Skin Sample
Tyler Mason

Diagnosis
Merkel cell carcinoma

Accession No.
3351

xT

Date of Birth
1982-05-02

Sex
Male

Physician
Dr. Cheryl Santos

Institution
Contreras LLC

Tumor specimen:
source Skin
CollectedDate 2023-09-23
ReceivedDate 2023-09-23
TumorPercentage 33%

Normal specimen:
source Blood
CollectedDate 2023-09-24
ReceivedDate 2023-09-29

GENOMIC VARIANTS

Somatic - Potentially Actionable		variant allele fraction
FLT3	c.2039C>T p.V592A Nonsense-LOF	3.72%
HDAC1	c.3113A>G p.Y303H Missensevariant(exon2)-GOF	12.51%

Somatic - Biologically Relevant		
PTEN	c.389G>C p.L182* Nonsense-LOF	29.33%
FGFR4	c.1162G>A p.G388R Frameshift-LOF	2.8%
PTPN11	c.1508G>C p.R130G Frameshift-GOF	1.35%
MSH2	c.1906G>C p.R130Q Frameshift-LOF	10.1%
MTOR	c.5664C>G p.R130P Nonsense-LOF	5.02%
CTNNB1	c.121A>G p.S37F Spliceregionvariant-GOF	1.29%

Germline - Pathogenic

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

Pertinent Negatives

MYCN PTCH1 HSP90B1

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

43 m/Mb 92%

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
HBA2	c.427T>C p.*143Qext*31 Nonsense-LOF NM_001011645	4.75%
CHEK2	c.1283C>T p.S428F Spliceregionvariant-GOF NM_001011645	8.73%
RNF43	c.380G>C p.R127P Nonsense-GOF NM_001011645	3.1%
BRAF	c.1406G>T p.L597R Missensevariant(exon2)-GOF NM_001011645	9.51%
HDAC1	c.3113A>G p.Y303H Frameshift-LOF NM_001011645	8.59%
PTEN	c.545T>G p.R130L Spliceregionvariant-LOF NM_001011645	1.81%
XPC	c.3113A>G p.S346P Missensevariant(exon2)-GOF NM_001011645	7.11%
APC	c.3920T>A p.I1307K Spliceregionvariant-GOF NM_001011645	4.81%
PRKCA	c.1387G>C p.D463H Frameshift-LOF NM_001011645	7.08%
AKT1	c.49G>A p.E17K Nonsense-GOF NM_001011645	1.93%
HBA2	c.427T>C p.*143Qext*31 Spliceregionvariant-GOF NM_001011645	3.18%
SDHB	c.487T>C p.S163P Stopgain-LOF NM_001011645	8.88%

LOW COVERAGE REGIONS

PHF6 SDHB

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

FLT3 c.2039C>T p.V592A Nonsense-LOF VAF: 3.72%

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 Missensevariant(exon2)-GOF VAF: 12.51%

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.

SOMATIC VARIANT DETAILS - BIOLOGICALLY RELEVANT

PTEN c.389G>C p.L182* Nonsense-LOF VAF: 29.33%

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.

FGFR4 c.1162G>A p.G388R Frameshift-LOF VAF: 2.8%

KRAS is a GDP/GTP binding protein that acts as an intracellular signal transducer. KRAS is involved in several pathways involved in cellular proliferation and survival, including the PI3K-AKT-mTOR pathway and the Ras-Raf-MEK-ERK pathway. Activating mutations, copy number gains, and overexpression of KRAS are associated with cancer progression.

PTPN11 c.1508G>C p.R130G Frameshift-GOF VAF: 1.35%

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.

MSH2 c.1906G>C p.R130Q Frameshift-LOF VAF: 10.1%

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.

MTOR c.5664C>G p.R130P Nonsense-LOF VAF: 5.02%

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.

CTNNB1 c.121A>G p.S37F Spliceregionvariant-GOF VAF: 1.29%

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

2023-09-22