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ENCYCLOPEDIC TUMOR ANALYSIS

TEST REPORT

Mr. ABC

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Mr. ABC

exaota®
ENCYCLOPEDIC TUMOR ANALYSIS

Patient Details

Name	:	Mr. ABC
Age	:	52 Years
Gender	:	Male
Address	:	---
Referring Doctor	:	Dr. XYZ

Specimen Details

Tumor Type	:	Adenocarcinoma of lung
Specimen Type	:	Blood, FFPE Tumor Block
Draw Date	:	02-Jan-2022 / 08.00 AM
Accession Date	:	03-Jan-2022 / 01.00 PM
Report Date	:	11-Jan-2022 / 11.00 AM

Specimen Analysis Summary

Tissue

FFPE Tumor Specimen	:	50% Neoplastic Cellularity (Rp682)
Tumor DNA/RNA	:	511 Genes (SNAs | Indels | CNAs | Fusion Transcripts | TMB)
RNA	:	20802 Genes
IHC	:	PD-L1 | AR | MLH1 | MSH2 | MSH6 | PMS2

Blood

cf Total Nucleic acids	:	52 Genes (SNAs | Indels | CNAs | Fusion Transcripts)
CTC- ICC	:	mTOR | VEGFR1 | VEGFR2 | VEGFA | EGFR
Pharmacogenetic analysis	:	23 Drugs
Chemosensitivity analysis	:	29 Drugs

Report Highlights

Targeted / Hormonal / Immunotherapy Drugs

(72 Clinical Trials Available: Refer to Page no. 31-46)

Indications	USFDA Approved* / NCCN recommended* (Lung Cancer)	Off Label Therapy*
Tumor Mutation Burden High 22 Mutations/Mb	☑ Pembrolizumab ☑ Atezolizumab ☑ Nivolumab ☑ Durvalumab	☑ Avelumab
VEGFR2/KDR ICC Positive	☑ Ramucirumab ☑ Cabozantinib ☑ Vandetanib	☑ Axitinib ☑ Sorafenib ☑ Ponatinib ☑ Lenvatinib ☑ Sunitinib ☑ Tivozanib ☑ Pazopanib ☑ Regorafenib
VEGFA ICC Positive	☑ Bevacizumab	☑ Ziv-Aflibercept
TACSTD2 (TROP2) Overexpression (+2.50 FC)	⊟ None	☑ Sacituzumab Govitecan
AR IHC Negative	⊟ None	☒ Abiraterone ☒ Bicalutamide ☒ Apalutamide ☒ Enzalutamide ☒ Darolutamide ☒ Flutamide ☒ Nilutamide ☒ Leuprolide

Biomarkers for Immune Checkpoint Inhibitors

Biomarker	Result
Tumor mutation burden (TMB)	22 Mutations / Mb
MMR Status	MMR-proficient
PD-L1 28-8	TPS - <1%
PD-L1 22C3	TPS - <1%
PD-L1 SP142	IC - <1%

Longitudinal Monitoring Biomarkers

Biomarker	Result
Highest Mutant Allele Frequency (HMAF)	3.6%
Number of CTCs detected	3 CTCs/ml

☑ SOC Drugs with Benefit ☑ Off Label Drugs with Benefit* ☒ Drugs without Clinical Benefit / with Potential Resistance

IHC: Immunohistochemistry; **SNA:** Single Nucleotide Alteration; **CNA:** Copy Number Alteration; **INDELS:** Insertion / Deletion Polymorphism; **TMB:** Tumor mutation burden; **ICC:** Immunocytochemistry; **MAF:** Mutant Allele Frequency; **SOC:** Standard of Care; **CTC:** Circulating Tumor Cells; **FC:** Fold change; **IC:** Tumor Infiltrating Immune Cells, **TPS** :Tumor Proportion Score, **MMR:** Mismatch Repair; **NCCN:** National Comprehensive Cancer Network.
*The USFDA approval or SOC recommendation may not be for the detected biomarker or alteration. The association of the detected biomarker or alteration and the drug may be based only on the literature evidence.

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Cytotoxic Drugs

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

Report Highlights

USFDA Approved / NCCN recommended (Lung Cancer)	
Drugs	**Result**
☑ Paclitaxel	74% CD
☑ Cisplatin	37% CD
☑ Etoposide	36% CD
☑ Gemcitabine	33% CD
☒ Carboplatin	<25% CD
☒ Docetaxel	<25% CD
☒ Pemetrexed	<25% CD
☒ Vinorelbine	<25% CD

Off Label Therapy	
Drugs	**Result**
☑ Topotecan	64% CD
☑ Irinotecan	62% CD
☑ Oxaliplatin	57% CD
☑ Mitomycin	53% CD
☑ Bleomycin	51% CD
☑ Cyclophosphamide	45% CD
☑ Vincristine	43% CD
☑ Dactinomycin	40% CD
☑ Cabazitaxel	36% CD
☒ 5FU/Capecitabine	<25% CD
☒ Ifosfamide	<25% CD
☒ Dacarbazine	<25% CD
☒ Doxorubicin	<25% CD
☒ Epirubicin	<25% CD
☒ Eribulin	<25% CD
☒ Melphalan	<25% CD
☒ Methotrexate	<25% CD
☒ Mitoxantrone	<25% CD
☒ Temozolomide	<25% CD
☒ Trabectedin	<25% CD
☒ Vinblastine	<25% CD

Additional Report Highlights

Indications for Non-Oncology Drugs

Drug	Indication
☑ Quercetin	WNT pathway activation - WNT5A (+5.22 FC), FZD6 (+4.28 FC) overexpression
☑ Celecoxib	WNT pathway activation - WNT5A (+5.22 FC), FZD6 (+4.28 FC) overexpression; MAPK pathway activation - MAPK10 (+2.97 FC), MAP3K5 (+2.84 FC) overexpression
☑ Atorvastatin	MAPK pathway activation - MAPK10 (+2.97 FC), MAP3K5 (+2.84 FC) overexpression
☑ Doxycycline	MMP9 (+5.08 FC), MMP12 (+9.89 FC), MMP25 (+3.34 FC) overexpression
☑ Berberine	MMP9 (+5.08 FC), MMP12 (+9.89 FC), MMP25 (+3.34 FC) overexpression
☑ Vitamin C/Ascorbic acid	SLC2A1 (GLUT1) (+4.53 FC) overexpression

Disease Relevant Findings

Biomarker	Result
EGFR	No mutations detected
KRAS	No mutations detected
BRAF	No mutations detected
ERBB2/HER2	No alterations detected
MET	No alterations detected

Biomarker	Result
ALK	No fusions detected
ROS1	No fusions detected
RET	No fusions detected
NTRK1/2/3	No fusions detected

☑ SOC Drugs with Benefit ☑ Off Label Drugs with Benefit* ☒ Drugs without Clinical Benefit / with Potential Resistance

Pharmacogenetics : Drugs with Contraindications

Drug	Indication	Drug	Indication
⊟		⊟	

Pharmacogenetics : Drugs with Increased Risk of Toxicity

Drug	Indication	Drug	Indication
⚠ 5-Fluorouracil	DPYD	⚠ Capecitabine	DPYD
⚠ Erdafitinib	CYP2C9	⚠ Gemcitabine	NT5C2
⚠ Irinotecan	UGT1A1	⚠ Sacituzumab govitecan	UGT1A1
⚠ Tegafur	DPYD		

Pharmacogenetics : Drugs with Labeled Risk of Toxicity

Drug	Indication	Drug	Indication
☑ Belinostat	UGT1A1	☑ Carboplatin	ERCC1, MTHFR
☑ Cisplatin	XPC, ERCC1	☑ Dabrafenib	G6PD
☑ Erlotinib	UGT1A1	☑ Gefitinib	CYP2D6
☑ Mercaptopurine	TPMT, NUDT15	☑ Methotrexate	ABCB1, MTHFR
☑ Nilotinib	UGT1A1	☑ Oxaliplatin	ERCC1
☑ Pazopanib	UGT1A1	☑ Rasburicase	G6PD
☑ Regorafenib	UGT1A1	☑ Thioguanine	TPMT, NUDT15
☑ Trametinib	G6PD	☑ Vincristine	CEP72

Summary of Other Genomic Alterations

Gene	Alteration Type (SNAs / Indels / CNAs/ Fusion)	Variant Classification	Therapeutic/Clinical Significance
TP53	p.S127F (Tissue MAF 28.85% at 6510X) p.S127F (Blood MAF 3.6% at 12500X)	Pathogenic	Refer to Page no. 04
KMT2D	p.E595* (Tissue MAF 17.75% at 4827X)	Likely Pathogenic	Refer to Page no. 04
NFE2L2	p.R34P (Tissue MAF 18.41% at 842X)	VUS	---
FLNB	p.E1169K (Tissue MAF 13.8% at 1753X)	VUS	---
FBXW7	p.S641L (Tissue MAF 20.4% at 1401X)	VUS	---
RAC1	p.D63H (Tissue MAF 16.67% at 1069X)	VUS	---
PTCH1	c.115G>C (Tissue MAF 13.7% at 341X)	VUS	---
MLH3	p.T1034S (Tissue MAF 46.72% at 2138X)	VUS	---
AXIN1	p.V683M (Tissue MAF 14.7% at 2493X)	VUS	---
RARA	c.179-5636G>C (Tissue MAF 45.65% at 1735X)	VUS	---

⊟ Not Applicable ⚠ Drugs with Increased Risk of Toxicity ☑ Drugs with Labeled Risk of Toxicity

VUS: Variant of unknown / uncertain significance

Tumor Mutation Burden (TMB)

Markers	Result
Tumor Mutation Burden (TMB)	**22 Mutations/Mb**
Interpretation	**Category**
High TMB	**Tier I (Level A)**

Patient's tumor mutation burden assessment based on targeted genomic profiling of 511 genes was found to be 22 Mutations/Mb.

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[1,2]. 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 [1,2]. Tumor mutation burden (TMB) is, thus, an informative biomarker for predicting response to immune checkpoint inhibitors like Pembrolizumab, Nivolumab, Atezolizumab, Avelumab, Durvalumab and Ipilimumab.

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[3-14].

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[15].

In various malignancies TMB >10 mutations/Mb have shown benefit from immune checkpoint inhibitors[3,9,12,16-20].

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

The median tumor mutation burden (TMB) (n=2102) for lung squamous cell carcinoma is reported to be 9.0 mutations/Mb, while the maximum TMB is 521.6 mutations/Mb (95% Confidence Interval, 10 - 12.7)[15].

High TMB (TMB-H) is indicative of potential benefit from immune checkpoint inhibitors. Tumor mutation burden (TMB) detected in the submitted sample is 22 mutations/Mb. Therefore in this case, the patient may derive benefit from immune checkpoint inhibitor therapy based on high TMB.

Genomic Findings

Single Nucleotide Alterations / Indels / Copy Number Alterations / Fusion

Gene/s (Transcript ID)	Variant
TP53 (NM_000546.5)	**c.380C>T, p.S127F; [p.(Ser127Phe)]**
Category : Tier I (Level B)	

Interpretation

TP53 mutations are commonly reported in non-small cell lung cancers and It is associated with an adverse prognosis in these patients[21-24].

Tp53 p.S127F lies within the DNA-binding domain of the TP53 protein and results in decreased TP53 transactivation[25,26]. In silico analysis predicts this variant to be a loss-of-function mutation. It is reported in tumors of large intestine, skin, pancreas and lung.

The TP53 gene provides instructions for making a protein called tumor protein p53 (or p53). This protein acts as a tumor suppressor, which means that it regulates cell division by keeping cells from growing and dividing too fast or in an uncontrolled way. Because p53 is essential for regulating cell division and preventing tumor formation, it has been nicknamed the "guardian of the genome".

Gene/s (Transcript ID)	Variant
KMT2D (NM_003482.4)	**c.1783G>T, p.E595*; [p.(Glu595Ter)]**
Category : Tier I (Level B)	

Interpretation

Mutations in KMT2D gene are reported in lung cancer and are associated with an adverse prognosis[27-31].

In silico analysis predicts KMT2D p.E595* to be a loss-of-function mutation. It is reported in tumors of haematopoietic and lymphoid system.

KMT2D, lysine methyltransferase 2D, is an epigenetic modifier and histone methyltransferase, which methylates H3K4 and is involved in transcriptional activation, mostly during development and cell differentiation.

