Skin Sample
Cheryl Schneider

Diagnosis
Squamous cell carcinoma

Accession No.
2254

xT

Date of Birth
1971-04-14

Sex
Female

Physician
Dr. Mr. Phillip Dillon II

Institution
Escobar-Franklin

Tumor specimen:
source Skin
CollectedDate 2024-02-22
ReceivedDate 2024-02-22
TumorPercentage 15%

Normal specimen:
source Blood
CollectedDate 2024-02-23
ReceivedDate 2024-02-25

GENOMIC VARIANTS

Somatic - Potentially Actionable		variant allele fraction
SIX1	c.530A>G p.Q177R Frameshift-LOF	18.49%
FGFR2	c.758C>G p.N549H Spliceregionvariant-GOF	27.38%
PIK3CA	c.3141T>G p.E542G Frameshift-LOF	28.72%
STAG2	c.3113A>G p.R1012X Frameshift-LOF	8.99%

Somatic - Biologically Relevant

FGFR3	c.1108G>T p.Y373C Nonsense-GOF	16.9%
DDR2	c.716T>G p.G370C Spliceregionvariant-LOF	9.37%

Germline - Pathogenic

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

Pertinent Negatives

PAX5 ZEB2 BRCA2 MAPK1

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

6 m/Mb 58%

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
DNMT3A	c.2711C>T p.P904L Spliceregionvariant-GOF NM_001011645	14.21%
SDHB	c.487T>C p.S163P Frameshift-GOF NM_001011645	17.2%
IDH1	c.394C>A p.R132C Spliceregionvariant-LOF NM_001011645	4.67%
ERBB2	c.2325_2326ins12 p.V777L Frameshift-GOF NM_001011645	3.39%
HDAC1	c.3113A>G p.Y303H Nonsense-LOF NM_001011645	6.9%
MPL	c.1544G>T p.W515L Nonsense-GOF NM_001011645	9.5%
MYD88	c.794T>C p.L265P Nonsense-GOF NM_001011645	9.99%
TEK	c.1354A>G p.N452D Stopgain-LOF NM_001011645	9.69%
HSD3B1	c.1100= p.T367N Spliceregionvariant-LOF NM_001011645	2.0%
CDKN2A	c.322G>T p.V51D Spliceregionvariant-GOF NM_001011645	5.83%
PTPN11	c.1508G>C p.G503A Nonsense-GOF NM_001011645	9.67%
FLT3	c.2039C>T p.N676S Nonsense-LOF NM_001011645	3.46%

LOW COVERAGE REGIONS

BRCA2 IDH2 CTNNB1

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

SIX1 c.530A>G p.Q177R Frameshift-LOF VAF: 18.49%

BCL11B encodes a C2H2-type zinc finger protein that functions as a transcriptional repressor and plays a role in T-cell development and survival. Loss of function mutations, copy number loss, and fusions resulting in the underexpression of BCL11B are associated with cancer progression.

FGFR2 c.758C>G p.N549H Spliceregionvariant-GOF VAF: 27.38%

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.

PIK3CA c.3141T>G p.E542G Frameshift-LOF VAF: 28.72%

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.

STAG2 c.3113A>G p.R1012X Frameshift-LOF VAF: 8.99%

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.

SOMATIC VARIANT DETAILS - BIOLOGICALLY RELEVANT

FGFR3 c.1108G>T p.Y373C Nonsense-GOF VAF: 16.9%

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.

DDR2 c.716T>G p.G370C Spliceregionvariant-LOF VAF: 9.37%

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

2024-02-21