# Pancreatic Sample
# Daniel Flores

Diagnosis
**Pancreatic neuroendocrine tumors 7682**

Accession No.

xT

Date of Birth
**1978-12-04**

Sex
**Male**

Physician
**Dr. Philip Marquez**

Institution
**Bishop-Thompson**

Tumor specimen:
source Pancreatic
CollectedDate 2023-05-09
ReceivedDate 2023-05-09
TumorPercentage 5%

Normal specimen:
source Blood
CollectedDate 2023-05-11
ReceivedDate 2023-05-11

## GENOMIC VARIANTS

| **Somatic - Potentially Actionable** | | **variant allele fraction** |
|---|---|---|
| **ARID2** | c.798G>A p.W266* Stopgain-LOF | 35.9% |
| **IDH1** | c.394_395delinsTC p.R132H Nonsense-GOF | 32.59% |
| **TOP2A** | c.3113A>G p.A1515S Stopgain-LOF | 25.8% |
| **Somatic - Biologically Relevant** | | |
| **FGFR3** | c.1111A>T p.A1515S Spliceregionvariant-LOF | 15.97% |
| **IDH1** | c.394_395delinsTC p.R132C Nonsense-LOF | 2.0% |

**Germline - Pathogenic**

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

**Pertinent Negatives**

PKLR BRCA1

## IMMUNOTHERAPY MARKERS

**Tumor Mutational Burden**

**48 m/Mb** 17%

**Microsatellite Instability Status**

Stable | **Equivocal** | High

## FDA-APPROVED THERAPIES, Current Diagnosis

| | | |
|---|---|---|
| KRAS G12C Inhibitors | **Sotorasib** | NCCN, Consensus, Non-Small Cell Lung Cancer<br>MSK OncoKB, Level 1<br>KRASp.G12C G12C-GOF |

## FDA-APPROVED THERAPIES, Other Indications

| | | |
|---|---|---|
| KRAS G12C Inhibitors | **Sotorasib** | NCCN, Consensus, Non-Small Cell Lung Cancer<br>MSK OncoKB, Level 1<br>KRASp.G12C G12C-GOF |

## ADDITIONAL INDICATORS

| | |
|---|---|
| **Unfavorable Prognosis** | NCCN, Consensus, Non-Small Cell Lung Cancer<br>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**<br>City, state - x mi<br>**KRAS mutation** |
| A Phase 1/2 Study of MRTX849 in Patients With Cancer Having a KRAS G12C Mutation KRYSTAL-1 | **Phase 1/2**<br>City, state - x mi<br>**KRAS mutation**<br>**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**<br>City, state - x mi<br>**NFE2L2 mutation**<br>**STK11 mutation** |

## VARIANTS OF UNKNOWN SIGNIFICANCE

| **Somatic** | **Mutation effect** | **Variant allele fraction** |
|---|---|---|
| MYD88 | c.794T>C p.L265P Spliceregionvariant-LOF<br>NM_001011645 | 11.73% |
| ERCC2 | c.3113A>G p.F332V Missensevariant(exon2)-GOF<br>NM_001011645 | 11.11% |
| PAX5 | c.547G>A p.P80R Spliceregionvariant-GOF<br>NM_001011645 | 5.47% |
| PAX5 | c.964G>A p.G183S Frameshift-GOF<br>NM_001011645 | 9.02% |
| H3.3 | c.3113A>G p.G35W Spliceregionvariant-LOF<br>NM_001011645 | 8.69% |
| HSP90B1 | c.3113A>G p.I66T Missensevariant(exon2)-GOF<br>NM_001011645 | 5.96% |
| PKLR | c.1436G>A p.R479H Stopgain-LOF<br>NM_001011645 | 4.81% |
| EZH2 | c.1936T>A p.Y646F Nonsense-LOF<br>NM_001011645 | 3.14% |
| **Germline** | **Mutation effect** | **Condition** |
| JAK3 | c.3113A>G p.L857P Missensevariant(exon2)-GOF<br>NM_001011645 | anyone |

## LOW COVERAGE REGIONS

ZEB2 TOP2A

## SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

**ARID2** c.798G>A p.W266* Stopgain-LOF VAF: 35.9%

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.

**IDH1** c.394_395delinsTC p.R132H Nonsense-GOF VAF: 32.59%

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.

**TOP2A** c.3113A>G p.A1515S Stopgain-LOF VAF: 25.8%

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.

## SOMATIC VARIANT DETAILS - BIOLOGICALLY RELEVANT

**FGFR3** c.1111A>T p.A1515S Spliceregionvariant-LOF VAF: 15.97%

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.

**IDH1** c.394_395delinsTC p.R132C Nonsense-LOF VAF: 2.0%

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.

## CLINICAL HISTORY

Diagnosed on

2023-05-06