Markers	Alteration type
EGFR (NM_005228)	Single nucleotide alterations and indels in exons 18, 19, 20 and 21 tested **Result :** Not detected

Interpretation

EGFR mutations were not detected in the submitted sample in the exons tested.

Significant association exists between EGFR mutations especially exon 19 deletions, exon 21, exon 18 and exon 20 mutations and sensitivity to tyrosine kinase inhibitor (TKI) therapy[32,33].

The EGFR gene encodes a transmembrane glycoprotein that is a member of the protein kinase superfamily. This protein is a receptor for members of the epidermal growth factor family. It is a cell surface protein that binds to epidermal growth factor. Binding of the protein to a ligand induces receptor dimerization and tyrosine auto-phosphorylation and leads to cell proliferation.

Markers	Alteration type
KRAS (NM_004985)	Single nucleotide alterations and indels in codons 12, 13, 61 and others in the tested exons **Result :** Not detected

Interpretation

KRAS mutations were not detected in the submitted sample in the exons tested.

Approximately 15-25% of patients with lung adenocarcinoma have tumor associated KRAS mutations. They have also been associated with a poor prognosis as well as resistance to chemotherapy and EGFR TKIs[33].

Markers	Alteration type
BRAF (NM_004333)	Single nucleotide alterations and indels in codons 469, 594, 596, 600 and others in the tested exons **Result :** Not detected

Interpretation

BRAF mutations were not detected in the submitted sample in the exons tested.

BRAF mutations in NSCLC are uncommon and seen in less than 5% of cases. Mechanisms of resistance to TKI therapy in EGFR mutated NSCLC includes mutations in BRAF gene [32-34].

The BRAF gene provides instructions for making a protein that helps transmit chemical signals from outside the cell to the cell's nucleus. It encodes a protein which is part of a signaling pathway known as the RAS/MAPK pathway, which controls several important cell functions like cell division, differentiation, and secretion.

Markers	Alteration type
MET (NM_000245)	Single nucleotide alterations and indels in the tested exons, including those resulting in exon 14 skipping; MET gene amplification, fusions **Result :** Not detected

Interpretation

MET copy number gain and mutations were not detected in the submitted sample in the exons tested.

MET alterations that result in exon 14 skipping are found in lung cancer in both the presence and absence of MET amplification. Exon 14 skipping results in the deletion of the juxta membrane domain of MET, which leads to enhanced signaling through the MET receptor pathway. Both pre-clinical and case report evidence suggest that tumors harboring MET with exon 14 alterations and/or MET amplifications have increased sensitivity to MET inhibitors[33,35].

MET gene encodes a member of the receptor tyrosine kinase family of proteins and the product of the protooncogene MET. The encoded preproprotein is proteolytically processed to generate alpha and beta subunits that are linked via disulfide bonds to form the mature receptor. Binding of its ligand, hepatocyte growth factor, induces dimerization and activation of the receptor, which plays a role in cellular survival, embryogenesis, and cellular migration and invasion. Mutations, amplification and overexpression of this gene are associated with multiple human cancers.

Markers	Alteration type
ERBB2/HER2 (NM_004448)	Single nucleotide alterations and indels in exon 20 and other tested exons **Result :** Not detected

Interpretation

ERBB2/HER2 mutations were not detected in the submitted sample in the exons tested.

ERBB2/HER2 mutations in NSCLC are uncommon and reported in 2-4% of cases. In cohorts of EGFR/KRAS/ALK-negative

NSCLC specimens, the frequency of HER2 mutations is 6%. Preclinical data suggest that the presence of mutation is associated with primary resistance to the first-generation EGFR TKIs, Erlotinib and Gefitinib. However, cells expressing the HER2 exon 20 mutations are sensitive to the irreversible dual EGFR and HER2 TKIs, Neratinib and Afatinib[34].

The ERBB2 gene encodes a member of the epidermal growth factor (EGF) receptor family of receptor tyrosine kinases. This protein has no ligand binding domain of its own and therefore cannot bind growth factors. However, it does bind tightly to other ligand-bound EGF receptor family members to form a heterodimer, stabilizing ligand binding and enhancing kinasemediated activation of downstream signaling pathways, such as those involving mitogen-activated protein kinase and phosphatidylinositol-3 kinase.

Markers	Alteration type
ALK (NM_004304)	Fusions/Rearrangements; Single nucleotide alterations and indels in the tested exons **Result :** Not detected

Interpretation

ALK fusions and mutations were not detected in the submitted sample.

Approximately 3-7% of lung tumors harbor ALK fusions. Multiple different ALK rearrangements have been described in NSCLC. The majority of these ALK fusion variants are comprised of portions of the echinoderm microtubule-associated protein-like 4 (EML4) gene with the ALK gene. In the vast majority of cases, ALK rearrangements are non-overlapping with other oncogenic mutations found in NSCLC[33].

Crizotinib, Ceritinib, Lorlatinib, Alectinib and Brigatinib are USFDA approved for NSCLC with ALK rearrangements.

Markers	Alteration type
ROS1 (NM_002944)	Fusions/Rearrangements; Single nucleotide alterations and indels in the tested exons **Result :** Not detected

Interpretation

ROS1 fusions and mutations were not detected in the submitted sample.

Approximately 2% of lung tumors harbor ROS1 fusions. Several different ROS1 rearrangements have been described in NSCLC. These include SLC34A2-ROS1, CD74-ROS1, EZR-ROS1, TPM3-ROS1, and SDC4-ROS1[33].

Crizotinib, Lorlatinib, Entrectinib and Ceritinib are USFDA approved for NSCLC with ROS1 rearrangements.

Markers	Alteration type
RET (NM_020975)	Fusions/Rearrangements; Single nucleotide alterations and indels in the tested exons **Result :** Not detected

Interpretation

RET fusions and mutations were not detected in the submitted sample.

Approximately 1% of lung cancers harbor RET rearrangements. Selpercatinib and Pralsetinib are USFDA approved for treatment of adult patients with metastatic RET fusion-positive NSCLC. Cabozantinib and Vandetanib are recommended as standard of care drugs for the treatment of NSCLC with RET rearrangements [33].

Markers	Alteration type
NTRK 1/2/3 (NM_001007792.1)	Fusions/Rearrangements **Result :** Not detected

Interpretation

NTRK 1/2/3 fusions were not detected in the submitted sample.

Gene rearrangements involving NTRK1/2/3 can generate fusion oncoproteins containing the kinase domains of TRKA/B/C, respectively. These fusions have been reported in multiple solid tumor types[36-38].

Larotrectinib and Entrectinib are USFDA approved for treatment of solid tumors with NTRK gene fusion without a known acquired resistance mutation.

Histopathological Analysis

Immunohistochemistry

Specimen

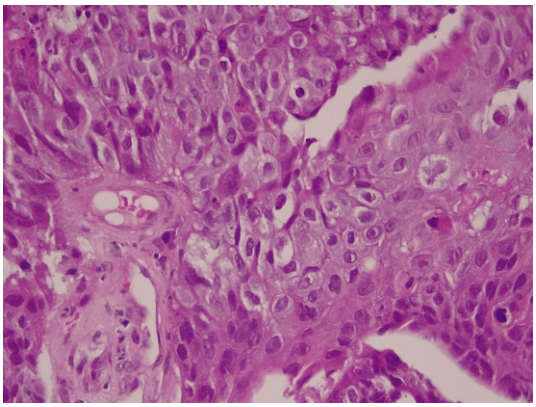
FFPE Block ID - RP682

Microscopy

Hematoxylin and eosin stained sections from representative areas reveal polypoidal bronchial mucosa covered by atypical epithelial cells. Cells are round to polygonal with moderate amount of eosinophilic cytoplasm and vesicular nuclei showing prominent nucleoli. Moderate pleomorphism is seen. Stroma is desmoplastic and shows moderate lymphoplasmacytic infiltrate as well as large areas of hemorrhages. Keratin pearls are not seen.

Impression

Bronchial biopsy (FFPE block) : Histological features are consistent with non-small cell lung carcinoma, in a known case of carcinoma of lung.



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

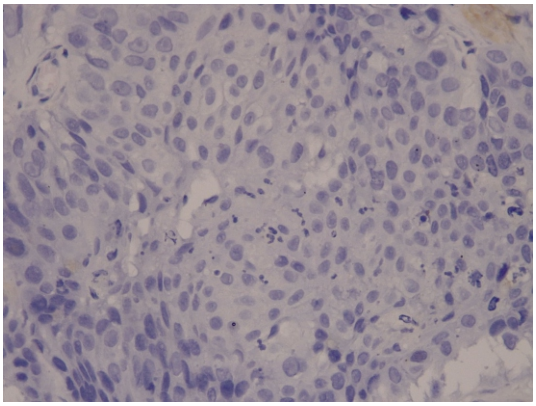
Immunohistochemistry (IHC) Analysis

Markers	Result
PD-L1 (Antibody clone 28-8)	**TPS - <1%**

Interpretation

PD-L1 (antibody clone 28-8) is immunoreactive in <1% of neoplastic cells.

Nivolumab is USFDA approved for the treatment of multiple tumor types, including non-small cell lung cancer. Nivolumab is also recommended as a standard of care drug (category 1) for the treatment of PD-L1 expression (PD-L1 ≥1%) positive lung cancers, as per NCCN guidelines [33].



PD-L1 (Antibody clone 28-8)

Markers	Result
PD-L1 (Antibody clone 22C3)	**TPS - <1%**

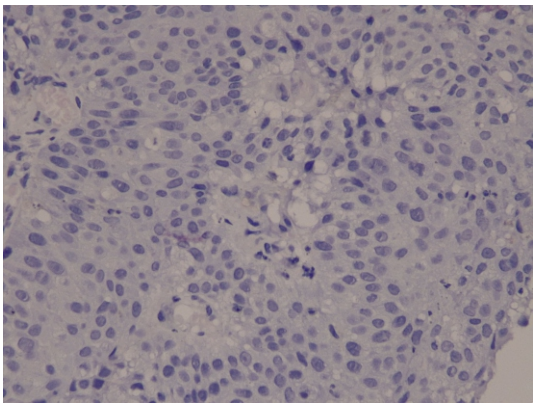
Interpretation

PD-L1 (antibody clone 22C3) is immunoreactive in <1% of neoplastic cells.

Pembrolizumab is USFDA approved for the treatment of multiple tumor types, including non-small cell lung cancer. Pembrolizumab is also recommended as a standard of care drug (category 1 and category 2B) for the treatment of PD-L1 expressing (≥1%) non-small cell lung cancers, as per NCCN guidelines [33].

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

Cemiplimab-rwlc is also recommended as a standard of care drug (category 1) for the treatment of PD-L1 expression (TPS ≥50%) positive tumors of non-small cell lung cancer, as per NCCN guidelines [33].



PD-L1 (Antibody clone 22C3)

Markers	Result
PD-L1 (Antibody clone: SP142)	**IC- <1%**

Interpretation

PD-L1 (antibody clone SP142) showed tumor infiltrating immune cells (IC) <1%.

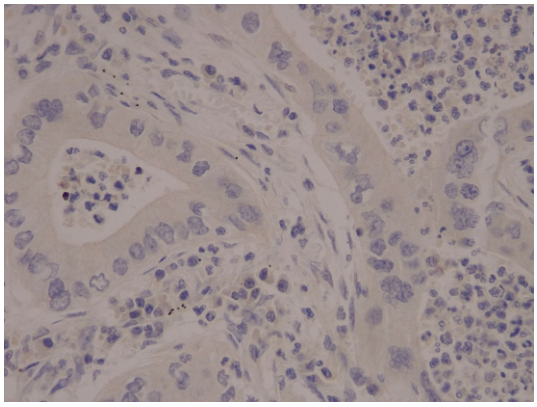
Atezolizumab is USFDA approved for the treatment of multiple tumor types, including non-small cell lung cancer. Atezolizumab is recommended as a standard of care drug (category 1) for the treatment of PD-L1 expression (≥1%) positive tumors of non-small cell lung cancer[33].

Markers	Result
AR	**Negative**

Interpretation

No staining of AR is indicative of potential lack of benefit from Abiraterone, Enzalutamide, Nilutamide, Apalutamide, Bicalutamide, Darolutamide, Leuprolide and Flutamide.

