exacta

ENCYCLOPEDIC TUMOR ANALYSIS

TEST REPORT

Ms. Raluca Rosca

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DATAR
CANCER GENETICS

Patient Details

Name	:	Ms. Raluca Rosca
Birth Date	:	
Gender	:	Female
Address	:	Romania
Referred by	:	Regina Maria

Specimen Details

Tumor Type	:	Glioblastoma
Specimen Type	:	Blood, FFPE Tumor Block
Collection Date	:	09-Jul-2025, 15-Jul-2025
Accession Date	:	10-Jul-2025, 16-Jul-2025
Report Date	:	26-Jul-2025

Specimen Analysis Summary

Tissue

FFPE Tumor Specimen	:	**100%** Neoplastic Cellularity (950075)
Tumor DNA/RNA	:	511 Genes (SNAs | Indels | CNAs | Fusion Transcripts | TMB)
mRNA	:	20802 Genes
IHC	:	PD-L1 | AR | MLH1 | MSH2 | MSH6 | PMS2

Blood

cf Total Nucleic acids	:	52 Genes (SNAs | Indels | CNAs)
CGC	:	GFAP | CD45
CTC- ICC	:	mTOR | VEGFR1 | VEGFR2 | VEGFA | EGFR
Chemosensitivity analysis	:	68 Drugs
Pharmacogenetic analysis	:	23 Drugs
Genomic DNA Analysis	:	30 Genes
19 Clinical Trials	:	Refer to page no. 43 - 48
Note	:	Addendum to follow for MGMT promoter methylation.

Report Highlights

Indications	Patient's Tumor Type Specific Therapies (Biomarker Directed)	Other Therapies
TMB - Low 2 Mutations/Mb	☐ None	☐ None
PD-L1 - 22C3 TPS - 0%	☐ None	☐ None
PD-L1 - 28-8 TPS - 0%	☐ None	☐ None
MMR proficient Intact nuclear expression of MLH1, MSH2, MSH6, PMS2	☐ None	☐ None
PTEN p.N31* (Novel) (Tissue MAF 26.8%)	☐ None	☑ Capivasertib
VEGFA Overexpression (+2.73 FC) ICC Positive	☐ None	☑ Bevacizumab
PTEN p.N31* (Novel) (Tissue MAF 26.8%) **EIF4EBP1 (4EBP1)** Overexpression (+2.09 FC) **EIF4EBP3 (4EBP3)** Overexpression (+2.55 FC)	☐ None	☑ Everolimus ☑ Temsirolimus
EGFR Overexpression (+2.44 FC)	☐ None	☑ Cetuximab ☑ Panitumumab ☑ Necitumumab
VEGFA Overexpression (+2.73 FC) ICC Positive **VEGFB** Overexpression (+2.73 FC)	☐ None	☑ Ziv-Aflibercept

Indications	Patient's Tumor Type Specific Therapies (Biomarker Directed)	Other Therapies	
VEGFR2/KDR ICC Positive	⊟ None	☑ Regorafenib ☑ Pazopanib ☑ Sunitinib ☑ Sorafenib ☑ Ponatinib ☑ Vandetanib	☑ Axitinib ☑ Lenvatinib ☑ Cabozantinib ☑ Tivozanib ☑ Ramucirumab ☑ Fruquintinib
AR IHC Negative	⊟ None	☒ Enzalutamide ☒ Nilutamide ☒ Darolutamide ☒ Flutamide	☒ Bicalutamide ☒ Apalutamide ☒ Leuprolide ☒ Abiraterone

☑ Drugs with Benefit ☒ Drugs without Clinical Benefit / with Potential Resistance

ICC: Immunocytochemistry; CGC: Circulating Glial Cells; MAF: Mutant Allele Frequency; IHC: Immunohistochemistry; TMB: Tumor mutation burden; MMR: Mismatch Repair; HRD: Homologous Recombination Deficiency; TPS: Tumor Proportion Score; MGMT: O6-Methylguanine-DNA methyltransferase; NCCN: National Comprehensive Cancer Network - Central Nervous System Cancers -Glioblastoma.

Longitudinal Monitoring Biomarkers

Biomarker	Result
Highest mutant allele frequency (HMAF)	0%
Number of CGCs detected	1 CGC/ml

Cytotoxic Drugs

Chemosensitivity Analysis : % Cell Death (CD) ± Molecular biomarker

USFDA Approved / NCCN recommended	
Drugs	Result
☑ Cisplatin	62% CD
☑ Vincristine	54% CD
☑ Etoposide	50% CD
☑ Temozolomide	46% CD
☑ Lomustine	41% CD
☑ Carboplatin	40% CD

Off Label Therapy	
Drugs	Result
☑ Epirubicin	52% CD
☑ Docetaxel	49% CD
☑ Paclitaxel	48% CD
☑ Ifosfamide	47% CD
☑ Thiotepa	46% CD
☑ 5-Fluorouracil/Capecitabine	45% CD
☑ Vinblastine	44% CD
☑ Methotrexate	43% CD
☑ Gemcitabine	42% CD
☑ Bleomycin	39% CD
☑ Doxorubicin	38% CD
☑ Mitomycin	37% CD
☑ Cabazitaxel	36% CD
☑ Oxaliplatin	35% CD
☑ Trabectedin	34% CD
☑ Topotecan	33% CD
☑ Pemetrexed	32% CD
☑ Dactinomycin	31% CD
☑ Mitoxantrone	30% CD
☑ Melphalan	29% CD
☑ Vinorelbine	28% CD
☑ Cyclophosphamide	27% CD
☑ Eribulin	25% CD
☒ Dacarbazine	<25% CD
☒ Irinotecan	<25% CD

☑ Drugs with Benefit ☒ Drugs without Clinical Benefit / with Potential Resistance

Report Highlights

Additional Report Highlights

Indications for Repurposed Drugs

Drug	Indication
☑ Ivermectin	55% CD
☑ Doxycycline	52% CD; MMP2 (+4.62 FC), MMP14 (+3.75 FC), MMP28 (+2.30 FC) overexpression
☑ Niclosamide	50% CD
☑ Helixor A	49% CD
☑ Fenbendazole	48% CD
☑ Chloroquine	48% CD
☑ Helixor M	47% CD
☑ Curcumin	46% CD; MMP2 (+4.62 FC), MMP14 (+3.75 FC), MMP28 (+2.30 FC) overexpression
☑ Genistein	45% CD
☑ Quercetin	44% CD; WNT signaling pathway - WNT5A (+3.31 FC) overexpression
☑ Atorvastatin	44% CD; MAPK pathway activation - MAPK7 (+3.14 FC) overexpression
☑ Artesunate	44% CD; WNT signaling pathway - WNT5A (+3.31 FC) overexpression; MMP2 (+4.62 FC), MMP14 (+3.75 FC), MMP28 (+2.30 FC) overexpression
☑ Diflunisal	43% CD
☑ Dihydroberberine	42% CD
☑ Iscador P	41% CD
☑ Pantoprazole	40% CD
☑ Indol-3-carbinol	39% CD
☑ Epigallocatechin gallate	38% CD; MAPK pathway activation - MAPK7 (+3.14 FC) overexpression; MMP2 (+4.62 FC), MMP14 (+3.75 FC), MMP28 (+2.30 FC) overexpression
☑ Iscador Qu	37% CD
☑ Resveratrol	36% CD; MMP2 (+4.62 FC), MMP14 (+3.75 FC), MMP28 (+2.30 FC) overexpression
☑ Aspirin	35% CD
☑ DMSO	35% CD
☑ Valproic acid	34% CD
☑ Propranolol	34% CD
☑ Hypericin	33% CD
☑ Vitamin C / Ascorbic Acid	32% CD
☑ Dichloroacetate	31% CD
☑ Mebendazole	30% CD; MAPK pathway activation - MAPK7 (+3.14 FC) overexpression; MMP2 (+4.62 FC), MMP14 (+3.75 FC), MMP28 (+2.30 FC) overexpression
☑ Melatonin	29% CD
☑ Hydroxy Itraconazole	28% CD
☑ Glibenclamide	27% CD
☑ Cannabidiol	26% CD; MMP2 (+4.62 FC), MMP14 (+3.75 FC), MMP28 (+2.30 FC) overexpression

Drug	Indication
☑ Metformin	24% CD; MAPK pathway activation - MAPK7 (+3.14 FC) overexpression; MMP2 (+4.62 FC), MMP14 (+3.75 FC), MMP28 (+2.30 FC) overexpression
☑ Helixor P	23% CD
☑ Salinomycin Sodium Salt	22% CD
☑ Bromelain	21% CD
☑ Calcitriol	20% CD
☑ Celecoxib	19% CD; WNT signaling pathway - WNT5A (+3.31 FC) overexpression; MAPK pathway activation - MAPK7 (+3.14 FC) overexpression
☑ Berberine	MMP2 (+4.62 FC), MMP14 (+3.75 FC), MMP28 (+2.30 FC) overexpression
☑ 6-Shogaol	MMP2 (+4.62 FC), MMP14 (+3.75 FC), MMP28 (+2.30 FC) overexpression

☑ Drugs with Benefit

Disease Relevant Findings

Biomarker	Result	Biomarker	Result
TERT c.-124C>T	Mutation detected	CDKN2A/B	Deletion detected
EGFRvIII	Not detected	TP53	No mutations detected
IDH1/2	No mutations detected	ATRX	No mutations detected
MYCN	No mutations detected	PDGFRA	No alterations detected
BRAF	No mutations detected	H3F3A G34	No mutations detected
H3F3A K27	No mutations detected	HIST1H3B	No mutations detected
TSC1/2	No mutations detected	MYB	No mutations detected
FGFR1/2/3	No alterations detected	MET	No alterations detected
MYBL1	No fusions detected	RET	No fusions detected
NTRK1/2/3	No fusions detected	1p/19q	Co-deletion not detected
NF1	No pathogenic/ likely pathogenic mutations detected		

Pharmacogenetics : Drugs with Contraindications

Drug	Indication
⊟ None	⊟ None

Pharmacogenetics - Drugs with Increased Risk of Toxicity

Drug	Indication	Drug	Indication
! Carboplatin	ERCC1, MTHFR	! Cisplatin	XPC, ERCC1
! Gemcitabine	NT5C2	! Oxaliplatin	ERCC1

Pharmacogenetics - Drugs with Labeled Risk of Toxicity

Drug	Indication	Drug	Indication
☑ 5-Fluorouracil	DPYD	☑ Belinostat	UGT1A1
☑ Capecitabine	DPYD	☑ Dabrafenib	G6PD

Drug	Indication	Drug	Indication
☑ Erdafitinib	CYP2C9	☑ Erlotinib	UGT1A1
☑ Gefitinib	CYP2D6	☑ Irinotecan	UGT1A1
☑ Mercaptopurine	TPMT, NUDT15	☑ Methotrexate	ABCB1, MTHFR
☑ Nilotinib	UGT1A1	☑ Pazopanib	UGT1A1
☑ Rasburicase	G6PD	☑ Regorafenib	UGT1A1
☑ Sacituzumab govitecan	UGT1A1	☑ Tegafur	DPYD
☑ Thioguanine	TPMT, NUDT15	☑ Trametinib	G6PD
☑ Vincristine	CEP72		

☐ Not Applicable ☐ Drugs with Increased Risk of Toxicity ☑ Drugs with Labeled Risk of Toxicity

Summary of Other Genomic Alterations

Gene	Alteration Type (SNAs / Indels / CNAs/ Fusion)	Variant Classification	Oncogenic Effect #	Therapeutic / Clinical Significance
TERT	c.-124C>T (Tissue MAF 30.56%)	Pathogenic	Likely Oncogenic	Refer to page no. 7
NF1	p.E445K (Tissue MAF 30.81%)	VUS	Unknown Oncogenic Effect	--
HDAC2	c.640-12T>C (Tissue MAF 62.23%)	VUS	Unknown Oncogenic Effect	--
MTAP	Copy number loss - Equivocal	---	Likely Oncogenic	Refer to page no. 9
CDKN2A/B	Copy number loss	---	Oncogenic	Refer to page no. 8
APC	p.N1808del	VUS (Germline)	---	---
NBN	p.I171V	VUS (Germline)	---	---

SNA: Single Nucleotide Alteration; CNA: Copy Number Alteration; INDELS: Insertion / Deletion; VUS: Variant of unknown/uncertain significance; # Oncogenic effect annotation is based on OncoKB.

Tumor Mutation Burden (TMB)

Genomic Findings Tissue

Markers	Result	Interpretation	Category
Tumor Mutation Burden (TMB)	2 Mutations/Mb	TMB - Low	Tier III

Tumor mutation burden (TMB), the total number of somatic coding mutations in a tumor, is a promising predictive biomarker for immunotherapy response in cancer patients (Chan et al., 2018; Fancello et al., 2019). The somatic mutations in tumor DNA can give rise to neoantigens, mutation-derived antigens that are recognized and targeted by the immune system, especially after treatment with agents that activate T cells. Therefore, more somatic mutations a tumor has, the more neoantigens it is likely to form, and TMB can represent a useful estimation of tumor neoantigenic load (Chan et al., 2018; Fancello et al., 2019). Tumor mutation burden (TMB) is, thus, an informative biomarker for predicting response to immune checkpoint inhibitors like Pembrolizumab, Nivolumab, Tremelimumab plus Durvalumab, Atezolizumab, Avelumab, Durvalumab and Ipilimumab (Hervieu et al., 2022; Wildsmith et al., 2023).

Clinical studies have shown associations between elevated TMB and efficacy of immune checkpoint inhibitors, alone or in combination with other agents, in multiple solid tumors including, lung cancer, urothelial carcinoma, melanoma, colorectal cancer, head and neck squamous cell carcinoma and other cancer types (Johnson et al., 2016; Goodman et al., 2017; Carbone et al., 2017; Hellmann et al., 2018; Eroglu et al., 2018; Miao et al., 2018; Rizvi et al., 2018; Powles et al., 2018; Socinski et al., 2018; Legrand et al., 2018; Chae et al., 2019; Ott et al., 2019).

