Skin Sample
Emily Rogers

Diagnosis
Merkel cell carcinoma

Accession No.
3060

xT

Date of Birth
1950-11-13

Sex
Male

Physician
Dr. Anthony Reed

Institution
Miller, Johnson and Chen

Tumor specimen:
source Skin
CollectedDate 2023-07-12
ReceivedDate 2023-07-13
TumorPercentage 98%

Normal specimen:
source Blood
CollectedDate 2023-07-15
ReceivedDate 2023-07-21

GENOMIC VARIANTS

Somatic - Potentially Actionable		variant allele fraction
PKLR	c.1436G>A p.R479H Nonsense-GOF	34.47%

Somatic - Biologically Relevant		
PDGFRB	c.3113A>G p.T681I Frameshift-LOF	24.67%
BTK	c.3113A>G p.T681I Nonsense-GOF	11.33%
PRKCA	c.1387G>C p.R479H Stopgain-LOF	17.88%

Germline - Pathogenic

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

Pertinent Negatives

CDKN2A BRCA1 IKZF1

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

8 m/Mb 90%

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**
NT5C2	c.1100G>A p.R367Q Frameshift-LOF NM_001011645	3.28%
FOXL2	c.402C>G p.C134W Frameshift-GOF NM_001011645	17.3%
PTCH1	c.3583A>T p.T1195S Nonsense-GOF NM_001011645	6.22%
AKT1	c.49G>A p.E17K Spliceregionvariant-GOF NM_001011645	9.05%
CHEK2	c.470T>C p.I157T Nonsense-GOF NM_001011645	8.56%
ARHGAP45	c.416G>A p.R139H Frameshift-GOF NM_001011645	5.47%
Germline	**Mutation effect**	**Condition**
MYO1G	c.145G>A p.V49M Missensevariant(exon2)-GOF NM_001011645	west
U2AF1	c.3113A>G p.Q157X Spliceregionvariant-GOF NM_001011645	nice

LOW COVERAGE REGIONS

KIT MTOR

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

PKLR c.1436G>A p.R479H Nonsense-GOF VAF: 34.47%

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

PDGFRB c.3113A>G p.T681I Frameshift-LOF VAF: 24.67%

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.

BTK c.3113A>G p.T681I Nonsense-GOF VAF: 11.33%

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.

PRKCA c.1387G>C p.R479H Stopgain-LOF VAF: 17.88%

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

2023-07-09