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



AR IHC **Negative**

Mismatch Repair (MMR) Status

Analysis of MMR Markers

Marker	Staining Pattern	Marker	Staining Pattern
MLH1	Intact nuclear expression	MSH6	Intact nuclear expression
MSH2	Intact nuclear expression	PMS2	Intact nuclear expression

Interpretation

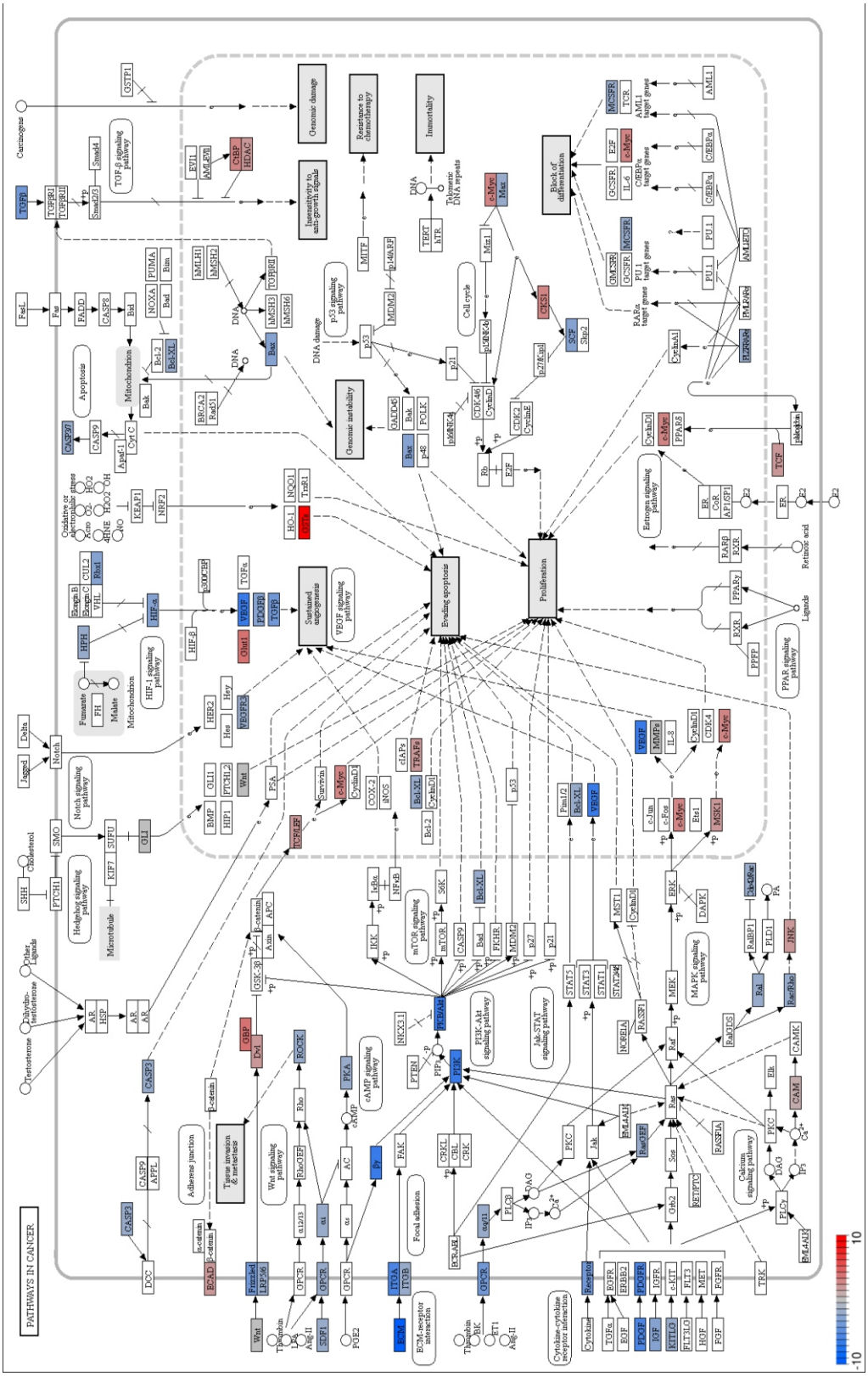
Immunohistochemistry (IHC) for four mismatch repair (MMR) proteins (MLH1, MSH2, MSH6 and PMS2) was performed on formalin-fixed, paraffin-embedded tissue taken from representative sections of the resection specimens. The tumor shows intact nuclear expression of MLH1, MSH2, MSH6, PMS2, which indicates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

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) [39,40]. 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-gxly for all dMMR/MSI-H solid tumors[41-44].

KEGG Pathway: 20802 Genes Analysis

KEGG Pathway -Tissue

Comprehensive Pathway Perturbation in Primary Tumor



Global Gene Expression Highlights

Gene Expression -Tissue

Out of **20802** protein coding genes analyzed in the tumor tissue, **5845** genes were expressed in the analyzed tumor tissue. **1845** genes were found to be differentially regulated in the tumor tissue.

List of Oncology Drugs with Potential Benefit

Gene/s	Result (Fold Change)
TACSTD2 (TROP2)	▲ +2.50 FC

Drugs With Benefit

☑ Sacituzumab Govitecan

Interpretation

Upregulation of TACSTD2 (TROP2) is suggestive of potential benefit from Sacituzumab Govitecan[45,47].

Sacituzumab Govitecan is USFDA approved for treatment of triple negative breast cancer.

In a multicenter study, Sacituzumab Govitecan in patients with metastatic non-small cell lung cancer (n=54) demonstrated objective response in 9 patients. Median progression-free survival and overall survival of 5.2 months and 9.5 months were reported, respectively[48].

List of Non-oncology Agents That May Provide Therapeutic Benefit

Gene/s	Result (Fold Change)
WNT5A	▲ +5.22 FC
FZD6	▲ +4.28 FC

Drugs With Benefit

☑ Quercetin ☑ Celecoxib

Interpretation

Quercetin inhibits cancer growth through inhibition of Wnt/ -catenin signalling pathway[49,50].
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[51,52].

Gene/s	Result (Fold Change)
MAPK10	▲ +2.97 FC
MAP3K5	▲ +2.84 FC

Drugs With Benefit

☑ Atorvastatin ☑ Celecoxib

Interpretation

Atorvastatin induces apoptosis in multiple cancers like pancreatic, breast, ovary, colon cancers; osteosarcoma and glioma by inhibiting MAPK-Bcl-2 signaling pathway[53-58].

Pre-clinical studies showed that low doses of Atorvastatin and Celecoxib in combination, inhibited tumor carcinogenesis more effectively than when they were given individually at higher doses[53,55,59].

Gene/s	Result (Fold Change)
MMP9	▲ +5.08 FC
MMP12	▲ +9.89 FC
MMP25	▲ +3.34 FC

Drugs With Benefit

☑ Doxycycline ☑ Berberine

Interpretation

The antibiotic agent, Doxycycline, non-selectively inhibits MMP activation and expression, and has been shown to suppress MMP activities in human cancer cells[60,61].

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[62-65].

Gene/s	Result (Fold Change)
SLC2A1 (GLUT1)	▲ +4.53 FC

Drugs With Benefit

☑ Vitamin C/Ascorbic acid

Interpretation

SLC2A1 (GLUT1) is capable of transporting oxidized form of Vitamin C (dehydroascorbic acid (DHA)), which inside the cells is reduced to ascorbic acid (AA). High-dose Vitamin C treatment induces cell death via the uptake and reduction of its oxidized form DHA back to Vitamin C[66,67].

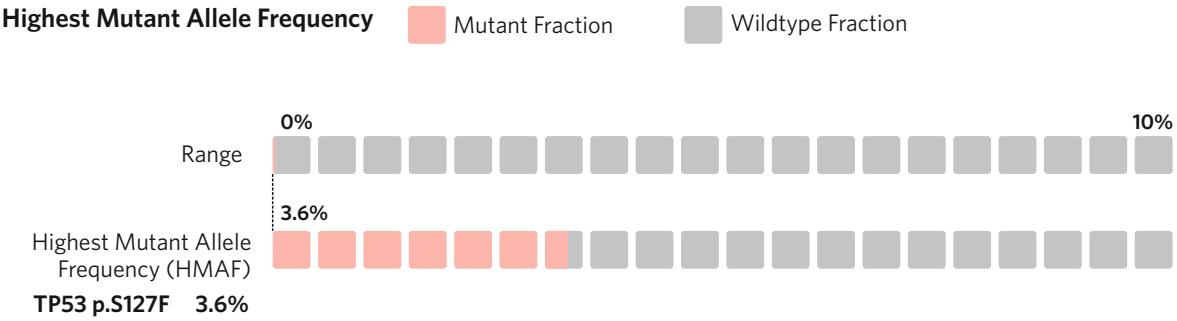
List of Oncology Drugs Without Therapeutic Benefit

⊟ Not Applicable

Cell Free Nucleic Acids: Somatic Genome Alterations

Cf-TNA

Highest Mutant Allele Frequency



TP53 p.S127F 3.6%

1. Highest mutant allele frequency of 3.6% was detected in the cell free nucleic acids isolated from patient's plasma.
2. Mutation in TP53 gene is suggestive of an adverse prognosis in lung cancer.
3. TP53 p.S127F variant was detected in both, tumor tissue as well as cell free nucleic acids analysis.

Genomic Findings

Single Nucleotide Alterations / Indels / Copy Number Alterations / Fusion

Gene/s (Transcript ID)	Variant
TP53 (NM_000546.5)	**c.380C>T, p.S127F; [p.(Ser127Phe)]**

Category : Tier I (Level B)

Interpretation

Kindly refer to clinical significance of TP53 p.S127F mentioned earlier.

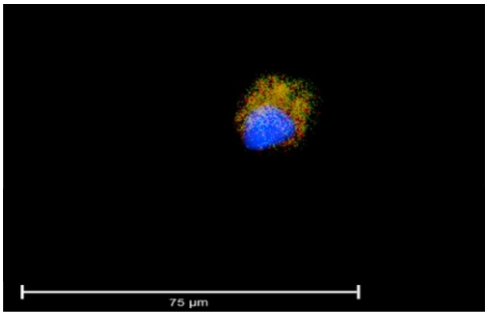
Circulating Tumor Cells Enumeration

CTCs

Circulating Tumor Cells (CTCs): **DETECTED**
Number of CTCs: **3 CTCs/ml peripheral blood**
CTCs are defined as EPCAM+ve, CK+ve, CD45-ve cells

Interpretation

3 CTCs/ml peripheral blood detected in the submitted sample.



Fluorescent microscopic image of CTC

Immunocytochemistry (ICC) Analysis on CTCs

ICC-CTCs

Markers	Result
VEGFR2/KDR	**Positive**

Interpretation

Positive staining of VEGFR2/KDR is indicative of potential benefit from Ramucirumab, Cabozantinib, Vandetanib, Axitinib, Lenvatinib, Pazopanib, Sorafenib, Sunitinib, Regorafenib, Ponatinib and Tivozanib[68-81].

Ramucirumab is USFDA approved for the treatment of multiple tumor types, including non-small cell lung cancer.

Ramucirumab is recommended as a standard of care drug for the treatment of non-small cell lung cancer[33].

Cabozantinib is USFDA approved for the treatment of hepatocellular carcinoma, advanced renal cell carcinoma and thyroid cancer.

Cabozantinib is recommended as a standard of care drug for the treatment of non-small cell lung cancer with RET rearrangements[33].

In a phase II randomized discontinuation trial, Cabozantinib in non-small-cell lung cancer (n=60) patients, selected without a prerequisite of RET fusion, showed clinical activity with disease-control rate of 38% at 12 weeks and tumor regression rate of 64%[82].

Vandetanib is USFDA approved for the treatment of medullary thyroid cancer.

Vandetanib is recommended as a standard of care drug for the treatment of non-small cell lung cancer with RET

rearrangements [33].

In a randomized phase II study, Vandetanib as a maintenance therapy in patients selected without a prerequisite of RET fusion in advanced non-small cell lung cancer (n=58) was well tolerated with median progression-free survival (PFS) of 4.5 months[83].

Axitinib is USFDA approved for the treatment of advanced renal cell carcinoma (RCC).

In a phase II study, Axitinib with doublet chemotherapy in patients with advanced NSCLC (n=38) showed anti-tumor activity with stable disease rate of 23.7% and median overall survival of 14.2 months[84].

