

كوماري عيراق

مجموعتي نويند ران

نوسينگري بهرله مانار

راكان الشيخ صبيح غازي الحنشل

نه ندامي ليژنه ي ده ستياكي



العراق

لنواب

لنائب

غازي الحنشل

النزاهة

مراجعة ملف المودع
لجنة النزاهة

العدد: ٢٦٤

التاريخ: ٢٠٢٦ / ٦ / ٢٠

السيد وزير الصحة المحترم

م/ استثناء من صرف العلاج

تحية طيبة ..

نرافق لكم طياً اصل الطلب المقدم من قبل المواطن (سمير حميد مجيد عبدالرحيم) من سكة محافظة نينوى، يعاني من مرض سرطان الرئة المتقدم منذ ستة اشهر عافانا وعافكم الله، وقد تلقا العلاج الكيميائي ولم تظهر أي استجابة له، وبعد اجراء الفحوصات الجينية اللازمة تبين ان حالته تحتاج الى العلاج المناعي (KEYTRUDA) المتوفر ضمن المؤسسات الصحية التابعة لوزارة الصحة. والذي يروم فيه من معاليكم التفضل بالموافقة على استثنائه وصرف العلاج المذكور أعلاه. راجين من سيادتكم التفضل بالموافقة له على صرف العلاج والنظر بعين العطف والإنسانية الى طلبه كونه متقاعد ومن محدودي الدخل ولكلفة العلاج العالية من ما يمنعه من شرائه .

راجين تدخلكم الشخصي واعلامنا ... مع التقدير .

المرفقات :

- اصل الطلب .
- التقارير الطبية .

نسخة الى :

- الارشيف للتأشير والحفظ .

التائب

راكان الشيخ صبيح غازي الحنشل

عضو لجنة النزاهة

الدورة السادسة

٢٠٢٦ / ٦ / ٢٠

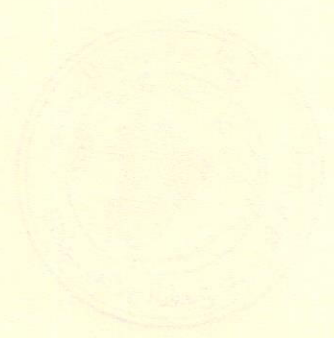


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السيد معالي وزير الصحة المحترم

م / استثناء صرف علاج

تحية طبية ...

إنني المريض (سمير حميد مجيد عبد عبد الرحيم) من سكنة مدينة الموصل، أعاني من سرطان الرئة المتقدم منذ ستة أشهر، وحسب التقارير الطبية المرفقة فقد تلقيت العلاج الكيماوي إلا أن حالتي لم تُظهر استجابة للعلاج.

وبعد إجراء الفحوصات الجينية اللازمة، ثبتت استفادتي من العلاج المناعي (Keytruda)، والمتوفر ضمن المؤسسات الصحية التابعة لوزارة الصحة. ونظراً لحاجتي الماسة لهذا العلاج واستمرار حالتي المرضية، أتقدم إلى سيادتكم راجياً التفضل بالموافقة على استثنائي وصرف العلاج المذكور.

علماً أن ظروف المادية صعبة كوني متقاعداً، كما أن سعر الدواء في الأسواق مرتفع جداً ولا أستطيع تحمل تكاليفه.

راجياً من سيادتكم النظر بعين العطف والإنسانية إلى طلبي هذا، والموافقة على شمولي بالعلاج.

مع فائق الاحترام والتقدير.



مقدم الطلب: سمير حميد مجيد

رقم الهاتف: ٠٧٧٤٠٩٣٩٠٥٣



المستشفى الاستشاري
Istishari Hospital

Patient Name: Samir Hameed Majeed	Exam Date & Time: 6:25 PM 4/11/2026
Patient ID: 425209	Accession: 17192437
Date Of Birth: 4/13/1958	
Gender: M	
Age: 67Y 11M	

BRAIN CT

No evidence of focal parenchymal lesion or acute hemorrhage.
Ventricular system appears normal to the age.
Normal basilar cisterns.
Normal brain stem and cerebellum.
No shift in the midline structures.
No epidural or subdural collections .
After administration of I.V. contrast , a tiny ill-defined non-mass-like patchy enhancement seen in the right parietal lobe superiorly and posteriorly, which could suggest an enhanced vessel, less likely enhanced lesion, for followup.
no evidence of other abnormal leptomeningeal or parenchymal enhancement could be seen .

