8.19%
HSD3B1	c.1100= p.T367= Spliceregionvariant-LOF NM_001011645	8.58%
PDGFRA	c.1153_1154delinsTT p.D842V Frameshift-LOF NM_001011645	4.59%

LOW COVERAGE REGIONS

ERCC2 DICER1 KLF1

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

PDGFRB c.3113A>G p.T681I Frameshift-GOF VAF: 22.86%

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.

CCND3 c.766_776del11 p.R256fs*64 Nonsense-GOF VAF: 5.48%

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.

SOMATIC VARIANT DETAILS - BIOLOGICALLY RELEVANT

ERBB2 c.2584A>G p.R896C Spliceregionvariant-LOF VAF: 1.03%

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.

MAPK1 c.964G>A p.L755P Nonsense-LOF VAF: 6.25%

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.

CDC73 c.1A>G p.L755S Nonsense-GOF VAF: 10.39%

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.

SDHA c.1660C>T p.R256fs*64 Frameshift-GOF VAF: 13.38%

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.

ABL1 c.3113A>G p.G660D Missensevariant(exon2)-GOF VAF: 7.63%

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.

KRAS c.36T>C p.G12C Nonsense-GOF VAF: 4.59%

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
2023-04-21