Colorectal Sample
Zachary Novak

Diagnosis
Adenocarcinoma

Accession No.
4643

xT

Date of Birth
1965-09-25

Sex
Male

Physician
Dr. Jennifer Walker

Institution
Doyle PLC

Tumor specimen:
source Colorectal
CollectedDate 2024-03-23
ReceivedDate 2024-03-30
TumorPercentage 47%

Normal specimen:
source Blood
CollectedDate 2024-03-30
ReceivedDate 2024-04-01

GENOMIC VARIANTS

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

DNMT3A	c.2711C>T p.P904L Spliceregionvariant-GOF	32.67%
STAT5B	c.1924A>C p.N642H Spliceregionvariant-GOF	15.84%
CALR	c.1092_1143del52 p.K385fs*47 Spliceregionvariant-GOF	21.4%
BRCA1	c.68_69delAG p.Q1756Pfs Missensevariant(exon2)-GOF	11.34%

Somatic - Biologically Relevant

BTK	c.3113A>G p.Q1756Pfs Frameshift-GOF	6.24%
XPC	c.3113A>G p.S346P Missensevariant(exon2)-GOF	6.23%

Germline - Pathogenic

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

Pertinent Negatives

NRAS · MUTYH · MYCN · ERBB2 · MET

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

37 m/Mb — 32%

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
CSF3R	c.3113A>G p.G751A Frameshift-GOF NM_001011645	5.5%
PHF6	c.3113A>G p.R225X Frameshift-GOF NM_001011645	1.07%
MET	c.3028G>A p.H1094Y Spliceregionvariant-GOF NM_001011645	10.59%
U2AF1	c.3113A>G p.R156X Spliceregionvariant-GOF NM_001011645	8.42%
STAG2	c.3113A>G p.R1012X Spliceregionvariant-GOF NM_001011645	3.98%
KRAS	c.37G>C p.Q61P Spliceregionvariant-LOF NM_001011645	9.26%
AKT1	c.49G>A p.E17K Nonsense-LOF NM_001011645	1.31%
SIX1	c.530A>G p.Q177R Spliceregionvariant-LOF NM_001011645	7.66%
DICER1	c.5438A>G p.E1813D Spliceregionvariant-LOF NM_001011645	1.35%
PTPN11	c.1508G>C p.G503A Nonsense-LOF NM_001011645	8.67%
RNF43	c.954G>T p.E318D Spliceregionvariant-GOF NM_001011645	9.32%
MYD88	c.794T>C p.L265P Frameshift-GOF NM_001011645	1.08%

LOW COVERAGE REGIONS

CHD6 TEK ALK

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

DNMT3A c.2711C>T p.P904L Spliceregionvariant-GOF VAF: 32.67%

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.

STAT5B c.1924A>C p.N642H Spliceregionvariant-GOF VAF: 15.84%

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.

CALR c.1092_1143del52 p.K385fs*47 Spliceregionvariant-GOF VAF: 21.4%

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.

BRCA1 c.68_69delAG p.Q1756Pfs Missensevariant(exon2)-GOF VAF: 11.34%

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

BTK c.3113A>G p.Q1756Pfs Frameshift-GOF VAF: 6.24%

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.

XPC c.3113A>G p.S346P Missensevariant(exon2)-GOF VAF: 6.23%

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

2024-03-20