

Summit™ Report

Patient Information	Provisional Diagnosis	Specimen	Physician Information
Name: John Smith DOB: 01/01/2000 Sex Assigned at Birth: Female MRN: 11xx22xx33	Diagnosis: Metastatic Renal Cell Carcinoma; Central Nervous System Neoplasm ICD10: R94.02	Type: CSF Collected: 7/2/2025 Received: 7/3/2025 Specimen ID: CASE 4 Abnormal Brain Scan	Institution: Belay Diagnostics Referring Physician: Provider Test

RESULT SUMMARY

POSITIVE

Clinically Significant Alterations Detected	TP53 Y220C (Tier 1A)
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Actionability Summary	0 therapeutic responses
	5 trials

ALTERATION DETAILS

Clinically Significant Genomic Variants				
Alteration	VAF	Type of Alteration	Classification	Clinical Implications
TP53 p.Y220C c.659A>G	4.8%	Substitution - Missense	Tier 1A	Potentially Relevant Clinical Trials; Diagnostic Implications

Aneuploidy Variants (Chromosome Arm Level Loss or Gain): None
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Clinical Implications: Associated with drug response = related to drug sensitivity or resistance as described in Drug Response section of this report; Potentially relevant clinical trials = gene is related to a trial in the Clinical Trials section of this report; Prognostic Implications = related to prognosis as described in Prognostic Implications section of this report; Diagnostic Implications = related to diagnosis as described in Diagnostic Implications

VAF: Variant Allelic Frequency

Variants of Unknown Significance (Tier 3): None
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ACTIONABILITY SUMMARY

FDA / NCCN Therapies for the Patient's Tumor Type (Tier 1A): None
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FDA / NCCN Therapies with Resistance / Decreased Response (Tier 1A): None
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Prognostic Implications per NCCN: None

Diagnostic Implications per WHO		
Biomarker	Diseases	Note
TP53 Y220C	Central Nervous System Neoplasm	Among central nervous system neoplasms, detection of TP53 mutations is an essential diagnostic criterion in the diagnosis of medulloblastoma, SHH-activated and TP53-mutant. TP53 mutations are reported in 10-15% of SHH-activated medulloblastomas, over half of which are germline. TP53 mutations are also desirable in the diagnoses of choroid plexus carcinoma (CPC) and astrocytoma, IDH-mutant. About 50% of CPCs carry TP53 mutations, whereas most IDH-mutant astrocytomas show widespread (> 50%) p53 expression (PMID:25040820).

CLINICAL TRIALS / INVESTIGATIONAL THERAPIES

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TP53 Y220C		
Therapy	Clinical Trial	Location/Sponsor
anti-KRAS and anti-TP53 peripheral blood lymphocytes + aldesleukin + cyclophosphamide + fludarabine; anti-KRAS and anti-TP53 peripheral blood lymphocytes + pembrolizumab + aldesleukin + cyclophosphamide + fludarabine	NCT03412877 (Phase 2) Administration of Autologous T-Cells Genetically Engineered to Express T-Cell Receptors Reactive Against Neoantigens in People With Metastatic Cancer	Bethesda, Maryland National Cancer Institute (NCI) IRC@nih.gov
cabozantinib	NCT05135975 (Phase 2) A Study of Cabozantinib as a Maintenance Agent to Prevent Progression or Recurrence in High-Risk Pediatric Solid Tumors	Birmingham, Alabama Nationwide Children's Hospital Madeline.Richardson3@nationwidechildrens.org
filgrastim + pegfilgrastim + carboplatin + cisplatin + cyclophosphamide + methotrexate + topotecan + vincristine	NCT05535166 (Phase 2) Molecular and Clinical Risk-Directed Therapy for Infants and Young Children With Newly Diagnosed Medulloblastoma	Palo Alto, California St. Jude Children's Research Hospital tabatha.doyle@stjude.org
niraparib	NCT04992013 (Phase 2) Niraparib in Tumors Metastatic to the CNS	Boston, Massachusetts Massachusetts General Hospital pbrastianos@mgh.harvard.edu
rezatapopt; pembrolizumab + rezatapopt	NCT04585750 (Phase 1/Phase 2) <i>FDA Fast Track</i> The Evaluation of PC14586 in Patients With Advanced Solid Tumors Harboring a TP53 Y220C Mutation (PYNNAACLE)	Los Angeles, California PMV Pharmaceuticals, Inc clinicaltrials@pmvpharma.com