Lenvatinib is USFDA approved for the treatment of endometrial, hepatocellular carcinoma, advanced renal cell carcinoma (RCC) and thyroid cancer.

In a clinical study, combination of Lenvatinib and best supportive care (BSC) versus BSC alone in third-line or greater non-small cell lung cancer showed improvement in both overall survival (38.4 vs 24.1 weeks) and progression free survival (20.9 vs 7.9 weeks) in heavily pretreated patients (n=135)[85].

Pazopanib is USFDA approved for treatment of advanced renal cell carcinoma and soft tissue sarcoma.

In a phase II study, Pazopanib in 32 evaluable patients with stage IV NSCLC, who failed at least two prior chemotherapy regimens showed overall response rate of 16% and overall survival of 26.4 weeks[86].

Sorafenib is USFDA approved for the treatment of advanced renal cell, hepatocellular and thyroid carcinoma.

In a randomized, double-blind, placebo-controlled, phase II trial, combination of Sorafenib and Erlotinib or Erlotinib alone in previously treated advanced non-small-cell lung cancer patients (n=168), showed disease control rates of 54% vs 38% and overall survival of 8 months vs 4.5 months[87].

Sunitinib is USFDA approved for the treatment of advanced renal cell carcinoma, gastrointestinal stromal tumor and pancreatic neuroendocrine tumors.

In a multicenter phase II trial, Sunitinib in previously treated, advanced NSCLC showed stable disease of 19% and was well tolerated in 63 evaluable patients[88].

In a phase II study, Sunitinib in patients with NSCLC (n= 64) showed manageable toxicity with progression-free survival of 9.4 weeks and median overall survival of 25.1 weeks[89].

Regorafenib is USFDA approved for the treatment of colorectal, hepatocellular cancers and gastrointestinal stromal tumors (GIST).

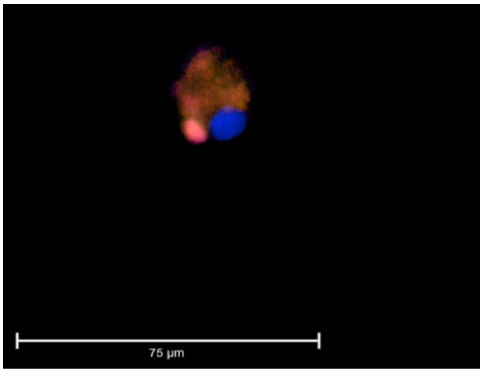
In a phase I study, Regorafenib in patients with advanced refractory NSCLC (n=17) was well tolerated and showed disease control rate of 76%[90].

Ponatinib is USFDA approved for the treatment of acute lymphoblastic leukemia and chronic myelogenous leukemia.

In a pre-clinical study, Ponatinib significantly inhibited the growth of NSCLC cells overexpressing FGFR1[91].

Tivozanib is USFDA approved for the treatment of relapsed or refractory advanced renal cell carcinoma.

In a pre-clinical study, Tivozanib showed activity as a single agent in lung tumor cells with KRAS or EGFR L858R/T790M mutations[92].



VEGFR2/KDR ICC **Positive**

Markers	Result
VEGFA	**Positive**

Interpretation

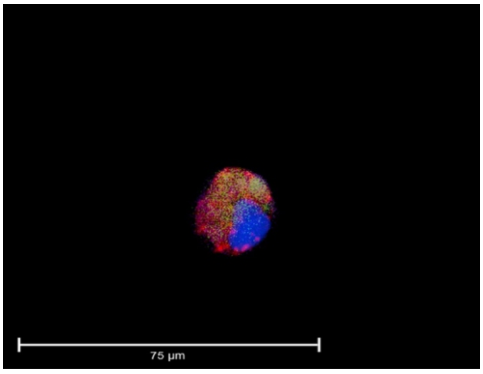
Positive staining of VEGFA is indicative of potential benefit from Bevacizumab and Ziv-Aflibercept[93,94].

Bevacizumab is USFDA approved for the treatment of multiple tumor types, including non-small cell lung cancer.

Bevacizumab is recommended as a standard of care drug (category 1) for the treatment of non-small cell lung cancer as per NCCN guidelines [33].

Ziv-Aflibercept is USFDA approved for the treatment of metastatic colorectal cancer.

In a multicenter, phase 2 study, Aflibercept in platinum- and Erlotinib-resistant adenocarcinoma of the lung (n=89) was well tolerated with single agent activity (overall response rate of 2.0%, 6-months and 12-months survival rates: 54% and 29%, respectively)[95].



VEGFA ICC **Positive**

Markers	Result
EGFR	**Negative**

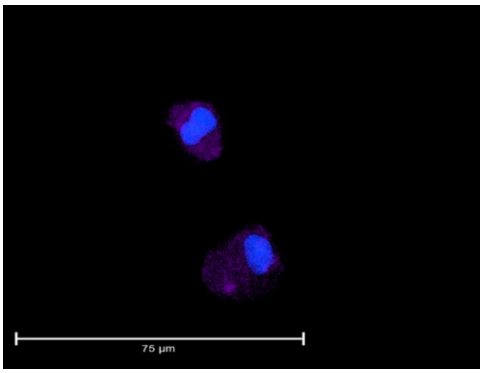
Interpretation

No staining of EGFR is indicative of potential lack of benefit from Cetuximab, Necitumumab and Panitumumab[96-99].

Cetuximab is USFDA approved for the treatment of head and neck and colorectal cancer.

Necitumumab is USFDA approved for the treatment of squamous non-small cell lung cancer.

Panitumumab is USFDA approved for treatment of colorectal cancer.



EGFR ICC **Negative**

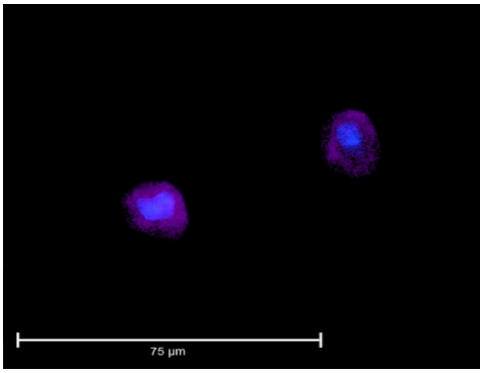
Markers	Result
VEGFR1/FLT1	**Negative**

Interpretation

No staining of VEGFR1/FLT1 is indicative of potential lack of benefit from Cabozantinib, Axitinib, Lenvatinib, Pazopanib, Sorafenib, Sunitinib, Regorafenib, Ponatinib and Tivozanib [68-81].

However, simultaneous positive staining of VEGFR2/KDR is indicative of potential benefit from Cabozantinib, Axitinib, Lenvatinib, Pazopanib, Sorafenib, Sunitinib, Regorafenib, Ponatinib and Tivozanib.

Kindly refer to USFDA labels of these drugs mentioned earlier.



VEGFR1/FLT1 ICC **Negative**

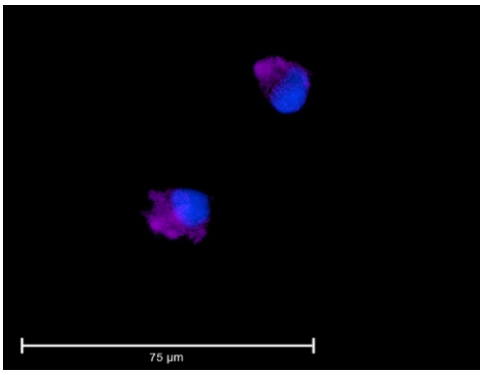
Markers	Result
mTOR	**Negative**

Interpretation

No staining of mTOR is indicative of potential lack of benefit from Everolimus and Temsirolimus[100-103].

Everolimus is USFDA approved for the treatment of renal cancer; hormone receptor-positive, HER2 negative breast cancer; neuroendocrine tumors of pancreatic, gastrointestinal (GI) or lung origin and subependymal giant cell astrocytoma.

Temsirolimus is USFDA approved for the treatment of patients with advanced renal cell carcinoma.



mTOR ICC **Negative**

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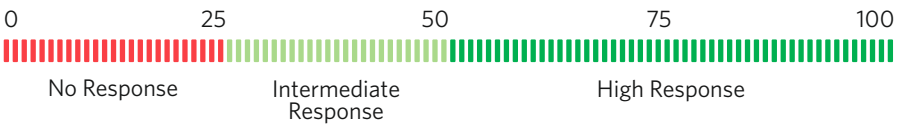
Chemosensitivity Analysis on CTCs

Chemosensitivity - Blood

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

Drug Names	% Cell Death	Drug Response
Paclitaxel	74	
Topotecan	64	
Irinotecan	62	
Oxaliplatin	57	
Mitomycin	53	
Bleomycin	51	
Cyclophosphamide	45	
Vincristine	43	
Dactinomycin	40	
Cisplatin	37	
Cabazitaxel	36	
Etoposide	36	
Gemcitabine	33	
5-Fluorouracil/Capecitabine	< 25	
Ifosfamide	< 25	
Carboplatin	< 25	
Dacarbazine	< 25	
Docetaxel	< 25	
Doxorubicin	< 25	
Epirubicin	< 25	
Eribulin	< 25	
Melphalan	< 25	
Methotrexate	< 25	
Mitoxantrone	< 25	
Pemetrexed	< 25	
Temozolomide	< 25	
Trabectedin	< 25	
Vinblastine	< 25	
Vinorelbine	< 25	

CHEMO SCALE



Pharmacogenetic Analysis

Pharmacogenetics

Drug with Contraindication	Drug with Increased Risk of Toxicity	Drug with Labelled Toxicity
☒ None	! 5-Fluorouracil	☑ Belinostat
	! Capecitabine	☑ Carboplatin
	! Erdafitinib	☑ Cisplatin
	! Gemcitabine	☑ Dabrafenib
	! Irinotecan	☑ Erlotinib
	! Sacituzumab govitecan	☑ Gefitinib
	! Tegafur	☑ Mercaptopurine
		☑ Methotrexate
		☑ Nilotinib
		☑ Oxaliplatin
		☑ Pazopanib
		☑ Rasburicase
		☑ Regorafenib
		☑ Thioguanine
		☑ Trametinib
		☑ Vincristine

Analysis of Pharmacogenetics Markers for Oncology Drugs

Drug
5-Fluorouracil

Gene Analysis
DPYD; *9A/HapB3

Evidence level : Level 1A

Interpretation

The patient has an intermediate metabolizer status for DPYD gene, leading to reduced DPD activity (approximately 50% reduced).

Patients with such genotype, when treated with 5-Fluorouracil, there is an increased risk for severe or even fatal drug toxicity. Reduce starting dose by 50% followed by titration of dose based on toxicity (increase the dose in patients experiencing no or clinically tolerable toxicity in the first two cycles to maintain efficacy; decrease the dose in patients who do not tolerate the starting dose to minimize toxicities) or therapeutic drug monitoring (if available) [104] .

Drug
Capecitabine

Gene Analysis
DPYD; *9A/HapB3

Evidence level : Level 1A

Interpretation

The patient has an intermediate metabolizer status for DPYD gene, leading to reduced DPD activity (approximately 50% reduced).

Patients with such genotype, when treated with Capecitabine, there is an increased risk for severe or even fatal drug toxicity. Reduce starting dose by 50% followed by titration of dose based on toxicity (increase the dose in patients experiencing no or clinically tolerable toxicity in the first two cycles to maintain efficacy; decrease the dose in patients who do not tolerate the starting dose to minimize toxicities) or therapeutic drug monitoring (if available) [105].

Drug	Gene Analysis
Erdafitinib	CYP2C9; *1/*3

Evidence level : Level 1A

Interpretation

The patient has an intermediate metabolizer status for CYP2C9 leading to reduced enzyme activity.

Patients with such genotype may have an increased plasma concentration of Erdafitinib and increased drug toxicity[106].

Drug	Gene Analysis
Gemcitabine	NT5C2; rs11598702 TT

Evidence level : Level 2B

Interpretation

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[107].

Drug	Gene Analysis
Irinotecan	UGT1A1; *1/*28

Evidence level : Level 1A

Interpretation

The patient has an intermediate metabolizer status for UGT1A1.

Patients with such genotype, who are treated with Irinotecan based regimens may have an increased risk of neutropenia, diarrhea, or asthenia[108].

