Pancreatic Sample
Heather Ellison

Diagnosis
Pancreatic neuroendocrine tumors 4816

Accession No.

xT

Date of Birth
1952-11-07

Sex
Male

Physician
Dr. Hector Flores

Institution
Jackson, Herrera and Anderson

Tumor specimen:
source Pancreatic
CollectedDate 2023-12-09
ReceivedDate 2023-12-12
TumorPercentage 72%

Normal specimen:
source Blood
CollectedDate 2023-12-13
ReceivedDate 2023-12-16

GENOMIC VARIANTS

Somatic - Potentially Actionable		variant allele fraction
BLM	c.2207_2212delinsTAGATTC p.Y736fs*4 Spliceregionvariant-GOF	19.6%
NCSTN	c.3113A>G p.A572G Stopgain-LOF	23.45%
NCSTN	c.3113A>G p.A572G Spliceregionvariant-LOF	25.26%
FLT3	c.1775T>G p.V592A Missensevariant(exon2)-GOF	4.84%

Somatic - Biologically Relevant

MYOD1	c.365T>G p.V592G Frameshift-LOF	10.31%

Germline - Pathogenic

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

Pertinent Negatives

SIX1 FGFR3

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

31 m/Mb 49%

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
NRAS	c.181C>A p.Q61E Stopgain-LOF NM_001011645	15.34%
FGFR3	c.1118A>G p.R248C Stopgain-LOF NM_001011645	1.41%
RNF43	c.954G>T p.E318D Missensevariant(exon2)-GOF NM_001011645	11.09%
PDGFRB	c.3113A>G p.T681I Nonsense-GOF NM_001011645	3.01%
HRAS	c.35G>T p.G12D Missensevariant(exon2)-GOF NM_001011645	2.79%
PIK3CA	c.1635G>C p.C420R Missensevariant(exon2)-GOF NM_001011645	7.25%
PDGFRA	c.1153_1154delinsTC p.K385X Nonsense-GOF NM_001011645	7.65%
DPYD	c.2846A>T p.Y186C Stopgain-LOF NM_001011645	6.81%
CHEK2	c.1283C>T p.I157T Spliceregionvariant-GOF NM_001011645	6.0%

LOW COVERAGE REGIONS

NCSTN MYD88 SDHB

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

BLM c.2207_2212delinsTAGATTC p.Y736fs*4 Spliceregionvariant-GOF VAF: 19.6%

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.

NCSTN c.3113A>G p.A572G Stopgain-LOF VAF: 23.45%

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.

NCSTN c.3113A>G p.A572G Spliceregionvariant-LOF VAF: 25.26%

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.

FLT3 c.1775T>G p.V592A Missensevariant(exon2)-GOF VAF: 4.84%

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

MYOD1 c.365T>G p.V592G Frameshift-LOF VAF: 10.31%

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

2023-12-08