TIER 1A THERAPY DETAILS

None

TEST DETAILS

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SNVs and Indels (32 genes, 112 amplicons)			
AKT1 NM_001014432.1 APC NM_000038.5 BRAF NM_004333.4 CD79B NM_000626.2 CDH1 NM_004360.3 CDKN2A NM_000077.4 CTNNB1 NM_001904.3 EGFR NM_005228.3	ERBB2 NM_004448.2 ERBB3 NM_001982.3 ERCC2 NM_000400.3 FBXW7 NM_033632.3 FGFR2 NM_000141.4 FGFR3 NM_000142.4 FUS NM_004960.3 GATA3 NM_001002295.1	GNAS NM_000516.4 H3-3A NM_002107.4 HRAS NM_005343.2 IDH1 NM_005896.2 IDH2 NM_002168.2 KRAS NM_004985.3 MYD88 NM_002468.4 NFE2L2 NM_006164.4	NRAS NM_002524.4 PIK3CA NM_006218.2 PTEN NM_000314.4 RAF1 NM_002880.3 SMAD4 NM_005359.5 TERT NM_198253.2 TP53 NM_000546.5 VHL NM_000551.3

Aneuploidy (chromosome arm level loss and gain)									
chr1p chr1q chr2p chr2q	chr3p chr3q chr4p chr4q	chr5p chr5q chr6p chr6q	chr7p chr7q chr8p chr8q	chr9p chr9q chr10p chr10q	chr11p chr11q chr12p chr12q	chr13q chr14q chr15q chr16p	chr16q chr17p chr17q chr18p	chr18q chr19p chr19q chr20p	chr20q chr21q chr22q

Methods and Limitations

The Summit™ next-generation sequencing (NGS) test investigates tumor DNA (tDNA) extracted from cerebrospinal fluid (CSF) for clinically relevant single/multi nucleotide variants (SNVs, MNVs, indels) and aneuploidy events associated with primary and metastatic central nervous system (CNS) cancers. Methodology involves targeted duplex sequencing of 32 key genes (SNVs, MNVs and Indels) and low pass whole genome sequencing (>0.1x) for the detection of chromosomal arm level loss or gain, aneuploidy (PMID: 37014860). Post target enrichment libraries, generated from 20-40ng of tDNA, are sequenced on the Illumina NovaSeq XPlus, generating 100 bp paired-end sequence reads. The LOD (limit of detection) for SNVs, MNVs and Indels was determined as 0.3% variant allelic fraction (VAF). Variants (mutations and aneuploidy) are called against the human genome build reference hg19 using the Summit™ Genome Analytics (SGA) pipeline (SNVs, MNVs, and Indels - version 1.0.0 and aneuploidy - version 0.6.0), developed at Belay Diagnostics.

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Tertiary analysis is performed using the precision oncology workbench (GenomOncology) based on the joint AMP/ASCO/CAP consensus guidelines for interpretation of sequence variants in cancer (PMID: 27993330). Please reach out to contact@belaydiagnostics.com for additional information or queries.

Disclaimers

This test was developed, and its performance characteristics determined by Belay Diagnostics Laboratory (CLIA# 14D2302605), which is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity testing. This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA). This test may be used for clinical purposes. However, the results of this test do not establish a diagnosis and should not be used alone for diagnosis or patient care decisions or otherwise replace the judgment of a treating physician and must always be interpreted in the context of all relevant clinical and pathological data.

This test is performed only to evaluate for somatic (i.e., tumor-specific) variants within the genes listed and cannot distinguish between germline and somatic alterations with absolute certainty. This test therefore does not report on incidental findings as defined by the American College for Medical Genetics and Genomics (ACMG) (PMID: 37347242). If a germline variant is suspected, follow-up germline testing using non-neoplastic (normal) tissue should be performed by a laboratory permitted to perform germline genetic testing along with genetic counseling. It is possible for a genomic variant to be present yet go undetected by our assay either due to the heterogeneous nature of the specimen or the limits of detection of our assay. Therefore, to the extent a particular genomic variant is not reported, Belay Diagnostics LLC does not guarantee that the variant does not exist in the specimen provided. Likely benign, and benign variants are not reported. For any reported variant of uncertain significance (VUS), if the classification changes, there is no obligation to send out a new report updating this information.

The information presented in the clinical trials and therapeutic sections of this report is compiled from public sources which are continuously updated. While we strive to ensure this information is accurate and complete, we cannot guarantee the accuracy or completeness of this information. This public sourced information is not ranked in order of potential or predicted efficacy and may not be complete. Specific eligibility criteria should be reviewed as applicable. This information may include associations between a genomic variant (or lack of a variant) and one or more therapeutic agents with potential clinical benefit (or lack of clinical benefit), including agents that are being studied in clinical research. The finding of a genomic variant does not necessarily indicate or demonstrate pharmacologic effectiveness (or lack thereof) of any agent or treatment regimen found in public source information. Similarly, the finding of "no clinically significant variant" does not necessarily indicate or demonstrate lack of pharmacologic effectiveness (or lack of effectiveness) of any agent or treatment regimen found in public source information. Belay Diagnostics expressly disclaims, and makes no representation of or warranty of, the accuracy or completeness with respect to the publicly available information included herein or reviewed or collected during creation of this report.

ACTIONABILITY REFERENCES

FDA: U.S. Food & Drug Administration (fda.gov)

NCCN: National Comprehensive Cancer Network® (NCCN®). Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. The NCCN Guidelines® and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

WHO: World Health Organization Classification of Tumours online (tumourclassification.iarc.who.int)

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