Analysis of tumor mutation burden (TMB) across more than 100,000 multiple solid cancer specimens suggests that patients with TMB >20 mutations/Mb may derive benefit from immune checkpoint inhibitors (Chalmers et al., 2017).

In various malignancies TMB >10 mutations/Mb have shown benefit from immune checkpoint inhibitors (Johnson et al., 2016; Legrand et al., 2018; Gerber et al., 2018; Georges et al., 2019; Zhu et al., 2019; Rizvi et al., 2020; Gullapalli et al., 2020; Ready, 2020).

Pembrolizumab has been USFDA approved for the treatment of patients with tumor mutation burden-high (TMB-H) [≥10 mutations/megabase (mut/Mb)] solid tumors.

Genomic Findings

Single Nucleotide Alterations / Indels / Copy Number Alterations / Fusion

Gene/s (Transcript ID)	Variant	Category:
TERT (NM_198253.3)	c.-124C>T	Tier I (Level A)

Interpretation: TERT promoter mutation is reported in glioblastoma and associated with an reduced overall survival (Nonoguchi et al., 2013; Mosrati et al., 2015; Eckel-Passow et al., 2015; Siraj et al., 2020; NCCN Guidelines, 2025). Some diffusely infiltrative astrocytomas lack the histologic features of glioblastoma (necrosis and/or microvascular proliferation) but having one or more of the molecular features of glioblastoma, including TERT promoter mutation, can be diagnosed as Glioblastoma, WHO grade IV (NCCN Guidelines, 2025).

Variant c.-124C>T, in TERT promoter region is reported to be a cancer-specific hotspot mutation and has been shown to be oncogenic (OncoKB, ClinVar, Blateau et al., 2020). TERT c.-124C>T, located at -124 bp upstream from the ATG start site confers enhanced TERT promoter activity by putatively generating consensus binding sites (GGAA) for ETS transcription factors within the TERT promoter region (Horn et al., 2013; Huang et al., 2013). This promoter mutation is associated with upregulation of TERT expression, suggesting it as a mechanism of telomerase activation in tumorigenesis (Huang et al., 2013; Arita et al., 2013). In silico analysis also predicts TERT c.-124C>T to be a pathogenic, gain-of-function mutation.

Telomerase is a ribonucleoprotein polymerase that maintains telomere ends by addition of the telomere repeat TTAGGG. The enzyme consists of a protein component with reverse transcriptase activity, encoded by this gene, and an RNA component which

serves as a template for the telomere repeat. Telomerase expression plays a role in cellular senescence, as it is normally repressed in postnatal somatic cells resulting in progressive shortening of telomeres.

Markers (Cytoband)	Result	Category:
CDKN2A/B (9p21.3)	Copy number loss	Tier I (Level A)

Interpretation: CDKN2A/B homozygous deletion is considered as an evidence of grade 4 status in IDH-mutant astrocytomas, even if such astrocytomas lack necrosis and microvascular proliferation, as per NCCN guidelines (NCCN Guidelines, 2025). CDKN2A and CDKN2B deletion results in constitutive CDK4/6 activity, leading to RB1 hyperphosphorylation and dysregulated cell cycle activity. Therefore, cell cycle control in CDKN2A-null but RB1-positive tumors can be restored by pharmacological inhibition of CDK4/6 (Eilers et al., 2015; Pan et al., 2017). Thus, copy number loss of CDKN2A and CDKN2B genes is indicative of potential therapeutic benefit from CDK4/6 inhibitors, Palbociclib, Ribociclib and Abemaciclib (Eilers et al., 2015; Pan et al., 2017). However conflicting evidence also exist. Other clinical studies have shown no significant correlation between CDKN2A loss and benefit from these drugs. (Finn et al., 2015).

Gene/s (Transcript ID)	Variant	Category:
PTEN (NM_000314.8)	c.90_91insTA, p.N31*; [p.(Asn31Ter)] (Novel)	Tier II (Level D)

Interpretation: Mutations in PTEN gene are reported in glioblastoma (Wang et al., 1997; Smith et al., 2001; Cancer Genome Atlas Research Network, 2008; Riddick and Fine, 2011; Xu et al., 2014; Han et al., 2016; Benitez et al., 2017; Hill et al., 2017; Shin et al., 2019). Loss of PTEN lipid phosphatase activity leads to phosphatidylinositol 3,4,5-triphosphate (PIP3) accumulation at the plasma membrane, which activates the AKT/mTOR pathway. Therefore, loss of function mutations in PTEN gene are suggestive of potential benefit from AKT inhibitor, Capivasertib as well as mTOR inhibitors, Everolimus and Temsirolimus (Dillon and Miller, 2014; Tian et al., 2019; Turner et al., 2023).

The USFDA has approved Capivasertib, an AKT inhibitor, with Fulvestrant for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer with one or more PIK3CA/AKT1/PTEN-alterations.
However, the efficacy of Capivasertib in glioblastoma is not well evaluated.

Everolimus is USFDA approved for treatment of hormone receptor-positive (HR+), HER2 negative (HER2-) breast cancer; neuroendocrine tumors of pancreatic, gastrointestinal, lung origin; renal cell carcinoma and subependymal giant cell astrocytoma.
Everolimus is recommended as a standard of care drug for subependymal giant cell astrocytoma (SEGA) as per NCCN guidelines (NCCN guidelines, 2025).
In the CPCT-03 study, evaluating the clinical benefit from Everolimus in patients with advanced solid tumors, with either a mutation or copy number loss of PTEN showed significant correlation between treatment response and PTEN status (P=0.046; onetailed Fisher's exact test) (n=5) (Weeber et al., 2017).
In a case study, treatment with Everolimus showed complete remission maintained at 33 months from diagnosis, in a patient with TSC2-mutant glioblastoma (Zureick et al., 2019).
In a clinical study, the combination of Everolimus and Carboplatin was shown to increase apoptosis as well as slow the growth and reduce tumor size in glioblastoma (Poore et al., 2019).

Temsirolimus is USFDA approved for the treatment of patients with advanced renal cell carcinoma.
In a phase II trial, Temsirolimus showed stable disease for >3 months in 1 out of 3 evaluable patients with glioblastoma (Geoerger et al., 2012).
In a phase II study, Temsirolimus in combination with Bevacizumab showed radiological stable disease (SD) in 2 of 10 patients with recurrent glioblastoma multiforme. Median progression-free survival of 8 weeks and overall survival of 15 weeks were reported (Lassen et al., 2013).

It is reported that, PTEN mutations were more common in the hyperprogressive disease (HPD) group on treatment with immune

checkpoint inhibitor therapy (71% HPD vs. 33.3% no HPD) in patients with high grade gliomas (Donovan et al., 2019).

Although functional characterization is not available for PTEN p.N31* novel variant, it is a truncating mutation in a tumor suppressor gene, and therefore is likely oncogenic and likely loss-of-function mutation (OncoKB). PTEN truncating mutations can produce several forms of C-terminally truncated PTEN proteins. Truncating mutations closer to the N-terminus result in loss of PTEN phosphatase function and an inability to negatively regulate PI3K/AKT pathway activity (Simpson et al., 2001). Public databases classify this as a likely pathogenic variant (Franklin, GeneBe). In silico analysis also predicts this novel mutation, to be a likely pathogenic, loss-of-function mutation.

The PTEN gene provides instructions for producing the phosphatidylinositol-3,4,5-trisphosphate 3-phosphatase protein. The PTEN enzyme modifies other proteins and lipids by removing phosphate groups. It helps control cell migration, adhesion and angiogenesis. Additionally, it is part of a pathway that mediates apoptosis or programmed cell death and also maintains genomic stability. Thus, PTEN enzyme prevents uncontrolled cell growth and acts as a tumor suppressor.

Markers (Cytoband)	Result	Category:
MTAP (9p21.3)	**Copy number loss - Equivocal**	**Tier II (Level D)**

Interpretation: Deletion of the MTAP gene occurs in 50% of all GBM cases, rendering it one of the most frequent genetic alterations in Glioblastoma, but its pathologic consequences remain unclear.

MTAP, a phosphorylase involved in methionine salvage pathways, is recurrently altered by deletion in various cancer types. MTAP (methylthioadenosine phosphorylase) loss is associated with reduced tumor-infiltrating lymphocytes (TILs) and poor overall survival in multiple tumor types, which can lead to resistance to immune checkpoint inhibitors (ICIs) (Gjuka et al., 2023; Chang et al., 2023; Seguchi et al., 2024). In a study focusing on the impact of MTAP loss on prognosis and efficacy of ICIs across advanced solid tumors, it was observed that patients with MTAP loss had significantly shorter progression-free survival when treated with ICIs, with a hazard ratio of 1.77 (Seguchi et al, 2024).

MTAP deletions are associated with homozygous deletions in the 9p21 chromosomal region that also includes the tumor suppressors CDKN2A, p16-INK4A, and p19-ARF (Marjon et al., 2016).

Pre-clinical studies with MTAP-deleted cancer cell lines demonstrated sensitivity to treatment with AMG 193 and MRTX1719 as measured by reduced tumor volume following treatment (Sacher et al., 2024).

Phase 1/2 Study of MRTX1719 in Solid Tumors With MTAP Deletion, currenly recruiting participant (NCT05245500).

AMG 193 is an orally available, small-molecule PRMT5 inhibitor that inhibits PRMT5 methyltransferase activity to increase expression of antiproliferative genes.

In the initial dose expansion results of the Phase I trial of AMG 193, patients with MTAP-null NSCLC (n=11) demonstrated an ORR of 18.2% and disease control rate (DCR) of 45.5%, patients with MTAP-null PDAC (n=16) demonstrated an ORR of 12.5% and a DCR of 43.8% and patients with MTAP-null biliary tract cancer (n=11) demonstrated an ORR of 18.2% and DCR of 36.4% (Sacher et al., 2024).

MRTX1719 is an orally available, small-molecule PRMT5-MTA complex inhibitor that targets the elevated expression of the PRMT5-MTA complex found in MTAP-deleted cells.

Preclinical studies in MTAP-deleted cancer cell lines, xenograft models and tumor biopsies demonstrate sensitivity to MRTX1719 as measured by inhibition of the production of PRMT5/MTAP metabolite SDMA, dose-dependent tumor shrinkage and inhibition of cellular proliferation (Engstrom et al., 2023).

Histopathological Analysis

Immunohistochemistry

Specimen

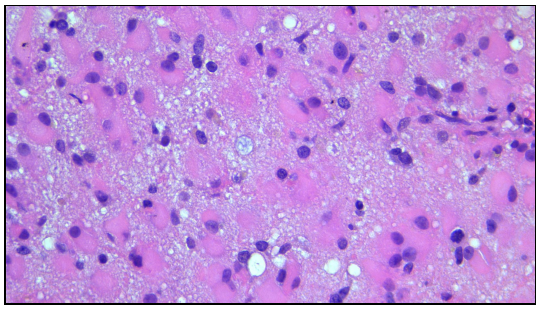
Received 1 FFPE block, Histopathological and Immunohistochemistry analysis is performed on block labelled as 950075

Microscopy

Infiltrating, hypercellular astrocytic neoplasm composed of predominantly gemostocytic astrocytes with hyperchromatic, elongated nuclei and irregular nuclear membranes. There is no mitosis, necrosis or microvascular proliferation in this specimen.

Impression

Histological features are consistent with glioblastoma, CNS WHO grade 4.



Light microscopic image of Haematoxylin & Eosin stained section of FFPE block (40X)

Immunohistochemistry (IHC) Analysis

Marker	Result
PD-L1 (Antibody clone 22C3)	TPS - 0%

Interpretation: PD-L1 (Antibody clone 22C3) is non-immunoreactive in neoplastic cells.

Pembrolizumab is USFDA approved for the treatment of melanoma, classical Hodgkin lymphoma, gastric or gastroesophageal junction adenocarcinoma, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors, primary mediastinal large B-cell lymphoma, merkel cell carcinoma, cervical, renal cell, endometrial, hepatocellular, urothelial, lung, esophageal, head and neck cancers.

Cemiplimab-rwlc is USFDA approved for treatment of cutaneous squamous cell carcinoma, basal cell carcinoma and PD-L1 expression (TPS ≥ 50%) positive non small cell lung tumors.

Marker	Result
PD-L1 (Antibody clone 28-8)	TPS - 0%

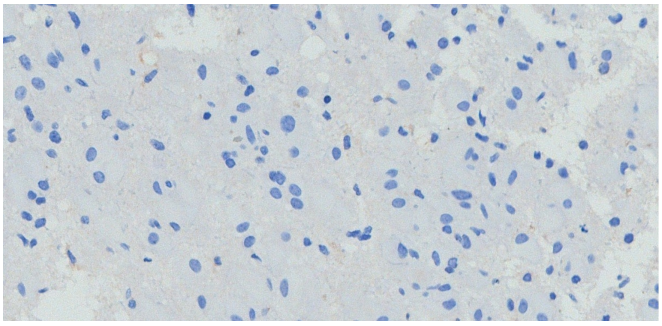
Interpretation: PD-L1 (Antibody clone 28-8) is non-immunoreactive in neoplastic cells.

Nivolumab is USFDA approved for the treatment of classic Hodgkin lymphoma, colorectal cancer, gastric (stomach) cancer, gastroesophageal junction adenocarcinoma, or esophageal cancer, malignant pleural mesothelioma, melanoma, non-small cell lung cancer, renal cell carcinoma, urothelial carcinoma, squamous cell carcinoma of the esophagus, head and neck.

