Colorectal Sample
Zoe Johnson

Diagnosis
Neuroendocrine tumors

Accession No.
6223

xT

Date of Birth
1971-06-01

Sex
Male

Physician
Dr. Andrew Lang

Institution
Willis-Ramos

Tumor specimen:
source Colorectal
CollectedDate 2024-03-30
ReceivedDate 2024-04-02
TumorPercentage 25%

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

GENOMIC VARIANTS

Somatic - Potentially Actionable — **variant allele fraction**

DPYD	c.557A>G p.I543V Frameshift-GOF	34.26%
H3.3	c.3113A>G p.G35R Stopgain-LOF	6.13%

Somatic - Biologically Relevant

PTCH1	c.3583A>T p.T1195S Nonsense-LOF	12.78%

Germline - Pathogenic

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

Pertinent Negatives

TOP2A KRAS BLM FBXW7 PHF6

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

19 m/Mb 74%

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**
EZH2	c.1936T>G p.Y646F Spliceregionvariant-GOF NM_001011645	13.29%
KRAS	c.37G>T p.G12Y Nonsense-LOF NM_001011645	6.41%
MAPK1	c.964G>A p.E322K Spliceregionvariant-LOF NM_001011645	1.26%
XPC	c.3113A>G p.S346P Frameshift-GOF NM_001011645	1.45%
PIK3CA	c.1635G>C p.E542K Stopgain-LOF NM_001011645	9.06%
ZEB2	c.3113A>G p.H1038R Nonsense-GOF NM_001011645	7.92%
KLF1	c.892G>C p.M39L Nonsense-GOF NM_001011645	5.8%
NCSTN	c.3113A>G p.A572G Spliceregionvariant-GOF NM_001011645	3.84%
Germline	**Mutation effect**	**Condition**
ERBB2	c.2524G>A p.L755X Missensevariant(exon2)-GOF NM_001011645	charge

LOW COVERAGE REGIONS

NF1

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

DPYD c.557A>G p.I543V Frameshift-GOF VAF: 34.26%

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.

H3.3 c.3113A>G p.G35R Stopgain-LOF VAF: 6.13%

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.

SOMATIC VARIANT DETAILS - BIOLOGICALLY RELEVANT

PTCH1 c.3583A>T p.T1195S Nonsense-LOF VAF: 12.78%

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.

CLINICAL HISTORY

Diagnosed on

2024-03-26