NECK CT

No evidence of pharyngeal or laryngeal masses .
Intact post nasal and para-pharyngeal spaces .
Unremarkable salivary glands .
No evidence of significant neck lymphadenopathy .
No evidence of soft tissue masses or fluid collections

CHEST CT

Almost total collapse of the left lung, with a few residual air bronchograms seen in the lower lobe, with evidence of an ill-defined area of soft tissue density seen at the infrahilar region on the left side, inseparable from the rest of the collapsed lung, however, it shows a distorted pulmonary architecture, with no obvious traversing vessels and appears slightly hyperdense in comparison with the Adjacent lung tissue, it measures roughly about 4 cm in diameter, after the administration of IV contrast, it shows less enhancement than the rest of the collapsed lung, findings could suggest a tumoral mass , however, the possibility of necrotic pneumonic infiltration could not be ruled out , for followup.
There is evidence of an ill-defined small soft tissue fullness seen at the distal end of the left main bronchus, with resultant abrupt cut-off of the bronchus at the level of the soft tissue density, (endobronchial invasion of the above-mentioned mass? Solitary endobronchial mass? Less likely mucous plug?)
Left-sided pleural effusion is noted.
Shifting of the mediastinal structure toward the left side, secondary to the total left lung collapse.
Multiple peripherally emphysematous bullae with fibrotic changes involving the right lung apex.
Also atelectatic bands with slight patchy opacity seen in the right lung base suggesting mild inflammatory changes.
The rest of the right lung field appears unremarkable with no evidence of obvious masses or lesions.
Few mediastinal and bilateral hilar lymph nodes are noted, the largest one measures about 2cm and located in the right hilum.
No right-sided pleural effusion.
The heart is not enlarged.

ABDOMEN AND PELVIC CT

A small hiatal hernia is noted.
The liver appears normal with no focal lesion or biliary tree dilatation.
Patent spleno-portal venous system.
Normal spleen and pancreas.

Normal both kidneys and supra renal glands.

Unremarkable abdominal aorta and its major branches.

Unremarkable bowel loops.

The prostate appears enlarged.

The urinary bladder shows diffuse wall thickening.

Clear mesenteric fat.

No abdominal or pelvic lymphadenopathy , masses or fluid collections.

No obvious bony lesions could be seen in the obtained bony structures.

Solid Tumor Profile Plus

Patient Name:	Hameed Majeed Majeed, Sameer	Ordering Physician:	Omar Al Rawi
Date of Birth:	01/01/1958	Accession #:	209933
Gender (M/F):	M	Specimen Type:	TISSUE
Client:	Tahleel Laboratories Technical Cons LLC	Specimen ID:	H26-613
Case #:	NGS26-008215		
Body Site:	LUNG		

MRN:	1794053	Tumor Type:	small cell lung cancer
Collected Date:	04/25/2026	Time:	12:00 AM
Received Date:	04/30/2026	Time:	12:20 PM
Reported Date:	05/15/2026	Time:	05:06 PM

Detected Genomic Alterations

Level 1 (FDA-Approved)	Level 2 (Standard of Care)	Level 3 (Clinical Evidence)	Level 4 (Biological Evidence)	Other
Tumor Mutation Burden High: 12 Mut/Mb	-Homologous recombination deficiency (HRD): Positive-High -No evidence of microsatellite instability	TP53, APC, SETD2, SUZ12, LYN	NKX2-1, DDX11, GALNT12, ABCG2 (?Germline), ASTN2 (?Germline)	-t(17;17)(q21;q21) LSM12::ETV4 fusion mRNA -Autosomal chromosomal structural analysis shows 3p-, 3q+, -4, 5q-, +8, -9, -10, -11, 13q-, 15q-, 19p- (distal)

Results Summary

- -Somatic mutations in TP53, APC, SETD2, NKX2-1, SUZ12, LYN, DDX11, and GALNT12 genes
- Possible germline mutation in ABCG2 and ASTN2 gene, heterozygous
- Tumor Mutation Burden High: 12 Mut/Mb
- Homologous recombination deficiency (HRD): Positive-High
- No evidence of microsatellite instability
- No evidence of EGFR, KRAS, BRAF, MET, ALK or ERBB2 mutations
- No evidence of fusion mRNA involving ALK, RET, ROS1, or NTRK
- EBV, HPV, TTV, and HTLV viral mRNA: Not detected
- HLA Genotyping:
 - HLA-A: A*24:03-A*24:03
 - HLA-B: B*44:02-B*18:01
 - HLA-C: C*16:04-C*12:03
- Autosomal chromosomal structural analysis shows 3p-, 3q+, -4, 5q-, +8, -9, -10, -11, 13q-, 15q-, 19p- (distal)
- Increased CK, MET mRNA
- High TMB suggests response to immune checkpoint inhibitors.