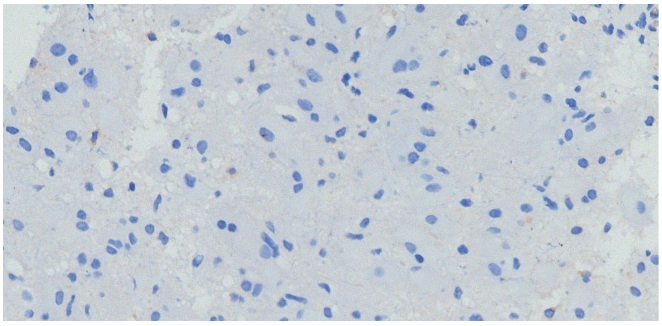
Marker	Result
AR	Negative

Interpretation: No staining for AR in neoplastic cells is indicative of potential lack of benefit from Enzalutamide, Bicalutamide, Nilutamide, Apalutamide, Darolutamide, Leuprolide, Flutamide and Abiraterone.

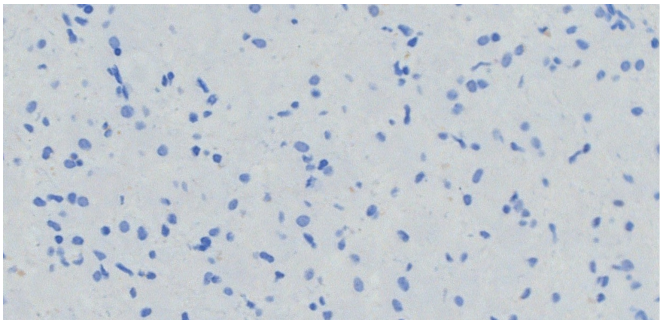
Enzalutamide, Bicalutamide, Nilutamide, Apalutamide, Darolutamide, Leuprolide, Flutamide and Abiraterone are USFDA approved for the treatment of metastatic prostate cancer.



PD-L1 (Antibody clone 22C3)



PD-L1 (Antibody clone 28-8)



AR IHC **Negative**

Mismatch Repair (MMR) Status

Immunohistochemistry

Marker	Staining pattern
MLH1	Intact nuclear expression
MSH2	Intact nuclear expression

Marker	Staining pattern
MSH6	Intact nuclear expression
PMS2	Intact nuclear expression

Interpretation:

Immunohistochemistry (IHC) for four mismatch repair (MMR) proteins (MLH1, MSH2, MSH6 and PMS2) was performed on formalin-fixed, paraffin-embedded tissue taken from representative sections of the resection specimens. The tumor shows intact nuclear expression of MLH1, MSH2, MSH6, PMS2, which indicates proficient mismatch repair (pMMR) status.

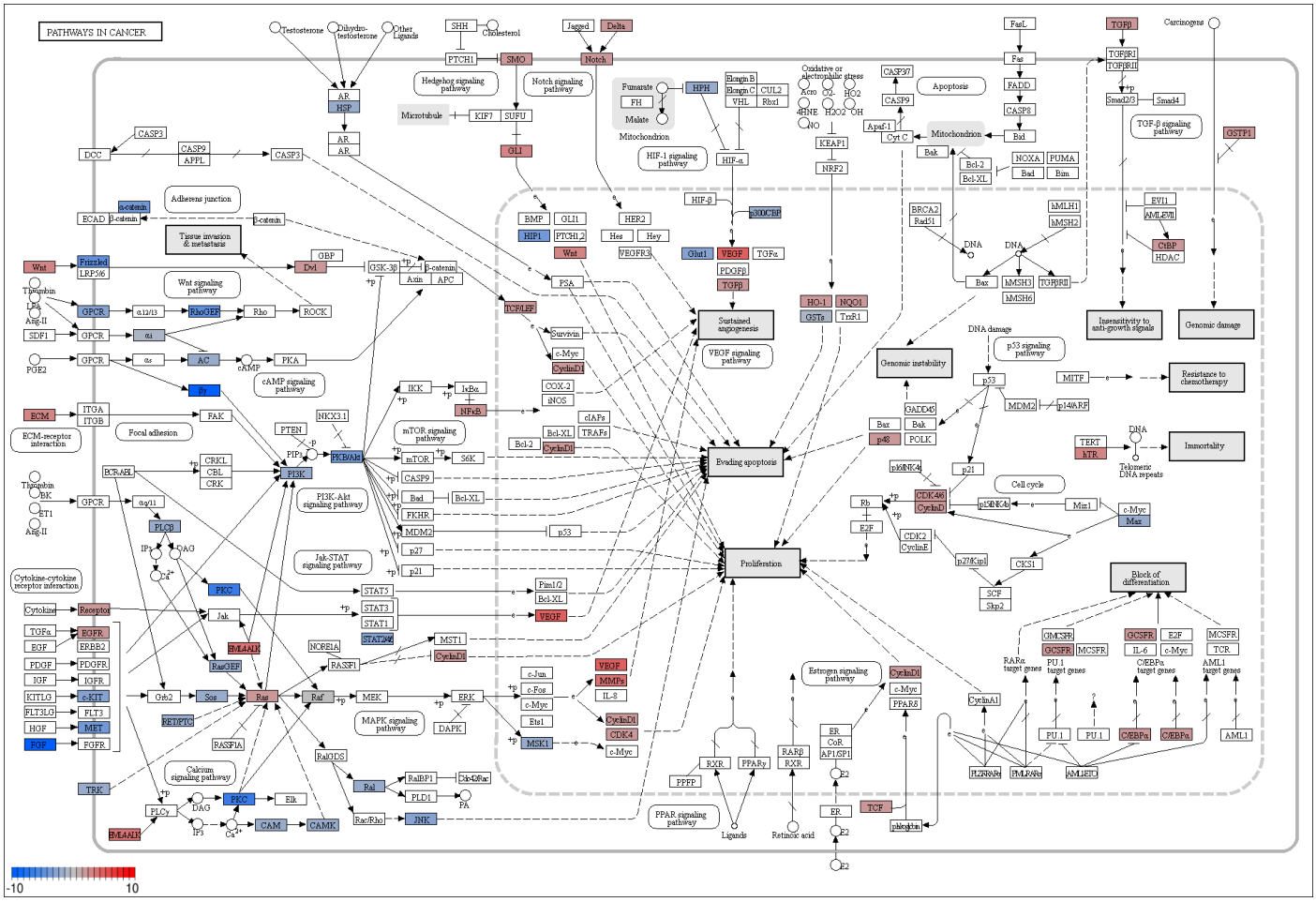
IHC for MMR proteins is used to identify MMR status: being diffusely positive (intact/retained nuclear staining) or showing loss of nuclear staining (MMR protein deficient) (Kanopiene et al, 2014; McCarthy et al, 2019). Loss of expression of MMR proteins may occur due to germline MMR gene mutations, somatic MMR gene inactivation or epigenetic silencing via promoter hypermethylation.

PD-1/PD-L1 checkpoints have important function in maintaining immune-tolerance and preventing effective antitumor immunity. Various clinical trials have demonstrated that mismatch repair deficiency (dMMR) or microsatellite instability-high (MSI-H) is significantly associated with long-term immunotherapy-related response and better prognosis in various tumors treated with immune checkpoint inhibitors. Tumors with dMMR or MSI-H are sensitive to immune checkpoint blockade (ICB), particularly to PD-1 and PD-L1 inhibitors. It is worth emphasizing that dMMR or MSI-H status could identify responders regardless of tumor location and tumor type, that is, they have the ability to guide different tumor immunotherapies in the same manner. Subsequently, USFDA approved Pembrolizumab and Dostarlimab for all dMMR/MSI-H solid tumors (Lemery et al., 2017; Zhao et al., 2019; Luchini et al., 2019; Andre et al., 2021).

KEGG Pathway: 20802 Genes Analysis

KEGG Pathway

Comprehensive Pathway Perturbation in Primary Tumor



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DATAR CANCER GENETICS

Global Gene Expression Highlights

Gene Expression - Tissue

Out of **20802** protein coding genes analyzed in the tumor tissue, **9478** genes were expressed in the analyzed tumor tissue.

2250 genes were found to be differentially regulated in the tumor tissue.

List of Oncology Drugs with Potential Benefit

Gene/s	Result (Fold change)	Drugs With Benefit
EGFR	▲ +2.44 FC	☑ Cetuximab ☑ Panitumumab ☑ Necitumumab

Interpretation: Upregulation of EGFR gene is suggestive of potential benefit from Cetuximab, Panitumumab, Necitumumab (Xu et al., 2016; Takeda and Nakagawa, 2019).

Cetuximab is USFDA approved for the treatment of head and neck and colorectal cancer.
In a pre-clinical study, Cetuximab effectively blocked glioblastoma cell invasion in an orthotopic xenograft model (Martens et al., 2008).

Panitumumab is USFDA approved for treatment of colorectal cancer.
In a pre-clinical study, Panitumumab demonstrated in vitro as well as in vivo anti-tumor activity against EGFRvIII-stratified glioma (Greenall et al., 2019).

Necitumumab is USFDA approved for the treatment of squamous non-small cell lung cancer.
However, its clinical efficacy in glioblastoma is not well evaluated.

Gene/s	Result (Fold change)	Drugs With Benefit
EIF4EBP1 (4EBP1)	▲ +2.09 FC	☑ Everolimus ☑ Temsirolimus

Interpretation: Overexpression of EIF4EBP1 (4EBP1) is suggestive of potential benefit from mTOR inhibitors, Everolimus and Temsirolimus (Li et al., 2013; Cha et al., 2015; Rutkovsky et al., 2019).

Kindly refer to USFDA labels/studies of these drugs mentioned earlier.

Gene/s	Result (Fold change)	Drugs With Benefit
EIF4EBP3 (4EBP3)	▲ +2.55 FC	☑ Everolimus ☑ Temsirolimus

Interpretation: Overexpression of EIF4EBP3 (4EBP3) is suggestive of potential benefit from mTOR inhibitors, Everolimus and Temsirolimus (Li et al., 2013; Cha et al., 2015; Rutkovsky et al., 2019).

Kindly refer to USFDA labels/studies of these drugs mentioned earlier.

Gene/s	Result (Fold change)	Drugs With Benefit
VEGFA	▲ +2.73 FC	☑ Bevacizumab ☑ Ziv-Aflibercept

Interpretation: Upregulation of VEGFA gene is suggestive of potential benefit from Bevacizumab and Ziv-Aflibercept (Ranieri et al., 2006; Otrock et al., 2011; Alidzanovic et al., 2016; Zhang et al., 2017).

Bevacizumab is USFDA approved for the treatment of multiple cancers including glioblastoma.
It is also recommended as a standard of care drug for the treatment of glioblastoma as per NCCN guidelines (NCCN guidelines, 2025).

Ziv-Aflibercept is USFDA approved for the treatment of metastatic colorectal cancer.
In a phase II study, treatment of Aflibercept in recurrent malignant glioma showed a 6-month progression-free survival rate of 7.7% in patients with glioblastoma (n=42). Overall radiographic response rate was 18% and median progression-free survival

was 12 weeks in patients with glioblastoma (de Groot et al., 2011).

Gene/s	Result (Fold change)	Drugs With Benefit
VEGFB	▲ +2.73 FC	☑ Ziv-Aflibercept

Interpretation: Upregulation of VEGFB is suggestive of potential benefit from Ziv-Aflibercept (Otrock et al., 2011; Zhang et al., 2017).

Kindly refer to USFDA labels/studies of this drug mentioned earlier.

List of Non-oncology Agents That May Provide Therapeutic Benefit

Markers	Result (Fold change)	Drugs
MAPK7	▲ +3.14 FC	☑ Atorvastatin ☑ Celecoxib ☑ Mebendazole ☑ Metformin ☑ Epigallocatechin-gallate (EGCG)

Interpretation: Atorvastatin induces apoptosis in multiple cancers by inhibiting MAPK-Bcl-2 signaling pathway (Reddy et al., 2006; Fromigue et al., 2006; Xiao et al., 2008; Bjarnadottir et al., 2013; Jones et al., 2018; Xu et al., 2018).

Several pre-clinical evidence demonstrate that Atorvastatin and Celecoxib and/or in combination, were more effective, than when given individually at higher doses. Inhibition of carcinogenesis by these agents is associated with the inhibition of cell proliferation and increase in apoptosis in tumor cells (Reddy et al, 2006; Xiao et al, 2008; Mármol et al, 2017; Huang et al., 2017; Li et al., 2018; Beckwitt et al., 2018; Ma et al., 2019).

Pre-clinical studies have demonstrated that Mebendazole inhibits the growth of various cancer cells by targeting the MAPK pathway (Simbulan et al., 2017; Younis et al., 2019; Guerini et al., 2019).

Metformin exhibits anti-tumor activity in cancer cells by inhibiting the MAPK pathway (Lei et al., 2017).

Several studies have shown that Epigallocatechin-gallate (EGCG) demonstrated anti-tumor effect by suppressing MAPK pathway (Singh et al., 2011; Negri et al., 2018).

Markers	Result (Fold change)	Drugs
MMP2	+4.62 FC	☑ Doxycycline ☑ Berberine ☑ Mebendazole ☑ Metformin ☑ Artesunate ☑ Cannabidiol ☑ Resveratrol ☑ Curcumin ☑ Epigallocatechin-gallate (EGCG) ☑ 6-Shogaol
MMP14	▲ +3.75 FC	
MMP28	+2.30 FC	

Interpretation: The antibiotic agent, Doxycycline, non-selectively inhibits MMP activation and expression, and has been shown to suppress MMP activities in human cancer cells (Tang et al., 2013; Cathcart et al., 2015).

Numerous studies have shown that Berberine and its derivatives demonstrate important anti-tumor effects. Berberine appears to exert its anticancer properties by inducing ROS production and prevention of cell migration via inhibition of the gene expression of MMP in various cancers (McCubrey et al, 2017; Li et al, 2018; Hu et al, 2019; Zhang et al, 2020).

Mebendazole is found to inhibit invasion and migration of cancer cells by supressing MMP activity (Pinto et al., 2015).

Metformin has been reported to block migration and invasion of tumor cells by inhibition of matrix metalloproteinase-9 (Hwang and Jeong, 2010).