Drug	Gene Analysis
Sacituzumab govitecan	UGT1A1; *1/*28

Evidence level : Level 1A

Interpretation

The patient has an intermediate metabolizer status for UGT1A1 gene leading to reduced UGT1A1 activity.

Patients with such genotype who are treated with Sacituzumab govitecan may have an increased risk of neutropenia and other adverse reactions[109].

Drug	Gene Analysis
Tegafur	DPYD; *9A/HapB3

Evidence level : Level 1A

Interpretation

The patient has an intermediate metabolizer status for DPYD gene, leading to reduced DPD activity (approximately 50% reduced).

Patients with such genotype, when treated with Tegafur, there is an increased risk for severe or even fatal drug toxicity. Reduce starting dose by 50% followed by titration of dose based on

toxicity (increase the dose in patients experiencing no or clinically tolerable toxicity in the first two cycles to maintain efficacy; decrease the dose in patients who do not tolerate the starting dose to minimize toxicities) or therapeutic drug monitoring (if available)[104].

Drug	Gene Analysis
Belinostat	UGT1A1; *1/*28

Evidence level : Level 1A

Interpretation

The patient has an intermediate metabolizer status for UGT1A1 gene leading to reduced UGT1A1 activity.

Such genotype does not affect the clearance of Belinostat significantly. Use as directed[110].

Drug	Gene Analysis
Carboplatin	ERCC1; rs11615 GG MTHFR; rs1801133 GG

Evidence level : Level 2A, 2B

Interpretation

The patient has favorable genotypes in the analysed MTHFR and ERCC1 gene variants.

Patients with this genotype may have a decreased risk of drug toxicity including nephrotoxicity, when treated with Carboplatin[111-113].

Pharmacogenetics

Drug	Gene Analysis
Cisplatin	**ERCC1; rs11615 GG** **XPC; rs2228001 TT**

Evidence level : Level 1B, 2B

Interpretation

The patient has favorable genotypes in the analysed XPC and ERCC1 gene variants.

Patients with such genotype may have a decreased but not non-existent risk of hearing loss, neutropenia and nephrotoxicity when treated with Cisplatin[112-114].

Drug	Gene Analysis
Dabrafenib	**G6PD; wildtype/wildtype**

Evidence level : Level 1A

Interpretation

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 [115].

Drug	Gene Analysis
Erlotinib	**UGT1A1; *1/*28**

Evidence level : Level 1A

Interpretation

The patient has an intermediate metabolizer status for UGT1A1.

Patients with such genotype, who are treated with Erlotinib may have an average risk of hyperbilirubinemia. Use as directed [116].

Drug	Gene Analysis
Gefitinib	**CYP2D6; *1/*35**

Evidence level : Level 1A

Interpretation

The patient has a normal metabolizer status for CYP2D6.

Patients with such genotype who are treated with Gefitinib may have normal metabolism of Gefitinib. Use as directed [117].

Drug	Gene Analysis
Mercaptopurine	**NUDT15; *1/*1** **TPMT; *1/*1**

Evidence level : Level 1A

Interpretation

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, lifethreatening 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 [118].

Drug	Gene Analysis
Methotrexate	**ABCB1; rs1045642 GG** **MTHFR; rs1801133 GG**

Evidence level : Level 2A

Interpretation

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[119].

Drug	Gene Analysis
Nilotinib	**UGT1A1; *1/*28**

Evidence level : Level 1A

Interpretation

The patient has an intermediate metabolizer status for UGT1A1.

Patients with such genotype, who are treated with Nilotinib may have an average risk of hyperbilirubinemia. Use as directed [120].

Drug	Gene Analysis
Oxaliplatin	**ERCC1; rs11615 GG**

Evidence level : Level 2B

Interpretation

The patient has a favorable genotype in analysed variant of ERCC1 gene.

Patients with this genotype when treated with Oxaliplatin may have decreased but not nonexistent risk for nephrotoxicity[112,113].

Drug	Gene Analysis
Pazopanib	**UGT1A1; *1/*28**

Evidence level : Level 1A

Interpretation

The patient has an intermediate metabolizer status for UGT1A1.

Patients with such genotype, who are treated with Pazopanib may have an average risk of hyperbilirubinemia. Use as directed [121].

Drug	Gene Analysis
Rasburicase	**G6PD; wildtype/ wildtype**

Evidence level : Level 1A

Interpretation

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 [122].

Drug	Gene Analysis
Regorafenib	**UGT1A1; *1/*28**

Evidence level : Level 1A

Interpretation

The patient has an intermediate metabolizer status for UGT1A1.

Patients with such genotype, who are treated with Regorafenib may have an average risk of hyperbilirubinemia. Use as directed [123].

Drug	Gene Analysis
Thioguanine	**NUDT15; *1/*1** **TPMT; *1/*1**

Evidence level : Level 1A

Interpretation

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 [124].

Drug	Gene Analysis
Trametinib	**G6PD; wildtype/ wildtype**

Evidence level : Level 2A

Interpretation

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 [125].

Drug	Gene Analysis
Vincristine	**CEP72; rs924607 CC**

Evidence level : Level 2B

Interpretation

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[126].

Tumor Tissue

Variant Allele Fraction and Coverage

Variant (Transcript ID)	Genomic co-ordinates	Allele fraction	Coverage (X)
TP53 (NM_000546.5) c.380C>T, p.S127F	chr17: 7578550G>A	28.85	6510
KMT2D (NM_003482.4) c.1783G>T, p.E595*	chr17:7578550G>A	28.85	6510
NFE2L2 (NM_006164.5) c.101G>C, p.R34P	chr2:178098944C>G	18.41	842
FLNB (NM_001164317.2) c.3505G>A, p.E1169K	chr3:58109198G>A	13.8	1753
FBXW7 (NM_033632.3) c.1922C>T, p.S641L	chr4:153244235G>A	20.4	1401
RAC1 (NM_018890.4) c.187G>C, p.D63H	chr7:6431634G>C	16.67	1069
PTCH1 (NM_001083603.3) c.115G>C	chr9:98278988C>G	13.7	341
MLH3 (NM_001040108.2) c.3101C>G, p.T1034S	chr14:75513258G>C	46.72	2138
AXIN1 (NM_003502.4) c.2047G>A, p.V683M	chr16:343627C>T	14.7	2493
RARA (NM_000964.4) c.179-5636G>C	chr17:38498932G>C	45.65	1735

In view of high allele frequency of MLH3 p.T1034S and RARA c.179-5636G>C variants, germline nature cannot be ruled out.

Due to minimum 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.

APC, ARID2 ATM. ATR, ATRX, BRCA1, BRCA2, BRIP1, CDKN2A, CHEK2, FANCC, KMT2A, MLH1, MSH2, NBN, NF1, PMS2, PTEN, RAD50, RB1, SMARCB1, TSC1, TSC2

Cell Free Nucleic Acids

Variant (Transcript ID)	Genomic co-ordinates	Allele fraction	Coverage (X)
TP53 (NM_000546.5) c.380C>T, p.S127F	chr17: 7578550G>A	3.6	12500

Criteria for Classification of Somatic Variants

The criteria/guidance used in this report is in accordance with the guidelines provided by the American College of Medical Genetics and Genomics (ACMG) for the interpretation and reporting of sequence variants in cancer. Somatic sequence variations are categorized into four tiers based on their clinical significance [127].

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.

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Gene List

Genes Analyzed in Tumor Tissue Analysis

SNAs / 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									

Fusion

AKT2	ALK	AR	AXL	BRAF	BRCA1	BRCA2	CDKN2A	EGFR	ERBB2
ERBB4	ERG	ESR1	ETV1	ETV4	ETV5	FGFR1	FGFR2	FGFR3	FGR
FLT3	JAK2	KRAS	MDM4	MET	MYB	MYBL1	NF1	NOTCH1	NOTCH4
NRG1	NTRK1	NTRK2	NTRK3	NUTM1	PDGFRA	PDGFRB	PIK3CA	PPARG	PRKACA
PRKACB	PTEN	RAD51B	RAF1	RB1	RELA	RET	ROS1	RSPO2	RSPO3
TERT									

* NO CNA

Gene List

Genes Analyzed in Cell Free Nucleic Acids Analysis

SNA 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						

Fusion Genes

ALK	BRAF	ERG	ETV1	FGFR1	FGFR2	FGFR3	MET	NTRK1	NTRK3
RET	ROS1								

CNA Genes

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

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

exacta®
ENCYCLOPEDIC TUMOR ANALYSIS

Drugs Tested in Chemosensitivity Analysis

Drug List

5-Fluorouracil/Capecitabine, Bleomycin, Cabazitaxel, Carboplatin, Cisplatin, Cyclophosphamide, Dacarbazine, Dactinomycin, Docetaxel, Doxorubicin, Epirubicin, Eribulin, Etoposide, Gemcitabine, Ifosfamide, Irinotecan, Melphalan, Methotrexate, Mitomycin, Mitoxantrone, Oxaliplatin, Paclitaxel, Pemetrexed, Temozolomide, Topotecan, Trabectedin, Vinblastine, Vincristine, Vinorelbine.

Antibody Details - Immunocytochemistry (ICC) Analysis

Marker	Clone
EPCAM	REA831
CK	REA764
CD45	HI30
mTOR	Polyclonal

Marker	Clone
VEGFR1	REA569
VEGFR2	REA1116
VEGFA	JH121
EGFR	Ep22

Antibody Details - Immunocytochemistry (ICC) Analysis

Antibody List

Marker	Clone	Vendor	Visualization System
PD-L1	SP142	Ventana	Optiview Universal DAB Detection Kit and Optiview Amplification Kit (on Ventana Benchmark XT platform)
AR	Ar441	Dako	Polymer Detection System
PD-L1	22C3	Dako	
PD-L1	28-8	Dako	
MLH1	ES05	Biogenex	
MSH2	FE11	Dako	
MSH6	EP49	Dako	
PMS2	Ep51	Dako	

PD-L1

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 U 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 U1%.

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) U 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 U1%. 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 U1% 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 PDL1 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.

PD-L1 (Clone: Sp142):

Ventana PD-L1 (SP142) assay is a qualitative immunohistochemical assay using rabbit monoclonal anti-PDL1 antibody (clone SP142), intended for use in the assessment of the programmed death-ligand 1 (PD-L1) protein in tumor cells and tumor infiltrating immune cells in the formalin-fixed, paraffin-embedded (FFPE) tissues with Optiview DAB Detection Kit and Optiview Amplification Kit on a BenchMark XT platform.

Determination of PD-L1 status is indication-specific and evaluation is based on either the proportion of tumor area occupied by PD-L1 expressing tumor-infiltrating immune cells (% IC) of any intensity or the percentage of PD-L1 expressing tumor cells (% TC) of any intensity.

VENTANA PD-L1 (SP142) Assay is indicated as an aid in identifying patients for treatment with Tecentriq (Atezolizumab). Cut-off of PD-L1 (SP142) in breast carcinoma is U 1% IC.

PD-L1 (Clone-SP142) testing performed by Referral laboratory.

Methods and Limitations

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. 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), analyzed at 800x minimum average depth using a customized in-house pipeline DCGL NGS Bioinformatics Pipeline v15, designed to accurately detect the somatic variants.

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.

Tumor Tissue mRNA Analysis

Tumor tissue was analyzed for mRNA expression detection using semiconductor based NGS 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 v5.9 designed to detect the significantly expressed genes.

Pharmacogenetic Analysis

Blood was analyzed for genotyping using semiconductor based NGS 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 P1 chip. The minimum average depth was 500x for panel of genes analyzed. High quality sequencing data (proportion of Q20 bases U75%) was analyzed using DCGL NGS Bioinformatics Pipeline v14.5. 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 98.55%.

IHC Analysis

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

CTC Enumeration and CTC-ICC Analysis

Enriched CTCs from the submitted peripheral blood were labelled with EPCAM, Cytokeratin and CD45 antibodies and analyzed by High content imaging platform. Analytical Validation of this assay shown sensitivity of 99.9% and specificity 99.9%.

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 C-TACs 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 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 99.9% and specificity 99.9%.

Disclaimer

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.

This test was developed, and its performance characteristics determined by Datar Cancer Genetics. It has not been cleared or approved by the U.S. Food and Drug Administration.