- Positive homologous recombination deficiency (HRD) suggests response to platinum-based chemotherapy and PARP inhibitors.
- APC mutation activates beta-catenin and WNT signaling pathway and suggests possible response to WNT and COX-2 inhibitors.
- SETD2 mutation suggests response to wee1 inhibitors.
- TP53 mutation suggests possible response to eprenetapopt (APR-246), Aurora kinase A and Wee1 inhibitors.
- The ABCG2 mutation is detected at high level raising the possibility of a germline abnormality. This gene is involved in membrane transport and possibly associated with drug response.
- The ASTN2 mutation is detected at high level, raising the possibility of a germline mutation. This mutation leads to early termination (loss of function). However, there is no data on its clinical relevance and should be classified as of "uncertain significance" at this time.
- See additional report information at the end of the report**

Tumor Heterogeneity

There are dominant abnormal clones with TP53, APC, SETD2, and NKX2-1 mutations. The SUZ12 and LYN mutations are detected in subclones. There are abnormal low-level clones with DDX11 and GALNT12 mutations.
The ABCG2 and ASTN2 mutations are detected at high levels, possible germline abnormalities.

Expression

Increased CK, MET mRNA

Diagnostic Implications

TP53, APC, SETD2,
NKX2-1, SUZ12, LYN,
DDX11, GALNT12,
ABCG2, ASTN2

The findings are consistent with aggressive neoplasm.
The ABCG2 and ASTN2 mutations are likely germline variants.

FDA-Approved Therapeutics

TMB-High Pembrolizumab

FDA-Approved Therapeutics in Other Tumor Types

HRD Positive Niraparib + platinum-based chemotherapy

Relevant Alteration Associated with Resistance

TP53 mutation is associated with resistance to therapy.

Levels 2, 3 & 4 (Standard of Care and Clinical/Biological Evidence)

TP53	Aurora kinase A inhibitors, Wee1 inhibitors, Chk1 inhibitors, kevetrin, APR-246, nutlins, gene therapy
APC	WNT, beta-catenin, and COX-2 inhibitors
SETD2	SETD2 mutation suggests response to WEE1 inhibitors
SUZ12	SUZ12 mutation may suggest sensitivity to bromodomain inhibitors.
LYN	Src family kinase inhibitors
TMB-High	Immunotherapy with checkpoint inhibitor
HRD Positive	PARP Inhibitors & Platinum based chemotherapy

Relevant Genes with NO Alteration

-No evidence of mutation in KRAS, NRAS, EGFR, BRAF, or BRCA 1/2 -No specific mutation in DPYD gene, associated with enzymatic deficiency	No evidence of fusion mRNA involving ALK, RET, ROS1, or NTRK	-No evidence of METex14 skipping or EGFRvIII -No evidence of ERBB2 (HER2) amplification
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Test Description:

This is a comprehensive molecular profile which uses next generation sequencing (NGS) to identify molecular abnormalities, including single nucleotide variants (SNVs), insertions/deletions (indels), copy number variants (CNVs), fusions, tumor mutational burden (TMB), microsatellite instability (MSI), homologous recombination deficiency (HRD), B- and T-cell clonality, and viruses (HPV, EBV, HTLV1, and TTV), in DNA of 434 genes and RNA in greater than 1600 genes implicated in solid tumors. Whenever possible, clinical relevance and implications of detected abnormalities are described below.