Artesunate inhibits invasion and metastasis in cancer cells through downregulating expression of MMPs (Rasheed et al., 2010;

Wang et al., 2016; Ma et al., 2019).

Cannabidiol showed anti-migratory and anti-invasive effects by inhibiting MMPs which in turn degraded the extra-cellular matrix (ECM), thus affecting metastasis of cancer to the distant organs (Chakravarti et al., 2014; Elbaz et al., 2015; Sharafi et al., 2019).

Multiple studies have shown that Resveratrol supresses invasion and growth of cancer cells by inhibiting expression of MMPs (Yu et al., 2008; Weng et al., 2010; Ko et al., 2017).

Curcumin exerts antitumor activity in cancer cells through downregulating MMP activity (Hong et al., 2006; Kumar et al., 2012; Hassan and Daghestani, 2012; Cao et al., 2014; Bachmeier et al., 2018).

Epigallocatechin-gallate (EGCG) is found to inhibit epithelial-mesenchimal transition (EMT) as well as cellular invasion in cancer cells by directly binding and downregulating collagenase activity of MMPs (Negri et al., 2018).

6-Shogaol is reported to inhibit cancer cell invasion by reducing MMP9 expression (Ling et al., 2010; Weng et al., 2010).

Markers	Result (Fold change)	Drugs	
WNT5A	▲ +3.31 FC	☑ Quercetin	☑ Celecoxib
		☑ Artesunate	

Interpretation: Quercetin inhibits cancer growth through inhibition of Wnt/β-catenin signalling pathway (Shan et al., 2009; Amado et al., 2011).

Celecoxib is one of the most commonly used non-steroidal anti-inflammatory drugs (NSAIDs), which have chemo-preventive activity against cancers. It acts by down-regulating the Wnt pathway activity (Gong et al., 2012; Huang et al., 2017).

Artesunate reduces growth, migration and invasion through inhibiting activated Wnt pathway in multiple tumor cells (Li et al., 2007; Chen et al., 2017; Zheng and Pan, 2018).

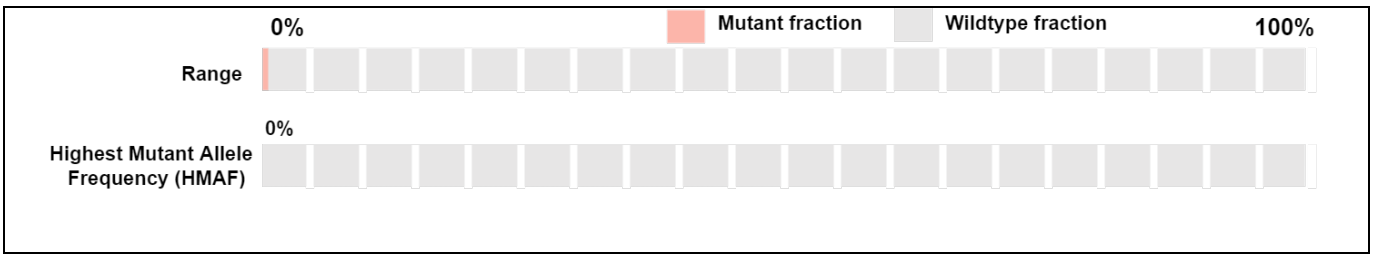
List of Oncology Drugs Without Therapeutic Benefit

None detected

Cell Free Nucleic Acids: Somatic Genome Alterations

cf-TNA

Figure 2:Highest Mutant Allele Frequency



No mutations were detected in the cell free nucleic acids isolated from patient's plasma.

Genomic Findings

Single Nucleotide Alterations / Indels / Copy Number Alterations

No somatic mutations/ amplifications detected

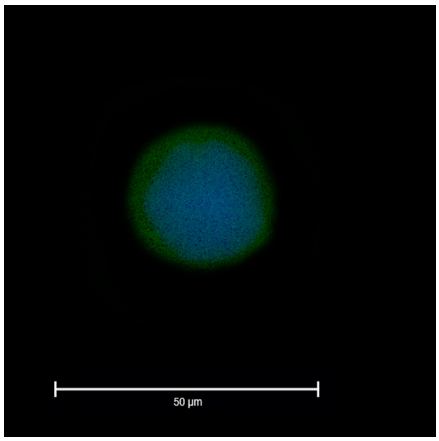
Circulating Glial Cell Enumeration

CGCs

Circulating Glial Cells (CGCs): **DETECTED**

Number of CGCs: **1 CGC/ml peripheral blood**

CGCs are defined as GFAP+ve, CD45-ve cells



Fluorescent microscopic image of CGC

Interpretation

1 CGC/ml peripheral blood detected in the submitted sample.

Recommendation

Circulating glial cell enumeration may be performed every 8 to 12 weeks to monitor disease status in consultation with the treating physician.

Immunocytochemistry (ICC) Analysis on Circulating Tumors and Associated Cells (CTCs)

ICC-CTCs

Markers	Result
VEGFR2/KDR	Positive

Interpretation: Positive staining for VEGFR2/KDR is indicative of potential benefit from Regorafenib, Axitinib, Pazopanib, Lenvatinib, Sunitinib, Cabozantinib, Sorafenib, Tivozanib, Ponatinib, Ramucirumab, Vandetanib and Fruquintinib (De Luca and Normanno, 2010; Paule et al., 2010; Chiang et al., 2012; Chu et al., 2013; Hepgur et al., 2013; Yamamoto et al., 2014; Li et al., 2014; Daudigeos-Dubus et al., 2015; Kim et al., 2015; Tannir et al., 2017; Ortega et al., 2017; Schmidinger and Danesi, 2018; Morse et al., 2019; Zhang et al., 2019; Jacob et al., 2020; Salgia et al., 2020; Liu et al., 2020).

Axitinib is USFDA approved for the treatment of advanced renal cell carcinoma (RCC).
In a randomized phase II study, Axitinib versus standard of care therapy for the treatment of recurrent glioblastoma (n=44), demonstrated tumor response of 28% in the Axitinib arm verses 23% in the control arm with manageable toxicity. Median progression-free and overall survival of 2.9 versus 2.6 months, and 10.3 versus 7.4 months for patients treated in the Axitinib versus control arm were reported, respectively (Neyns et al., 2014).
In a randomized phase II trial, comparing Axitinib monotherapy versus Axitinib plus Lomustine showed response rate of 28% versus 38% and 6-months progression-free survival of 26% versus 17% in patients with recurrent glioblastoma (n=79) (Duerinck et al., 2018).

Cabozantinib is USFDA approved for the treatment of hepatocellular carcinoma, advanced renal cell carcinoma (RCC) and thyroid cancer.
In a pre-clinical study, Cabozantinib inhibits the growth of tumor cell in glioma (Yakes et al., 2011).
In a phase 2 study, Cabozantinib as a maintenance agent to prevent progression or recurrence in high-risk pediatric solid tumors is currently recruiting participants (NCT05135975).

Lenvatinib is USFDA approved for the treatment of endometrial, hepatocellular carcinoma, advanced renal cell carcinoma (RCC) and thyroid cancer.
In a phase II trial, Lenvatinib was shown to be active (stable disease: 28%, 6-month overall survival rate: 28%) and well tolerated in 32 evaluable patients with recurrent glioblastoma (Reardon et al., 2012).

Ponatinib is USFDA approved for the treatment of acute lymphoblastic leukemia and chronic myelogenous leukemia.
In a pre-clinical study, Ponatinib reduced cell viability, induced cell apoptosis in a dose-dependent manner in malignant glioblastoma cells in vitro as well as reduced the tumor volume and increased apoptosis in pre-clinical model of glioblastoma (Zhang et al., 2014).

Pazopanib is USFDA approved for the treatment of soft tissue sarcoma and renal cell carcinoma.
In a phase I/II trial, Pazopanib in combination with Lapatinib demonstrated partial response rate of 5% and stable disease lasting ≥8 weeks in 34% patients with relapsed malignant glioma (n=41) (Reardon et al., 2013).
In a case study, treatment of Pazopanib patient achieved complete remission in diffuse midline glioma (Xiang-yuet al., 2019).

Regorafenib is USFDA approved for the treatment of colorectal, hepatocellular cancers and gastrointestinal stromal tumors.
In a clinical study, treatment of Regorafenib in 24 patients with advanced high-grade gliomas (including 1 diffuse midline glioma) showed partial response in 18 patients and median progression-free survival rate of 2.1 months (Lazaridis et al., 2019).

Sorafenib is USFDA approved for the treatment of advanced renal cell, hepatocellular and thyroid cancer.
Phase II study, treatment of Sorafenib in children with recurrent or progressive low-grade astrocytomas (n=11) showed median time to progression of 2.8 months (Karajannis et al., 2014).

Sunitinib is USFDA approved for the treatment of advanced renal cell carcinoma, gastrointestinal stromal tumor and pancreatic neuroendocrine tumors.
In a clinical study, combination of Sunitinib Malate and Lomustine for patients with Temozolomide-refractory recurrent anaplastic or low-grade glioma (n=13) showed complete response in 1 patient, stable disease in 3 patients. Median progression-free survival rate of 1.8 months with 6-month progression-free survival rate of 15% and median overall survival rate of 6.7 months were reported (Duerinck et al., 2015).
In a phase I and pharmacokinetic study of Sunitinib in 4 patients with sarcoma and glioma showed stable disease for 2 to 9 cycles in pediatric patients with refractory solid tumors (n=23) (DuBois et al., 2011).

Tivozanib is USFDA approved for the treatment of renal cell carcinoma.
In a phase II study, treatment of Tivozanib in recurrent glioblastoma (n=10), demonstrated complete response in 1, partial response in 1 and stable disease in 4 patients with the median progression-free and overall survival of 2.3 and 8.1 months, respectively (Kalpathy-Cramer et al., 2017).

Ramucirumab is USFDA approved for the treatment of non-small cell lung cancer, stomach adenocarcinoma or gastroesophageal junction adenocarcinoma and colorectal cancer.
In a clinical study, the treatment of Ramucirumab and Olaratumab in patients with recurrent glioblastoma (n=28) demonstrated potent anti-angiogeneic effect and decreased T2 volume, contrast enhanced volume and intensity in 28 days (Blakeley et al., 2013; NCT00895180).

Vandetanib is USFDA approved for the treatment of medullary thyroid cancer.
In a phase I and dose expansion cohort study, combination of Vandetanib and Sirolimus in patients with recurrent glioblastoma showed partial response in 2 of 19 patients. The progression-free survival at 6 months (PFS6) was 15.8 % (Chheda et al., 2015).

Fruquintinib is USFDA approved kinase inhibitor indicated for the treatment of adult patients with metastatic colorectal cancer (mCRC) who have been previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-VEGF therapy, and, if RAS wild-type and medically appropriate, an anti-EGFR therapy.
However, efficacy of this drug in glioblastoma is not well evaluated.

Markers	Result
VEGFA	Positive

Interpretation: Positive staining for VEGFA is indicative of potential benefit from Bevacizumab and Ziv-Aflibercept (Weickhardt et al., 2011; Tsai et al., 2015).

Kindly refer to USFDA labels/studies of these drugs mentioned earlier.

Markers	Result
VEGFR1/FLT1	Negative

Interpretation: No staining for VEGFR1/FLT1 is indicative of potential lack of benefit from Regorafenib, Axitinib, Pazopanib,

Lenvatinib, Sunitinib, Cabozantinib, Sorafenib, Tivozanib, Ponatinib and Fruquintinib (De Luca and Normanno, 2010; Paule et al., 2010; Chiang et al., 2012; Chu et al., 2013; Hepgur et al., 2013; Yamamoto et al., 2014; Li et al., 2014; Daudigeos-Dubus et al., 2015; Kim et al., 2015; Tannir et al., 2017; Ortega et al., 2017; Schmidinger and Danesi, 2018; Morse et al., 2019; Zhang et al., 2019; Jacob et al., 2020; Salgia et al., 2020; Liu et al., 2020).

However, simultaneous positive staining for VEGFR2/KDR is indicative of potential benefit from these drugs.
Kindly refer to USFDA labels of these drugs mentioned earlier.

Markers	Result
mTOR	Negative

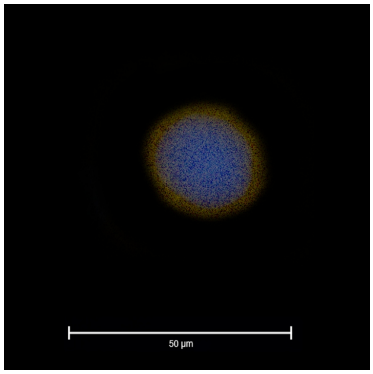
Interpretation: No staining for mTOR is indicative of potential lack of benefit from Everolimus and Temsirolimus (Li et al., 2014; Rodriguez-Moreno et al., 2017; Du et al., 2018; Kuo et al., 2019).

However, simultaneous inactivating novel PTEN p.N31* mutation, overexpression of EIF4EBP1 (4EBP1) and EIF4EBP3 (4EBP3) are suggestive of potential benefit from mTOR inhibitors, Everolimus and Temsirolimus.
Kindly refer to USFDA labels of these drugs mentioned earlier.

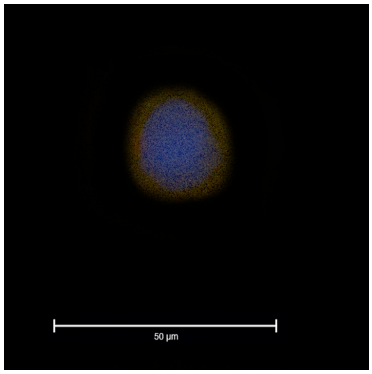
Markers	Result
EGFR	Negative

Interpretation: No staining for EGFR is indicative of potential lack of benefit from Cetuximab, Panitumumab and Necitumumab (Douillard et al., 2014; Trivedi et al., 2016; Thakur and Wozniak, 2017; Caratelli et al., 2020).