This laboratory is certified under the Clinical Laboratory Improvement Amendments (CLIA)-USA as qualified to perform high complexity clinical laboratory testing.

The Patient Analysis raw data may be shared on written request by the individual patient.

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.

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****End of Report****

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Clinical Trials Relevant to Patient's Genomic Findings

Tumor Mutational Burden

NCT number:
NCT03767075

Phase: II

Treatment:
Atezolizumab

Cancer Type:
Unspecified Solid Tumor

Study Title:
Basket of Baskets: A Modular, Open-label, Phase II, Multicentre Study To Evaluate Targeted Agents in Molecularly Selected Populations With Advanced Solid Tumours

Variant Classification:
Tumor Mutational Burden

Locations:
France, Germany, Netherlands, Spain, Sweden, United Kingdom

NCT number:
NCT04185831

Phase: II

Treatment:
Atezolizumab

Cancer Type:
Unspecified Solid Tumor

Study Title:
MEGALiT - a Multicenter, Basket and Umbrella Explorative Trial on the Efficacy and Safety of Molecular Profile Selected Commercially Available Targeted Anti-cancer Drugs in Patients With Advanced Cancers Progressive on Standard Therapy

Variant Classification:
Tumor Mutational Burden

Locations:
Sweden

NCT number:
NCT04551521

Phase: II

Treatment:
Atezolizumab

Cancer Type:
Unspecified Solid Tumor

Study Title:
Continuous ReAssessment With Flexible ExTension in Rare Malignancies - CRAFT: The NCT-PMO-1602 Phase II Trial

Variant Classification:
Tumor Mutational Burden

Locations:
Germany

NCT number:
NCT04589845

Phase: II

Treatment:
Atezolizumab

Cancer Type:
Unspecified Solid Tumor

Study Title:
Tumor-Agnostic Precision Immunooncology and Somatic Targeting Rational for You (TAPISTRY) Phase II Platform Trial

Variant Classification:
Tumor Mutational Burden

Locations:
Australia, Belgium, Brazil, Canada, China, Germany, Hong Kong, Israel, Italy, New Zealand, Poland, Portugal, Republic of Korea, Singapore, Spain, Switzerland, Taiwan, United States

Contacts:
Reference Study ID Number: BO41932 [888-662-6728; Global-Roche-Genentech-Trials@gene.com]

NCT number:
NCT04591431

Phase: II

Treatment:
Atezolizumab, Nivolumab, Ipilimumab

Cancer Type:
Non-Small Cell Lung Cancer

Study Title:
The Rome Trial From Histology to Target: the Road to Personalize Target Therapy and Immunotherapy

Variant Classification:
Tumor Mutational Burden

Locations:
Italy

Clinical Trials Relevant to Patient's Genomic Findings

Clinical Trials

TP53 mutation

NCT number: NCT03096054
Phase: I
Treatment: LY3143921
Cancer Type: Non-Small Cell Lung Cancer

Study Title: A Cancer Research UK (CR-UK) Phase I Trial of LY3143921 a Cdc7 Inhibitor in Adult Patients With Advanced Solid Tumours
Variant Classification: TP53 mutation
Locations: United Kingdom

NCT number: NCT04383938
Phase: I /II
Treatment: Eprenetapopt, Pembrolizumab
Cancer Type: Non-Small Cell Lung Cancer

Study Title: Study of APR-246 in Combination With Pembrolizumab in Subjects With Solid Tumor Malignancies
Variant Classification: TP53 mutation status
Locations: United Kingdom
Contacts: Dr. Eyal Attar [617-804-6947; info@aprea.com]

NCT number: NCT04169841
Phase: II
Treatment: Durvalumab, Tremelimumab, Olaparib
Cancer Type: Non-Small Cell Lung Cancer

Study Title: Precision Medicine Phase II Study Evaluating the Efficacy of a Double Immunotherapy by Durvalumab and Tremelimumab Combined With Olaparib in Patients With Solid Cancers and Carriers of Homologous Recombination Repair Genes Mutation in Response or Stable After Olaparib Treatment
Variant Classification: HRR mutation
Locations: France

NCT number: NCT04940637
Phase: II
Treatment: Niraparib, Dostarlimab
Cancer Type: Non-Small Cell Lung Cancer

Study Title: A Phase II, Open-Label, Single Arm, Prospective, Multicenter Study of Niraparib Plus Dostarlimab in Patients With Advanced NSCLC and/or MPM, and Positive for PD-L1 Expression and Germline or Somatic Mutations in the HRR Genes
Variant Classification: HRR mutation
Locations: Italy

NCT number: No NCT ID
Phase: I/II
Treatment: Sintilimab
Cancer Type: Non-Small Cell Lung Cancer

Other identifiers: ChiCTR1900023234
Study Title: Single-arm Exploratory Study for Sintilimab Second-line or Later-line Treatment of Advanced Non-small Cell Lung Cancer with DDR Pathway Gene Mutation
Variant Classification: DNA repair mutation
Locations: China

NCT number:
NCT04095273

Phase: I

Treatment:
BAY-1895344, Pembrolizumab

Cancer Type:
Non-Small Cell Lung Cancer

Study Title:
A Multicenter, Non-randomized, Open-label Phase Ib Study to Determine the Maximum Tolerated and Recommended Phase II Dose of the ATR Inhibitor BAY1895344 in Combination With Pembrolizumab and to Characterize Its Safety, Tolerability, Pharmacokinetics and Preliminary Anti-tumor Activity in Patients With Advanced Solid Tumors

Variant Classification:
DNA repair mutation

Locations:
Germany, Spain, Switzerland, United States

Contacts:
Bayer Clinical Trials Contact [clinical-trials-contact@bayer.com]

NCT number:
NCT04293094

Phase: I

Treatment:
AMG-650

Cancer Type:
Unspecified Solid Tumor

Study Title:
A Phase I, Multicenter, Open-label, Dose-Exploration and Dose-Expansion Study Evaluating the Safety, Tolerability, Pharmacokinetics, and E icacy of AMG 650 in Subjects With Advanced Solid Tumors

Variant Classification:
TP53 mutation

Locations:
Australia, Belgium, Canada, Italy, Japan, Spain, United States

Contacts:
Amgen Call Center [866-572-6436; medinfo@amgen.com]

NCT number:
NCT02029001

Phase: III

Treatment:
Olaparib

Cancer Type:
Unspecified Solid Tumor

Study Title:
A Two-period, Multicenter, Randomized, Open-label, Phase II Study Evaluating the Clinical Benefit of a Maintenance Treatment Targeting Tumor Molecular Alterations in Patients with Progressive Locally-advanced or Metastatic Solid Tumors.

Variant Classification:
HRR mutation

Locations:
France

NCT number:
NCT04123366

Phase: II

Treatment:
Olaparib, Pembrolizumab

Cancer Type:
Unspecified Solid Tumor

Study Title:
A Phase II Study of Olaparib in Combination With Pembrolizumab in Participants With Previously Treated, Homologous Recombination Repair Mutation (HRRm) and/or Homologous Recombination Deficiency (HRD)-Positive Advanced Cancer

Variant Classification:
HRR mutation

Locations:
Argentina, Australia, Canada, Colombia, France, Germany, Guatemala, Israel, Italy, Japan, Latvia, Mexico, Peru, Poland, Puerto Rico, Republic of Korea, Romania, South Africa, Spain, Sweden, Turkey, Ukraine, United States

Contacts:
Toll Free Number [888-577-8839; Trialsites@merck.com]

Clinical Trials

NCT number:
NCT04174716

Phase: I/II

Treatment:
Venadaparib

Cancer Type:
Unspecified Solid Tumor

Study Title:
An Open-label, Multi-center, Phase Ib/IIa Basket Trial of IDX-1197 in Patients With Homologous Recombination Repair Mutated Solid Tumors

Variant Classification:
HRR mutation

Locations:
Republic of Korea

NCT number:
NCT03767075

Phase: II

Treatment:
Atezolizumab

Cancer Type:
Unspecified Solid Tumor

Study Title:
Basket of Baskets: A Modular, Open-label, Phase II, Multicentre Study To Evaluate Targeted Agents in Molecularly Selected Populations With Advanced Solid Tumours

Variant Classification:
DNA repair mutation

Locations:
France, Germany, Netherlands, Spain, Sweden, United Kingdom

NCT number:
NCT04905914

Phase: I / II

Treatment:
ATRN-119

Cancer Type:
Unspecified Solid Tumor

Study Title:
A Phase I/IIa, Open-Label, Safety, Pharmacokinetic, And Preliminary Efficacy Study Of Oral ATRN-119 In Patients With Advanced Solid Tumors

Variant Classification:
DNA repair mutation

Locations:
United States

Locations:
Robert Hasson [619-540-6253; rhasson@pacificlinkconsulting.com]

NCT number:
NCT04901702

Phase: I / II

Treatment:
Talazoparib, Chemotherapy

Cancer Type:
Unspecified Solid Tumor

Study Title:
A Randomized Phase I/II Study of Talazoparib or Temozolomide in Combination With Onivyde in Children With Recurrent Solid Malignancies and Ewing Sarcoma

Variant Classification:
HRR pathway

Locations:
Canada, United States

Locations:
Dr. Sara Federico [866-278-5833; referralinfo@stjude.org]

NCT number:
NCT03155620

Phase: II

Treatment:
Olaparib

Cancer Type:
Unspecified Solid Tumor

Study Title:
NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice) Screening Protocol

Variant Classification:
DNA repair pathway

Locations:
Puerto Rico, United States

Locations:
Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

NCT number:
NCT03233204

Phase: II

Treatment:
Olaparib

Cancer Type:
Unspecified Solid Tumor

Study Title:
NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice)- Phase 2 Subprotocol of Olaparib in Patients With Tumors Harboring Defects in DNA Damage Repair Genes

Variant Classification:
DNA repair pathway

Locations:
Puerto Rico, United States

Contacts:
Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

NCT number:
NCT04267939

Phase: I

Treatment:
BAY-1895344, Niraparib

Cancer Type:
Unspecified Solid Tumor

Study Title:
An Open-label Phase Ib Study to Determine the Maximum Tolerated and/or Recommended Phase II Dose of the ATR Inhibitor BAY 1895344 in Combination With PARP Inhibitor Niraparib, in Patients With Recurrent Advanced Solid Tumors and Ovarian Cancer

Variant Classification:
DNA repair pathway

Locations:
United States

Contacts:
Bayer Clinical Trials Contact [888-842-2937; clinical-trials-contact@bayer.com]

NCT number:
NCT04693468

Phase: I

Treatment:
Talazoparib, Palbociclib, Axitinib, Crizotinib

Cancer Type:
Unspecified Solid Tumor

Study Title:
Modular Phase IB Hypothesis-Testing, Biomarker-Driven, Talazoparib Combination Trial (TalaCom)

Variant Classification:
DNA repair pathway

Locations:
United States

Contacts:
Timothy A. Yap [713-563-1784; tyap@mdanderson.org]

NCT number:
NCT03096054

Phase: I

Treatment:
Ly3143921

Cancer Type:
Non-Small Cell Lung Cancer

Study Title:
A Cancer Research UK (CR-UK) Phase I Trial of LY3143921 a Cdc7 Inhibitor in Adult Patients With Advanced Solid Tumours

Variant Classification:
TP53 mutation

Locations:
United Kingdom

NCT number:
NCT04383938

Phase: I / II

Treatment:
Eprenetapopt, Pembrolizumab

Cancer Type:
Non-Small Cell Lung Cancer

Study Title:
Study of APR-246 in Combination With Pembrolizumab in Subjects With Solid Tumor Malignancies

Variant Classification:
TP53 mutation status

Locations:
United States

Contacts:
Dr. Eyal Attar [617-804-6947; info@aprea.com]

NCT number:
NCT04169841

Phase: II

Treatment:
Durvalumab, Tremelimumab, Olaparib

Cancer Type:
Non-Small Cell Lung Cancer

Study Title:
Precision Medicine Phase II Study Evaluating the Efficacy of a Double Immunotherapy by Durvalumab and Tremelimumab Combined With Olaparib in Patients With Solid Cancers and Carriers of Homologous Recombination Repair Genes Mutation in Response or Stable After Olaparib Treatment