Biological relevance of detected Alterations

- TP53. This gene encodes a tumor suppressor protein containing transcriptional activation, DNA binding, and oligomerization domains. The encoded protein responds to diverse cellular stresses to regulate expression of target genes, thereby inducing cell cycle arrest, apoptosis, senescence, DNA repair, or changes in metabolism. Mutations in this gene are associated with a variety of human cancers, including hereditary cancers such as Li-Fraumeni syndrome. Alternative splicing of this gene and the use of alternate promoters result in multiple transcript variants and isoforms. Additional isoforms have also been shown to result from the use of alternate translation initiation codons from identical transcript variants (PMIDs: 12032546, 20937277). [provided by RefSeq, Dec 2016]
- APC. This gene encodes a tumor suppressor protein that acts as an antagonist of the Wnt signaling pathway. It is also involved in other processes including cell migration and adhesion, transcriptional activation, and apoptosis. Defects in this gene cause familial adenomatous polyposis (FAP), an autosomal dominant pre-malignant disease that usually progresses to malignancy. Mutations in the APC gene have been found to occur in most colorectal cancers. Disease-associated mutations tend to be clustered in a small region designated the mutation cluster region (MCR) and result in a truncated protein product. [provided by RefSeq, Dec 2019]
- SETD2. Huntington's disease (HD), a neurodegenerative disorder characterized by loss of striatal neurons, is caused by an expansion of a polyglutamine tract in the HD protein huntingtin. This gene encodes a protein belonging to a class of huntingtin interacting proteins characterized by WW motifs. This protein is a histone methyltransferase that is specific for lysine-36 of histone H3, and methylation of this residue is associated with active chromatin. This protein also contains a novel transcriptional activation domain and has been found associated with hyperphosphorylated RNA polymerase II. [provided by RefSeq, Aug 2008]

- **NKX2-1.** This gene encodes a protein initially identified as a thyroid-specific transcription factor. The encoded protein binds to the thyroglobulin promoter and regulates the expression of thyroid-specific genes but has also been shown to regulate the expression of genes involved in morphogenesis. Mutations and deletions in this gene are associated with benign hereditary chorea, choreoathetosis, congenital hypothyroidism, and neonatal respiratory distress, and may be associated with thyroid cancer. Multiple transcript variants encoding different isoforms have been found for this gene. This gene shares the symbol/alias 'TTF1' with another gene, transcription termination factor 1, which plays a role in ribosomal gene transcription. [provided by RefSeq, Feb 2014]
- **SUZ12.** This zinc finger gene has been identified at the breakpoints of a recurrent chromosomal translocation reported in endometrial stromal sarcoma. Recombination of these breakpoints results in the fusion of this gene and JAZF1. The protein encoded by this gene contains a zinc finger domain in the C terminus of the coding region. [provided by RefSeq, Jul 2009]
- **LYN.** This gene encodes a tyrosine protein kinase, which maybe involved in the regulation of mast cell degranulation, and erythroid differentiation. Alternatively spliced transcript variants encoding different isoforms have been found for this gene. [provided by RefSeq, Jul 2011]
- **DDX11.** DEAD box proteins, characterized by the conserved motif Asp-Glu-Ala-Asp (DEAD), are putative RNA helicases. They are implicated in a number of cellular processes involving alteration of RNA secondary structure such as translation initiation, nuclear and mitochondrial splicing, and ribosome and spliceosome assembly. Based on their distribution patterns, some members of this family are believed to be involved in embryogenesis, spermatogenesis, and cellular growth and division. This gene encodes a DEAD box protein, which is an enzyme that possesses both ATPase and DNA helicase activities. This gene is a homolog of the yeast CHL1 gene, and may function to maintain chromosome transmission fidelity and genome stability. Alternative splicing results in multiple transcript variants encoding distinct isoforms. [provided by RefSeq, Jul 2008]
- **GALNT12.** This gene encodes a member of a family of UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferases, which catalyze the transfer of N-acetylgalactosamine (GalNAc) from UDP-GalNAc to a serine or threonine residue on a polypeptide acceptor in the initial step of O-linked protein glycosylation. Mutations in this gene are associated with an increased susceptibility to colorectal cancer. [provided by RefSeq, Mar 2011]
- **ABCG2.** The membrane-associated protein encoded by this gene is included in the superfamily of ATP-binding cassette (ABC) transporters. ABC proteins transport various molecules across extra- and intra-cellular membranes. ABC genes are divided into seven distinct subfamilies (ABC1, MDR/TAP, MRP, ALD, OABP, GCN20, White). This protein is a member of the White subfamily. Alternatively referred to as a breast cancer resistance protein, this protein functions as a xenobiotic transporter which may play a major role in multi-drug resistance. It likely serves as a cellular defense mechanism in response to mitoxantrone and anthracycline exposure. Significant expression of this protein has been observed in the placenta, which may suggest a potential role for this molecule in placenta tissue. Multiple transcript variants encoding different isoforms have been found for this gene. [provided by RefSeq, Apr 2012]
- **ASTN2.** This gene encodes a protein that is expressed in the brain and may function in neuronal migration, based on functional studies of the related astrotactin 1 gene in human and mouse. A deletion at this locus has been associated with schizophrenia. Multiple transcript variants encoding different proteins have been found for this locus. [provided by RefSeq, May 2010]