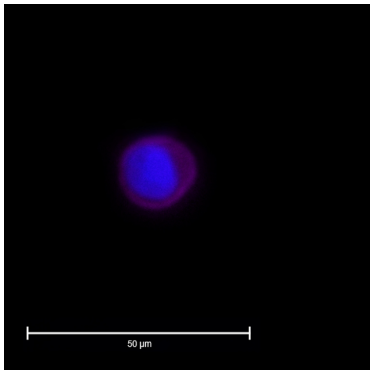
However, simultaneous upregulation of EGFR gene is suggestive of potential benefit from these drugs.
Kindly refer to USFDA labels of these drugs mentioned earlier.



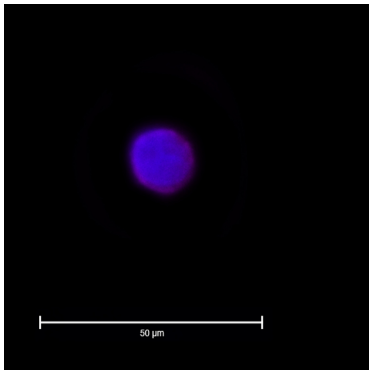
VEGFR2/KDR ICC **Positive**



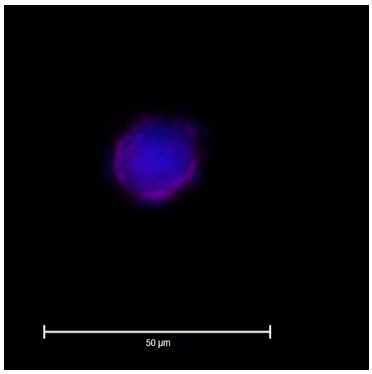
VEGFA ICC **Positive**



VEGFR1/FLT1 ICC **Negative**



mTOR ICC **Negative**



EGFR ICC **Negative**

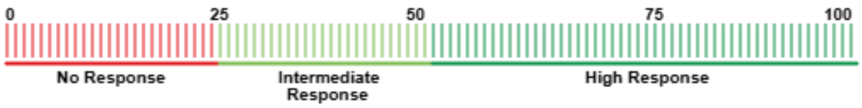
Chemosensitivity Analysis on CTCs

Chemosensitivity

Chemosensitivity assay performed on cultured circulating tumor and its associated cells indicates the effectiveness of chemotherapeutic drugs in descending order of efficacy.

Drug Names	% Cell Death	Drug Response
Cisplatin	62	
Vincristine	54	
Epirubicin	52	
Etoposide	50	
Docetaxel	49	
Paclitaxel	48	
Ifosfamide	47	
Thiotepa	46	
Temozolomide	46	
5-Fluorouracil/Capecitabine	45	
Vinblastine	44	
Methotrexate	43	
Gemcitabine	42	
Lomustine	41	
Carboplatin	40	
Bleomycin	39	
Doxorubicin	38	
Mitomycin	37	
Cabazitaxel	36	
Oxaliplatin	35	
Trabectedin	34	
Topotecan	33	
Pemetrexed	32	
Dactinomycin	31	
Mitoxantrone	30	
Melphalan	29	
Vinorelbine	28	
Cyclophosphamide	27	
Eribulin	25	
Dacarbazine	< 25	
Irinotecan	< 25	

CHEMO SCALE

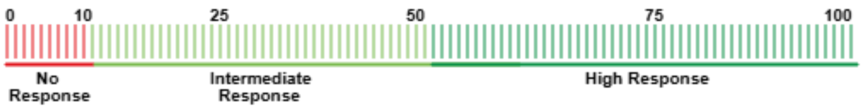


Response to Repurposed Drugs

Chemosensitivity

Drug Names	% Cell Death	Drug Response
Ivermectin	55	
Doxycycline	52	
Niclosamide	50	
Helixor A	49	
Fenbendazole	48	
Chloroquine	48	
Helixor M	47	
Curcumin	46	
Genistein	45	
Quercetin	44	
Atorvastatin	44	
Artesunate	44	
Diflunisal	43	
Dihydroberberine	42	
Iscador P	41	
Pantoprazole	40	
Indol-3-carbinol	39	
Epigallocatechin gallate	38	
Iscador Qu	37	
Resveratrol	36	
Aspirin	35	
DMSO	35	
Valproic acid	34	
Propranolol	34	
Hypericin	33	
Vitamin C	32	
Dichloroacetate	31	
Mebendazole	30	
Melatonin	29	
Hydroxy Itraconazole	28	
Glibenclamide	27	
Cannabidiol	26	
Metformin	24	
Helixor P	23	
Salinomycin Sodium Salt	22	
Bromelain	21	
Calcitriol	20	
Celecoxib	19	

CHEMO SCALE



Pharmacogenetic Analysis

Pharmacogenetics

Drug with Contraindication

- None

Drug with Increased Risk of Toxicity

- Carboplatin
- Cisplatin
- Gemcitabine
- Oxaliplatin

Drug with Labelled Toxicity

- 5-Fluorouracil
- Belinostat
- Capecitabine
- Dabrafenib
- Erdafitinib
- Erlotinib
- Gefitinib
- Irinotecan
- Mercaptopurine
- Methotrexate
- Nilotinib
- Pazopanib
- Rasburicase
- Regorafenib
- Sacituzumab govitecan
- Tegafur
- Thioguanine
- Trametinib
- Vincristine

Drug	Gene Analysis	Interpretation
Carboplatin Evidence level : Level 2A,2B	ERCC1; rs11615 AA MTHFR; rs1801133 GG	The patient has an unfavorable genotype in the analysed ERCC1 gene variant. Patients with this genotype may have an increased risk of nephrotoxicity, when treated with Carboplatin (Patino-Garcia et al., 2009; Khrunin et al., 2010; Tzvetkov et al., 2011).
Cisplatin Evidence level : Level 1B,2B	ERCC1; rs11615 AA XPC; rs2228001 GG	The patient has unfavorable genotypes in the analysed XPC and ERCC1 gene variants. Patients with such genotype may have an increased risk of toxicity including hearing loss, neutropenia and nephrotoxicity when treated with Cisplatin (Sakano et al., 2010; Khrunin et al., 2010; Tzvetkov et al., 2011).
Gemcitabine Evidence level : Level 2B	NT5C2; rs11598702 TT	The patient has an unfavorable genotype in the analysed variant of NT5C2 gene. Patients with such genotype may have a decreased clearance of Gemcitabine and an increased risk of toxicity (Mitra et al., 2012).
Oxaliplatin Evidence level : Level 2B	ERCC1; rs11615 AA	The patient has an unfavorable genotype in ERCC1 gene. Patients with such genotype when treated with Oxaliplatin may have an increased risk for nephrotoxicity (Khrunin et al., 2010; Tzvetkov et al., 2011).
5-Fluorouracil Evidence level : Level 1A	DPYD; *1/*1	The patient has a normal metabolizer status for DPYD gene leading to normal DPYD activity. Labelled risk for 5-Fluorouracil toxicity. Use as directed (Fluorouracil FDA Label).
Belinostat Evidence level : Level 1A	UGT1A1; *1/*1	The patient has a normal metabolizer status for UGT1A1 gene leading to reference UGT1A1 activity. Such genotype does not affect the clearance of Belinostat. Use as directed (Belinostat FDA Label).
Capecitabine Evidence level : Level 1A	DPYD; *1/*1	The patient has a normal metabolizer status for DPYD gene leading to normal DPYD activity. Labelled risk for Capecitabine toxicity. Use as directed (Capecitabine FDA Label).
Dabrafenib Evidence level : Level 1A	G6PD; wildtype/wildtype	The patient is not a carrier of G6PD deficient genotype. Patients with such genotype who are treated with Dabrafenib may have a reduced risk of hemolysis (Dabrafenib FDA Label).

Drug	Gene Analysis	Interpretation
Erdafitinib Evidence level : Level 1A	**CYP2C9; *1/*1**	The patient has a normal metabolizer status for CYP2C9 leading to an optimal enzyme activity. Patients with such genotype may have an optimal plasma concentration of Erdafitinib. Use as directed (Erdafitinib FDA Label).
Erlotinib Evidence level : Level 1A	**UGT1A1; *1/*1**	The patient has a normal metabolizer status for UGT1A1. Patients with such genotype who are treated with Erlotinib may have an average risk of hyperbilirubinemia. Use as directed (Erlotinib EMA Label).
Gefitinib Evidence level : Level 1A	**CYP2D6; *1/*4**	The patient has an intermediate metabolizer status for CYP2D6. Patients with such genotype who are treated with Gefitinib may have normal metabolism of Gefitinib. Use as directed (Gefitinib FDA Label).
Irinotecan Evidence level : Level 1A	**UGT1A1; *1/*1**	The patient has a normal metabolizer status for UGT1A1. Patients with such genotype who are treated with Irinotecan - based regimens may have an average risk of neutropenia, diarrhea, or asthenia (Irinotecan FDA Label).
Mercaptopurine Evidence level : Level 1A	**NUDT15; *1/*1** **TPMT; *1/*1**	The patient is a normal metabolizer for TPMT and NUDT 15 genes. Patients with such metabolizer status who are treated with Mercaptopurine may have an increased inactivation of Mercaptopurine and a decreased risk of developing severe, life-threatening myelotoxicity. Use as directed. Start with normal starting dose and adjust doses of Mercaptopurine based on disease-specific guidelines. Allow 2 weeks to reach steady state after each dose adjustment (Mercaptopurine FDA Label).
Methotrexate Evidence level : Level 2A	**ABCB1; rs1045642 AG** **MTHFR; rs1801133 GG**	The patient has favorable genotypes in the analysed variants of ABCB1 and MTHFR genes. Patients with such genotypes when treated with Methotrexate, may have a decreased risk of toxicity (Suthandiram et al., 2014).
Nilotinib Evidence level : Level 1A	**UGT1A1; *1/*1**	The patient has a normal metabolizer status for UGT1A1. Patients with such genotype who are treated with Nilotinib may have an average risk of hyperbilirubinemia. Use as directed (Nilotinib FDA Label).
Pazopanib Evidence level : Level 1A	**UGT1A1; *1/*1**	The patient has a normal metabolizer status for UGT1A1. Patients with such genotype who are treated with Pazopanib may have an average risk of hyperbilirubinemia. Use as directed (Pazopanib FDA Label).

Drug	Gene Analysis	Interpretation
Rasburicase Evidence level : Level 1A	**G6PD; wildtype/wildtype**	The patient is not a carrier of G6PD deficient genotype. Patients with such genotype who are treated with Rasburicase may have a reduced risk of hemolysis (Rasburicase FDA Label).
Regorafenib Evidence level : Level 1A	**UGT1A1; *1/*1**	The patient has a normal metabolizer status for UGT1A1. Patients with such genotype who are treated with Regorafenib may have an average risk of hyperbilirubinemia. Use as directed (Regorafenib EMA Label).
Sacituzumab govitecan Evidence level : Level 1A	**UGT1A1; *1/*1**	The patient has a normal metabolizer status for UGT1A1 gene leading to reference UGT1A1 activity. Patients with such genotype who are treated with Sacituzumab govitecan may have an average risk of neutropenia and other adverse reactions. Use as directed (Sacituzumab govitecan FDA Label).
Tegafur Evidence level : Level 1A	**DPYD; *1/*1**	The patient has a normal metabolizer status for DPYD gene leading to normal DPYD activity. Labelled risk for Tegafur toxicity. Use as directed (Fluorouracil FDA Label).
Thioguanine Evidence level : Level 1A	**NUDT15; *1/*1** **TPMT; *1/*1**	The patient is a normal metabolizer for TPMT and NUDT 15 genes. Patients with such metabolizer status who are treated with Thioguanine may have an increased inactivation of Thioguanine and a decreased risk of developing severe, life-threatening myelotoxicity. Use as directed. Start with normal starting dose and adjust doses of Thioguanine based on disease-specific guidelines. Allow 2 weeks to reach steady state after each dose adjustment (Thioguanine FDA Label).
Trametinib Evidence level : Level 1A	**G6PD; wildtype/wildtype**	The patient is not a carrier of G6PD deficient genotype. Patients with such genotype who are treated with Trametinib may have a reduced risk of hemolysis (Trametinib FDA Label).
Vincristine Evidence level : Level 2B	**CEP72; rs924607 CT**	The patient has a favorable genotype in the analysed variant of CEP72 gene. Patients with such genotypes who are treated with Vincristine may have a decreased, but not absent, risk of peripheral nervous system diseases (Diouf et al., 2015).

Tissue Based Analysis

Variant Allele Fraction and Coverage

Variant (Transcript ID)	Genomic co-ordinates	Allele fraction	Coverage (X)
TERT (NM_198253.3) c.-124C>T	chr5: 1295228G>A	30.56	72
NF1 (NM_001042492.3) c.1333G>A, p.E445K	chr17: 29533330G>A	30.81	1332
PTEN (NM_000314.8) c.90_91insTA, p.N31*	chr10: 89653793del>TA	26.8	615
HDAC2 (NM_001527.4) c.640-12T>C	chr6: 114270436A>G	62.23	775

Due to suboptimal coverage or no sequence, the presence or absence of variants contained within certain target regions of the genes listed below could not be meaningfully assessed.
TSC2

CNV Details

Tissue Based Analysis

Marker	Cytoband	Copy Number
MTAP	9p21.3	Copy number loss - Equivocal
CDKN2A/B	9p21.3	Copy number loss

Blood Based Analysis

Variant Allele Fraction and Coverage

Variant (Transcript ID)	Genomic co-ordinates	Allele fraction	Coverage (X)
APC (NM_000038.6) c.5424_5426del, p.N1808del	chr5: 112176715delCAA	49.94	806
NBN (NM_002485.4) c.511A>G, p.I171V	chr8: 90990521T>C	49.5	3944

Criteria for Classification of Somatic Variants

Analysis Criteria

The criteria/guidance used in this report is in accordance with the guidelines provided by the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists (AMP/ASCO/CAP) for the interpretation and reporting of sequence variants in cancer. Somatic sequence variations are categorized into four tiers based on their clinical significance (Li et al, 2017).