Variant Classification:
HRR mutation

Locations:
France

NCT number:
NCT04940637

Phase: II

Treatment:
Niraparib, Dostarlimab

Cancer Type:
Non-Small Cell Lung Cancer

Study Title:
A Phase II, Open-Label, Single Arm, Prospective, Multicenter Study of Niraparib Plus Dostarlimab in Patients With Advanced NSCLC and/or MPM, and Positive for PD-L1 Expression and Germline or Somatic Mutations in the HRR Genes

Variant Classification:
HRR mutation

Locations:
Italy

NCT number:
No NCT ID

Phase: I / II

Treatment:
Sintilimab

Cancer Type:
Non-Small Cell Lung Cancer

Other identifiers: ChiCTR1900023234

Study Title:
Single-arm Exploratory Study for Sintilimab Second-line or Later-line Treatment of Advanced Non-small Cell Lung Cancer with DDR Pathway Gene Mutation

Variant Classification:
DNA repair mutation

Locations:
China

NCT number:
NCT04095273

Phase: I

Treatment:
BAY-1895344, Pembrolizumab

Cancer Type:
Non-Small Cell Lung Cancer

Study Title:
A Multicenter, Non-randomized, Open-label Phase Ib Study to Determine the Maximum Tolerated and Recommended Phase II Dose of the ATR Inhibitor BAY1895344 in Combination With Pembrolizumab and to Characterize Its Safety, Tolerability, Pharmacokinetics and Preliminary Anti-tumor Activity in Patients With Advanced Solid Tumors

Variant Classification:
DNA repair mutation

Locations:
Germany, Spain, Switzerland, United States

Contacts:
Bayer Clinical Trials Contact [clinical-trials-contact@bayer.com]

NCT number:
NCT04293094

Phase: I

Treatment:
AMG-650

Cancer Type:
Unspecified Solid Tumor

Study Title:
A Phase I, Multicenter, Open-label, Dose-Exploration and Dose-Expansion Study Evaluating the Safety, Tolerability, Pharmacokinetics, and Efficacy of AMG 650 in Subjects With Advanced Solid Tumors

Variant Classification:
TP53 mutation

Locations:
Australia, Belgium, Canada, Italy, Japan, Spain, United States

Contacts:
Amgen Call Center [866-572-6436; medinfo@amgen.com]

NCT number:
NCT02029001

Phase: II

Treatment:
Olaparib

Cancer Type:
Unspecified Solid Tumor

Study Title:
A Two-period, Multicenter, Randomized, Open-label, Phase II Study Evaluating the Clinical Benefit of a Maintenance Treatment Targeting Tumor Molecular Alterations in Patients with Progressive Locally-advanced or Metastatic Solid

Variant Classification:
HRR mutation

Locations:
France

NCT number:
NCT04123366

Phase: II

Treatment:
Olaparib, Pembrolizumab

Cancer Type:
Unspecified Solid Tumor

Study Title:
A Phase II Study of Olaparib in Combination With Pembrolizumab in Participants With Previously Treated, Homologous Recombination Repair Mutation (HRRm) and/or Homologous Recombination Deficiency (HRD)-Positive Advanced Cancer

Variant Classification:
HRR mutation

Locations:
Argentina, Australia, Canada, Colombia, France, Germany, Guatemala, Israel, Italy, Japan, Latvia, Mexico, Peru, Poland, Puerto Rico, Republic of Korea, Romania, South Africa, Spain, Sweden, Turkey, Ukraine, United States

Contacts:
Toll Free Number [888-577-8839; Trialsites@merck.com]

NCT number:
NCT04174716

Phase: I/II

Treatment:
Venadaparib

Cancer Type:
Unspecified Solid Tumor

Study Title:
An Open-label, Multi-center, Phase Ib/IIa Basket Trial of IDX-1197 in Patients With Homologous Recombination Repair Mutated Solid Tumors

Variant Classification:
HRR mutation

Locations:
Republic of Korea

NCT number:
NCT03767075

Phase: II

Treatment:
Atezolizumab

Cancer Type:
Unspecified Solid Tumor

Study Title:
Basket of Baskets: A Modular, Open-label, Phase II, Multicentre Study To Evaluate Targeted Agents in Molecularly Selected Populations With Advanced Solid Tumours

Variant Classification:
DNA repair mutation

Locations:
France, Germany, Netherlands, Spain, Sweden, United Kingdom

Clinical Trials

NCT number: NCT04905914
Phase: I / II
Treatment: ATRN-119
Cancer Type: Unspecified Solid Tumor

Study Title: A Phase I/IIa, Open-Label, Safety, Pharmacokinetic, And Preliminary Efficacy Study Of Oral ATRN-119 In Patients With Advanced Solid Tumors
Variant Classification: DNA repair mutation
Locations: United States
Contacts: Robert Hasson [619-540-6253; rhasson@pacificlinkconsulting.com]

NCT number: NCT04901702
Phase: I / II
Treatment: Talazoparib, Chemotherapy
Cancer Type: Unspecified Solid Tumor

Study Title: A Randomized Phase I/II Study of Talazoparib or Temozolomide in Combination With Onivyde in Children With Recurrent Solid Malignancies and Ewing Sarcoma
Variant Classification: HRR pathway
Locations: Canada, United States
Contacts: Dr. Sara Federico [866-278-5833; referralinfo@stjude.org]

NCT number: NCT03155620
Phase: II
Treatment: Olaparib
Cancer Type: Unspecified Solid Tumor

Study Title: NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice) Screening Protocol
Variant Classification: DNA repair pathway
Locations: Puerto Rico, United States
Contacts: Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

NCT number: NCT03233204
Phase: II
Treatment: Olaparib
Cancer Type: Unspecified Solid Tumor

Study Title: NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice)- Phase 2 Subprotocol of Olaparib in Patients With Tumors Harboring Defects in DNA Damage Repair Genes
Variant Classification: DNA repair pathway
Locations: Puerto Rico, United States
Contacts: Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

NCT number: NCT04267939
Phase: I
Treatment: BAY-1895344, Niraparib
Cancer Type: Unspecified Solid Tumor

Study Title: An Open-label Phase Ib Study to Determine the Maximum Tolerated and/or Recommended Phase II Dose of the ATR Inhibitor BAY 1895344 in Combination With PARP Inhibitor Niraparib, in Patients With Recurrent Advanced Solid Tumors and Ovarian Cancer
Variant Classification: DNA repair pathway
Locations: United States
Contacts: Bayer Clinical Trials Contact [888-842-2937; clinical-trials-contact@bayer.com]

NCT number: NCT04693468
Phase: I
Treatment: Talazoparib, Palbociclib, Axitinib, Crizotinib
Cancer Type: Unspecified Solid Tumor

Study Title: Modular Phase IB Hypothesis-Testing, Biomarker-Driven, Talazoparib Combination Trial (TalaCom)
Variant Classification: DNA repair pathway
Locations: United States
Contacts: Timothy A. Yap [713-563-1784; tyap@mdanderson.org]

NCT number: NCT04293094
Phase: I
Treatment: AMG-650
Cancer Type: Unspecified Solid Tumor

Study Title: A Phase I, Multicenter, Open-label, Dose-Exploration and Dose-Expansion Study Evaluating the Safety, Tolerability, Pharmacokinetics, and Efficacy of AMG 650 in Subjects With Advanced Solid Tumors
Variant Classification: TP53 mutation
Locations: Australia, Belgium, Canada, Italy, Japan, Spain, United States
Contacts: Amgen Call Center [866-572-6436; medinfo@amgen.com]

NCT number: NCT03096054
Phase: I
Treatment: Ly3143921
Cancer Type: Non-Small Cell Lung Cancer

Study Title: A Cancer Research UK (CR-UK) Phase I Trial of LY3143921 a Cdc7 Inhibitor in Adult Patients With Advanced Solid Tumours
Variant Classification: TP53 mutation
Locations: United Kingdom

NCT number: NCT04383938
Phase: I / II
Treatment: Eprenetapopt, Pembrolizumab
Cancer Type: Non-Small Cell Lung Cancer

Study Title: Study of APR-246 in Combination With Pembrolizumab in Subjects With Solid Tumor Malignancies
Variant Classification: TP53 mutation status
Locations: United States
Contacts: Dr. Eyal Attar [617-804-6947; info@aprea.com]

NCT number: NCT04169841
Phase: II
Treatment: Durvalumab, Tremelimumab, Olaparib
Cancer Type: Non-Small Cell Lung Cancer

Study Title: Precision Medicine Phase II Study Evaluating the Efficacy of a Double Immunotherapy by Durvalumab and Tremelimumab Combined With Olaparib in Patients With Solid Cancers and Carriers of Homologous Recombination Repair Genes Mutation in Response or Stable After Olaparib Treatment
Variant Classification: HRR mutation
Locations: France

NCT number: NCT04940637
Phase: II
Treatment: Niraparib, Dostarlimab
Cancer Type: Non-Small Cell Lung Cancer

Study Title: A Phase II, Open-Label, Single Arm, Prospective, Multicenter Study of Niraparib Plus Dostarlimab in Patients With Advanced NSCLC and/or MPM, and Positive for PD-L1 Expression and Germline or Somatic Mutations in the HRR Genes
Variant Classification: HRR mutation
Locations: Italy

NCT number: NCT02029001
Phase: II
Treatment: Olaparib
Cancer Type: Unspecified Solid Tumor

Study Title: A Two-period, Multicenter, Randomized, Open-label, Phase II Study Evaluating the Clinical Benefit of a Maintenance Treatment Targeting Tumor Molecular Alterations in Patients with Progressive Locally-advanced or Metastatic Solid Tumors.
Variant Classification: HRR mutation
Locations: France

NCT number: NCT04939662
Phase: II
Treatment: Olaparib, Bevacizumab
Cancer Type: Small Cell Lung Cancer

Study Title: Phase II, Single-arm Study of Olaparib and Bevacizumab Combination Therapy in Relapsed Small Cell Lung Cancer Subjects With DNA Damage Response and the Repair Pathway Alteration, ATM Deficiency, SLFN11 Positive, or POU2F3 Positive
Variant Classification: HRR mutation
Locations: Republic of Korea

NCT number: NCT04123366
Phase: II
Treatment: Olaparib, Pembrolizumab
Cancer Type: Unspecified Solid Tumor

Study Title: A Phase II Study of Olaparib in Combination With Pembrolizumab in Participants With Previously Treated, Homologous Recombination Repair Mutation (HRRm) and/or Homologous Recombination Deficiency (HRD)-Positive Advanced Cancer
Variant Classification: HRR mutation
Locations: Argentina, Australia, Canada, Colombia, France, Germany, Guatemala, Israel, Italy, Japan, Latvia, Mexico, Peru, Poland, Puerto Rico, Republic of Korea, Romania, South Africa, Spain, Sweden, Turkey, Ukraine, United States
Contacts: Toll Free Number [888-577-8839; Trialsites@merck.com]

NCT number: NCT04174716
Phase: I / II
Treatment: Venadaparib
Cancer Type: Unspecified Solid Tumor

Study Title: An Open-label, Multi-center, Phase Ib/IIa Basket Trial of IDX-1197 in Patients With Homologous Recombination Repair Mutated Solid Tumors
Variant Classification: HRR mutation
Locations: Republic of Korea

Clinical Trials

NCT number: NCT05002868
Phase: I
Treatment: Rp12146
Cancer Type: Small Cell Lung Cancer

Study Title: A Multi-center, Open-label, Phase I/Ib Study to Assess the Safety, Pharmacokinetics and Anti-tumor Activity of RP12146, a Poly (ADP-ribose) Polymerase (PARP) Inhibitor, in Patients With Locally Advanced or Metastatic Solid Tumors
Variant Classification: HRR mutation
Locations: Poland

NCT number: NCT03767075
Phase: II
Treatment: Atezolizumab
Cancer Type: Unspecified Solid Tumor

Study Title: Basket of Baskets: A Modular, Open-label, Phase II, Multicentre Study To Evaluate Targeted Agents in Molecularly Selected Populations With Advanced Solid Tumours
Variant Classification: DNA repair mutation
Locations: France, Germany, Netherlands, Spain, Sweden, United Kingdom

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NCT number: NCT04905914
Phase: I / II
Treatment: ATRN-119
Cancer Type: Unspecified Solid Tumor

Study Title: A Phase I/IIa, Open-Label, Safety, Pharmacokinetic, And Preliminary Efficacy Study Of Oral ATRN-119 In Patients With Advanced Solid Tumors
Variant Classification: DNA repair mutation
Locations: United States
Contacts: Robert Hasson [619-540-6253; rhasson@pacificlinkconsulting.com]