Drug Information

Pembrolizumab (Keytruda)

Pembrolizumab is a highly selective IgG4-kappa humanized monoclonal antibody against PD-1 receptor. It was generated by grafting the variable sequences of a very high-affinity mouse antihuman PD-1 antibody onto a human IgG4-kappa isotype with the containing a stabilizing S228P Fc mutation.

Olaparib (Lynparza)

Olaparib (Lynparza) is an antineoplastic agent, Poly(ADP-ribose) Polymerase 1;2;3 inhibitor. (PARP1;2;3 inhibitor).

Lynparza is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated for the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza.

Talazoparib

Talazoparib is a poly(ADP-ribose) Polymerase 1, 2 (PARP 1;2 inhibitor).

Talazoparib was approved by the FDA for use in germline BRCA mutated, HER2 negative, locally advanced or metastatic breast cancer on October 16, 2018 under the trade name Talzenna. Talazoparib prevents PARP-mediated repair of DNA damage in cancer cells, allowing accumulation of damage and PARP-DNA complexes. Repair related errors by error prone secondary repair pathways may also contribute to the cytotoxicity of Talazoparib. Talazoparib is indicated for the treatment of deleterious or suspected deleterious germline BRCA mutated, HER2 negative locally advanced or metastatic breast cancer in adults.

Nilotinib

Nilotinib is a transduction inhibitor that targets BCR-ABL, c-kit and PDGF, for the potential treatment of various leukemias, including chronic myeloid leukemia (CML).

Bosutinib

Bosutinib is a tyrosine kinase inhibitor. Although it is able to inhibit several tyrosine kinases such as Src, Lyn, and Hck, which are members of the Src-family of kinases, its primary target is the Bcr-Abl kinase.

The Bcr-Abl gene is a chimeric oncogene created from the fusion of the breakpoint-cluster (Bcr) gene and Abelson (Abl) tyrosine gene. This chromosomal abnormality results in the formation of what is commonly known as the Philadelphia chromosome or Philadelphia translocation. The Bcr-Abl gene expresses a particular kinase that promotes the progression of CML. A decrease in the growth and size of the CML tumour has been observed following administration of bosutinib. Bosutinib did not inhibit the T315I and V299L mutant cells.

Potential Clinical Trials

Trial URL	Status	Title	Disease	Drug	Sites
https://clinicaltrials.gov/study/NCT05902988	Recruiting	A Phase I/II Study of VLS-1488 (an Oral KIF18A Inhibitor) in Subjects With Advanced Cancer	Lung Cancer	VLS-1488	Memorial Sloan Kettering Cancer Center, New York, New York 10065
https://clinicaltrials.gov/study/NCT07444814	Recruiting	A Phase 1 First-in-Human Study of PTK7-Directed Antibody Drug Conjugate HWK-007 in Participants With Advanced Solid Tumors	Lung Cancer	HWK-007	Hackensack University Medical Center - John Theurer Cancer Center, Hackensack, New Jersey 07601
https://clinicaltrials.gov/study/NCT07397338	Recruiting	A Phase 1/2 Open-Label, Multicenter Study of RAS(ON) Inhibitors in Combination With Ivonescimab With or Without Other Anti-Cancer Agents in Patients With Solid Tumors	Lung Cancer	Daraxonrasib, Elironrasib, Zoldonrasib, Ivonescimab, Carboplatin/Cisplatin + Pemetrexed (Dose Expansion Only), cetuximab (Cohort C2 Only), Carboplatin/Cisplatin + Pemetrexed (Cohort B2 Only), Daraxonrasib (Cohort B1 only)	NEXT Virginia, Fairfax, Virginia 22031