The 'oncogenic effect' categories in this report are derived from OncoKB and reflect each variant's predicted role in cancer as oncogenic, likely oncogenic, likely neutral, or inconclusive/unknown.

Tier I: Variants/biomarkers with strong clinical significance (therapeutic, prognostic and/or diagnostic)
Level A evidence: FDA approved therapies or standard guidelines for a specific tumor type.
Level B evidence: Statistically significant studies with consensus for specific tumor type.

Tier II: Biomarkers with potential clinical significance (therapeutic, prognostic and/or diagnostic)
Level C evidence: FDA approved therapies or standard guidelines for a different tumor type (off-label use of the drug). An inclusion criteria for clinical trials.

Level D evidence: No consensus among different studies.

Tier III: Biomarker whose association with cancer is not evident from available literature and is not frequently present in general population.

Tier IV: Biomarker whose association with cancer has not been reported till date and is frequently present in general population. This category of variants is not included in this report as per guidelines.

Criteria of Classification for Pharmacogenetic Analysis

Each variant-drug combination can be graded based on the measure of confidence in the association and the strength of prescribing recommendation.

Level 1: Evidence based on pharmacogenetics guidelines or well-established association studies

Level 2: Evidence of moderate variant-drug association from studies.

Level 3: Evidence suggests no consensus among different studies.

Drug Metabolizer Status Categories

Based on the different combination of haplotypes an individual inherits in each drug metabolizing gene, a drug metabolizer status can be predicted. There are 4 different drug metabolizer status types:

Poor Metabolizers (also called "PM"), Poor metabolizers have two non-functional alleles and therefore have little to no enzyme activity.

Intermediate Metabolizers (also called "IM"), Intermediate metabolizers have one non-functional allele and one normally functioning allele, and therefore have decreased enzyme activity.

Normal Metabolizers (also called "NM") Normal metabolizers have 2 normally functioning alleles and therefore have normal enzyme activity.

Ultra-Rapid Metabolizers (also called "UM"). Ultra-rapid metabolizers have one or more alleles which result in increased enzyme activity compared to extensive metabolizers.
The impact of each metabolizer type on medication response depends on the role of the enzyme in the metabolism of the specific drug in question. For example, for a drug that is inactivated by the enzyme, an ultra-rapid metabolizer may need a higher dose of the drug to reach a therapeutic range while for another drug, that is activated by the enzyme; ultra-rapid metabolizer status may be associated with increased exposure to the drug and therefore an increased risk of adverse drug reactions.

Criteria for Classification of Germline Variants

The American College of Medical Genetics and Genomics (ACMG) developed guidance for the interpretation of sequence variants and recommended the use of following specific standard terminology to describe variants identified in genes that cause Mendelian disorders (Richards et al.,2015).

Pathogenic: Functional or expression evidence suggests deleterious effect on gene function.

Likely Pathogenic/Probably Deleterious: Limited or no functional evidence available, but overall biological expectations suggestive of deleterious effect.

Variants of unknown significance (VUS): Little or nothing has been reported on this variant or its effects.

Likely Benign: The variant has been seen in cases, but also in controls. Variant may be present in a high percentage of the population, and may be present in a non-conserved region.

Benign: Established in the literature as a variant that is not associated with Mendelian (single-gene inherited) disease, or known to have an allele frequency that is far too high to be compatible with the prevalence of disease, mode of inheritance and penetrance patterns known for that condition.

Guide to Interpretation for MMR IHC

- Heterogenous staining pattern: Loss of MMR protein IHC staining admixed with areas of strong and diffuse retained MMR protein expression is defined as heterogenous staining pattern. However, this pattern should not be regarded as MMR IHC-Intact/retained or artefactual. Heterogeneous staining can be observed with any of the four IHC markers. If MSH2 protein is intact, possibility of Lynch syndrome is extremely unlikely.
- No loss of nuclear expression of mismatch repair (MMR) proteins: Low probability of microsatellite instability-high (MSI-H).
- Loss of nuclear expression of MLH1 and PMS2: Testing for methylation of the MLH1 promoter and/or mutation of BRAF is indicated (the presence of BRAF V600E mutation and/or MLH1 methylation suggests that the tumor is sporadic and germline evaluation is probably not indicated; absence of both MLH1 methylation and of BRAF V600E mutation suggests the possibility of Lynch syndrome, and sequencing and/or large deletion/duplication testing of germline MLH1 may be indicated).
- Loss of nuclear expression of MSH2 and MSH6: High probability of Lynch syndrome (sequencing and/or large deletion/duplication testing of germline MSH2 may be indicated, and, if negative, sequencing and/or large deletion/duplication testing of germline MSH6 may be indicated).
- Loss of nuclear expression of MSH6 only: High probability of Lynch syndrome (sequencing and/or large deletion/duplication testing of germline MSH6 may be indicated).
- Loss of nuclear expression of PMS2 only: High probability of Lynch syndrome (sequencing and/or large deletion/duplication testing of germline PMS2 may be indicated).

Genes Analyzed in Tumor Tissue Analysis

Gene List

SNVs/Indels/CNAs:

ABCB1	ABL1	ABL2	ABRAXAS1	ACVR1*	ACVR1B	ACVR2A	ADAMTS12	ADAMTS2	AKT1
AKT2	AKT3	ALK	AMER1	APC	AR	ARAF	ARHGAP35	ARID1A	ARID1B
ARID2	ARID5B	ASXL1	ASXL2	ATM	ATP1A1*	ATR	ATRX	AURKA	AURKC
AXIN1	AXIN2	AXL	B2M	BAP1	BARD1	BCL2	BCL2L12	BCL6	BCOR
BCR*	BLM	BMP5*	BMPR2	BRAF	BRCA1	BRCA2	BRIP1	BTK*	CACNA1D*
CALR*	CARD11	CASP8	CBFB	CBL	CCND1	CCND2	CCND3	CCNE1	CD274
CD276	CD79B*	CDC73	CDH1	CDH10	CDK12	CDK4	CDK6	CDKN1A	CDKN1B
CDKN2A	CDKN2B	CDKN2C	CHD4	CHEK1	CHEK2	CIC	CIITA*	CREBBP	CSF1R*
CSMD3	CTCF	CTLA4	CTNNB1*	CTNND2	CUL1*	CUL3	CUL4A	CUL4B	CYLD
CYP2C9	CYP2D6*	CYSLTR2*	DAXX	DDR1	DDR2	DDX3X	DGCR8*	DICER1	DNMT3A
DOCK3	DPYD	DROSHA*	DSC1	DSC3	E2F1*	EGFR	EIF1AX	ELF3	EMSY
ENO1	EP300	EPAS1*	EPCAM	EPHA2	ERAP1	ERAP2	ERBB2	ERBB3	ERBB4
ERCC2	ERCC4	ERCC5*	ERRFI1	ESR1	ETV6	EZH2	FAM135B	FANCA	FANCC
FANCD2	FANCE	FANCF	FANCG	FANCI	FANCL	FANCM	FAS*	FAT1	FBXW7
FGF19	FGF23	FGF3	FGF4	FGF7*	FGF9	FGFR1	FGFR2	FGFR3	FGFR4
FLT3	FLT4	FOXA1	FOXL2*	FOXO1*	FUBP1	FYN	GATA2	GATA3	GLI1*
GLI3	GNA11*	GNA13	GNAQ*	GNAS	GPS2	H3F3A	H3F3B	HDAC2	HDAC9
HIF1A*	HIST1H2BD*	HIST1H3B*	HLA-A	HLA-B	HNF1A	HRAS*	ID3*	IDH1*	IDH2
IGF1R	IKBKB	IL6ST*	IL7R	INPP4B	IRF4*	IRS4*	JAK1	JAK2	JAK3
KDM5C	KDM6A	KDR	KEAP1	KIT	KLF4*	KLF5	KLHL13*	KMT2A	KMT2B
KMT2C	KMT2D	KNSTRN*	KRAS	LARP4B	LATS1	LATS2	MAGOH	MAP2K1	MAP2K2*
MAP2K4	MAP2K7	MAP3K1	MAP3K4	MAPK1	MAPK8	MAX	MCL1	MDM2	MDM4
MECOM	MED12*	MEF2B	MEN1	MET	MGA	MITF	MLH1	MLH3	MPL
MRE11	MSH2	MSH3	MSH6	MTAP	MTOR	MTUS2*	MUTYH	MYC	MYCL
MYCN	MYD88	MYOD1*	NBN	NCOR1	NF1	NF2	NFE2L2	NOTCH1	NOTCH2
NOTCH3	NOTCH4	NRAS	NSD2*	NT5C2*	NTRK1	NTRK2*	NTRK3	NUP93*	PALB2
PARP1	PARP2	PARP3	PARP4	PAX5*	PBRM1	PCBP1	PDCD1	PDCD1LG2	PDGFRA

PDGFRB	PDIA3	PGD	PHF6	PIK3C2B	PIK3CA	PIK3CB	PIK3CD*	PIK3CG*	PIK3R1
PIK3R2	PIM1	PLCG1	PMS1	PMS2	POLD1	POLE	POT1	PPM1D	PPP2R1A
PPP2R2A	PPP6C	PRDM1	PRDM9	PRKACA	PRKAR1A	PSMB10*	PSMB8*	PSMB9*	PTCH1
PTEN	PTPN11	PTPRD*	PTPRT	PXDNL	RAC1	RAD50	RAD51	RAD51B	RAD51C
RAD51D	RAD52	RAD54L	RAF1	RARA	RASA1	RASA2	RB1	RBM10	RECQL4
RET	RGS7*	RHEB	RHOA*	RICTOR	RIT1	RNASEH2A	RNASEH2B	RNASEH2C*	RNF43
ROS1	RPA1	RPL10*	RPL22*	RPL5*	RPS6KB1	RPTOR	RUNX1	RUNX1T1*	SDHA
SDHB	SDHC*	SDHD	SETBP1	SETD2	SF3B1	SIX1*	SIX2*	SLCO1B3	SLX4
SMAD2	SMAD4	SMARCA4	SMARCB1	SMC1A	SMO	SNCAIP*	SOCS1*	SOS1*	SOX2*
SOX9	SPEN	SPOP	SRC	SRSF2*	STAG2	STAT1*	STAT3	STAT5B*	STAT6
STK11	SUFU	TAF1*	TAP1	TAP2	TBX3	TCF7L2	TERT	TET2	TGFBR1*
TGFBR2	TMEM132D*	TNFAIP3	TNFRSF14	TOP1	TP53	TP63	TPMT	TPP2	TRRAP*
TSC1	TSC2	TSHR*	U2AF1	UGT1A1*	USP8	USP9X	VHL	WAS*	WT1
XPO1	XRCC2	XRCC3	YAP1	YES1	ZBTB20*	ZFHX3	ZMYM3	ZNF217	ZNF429
ZRSR2									

* NO CNA

Fusion:

AKT1	AKT2	AKT3	ALK	AR	BRAF	BRCA1	CDKN2A	EGFR	ERBB2
ERBB4	ERG	ESR1	ETV1	ETV4	ETV5	FGFR1	FGFR2	FGFR3	MAP3K8
MET	MTAP	MYB	MYBL1	NOTCH1	NOTCH2	NOTCH3	NRG1	NTRK1	NTRK2
NTRK3	NUTM1	PIK3CA	PIK3CB	PPARG	PRKACA	PRKACB	RAF1	RARA	RELA
RET	ROS1	RSPO2	RSPO3	STAT6	TERT	TFE3	TFEB	YAP1	

Genes Analyzed in Cell Free Nucleic Acids Analysis

SNV Genes:

AKT1	ALK	APC	AR	ARAF	BRAF	CHEK2	CTNNB1	DDR2	EGFR
ERBB2	ERBB3	ESR1	FBXW7	FGFR1	FGFR2	FGFR3	FGFR4	FLT3	GNA11
GNAQ	GNAS	HRAS	IDH1	IDH2	KIT	KRAS	MAP2K1	MAP2K2	MET
MTOR	NRAS	NTRK1	NTRK3	PDGFRA	PIK3CA	PTEN	RAF1	RET	ROS1
SF3B1	SMAD4	SMO	TP53						

CNV Genes:

CCND1	CCND2	CCND3	CDK4	CDK6	EGFR	ERBB2	FGFR1	FGFR2	FGFR3
MET	MYC								

Genes Analyzed in Genomic DNA Analysis

APC	ATM	AXIN2	BLM	BMPR1A
BRCA1	BRCA2	CDH1	CHEK2	EPCAM
FANCA	GALNT12	GREM1	HOXB13	MLH1
MLH3	MSH2	MSH6	MUTYH	NBN
NTHL1	PALB2	PMS2	POLD1	POLE
PTEN	RAD51D	SMAD4	STK11	TP53