NCT number: No NCT ID
Phase: I / II
Treatment: Sintilimab
Cancer Type: Non-Small Cell Lung Cancer

Other identifiers: ChiCTR1900023234
Study Title: Single-arm Exploratory Study for Sintilimab Second-line or Later-line Treatment of Advanced Non-small Cell Lung Cancer with DDR Pathway Gene Mutation
Variant Classification: DNA repair mutation
Locations: China

NCT number: NCT04901702
Phase: I / II
Treatment: Talazoparib, Chemotherapy
Cancer Type: Unspecified Solid Tumor

Study Title: A Randomized Phase I/II Study of Talazoparib or Temozolomide in Combination With Onivyde in Children With Recurrent Solid Malignancies and Ewing Sarcoma
Variant Classification: HRR mutation
Locations: Canada, United States
Contacts: Dr. Sara Federico [866-278-5833; referralinfo@stjude.org]

Clinical Trials

NCT number: NCT04095273
Phase: I
Treatment: BAY-1895344, Pembrolizumab
Cancer Type: Non-Small Cell Lung Cancer

Study Title: A Multicenter, Non-randomized, Open-label Phase Ib Study to Determine the Maximum Tolerated and Recommended Phase II Dose of the ATR Inhibitor BAY1895344 in Combination With Pembrolizumab and to Characterize Its Safety, Tolerability, Pharmacokinetics and Preliminary Anti-tumor Activity in Patients With Advanced Solid Tumors
Variant Classification: DNA repair mutation
Locations: Germany, Spain, Switzerland, United States
Contacts: Bayer Clinical Trials Contact [clinical-trials-contact@bayer.com]

NCT number: NCT03155620
Phase: II
Treatment: Olaparib
Cancer Type: Unspecified Solid Tumor

Study Title: NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice) Screening Protocol
Variant Classification: DNA repair pathway
Locations: Puerto Rico, United States
Contacts: Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

NCT number: NCT03233204
Phase: II
Treatment: Olaparib
Cancer Type: Unspecified Solid Tumor

Study Title: NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice)- Phase 2 Subprotocol of Olaparib in Patients With Tumors Harboring Defects in DNA Damage Repair Genes
Variant Classification: DNA repair pathway
Locations: Puerto Rico, United States
Contacts: Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

NCT number: NCT04267939
Phase: I
Treatment: BAY-1895344, Niraparib
Cancer Type: Unspecified Solid Tumor

Study Title: An Open-label Phase Ib Study to Determine the Maximum Tolerated and/or Recommended Phase II Dose of the ATR Inhibitor BAY 1895344 in Combination With PARP Inhibitor Niraparib, in Patients With Recurrent Advanced Solid Tumors and Ovarian Cancer
Variant Classification: DNA repair pathway
Locations: United States
Contacts: Bayer Clinical Trials Contact [888-842-2937; clinical-trials-contact@bayer.com]

NCT number: NCT04693468
Phase: I
Treatment: Talazoparib, Palbociclib, Axitinib, Crizotinib
Cancer Type: Unspecified Solid Tumor

Study Title: Modular Phase IB Hypothesis-Testing, Biomarker-Driven, Talazoparib Combination Trial (TalaCom)
Variant Classification: DNA repair pathway
Locations: United States
Contacts: Timothy A. Yap [713-563-1784; tyap@mdanderson.org]

NCT number: NCT04293094
Phase: I
Treatment: AMG-650
Cancer Type: Unspecified Solid Tumor

Study Title: A Phase I, Multicenter, Open-label, Dose-Exploration and Dose-Expansion Study Evaluating the Safety, Tolerability, Pharmacokinetics, and E icacy of AMG 650 in Subjects With Advanced Solid Tumors
Variant Classification: TP53 mutation
Locations: Australia, Belgium, Canada, Italy, Japan, Spain, United States
Contacts: Amgen Call Center [866-572-6436; medinfo@amgen.com]

NCT number: NCT03096054
Phase: I
Treatment: Ly3143921
Cancer Type: Non-Small Cell Lung Cancer

Study Title: A Cancer Research UK (CR-UK) Phase I Trial of LY3143921 a Cdc7 Inhibitor in Adult Patients With Advanced Solid Tumours
Variant Classification: TP53 mutation
Locations: United Kingdom

NCT number: NCT04383938
Phase: I / II
Treatment: Eprenetapopt, Pembrolizumab
Cancer Type: Non-Small Cell Lung Cancer

Study Title: Study of APR-246 in Combination With Pembrolizumab in Subjects With Solid Tumor Malignancies
Variant Classification: TP53 mutation status
Locations: United States
Contacts: Dr. Eyal Attar [617-804-6947; info@aprea.com]

NCT number: NCT04169841
Phase: II
Treatment: Durvalumab, Tremelimumab, Olaparib
Cancer Type: Non-Small Cell Lung Cancer

Study Title: Precision Medicine Phase II Study Evaluating the Efficacy of a Double Immunotherapy by Durvalumab and Tremelimumab Combined With Olaparib in Patients With Solid Cancers and Carriers of Homologous Recombination Repair Genes Mutation in Response or Stable After Olaparib Treatment
Variant Classification: HRR mutation
Locations: France

NCT number: NCT04940637
Phase: II
Treatment: Niraparib, Dostarlimab
Cancer Type: Non-Small Cell Lung Cancer

Study Title: A Phase II, Open-Label, Single Arm, Prospective, Multicenter Study of Niraparib Plus Dostarlimab in Patients With Advanced NSCLC and/or MPM, and Positive for PD-L1 Expression and Germline or Somatic Mutations in the HRR Genes
Variant Classification: HRR mutation
Locations: Italy

NCT number: NCT02029001
Phase: II
Treatment: Olaparib
Cancer Type: Unspecified Solid Tumor

Study Title: A Two-period, Multicenter, Randomized, Open-label, Phase II Study Evaluating the Clinical Benefit of a Maintenance Treatment Targeting Tumor Molecular Alterations in Patients with Progressive Locally-advanced or Metastatic Solid Tumors.
Variant Classification: HRR mutation
Locations: France

NCT number: NCT04939662
Phase: II
Treatment: Olaparib, Bevacizumab
Cancer Type: Small Cell Lung Cancer

Study Title: Phase II, Single-arm Study of Olaparib and Bevacizumab Combination Therapy in Relapsed Small Cell Lung Cancer Subjects With DNA Damage Response and the Repair Pathway Alteration, ATM Deficiency, SLFN11 Positive, or POU2F3 Positive
Variant Classification: HRR mutation
Locations: Republic of Korea

NCT number: NCT04123366
Phase: II
Treatment: Olaparib, Pembrolizumab
Cancer Type: Unspecified Solid Tumor

Study Title: A Phase II Study of Olaparib in Combination With Pembrolizumab in Participants With Previously Treated, Homologous Recombination Repair Mutation (HRRm) and/or Homologous Recombination Deficiency (HRD)-Positive Advanced Cancer
Variant Classification: HRR mutation
Locations: Argentina, Australia, Canada, Colombia, France, Germany, Guatemala, Israel, Italy, Japan, Latvia, Mexico, Peru, Poland, Puerto Rico, Republic of Korea, Romania, South Africa, Spain, Sweden, Turkey, Ukraine, United States
Contacts: Toll Free Number [888-577-8839; Trialsites@merck.com]

NCT number: NCT04174716
Phase: I / II
Treatment: Venadaparib
Cancer Type: Unspecified Solid Tumor

Study Title: An Open-label, Multi-center, Phase Ib/IIa Basket Trial of IDX-1197 in Patients With Homologous Recombination Repair Mutated Solid Tumors
Variant Classification: HRR mutation
Locations: Republic of Korea

NCT number: NCT05002868
Phase: I
Treatment: Rp12146
Cancer Type: Small Cell Lung Cancer

Study Title: A Multi-center, Open-label, Phase I/Ib Study to Assess the Safety, Pharmacokinetics and Anti-tumor Activity of RP12146, a Poly (ADP-ribose) Polymerase (PARP) Inhibitor, in Patients With Locally Advanced or Metastatic Solid Tumors
Variant Classification: HRR mutation
Locations: Poland

NCT number: NCT03767075
Phase: II
Treatment: Atezolizumab
Cancer Type: Unspecified Solid Tumor

Study Title: Basket of Baskets: A Modular, Open-label, Phase II, Multicentre Study To Evaluate Targeted Agents in Molecularly Selected Populations With Advanced Solid Tumours
Variant Classification: DNA repair mutation
Locations: France, Germany, Netherlands, Spain, Sweden, United Kingdom

NCT number: NCT04905914
Phase: I / II
Treatment: ATRN-119
Cancer Type: Unspecified Solid Tumor

Study Title: A Phase I/IIa, Open-Label, Safety, Pharmacokinetic, And Preliminary Efficacy Study Of Oral ATRN-119 In Patients With Advanced Solid Tumors
Variant Classification: DNA repair mutation
Locations: United States
Contacts: Robert Hasson [619-540-6253; rhasson@pacificlinkconsulting.com]

NCT number: No NCT ID
Phase: I / II
Treatment: Sintilimab
Cancer Type: Non-Small Cell Lung Cancer

Other identifiers: ChiCTR1900023234
Study Title: Single-arm Exploratory Study for Sintilimab Second-line or Later-line Treatment of Advanced Non-small Cell Lung Cancer with DDR Pathway Gene Mutation
Variant Classification: DNA repair mutation
Locations: China

NCT number: NCT04901702
Phase: I / II
Treatment: Talazoparib, Chemotherapy
Cancer Type: Unspecified Solid Tumor

Study Title: A Randomized Phase I/II Study of Talazoparib or Temozolomide in Combination With Onivyde in Children With Recurrent Solid Malignancies and Ewing Sarcoma
Variant Classification: HRR pathway
Locations: Canada, United States
Contacts: Dr. Sara Federico [866-278-5833; referralinfo@stjude.org]

NCT number: NCT04095273
Phase: I
Treatment: BAY-1895344, Pembrolizumab
Cancer Type: Non-Small Cell Lung Cancer

Study Title: A Multicenter, Non-randomized, Open-label Phase Ib Study to Determine the Maximum Tolerated and Recommended Phase II Dose of the ATR Inhibitor BAY1895344 in Combination With Pembrolizumab and to Characterize Its Safety, Tolerability, Pharmacokinetics and Preliminary Anti-tumor Activity in Patients With Advanced Solid Tumors
Variant Classification: DNA repair mutation
Locations: Germany, Spain, Switzerland, United States
Contacts: Bayer Clinical Trials Contact [clinical-trials-contact@bayer.com]

NCT number: NCT03155620
Phase: II
Treatment: Olaparib
Cancer Type: Unspecified Solid Tumor

Study Title: NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice) Screening Protocol
Variant Classification: DNA repair pathway
Locations: Puerto Rico, United States
Contacts: Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

NCT number: NCT03233204
Phase: II
Treatment: Olaparib
Cancer Type: Unspecified Solid Tumor

Study Title: NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice)- Phase 2 Subprotocol of Olaparib in Patients With Tumors Harboring Defects in DNA Damage Repair Genes
Variant Classification: DNA repair pathway
Locations: Puerto Rico, United States
Contacts: Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

NCT number: NCT04267939
Phase: I
Treatment: BAY-1895344, Niraparib
Cancer Type: Unspecified Solid Tumor

Study Title: An Open-label Phase Ib Study to Determine the Maximum Tolerated and/or Recommended Phase II Dose of the ATR Inhibitor BAY 1895344 in Combination With PARP Inhibitor Niraparib, in Patients With Recurrent Advanced Solid Tumors and Ovarian Cancer
Variant Classification: DNA repair pathway
Locations: United States
Contacts: Bayer Clinical Trials Contact [888-842-2937; clinical-trials-contact@bayer.com]

NCT number: NCT04693468
Phase: I
Treatment: Talazoparib, Palbociclib, Axitinib, Crizotinib
Cancer Type: Unspecified Solid Tumor

Study Title: Modular Phase IB Hypothesis-Testing, Biomarker-Driven, Talazoparib Combination Trial (TalaCom)
Variant Classification: DNA repair pathway
Locations: United States
Contacts: Timothy A. Yap [713-563-1784; tyap@mdanderson.org]

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