Skin Sample
Samantha Foster

Diagnosis
Merkel cell carcinoma

Accession No.
6890

xT

Date of Birth
1934-04-13

Sex
Male

Physician
Dr. Jared Brooks

Institution
Morgan-Carrillo

Tumor specimen:
source Skin
CollectedDate 2023-10-26
ReceivedDate 2023-10-26
TumorPercentage 70%

Normal specimen:
source Blood
CollectedDate 2023-10-30
ReceivedDate 2023-11-01

GENOMIC VARIANTS

Somatic - Potentially Actionable		variant allele fraction
NRAS	c.181C>G p.Q61X Nonsense-GOF	7.27%
HDAC1	c.3113A>G p.Y303H Frameshift-GOF	32.68%

Somatic - Biologically Relevant		
FGFR2	c.1124A>G p.C382R Missensevariant(exon2)-GOF	14.51%
BRCA1	c.5265_5266insC p.S372C Frameshift-GOF	17.58%
STAG2	c.3113A>G p.V679F Spliceregionvariant-GOF	5.5%
MYD88	c.794T>C p.Y375C Nonsense-GOF	9.14%
CALR	c.1092_1143del52 p.L367fs*46 Spliceregionvariant-GOF	5.27%
FLT3	c.2525A>G p.Y375C Spliceregionvariant-GOF	2.1%

Germline - Pathogenic

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

Pertinent Negatives

CSF3R

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

31 m/Mb 1%

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
CHEK2	c.470T>C p.I157T Nonsense-GOF NM_001011645	18.29%
SIX1	c.530A>G p.Q177R Spliceregionvariant-GOF NM_001011645	17.47%
CSF1R	c.1085A>G p.H362R Stopgain-LOF NM_001011645	1.77%
ZEB2	c.3113A>G p.H1038R Nonsense-LOF NM_001011645	8.68%
CHEK2	c.470T>C p.I157T Stopgain-LOF NM_001011645	6.79%
HDAC1	c.3113A>G p.Y303H Nonsense-LOF NM_001011645	5.96%
NRAS	c.37G>A p.G13V Frameshift-LOF NM_001011645	9.25%
BLM	c.2207_2212delinsTAGATTC p.Y736fs*4 Stopgain-LOF NM_001011645	8.19%
FOXL2	c.402C>G p.C134W Frameshift-GOF NM_001011645	2.98%
CALR	c.1154_1155insTTGTC p.L367fs*46 Missensevariant(exon2)-GOF NM_001011645	3.66%

Electronically signed by	CLIA number	Date Signed/Reported	Laboratory Medical Director	ID #	Pipeline version
Jared Brooks	14D2114007	2023-10-26	Dr. Lauren Freeman	6890	3.2.0

LOW COVERAGE REGIONS

STAG2 DPYD CHEK2

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

NRAS c.181C>G p.Q61X Nonsense-GOF VAF: 7.27%

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.

HDAC1 c.3113A>G p.Y303H Frameshift-GOF VAF: 32.68%

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

FGFR2 c.1124A>G p.C382R Missensevariant(exon2)-GOF VAF: 14.51%

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.

BRCA1 c.5265_5266insC p.S372C Frameshift-GOF VAF: 17.58%

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.

STAG2 c.3113A>G p.V679F Spliceregionvariant-GOF VAF: 5.5%

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.

MYD88 c.794T>C p.Y375C Nonsense-GOF VAF: 9.14%

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.

CALR c.1092_1143del52 p.L367fs*46 Spliceregionvariant-GOF VAF: 5.27%

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.

FLT3 c.2525A>G p.Y375C Spliceregionvariant-GOF VAF: 2.1%

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
2023-10-22