Tumor Tissue Gene Expression Analysis

Tumor tissue RNA: 20802 mRNA

Genes Analyzed for Pharmacogenetics

Genes	Variants Analyzed
ABCB1	c.3435T>C
CEP72	n.366+1469G>A
CYP2C9	*1, *2, *3, *4, *5, *6, *7, *8, *9, *10, *11, *12, *13, *14, *15, *16, *18, *35
CYP2D6	*1, *2, *3, *4, *6, *7, *8, *9, *10, *11, *12, *15, *17, *19, *20, *29, *35, *38, *41, *42, *44, *56 and *5, XN
DPYD	*1, *10, *11, *12, *13, *2A, *3, *4, *5, *6, *7, *8, *9A, *9B, c.1024G>A, c.1057C>T, c.1314T>G, c.1896T>C, c.2279C>T, c.2639G>T, c.2846A>T, c.2872A>G, c.2933A>G, c.496A>G, c.557A>G, c.61C>T, c.62G>A, c.1129-5923C>G (HapB3), c.1236G>A (HapB3)
ERCC1	c.354T>C
G6PD	Gaohe; Sunderland; Orissa; Murcia Oristano; Ube Konan; Vancouver; Santa Maria; G6PD A- 680T_376G; Mt Sinai; Sierra Leone; G6PD A- 968C_376G; Ananindeua; Taipei Chinese-3; Malaga; Mediterranean Haplotype; Mediterranean_Dallas_Panama_Sassari_Cagliari_ Birmingham; Coimbra Shunde; Sibari; Cincinnati; Minnesota_Marion_Gastonia_LeJeune; Nanning; Chinese-5; Ierapetra; Serres; Iowa_Walter Reed_Springfield; Guadalajara; Riverside; Asahi; Ludhiana; Pawnee; Surabaya; Japan_Shinagawa; Puerto Limon; Alhambra; Nashville_Anaheim_Portici; Beverly Hills_Genova_Iwate_Niigata_Yamaguchi; Tomah; Montpellier; Loma Linda; Mira d'Aire; Chatham; Rehevot; Kalyan-Kerala_Jamnaga_Rohini; Viangchan_Jammu; Seattle_Lodi_Modena_Ferrara II_Athens-like; Aveiro; Nilgiri; Nankang; Ilesha; Crispim; Sao Borja; Lagosanto; Namouru; A- 202A_376G; Hechi; Metaponto; Aures; Acrokorinthos; A; Vanua Lava; Mediterranean_Dallas_Panama_Sassari_Cagliari_Birmingham; wildtype; 202G>A_376A>G_1264C>G
MTHFR	c.665C>T
NT5C2	c.175+1178A>G
NUDT15	*1, *2, *3, *4, *5, *6
TPMT	*1, *2, *3A, *3B, *3C, *4, *5, *6, *7, *8, *9, *10, *11, *12, *13, *14, *15, *16, *20, *21, *23, *24, *25, *26, *29, *31, *32, *33, *34, *37
UGT1A1	*1, *28
XPC	c.2815C>A

Drugs Tested in Chemosensitivity Analysis

Drug List

5-Fluorouracil/Capecitabine, Artesunate, Aspirin, Atorvastatin, Bleomycin, Bromelain, Cabazitaxel, Calcitriol, Cannabidiol, Carboplatin, Celecoxib, Chloroquine, Cisplatin, Curcumin, Cyclophosphamide, DMSO, Dacarbazine, Dactinomycin, Dichloroacetate, Diflunisal, Dihydroberberine, Docetaxel, Doxorubicin, Doxycycline, Epigallocatechin gallate, Epirubicin, Eribulin, Etoposide, Fenbendazole, Gemcitabine, Genistein, Glibenclamide, Helixor A, Helixor M, Helixor P, Hydroxy Itraconazole, Hypericin, Ifosfamide, Indol-3-carbinol, Irinotecan, Iscador P, Iscador Qu, Ivermectin, Lomustine, Mebendazole, Melatonin, Melphalan, Metformin, Methotrexate, Mitomycin, Mitoxantrone, Niclosamide, Oxaliplatin, Paclitaxel, Pantoprazole, Pemetrexed, Propranolol, Quercetin, Resveratrol, Salinomycin Sodium Salt, Temozolomide, Thiotepa, Topotecan, Trabectedin, Valproic acid, Vinblastine, Vincristine, Vinorelbine, Vitamin C

Antibody Details - Immunocytochemistry (ICC) Analysis

Antibody

Marker	Clone	Marker	Clone
GFAP	REA764	CD45	HI30
mTOR	Polyclonal	VEGFR1	REA569
VEGFR2	REA1116	VEGFA	JH121
EGFR	EP22		

Antibody Details - Immunohistochemistry (IHC) Analysis

Antibody List

Marker	Clone	Vendor	Visualization System
AR	AR27	Leica	Polymer Detection System
PD-L1	22C3	Dako	
PD-L1	28-8	Dako	
MLH1	ES05	Leica	
MSH2	79H11	Leica	
MSH6	PU29	Leica	
PMS2	M0R4G	Leica	

PD-L1

PD-L1 Interpretation

PD-L1 (Clone: 22C3): PD-L1 protein expression is determined by using Tumor Proportion Score (TPS), which is the percentage of viable tumor cells showing partial or complete membrane staining. PD-L1 IHC 22C3 pharmDx is indicated as an aid in identifying NSCLC patients for treatment with KEYTRUDA® (Pembrolizumab). According to PD-L1 IHC 22C3 pharmDx literature, specimen should be considered PD-L1 positive if TPS ≥ 50% of the viable tumor cells exhibit membrane staining at any intensity. However, an open-label, phase 3 KEYNOTE-042 study proved Pembrolizumab to be superior over platinum-based chemotherapy in patients with previously untreated advanced/metastatic NSCLC without sensitizing EGFR or ALK alterations and a PD-L1 TPS ≥1%.

Phase 3 trial of Cemiplimab versus platinum-based chemotherapies showed that Cemiplimab is indicated for the first-line treatment of patients with NSCLC whose tumors have high PD-L1 expression [Tumor Proportion Score (TPS) ≥ 50%] as determined by an FDA-approved test, with no EGFR, ALK or ROS1 aberrations (NCT03088540).

#PD-L1 IHC 22C3 pharmDx is a qualitative immunohistochemical assay using monoclonal Mouse Anti-PD-L1, Clone 22C3 intended for use in the detection of PD-L1 protein in formalin-fixed, paraffin-embedded (FFPE) non-small cell lung cancer (NSCLC) tissue.

PD-L1 (Clone: 28-8): PD-L1 protein expression is defined as the percentage of tumor cells exhibiting positive complete circumferential or partial linear plasma membrane staining at any intensity. Cytoplasmic staining, if present, is not considered positive for scoring purposes. Non-malignant cells and immune cells (e.g. such as infiltrating lymphocytes or macrophages) may also stain with PD-L1; however, these are not included in the scoring for the determination of PD-L1 positivity.

PD-L1 expression cut off for non-squamous non-small cell lung carcinoma is ≥ 1%. PD-L1 expression as detected by PD-L1 28-8 pharmDx in non-squamous NSCLC may be associated with enhanced survival from OPDIVO® (Nivolumab).

PD-L1 expression cut off is ≥ 1% for squamous cell carcinoma of the head and neck (SCCHN), Urothelial carcinoma (UC) and melanoma. Detection of PD-L1 expressing tumor cells in SCCHN and UC patient specimens may indicate an enhanced survival benefit

to OPDIVO® (Nivolumab) treatment for the patients. Clinical study CHECKMATE-067 investigated the clinical validity of PD-L1 IHC 28-8 pharmDx for the assessment of PD-L1 expression in melanoma patients treated with OPDIVO®, OPDIVO® in combination with YERVOY® (Ipilimumab), and YERVOY® alone.

#PD-L1 IHC 28-8 pharmDx is a qualitative immunohistochemical assay using monoclonal Rabbit Anti-PD-L1, Clone 28-8 intended for use in the detection of PD-L1 protein in formalin-fixed, paraffin-embedded (FFPE) non-squamous non-small cell lung cancer (NSCLC), squamous cell carcinoma of the head and neck (SCCHN), urothelial carcinoma (UC), and melanoma tissues.

Methods and Limitations

Methods

Tumor tissue analysis:

FFPE tissue was analyzed for mutation, copy number alterations and fusion detection using semiconductor based Next Generation Sequencing technology. High quality FFPE tissue DNA and RNA extracted from the submitted specimen was subjected to target enrichment by multiplex PCR amplification using Oncomine Comprehensive Assay Plus panel targeting 511 Oncogenes and Tumor suppressor genes. (see gene list in the 'Gene Analyzed' section). Enriched DNA sequences were ligated with platform specific adaptor molecules and were sequenced using semiconductor chip. Sequenced data was aligned with the human genome (hg19) and libraries are sequenced to target 1000x average coverage with >95% of amplicons with atleast 100 reads using a customized in-house pipeline DCGL NGS Bioinformatics Pipeline v15.6 and DCGL NGS Bioinformatics Pipeline v10.8, designed to accurately detect the somatic variants.

Regarding copy number losses identified in the assay, a “copy number loss” denotes homozygous deletion in the gene, indicating loss of the gene. Conversely, an alteration labeled as “Loss – equivocal” indicates that the analysis suggests but does not definitely confirm, a homozygous deletion of the gene in question.

The lower limit of detection of the mutations targeted is 5%, and variants present below 5% may not be detectable with this assay, whereas analytical sensitivity is 98.24% and specificity is 99.78% for SNV, CNV and Fusion.

This test does not distinguish between somatic and germline variants. Therefore, germline testing with genetic counseling may be warranted for specific genetic variants with potential actionable implications in the germline context when clinically appropriate.

This test does not detect gene variants other than those listed. Alterations in the primer binding regions can affect the testing, and ultimately, the genotyping assessments made. Rare diagnostic errors may occur due to primer site mutations. Tumor panel has limitations in detecting the following types of mutations (this might not be exhaustive): large rearrangements, epigenetic factors, mutations in repetitive or high GC rich regions and mutations in gene with corresponding pseudo genes or other highly homologous sequences. Presence of PCR inhibitors in the sample may prevent DNA amplification for mutation analysis. Rare and novel mutations may be clinically uncharacterized.

Cell free nucleic acids analysis:

Cell free nucleic acids were analyzed for mutation detection using semiconductor based Next Generation Sequencing technology. Cell free nucleic acids extracted from the plasma of submitted specimen was subjected to target enrichment by multiplex PCR amplification using Oncomine Pan-Cancer Cell-Free panel (see gene list in the 'Genes analyzed section'). Enriched DNA sequences were ligated with platform specific adaptor molecules and were sequenced on semiconductor chip. Sequenced data was aligned with the human genome (hg19), analyzed at 17000x median target coverage (with median molecular tag coverage 1250x) using a customized in-house pipeline DCGL NGS Bioinformatics Pipeline v11.14, designed to accurately detect the rare somatic variants. Lower limit of detection of the mutations targeted is 0.1% and variants present below 0.1% may not be detectable with this assay, whereas analytical sensitivity is 97.06% and specificity is 100% for SNV, CNV.

A negative test result does not exclude the possibility of mutations being present in the test sample probably due to the reads representing minor allele fraction is below the detectable limit of the assay or other limiting technical/analytical factors. The scope of copy number variations analysis includes copy number gain/amplification of the detected gene(s).

The clinical sensitivity of most assays for detection of alterations in cell free nucleic acids is limited as compared with tumor tissue-based testing. This may result from a high ratio of normal to tumor DNA or excess degradation of cell free nucleic acids or may simply reflect the biologic heterogeneity of solid tumors, some of which may shed abundant nucleic acid into the circulation

and others that may not. Tumor type, size, disease stage, sites of metastasis, histologic grade, or other features may also affect levels, however, much remains to be elucidated.

Tumor tissue mRNA analysis:

Tumor tissue was analyzed for mRNA expression detection using semiconductor based Next Generation Sequencing method. High quality RNA was extracted from the submitted specimens along with healthy tissue sample and subjected to mRNA library preparation using a Ion AmpliSeq Transcriptome Human Gene Expression targeted panel. RNA sequencing was performed to achieve at least 4 million mappable high-quality reads for the paired analysis. Sequence reads were aligned to the hg19 transcriptome reference sequence in Torrent Suite Software using the Ion Torrent Mapping Alignment Program. Differential Gene Expression analysis was performed using a customized in-house pipeline DCGL NGS Bioinformatics Pipeline vS5.12 designed to detect the Significantly expressed genes.

Pharmacogenetic analysis:

Blood was analyzed for genotyping using semiconductor based Next Generation Sequencing technology. High quality genomic DNA was extracted from the submitted specimen and subjected to target enrichment by high multiplex PCR amplification using Ion AmpliSeq panel targeting variants of genes. Enriched DNA sequences were ligated with platform specific adaptor molecules and was sequenced on using semiconductor chip. The minimum average depth was 500x for panel of genes analyzed. High quality sequencing data (proportion of Q20 bases ≥75%) was analyzed using DCGL NGS Bioinformatics Pipeline vS14.7. This test does not detect polymorphisms other than those listed. Drug metabolism may be affected by non-genetic factors. DNA testing does not replace the need for clinical and therapeutic drug monitoring. Analytical Validation of this assay shown sensitivity of 100% and specificity 100%.

Genomic DNA analysis:

EDTA blood was analysed for mutation detection using semiconductor based Next Generation Sequencing technology. High quality genomic DNA was extracted from the submitted specimen and subjected to target enrichment by high multiplex PCR amplification using Ion AmpliSeq panel targeting mutation of genes mentioned above. Enriched DNA sequences were ligated with platform specific adaptor molecules and was sequenced on using semiconductor chip. Sequenced data was aligned with the human genome (hg19), analyzed at 500x average target depth (with >=90% amplicons with atleast 100 reads) using a customized in-house pipeline DCGL NGS Bioinformatics Pipeline v2.17, designed to accurately detect the germline variants.

Analytical Validation of this assay shown sensitivity of 100% and specificity 100%.

Pathogenic/likely pathogenic mutation if detected in the sample is confirmed by gold standard Sanger Sequencing method. Sanger sequencing data is analyzed using SeqScape Software ver 3.0.

IHC analysis:

FFPE tissue was analyzed for immunohistochemistry. The test results relate specifically to the sample received in the lab. The pre-analytical variables like cold ischemia time, fixative and duration of fixation, which are beyond the control of DCGL laboratory, may affect the test results.

CGC Enumeration and ICC analysis:

Enriched CGCs from the submitted peripheral blood were labelled with GFAP and CD45 antibodies and analyzed by High content imaging platform. Analytical Validation of this assay shown sensitivity of 99.99% and specificity 99.99%.

Circulating Tumor and associated cells from the submitted peripheral blood were analyzed through Cell stabilization protocol using Cell Wizard System. Cells were labelled with mTOR, VEGFR1, VEGFR2, VEGF-A and EGFR antibodies and analyzed by Fluorescent microscopy for Immunocytochemistry (ICC).

