Skin Sample
Julia Chambers

Diagnosis
Merkel cell carcinoma

Accession No.
7434

xT

Date of Birth
1987-02-13

Sex
Female

Physician
Dr. Jennifer Knight

Institution
Becker, Adams and Nelson

Tumor specimen:
source Skin
CollectedDate 2023-05-07
ReceivedDate 2023-05-14
TumorPercentage 6%

Normal specimen:
source Blood
CollectedDate 2023-05-14
ReceivedDate 2023-05-16

GENOMIC VARIANTS

Somatic - Potentially Actionable		variant allele fraction
ARID2	c.798G>A p.W266* Spliceregionvariant-LOF	33.12%
CALR	c.1154_1155insTTGTC p.K385fs*47 Missensevariant(exon2)-GOF	34.25%

Somatic - Biologically Relevant		
NOTCH1	c.7398_7407del p.S2467Afs*15 Nonsense-GOF	9.15%
MYO1G	c.145G>A p.G1196D Frameshift-LOF	1.3%
PTEN	c.389G>A p.G1196D Nonsense-GOF	2.36%
HBA2	c.427T>C p.S2467Gfs*11 Frameshift-LOF	4.49%

Germline - Pathogenic

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

Pertinent Negatives

B2M PAX5 FGFR1

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

33 m/Mb 47%

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
KLF4	c.1225A>C p.K409Q Frameshift-LOF NM_001011645	5.63%
U2AF1	c.3113A>G p.R156X Nonsense-GOF NM_001011645	7.36%
DNMT3A	c.2711C>T p.P904L Nonsense-LOF NM_001011645	7.03%
BRAF	c.1798_1799delinsAG p.V600A Spliceregionvariant-GOF NM_001011645	5.63%
RB1	c.3113A>G p.F650S Nonsense-LOF NM_001011645	4.38%
ZEB2	c.3113A>G p.H1038R Frameshift-LOF NM_001011645	9.93%
ZEB2	c.3113A>G p.H1038R Spliceregionvariant-GOF NM_001011645	4.81%
MTOR	c.5662T>C p.G1954R Nonsense-LOF NM_001011645	4.41%
BRAF	c.1405G>C p.L597V Nonsense-LOF NM_001011645	3.01%
U2AF1	c.3113A>G p.S34X Spliceregionvariant-LOF NM_001011645	1.45%
FGFR3	c.1138G>A p.G380R Frameshift-GOF NM_001011645	1.09%
KIT	c.2492T>C p.D820Y Missensevariant(exon2)-GOF NM_001011645	2.89%

LOW COVERAGE REGIONS

CDKN2A

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

ARID2 c.798G>A p.W266* Spliceregionvariant-LOF VAF: 33.12%

ARID2 encodes a protein that is a subunit of the SWI/SNF chromatin remodeling complex SWI/SNF-B or PBAF. This complex functions in ligand-dependent transcriptional activation. Loss of function mutations and copy number loss of ARID2 are associated with cancer progression.

CALR c.1154_1155insTTGTC p.K385fs*47 Missensevariant(exon2)-GOF VAF: 34.25%

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

NOTCH1 c.7398_7407del p.S2467Afs*15 Nonsense-GOF VAF: 9.15%

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.

MYO1G c.145G>A p.G1196D Frameshift-LOF VAF: 1.3%

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.

PTEN c.389G>A p.G1196D Nonsense-GOF VAF: 2.36%

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.

HBA2 c.427T>C p.S2467Gfs*11 Frameshift-LOF VAF: 4.49%

ARID2 encodes a protein that is a subunit of the SWI/SNF chromatin remodeling complex SWI/SNF-B or PBAF. This complex functions in ligand-dependent transcriptional activation. Loss of function mutations and copy number loss of ARID2 are associated with cancer progression.

CLINICAL HISTORY

Diagnosed on

2023-05-06