Blood based Chemosensitivity analysis:

Circulating tumor and its associated cells were isolated from the submitted peripheral blood sample. The live cancer cells were tested against multiple chemotherapy agents. The number of drugs selected for testing depend on the number of circulating tumor associated cells isolated from the submitted sample.

A defined number of cells were incubated with different drugs with respective drug concentrations, mean peak plasma concentration and cell death events were measured. The extent of cell death was determined either using Varioskan LUX platform. Percent cell death was calculated to evaluate the response level of the drug. Appropriate positive and negative controls

were tested and evaluated in a similar manner simultaneously with the test sample.

Analytical Validation of this assay shown sensitivity of 99.99% and specificity 99.99%.

The performance of the assay specific reagents used in this assay has been established and its performance characteristics defined by Datar Cancer Genetics. This test may not detect all variants in non-coding regions that could affect copy number changes encompassing all or a large portion of the gene. Tumor mutation analysis panel testing is limited in detecting the following types of mutations (this might not be exhaustive): large rearrangements and deletion/ duplications, epigenetic factors, mutations in repetitive or high GC rich regions and mutations in gene with corresponding pseudo genes or other highly homologous sequences. Presence of PCR inhibitors in the sample may prevent DNA amplification for mutation analysis. Rare and novel mutations may be clinically uncharacterized.

Also note that the current knowledge on the genetic of the disease or pathogenic disorder or on the inheritance of the genes may be incomplete. If the test identifies the genetic cause of the disorder, it is possible that this knowledge may or may not help with the prognosis and management of the disease.

Important Information for Patients:

This test is a Laboratory Developed Test, and its performance characteristics were determined by Datar Cancer Genetics UK Private Limited, United Kingdom. It has not been cleared or approved by the U.S. Food and Drug Administration.
This facility is certified by the College of American Pathologists (CAP) and under the Clinical Laboratory Improvement Amendments (CLIA)-USA as qualified to perform high complexity clinical laboratory testing.

Disclaimer

This report documents the genetic alterations detected in the submitted sample material. Information in this report is provided for information purpose only and should only be considered in conjunction with all other relevant information regarding a particular patient, before the patient's treating physician recommends a course of treatment.

Decisions on patient care and treatment must be based on the independent medical judgment of the treating physicians, taking into consideration all applicable information concerning the patient's condition, such as personal and family history, physician's examination, information from other diagnostic test and patient references, in accordance with the standard of care in a given community. A treating physician's decisions should not be based on a single test or on the information contained in this report.

This information in this report does not constitute a treatment recommendation by Datar Cancer Genetics, either to use or not to use any specific therapeutic agent, and should not be interpreted as treatment advice. Decisions on patient care and treatment rest solely within the discretion of the patient's treating physician.

Standard of Care (SoC) drugs for a patient's cancer type are identified and indicated based on the diagnostic information (tissue and subtype) provided in the test requisition form (TRF), and the corresponding standard treatment guidelines (e.g., NCCN) for that cancer type.

The chemosensitivity videos are provided as additional information, are intended to be informative only, and are not intended to be conclusive or prescriptive for the selection of any anticancer drug(s).

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End of Report

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Clinical Trials Relevant to Patient's Genomic Findings

Clinical Trials

TERT promoter mutation

NCT number: NCT05271240 **Phase: III** **Treatment:** Bevacizumab, Chemotherapy, Radiation Therapy **Cancer Type:** Glioblastoma IDH-wildtype (Grade 4)	**Study Title:** A Phase III Randomized Trial of Repeated Superselective Intraarterial Cerebral Infusion (SIACI) of Bevacizumab (Avastin) With Temozolomide and Radiation Compared to Temozolomide and Radiation Alone in Newly Diagnosed Glioblastoma (GBM) **Variant Classification:** TERT promoter mutation **Locations:** United States **Contacts:** Dr. John Boockvar [212-434-3900; jboockvar@northwell.edu]
NCT number: NCT05463848 **Phase: II** **Treatment:** Pembrolizumab, Olaparib, Chemotherapy **Cancer Type:** Glioblastoma IDH-wildtype (Grade 4)	**Study Title:** A Surgical "Window-of-Opportunity" and Phase II Trial of Pembrolizumab, Olaparib and Temozolomide in Recurrent Glioblastoma **Variant Classification:** TERT promoter mutation **Locations:** United States **Contacts:** Dr. Luis N. Gonzalez [617-732-7432; lgonzalez-castro@partners.org]
NCT number: NCT04910022 **Phase: I/II** **Treatment:** NMS-P293, Chemotherapy **Cancer Type:** Glioblastoma IDH-wildtype (Grade 4)	**Study Title:** A Phase I/II Combination Study of NMS-03305293 and Temozolomide in Adult Patients With Recurrent Glioblastoma **Variant Classification:** TERT promoter mutation **Locations:** Italy, Netherlands, Puerto Rico, Switzerland, United States **Contacts:** Domenico Roberti [clinicaltrials@nervianoms.com]

CDKN2A deletion

NCT number:
NCT04983810

Phase: I/II

Treatment:
Fadraciclib

Cancer Type:
Unspecified Solid Tumor

Study Title:
A Phase I/II, Open-label, Multicenter Study to Investigate the Safety, Pharmacokinetics, and Efficacy of Fadraciclib (CYC065), an Oral CDK 2/9 Inhibitor, in Subjects with Advanced Solid Tumors and Lymphoma

Variant Classification:
CDKN2A aberration, CDKN2B aberration

Locations:
Republic of Korea, Spain, United States

Contacts:
Dr. Mark H. Kirschbaum [626-316-3394; mkirschbaum@cyclacel.com]

NCT number:
NCT02896335

Phase: II

Treatment:
Palbociclib

Cancer Type:
Unspecified Solid Tumor

Study Title:
Phase II Trial of Palbociclib and Pembrolizumab in Central Nervous System Metastases

Variant Classification:
CDKN2A deletion

Locations:
United States

Contacts:
Dr. Priscilla Brastianos [617-724-8770; PBRASTIANOS@mgh.harvard.edu]

NCT number:
NCT02693535

Phase: II

Treatment:
Palbociclib, Abemaciclib

Cancer Type:
Unspecified Solid Tumor

Study Title:
Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Variant Classification:
CDKN2A deletion

Locations:
United States

Contacts:
Pam Mangat [tapur@asco.org]

NCT number:
NCT05843253

Phase: II

Treatment:
Ribociclib, Everolimus

Cancer Type:
Astrocytoma IDH-mutant (Grade 3), Astrocytoma IDH-mutant (Grade 4), Diffuse Hemispheric Glioma, H3 G34-mutant (Grade 4), Diffuse Midline Glioma H3 K27-altered (Grade 4), Diffuse Pediatric-type High-Grade Glioma, H3-wildtype and IDH-wildtype (Grade 4), Glioblastoma IDH-wildtype (Grade 4), Infant-type Hemispheric Glioma, Oligodendroglioma IDH-mutant and 1p/19q-codeleted (Grade 3), Pleomorphic Xanthoastrocytoma (Grade 2,3)

Study Title:
PhaseII Study of Ribociclib and Everolimus Following Radiotherapy in Pediatric and Young Adult Patients Newly Diagnosed With HGG Including DIPG, Which Harbor Alterations of the Cell Cycle and/or PI3K/mTOR Pathways

Variant Classification:
CDKN2A deletion

Locations:
United States

Contacts:
Amy K. Jones [614-722-3284; Target@nationwidechildrens.org]

NCT number:
NCT05866692

Phase: I

Treatment:
TY-2699a

Cancer Type:
Unspecified Solid Tumor

Study Title:
A Phase I, Multicenter, Open-label Study of TY-2699a, Administered Orally in Adult Patients With Locally Advanced or Metastatic Solid Tumors

Variant Classification:
Rb pathway

Locations:
China

NF1 deletion

NCT number:
NCT05009992

Phase: II

Treatment:
Dordaviprone, Targeted Therapy

Cancer Type:
Diffuse Midline Glioma H3 K27-altered (Grade 4)

Study Title:
A Combination Therapy Trial Using an Adaptive Platform Design for Children and Young Adults With Diffuse Midline Gliomas (DMGs) Including Diffuse Intrinsic Pontine Gliomas (DIPGs) at Initial Diagnosis, Post-Radiation Therapy and at Time of Progression

Variant Classification:
NF1 aberration

Locations:
Netherlands, United States

Contacts:
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NCT number:
NCT06104488

Phase: I

Treatment:
Avutometinib

Cancer Type:
Central Nervous System Tumors

Study Title:
A Multi-Center Phase I Dose Escalation Study of Avutometinib, a RAF/MEK Clamp, in Pediatric Patients With Refractory or Recurrent Solid Tumors Harboring Activating MAPK Pathway Alterations

Variant Classification:
NF1 aberration

Locations:
United States

Contacts:
Dr. Sameer Farouk Sait [212-639-3449; faroukss@mskcc.org]

NCT number:
NCT03905148

Phase: I/II

Treatment:
Mirdametinib, Lifirafenib

Cancer Type:
Unspecified Solid Tumor

Study Title:
A Phase Ib, Open-Label, Dose-escalation and Expansion Study to Investigate the Safety, Pharmacokinetics and Antitumor Activities of a RAF Dimer Inhibitor BGB-283 in Combination With MEK Inhibitor PD-0325901 in Patients With Advanced or Refractory Solid Tumors

Variant Classification:
RAS/RAF/MEK/ERK pathway

Locations:
Australia, United States

Contacts:
BeiGene [877-828-5568; clinicaltrials@beigene.com]

NCT number:
NCT05354843

Phase: I

Treatment:
ET0038

Cancer Type:
Unspecified Solid Tumor

Study Title:
A Phase I, Open-Label, Multi-Center Dose Finding Study to Investigate the Safety, Pharmacokinetics, and Preliminary Efficacy of SHP2 Inhibitor ET0038 Monotherapy in Patients With Advanced Solid Tumors

Variant Classification:
RAS/RAF/MEK/ERK pathway

Locations:
China

NCT number:
NCT06326411

Phase: I

Treatment:
Nest-1

Cancer Type:
Unspecified Solid Tumor

Study Title:
A Phase I, Open Label Single-arm Two-part Study to Investigate Safety, Pharmacokinetics, and Preliminary Efficacy of Pan-RAF/MEK Glue NST-628 Oral Tablets in Subject With Solid Tumors Harboring Genetic Alterations in the MAPK Pathway and With Other Solid Tumors

Variant Classification:
RAS/RAF/MEK/ERK pathway

Locations:
Australia, United States

Contacts:
CMO [617-468-4292; info@nestedtx.com]

CDKN2B deletion

NCT number:
NCT04983810

Phase: I/II

Treatment:
Fadraciclib

Cancer Type:
Unspecified Solid Tumor

Study Title:
A Phase I/II, Open-label, Multicenter Study to Investigate the Safety, Pharmacokinetics, and Efficacy of Fadraciclib (CYC065), an Oral CDK 2/9 Inhibitor, in Subjects with Advanced Solid Tumors and Lymphoma

Variant Classification:
CDKN2A aberration, CDKN2B aberration

Locations:
Republic of Korea, Spain, United States

Contacts:
Dr. Mark H. Kirschbaum [626-316-3394; mkirschbaum@cyclacel.com]

NCT number:
NCT02693535

Phase: II

Treatment:
Palbociclib, Abemaciclib

Cancer Type:
Unspecified Solid Tumor

Study Title:
Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Variant Classification:
CDKN2B deletion

Locations:
United States

Contacts:
Pam Mangat [tapur@asco.org]

NCT number:
NCT05843253

Phase: II

Treatment:
Ribociclib, Everolimus

Cancer Type:
Astrocytoma IDH-mutant (Grade 3), Astrocytoma IDH-mutant (Grade 4), Diffuse Hemispheric Glioma, H3 G34-mutant (Grade 4), Diffuse Midline Glioma H3 K27-altered (Grade 4), Diffuse Pediatric-type High-Grade Glioma, H3-wildtype and IDH-wildtype (Grade 4), Glioblastoma IDH-wildtype (Grade 4), Infant-type Hemispheric Glioma, Oligodendroglioma IDH-mutant and 1p/19q-codeleted (Grade 3), Pleomorphic Xanthoastrocytoma (Grade 2,3)

Study Title:
PhaseII Study of Ribociclib and Everolimus Following Radiotherapy in Pediatric and Young Adult Patients Newly Diagnosed With HGG Including DIPG, Which Harbor Alterations of the Cell Cycle and/or PI3K/mTOR Pathways

Variant Classification:
CDKN2B deletion

Locations:
United States

Contacts:
Amy K. Jones [614-722-3284; Target@nationwidechildrens.org]

MTAP deletion

NCT number:
NCT05245500

Phase: I/II

Treatment:
MRTX1719

Cancer Type:
Unspecified Solid Tumor

Study Title:
A Phase I/II Multiple Expansion Cohort Trial of MRTX1719 in Patients With Advanced Solid Tumors With Homozygous MTAP Deletion

Variant Classification:
MTAP deletion

Locations:
United States

Contacts:
BMS Clinical Trials Contact Center www.BMSClinicalTrials.com [855-907-3286; Clinical.Trials@bms.com]

NCT number:
No NCT ID

Phase: I

Treatment:
GTA-182

Cancer Type:
Unspecified Solid Tumor

Other identifiers: CTR20243795, GTA182-101

Study Title:
A Phase I clinical study evaluating the safety and tolerability of GTA182 in subjects with MTAPnull/lost advanced solid tumors through dose escalation and expansion

Variant Classification:
MTAP deletion

Locations:
China

NCT number:
NCT06414460

Phase: I

Treatment:
ISM-3412

Cancer Type:
Unspecified Solid Tumor

Study Title:
A Phase I, Open-Label, Multicenter, First-in-Human Study to Evaluate the Safety, Tolerability, Pharmacokinetics/Pharmacodynamics, and Preliminary Efficacy of ISM3412 in Participants With Locally Advanced/Metastatic Solid Tumors

Variant Classification:
MTAP deletion

Locations:
China

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