Detailed Results

Single Nucleotide Variant (SNV) and Insertions-Deletions (INDELS)								
Gene name	Hgvsp	Hgvsc	Amino acids	Codons	Consequence	Allele frequency	Read depth	Predicted effect on protein
TP53	0	NM_000546.5:c.375+1G>A	0	0	splice_donor_variant	85.66	244	0
APC	NP_000029.2:p.Ser1344Ter	NM_000038.5:c.4031C>A	S/*	tCa/tAa	stop_gained	74.42	473	0
SETD2	NP_054878.5:p.Ser185Ter	NM_014159.6:c.554C>G	S/*	tCa/tGa	stop_gained	64.96	234	0
NKX2-1	NP_001073136.1:p.Ala146Val	NM_001079668.2:c.437C>T	A/V	gCc/gTc	missense_variant	62.07	29	deleterious

Niraparib (Zejula)

Niraparib (ZEJULA) is an inhibitor of poly (ADP-ribose) polymerase (PARP) with potential antineoplastic activity. PARP Inhibitor MK4827 inhibits PARP activity, enhancing the accumulation of DNA strand breaks and promoting genomic instability and apoptosis. The PARP family of proteins detect and repair single strand DNA breaks by the base-excision repair (BER) pathway. The specific PARP family member target for PARP inhibitor MK4827 is unknown. (NCI Thesaurus)

ZEJULA is a poly(ADP-ribose) polymerase (PARP) inhibitor indicated for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.

Rucaparib (Rubraca)

Rucaparib is a potent mammalian poly(ADP-ribose) polymerase 1, 2 and 3 inhibitor with anticancer properties (PARP 1;2;3 inhibitor).

Rucaparib is an inhibitor of PARP-1, PARP-2, and PARP-3. Via an inhibitory effect on the PARP enzymatic activity, rucaparib decreases the formation of PARP-DNA complexes resulting in DNA damage, apoptosis, and cell death. It is proposed that PARP inhibition specifically targets tumor cells with preexisting HRD, such as those cells possessing mutations in the BRCA1 or BRCA2 genes.

APR-246

APR-246 is a first-in-class agent targeting mutant p53. In vitro and in vivo preclinical models have demonstrated that APR-246 has excellent efficacy in OC (both adenocarcinoma and squamous cell carcinoma) and potentially synergises with chemotherapies used in the treatment of OC, restoring sensitivity to chemotherapy-resistant tumours. An initial phase I clinical trial has shown APR-246 to be safe in humans and early results from a currently running phase Ib/II trial of APR-246 with carboplatin and liposomal doxorubicin in ovarian cancer have been promising. Together, these data provide a strong rationale for investigating the efficacy of APR-246 in OC.

APR-246 has been used in trials studying the treatment of Prostatic Neoplasms, Hematologic Neoplasms, and Platinum Sensitive Recurrent High-grade Serous Ovarian Cancer With Mutated p53.

APR-246 is an analogue of PRIMA-1, which modifies the core domain of mutant p53, resulting in restoration of wild-type p53 conformation and reactivation of normal p53 function, leading to increased cell cycle arrest and tumor cell death (PMID: 20498645).

Sulindac

Sulindac is a COX-1/COX-2 inhibitor. It is being evaluated as a potential cancer chemo-preventive and therapeutic drug in clinical trials for a variety of malignancies.

Celecoxib

Celecoxib is a selective cyclooxygenase-2 (COX-2) inhibitor, is a nonsteroidal anti-inflammatory drug (NSAID). It is used to manage symptoms of various types of arthritis pain and in familial adenomatous polyposis (FAP) to reduce precancerous polyps in the colon. It is marketed by Pfizer under the brand name Celebrex, and was initially granted FDA approval in 1998. Interestingly, selective COX-2 inhibitors (especially celecoxib), have been evaluated as potential cancer chemopreventive and therapeutic drugs in clinical trials for a variety of malignancies.

Birabresib

Birabresib (OTX015 or MK-8628) is a potent BET bromodomain inhibitor, which targets the BET bromodomain proteins 2, 3, and 4 (BRD2/3/4). BRDs 2, 3, and 4 are considered potential cancer targets because of their pivotal role in regulating the transcription of growth-promoting genes and cell cycle regulators. OTX015 is the first BRD2/3/4 inhibitor to enter clinical trials. Upon administration, birabresib binds to the acetylated lysine recognition motifs on the bromodomain of BET proteins, thereby preventing the interaction between the BET proteins and acetylated histone peptides. This disrupts chromatin remodeling and gene expression.

Imatinib

Imatinib is indicated treatment of Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML), Ph+ acute lymphoblastic leukaemia, myelodysplastic/myeloproliferative diseases, aggressive systemic mastocytosis, hypereosinophilic syndrome and/or chronic eosinophilic leukemia (CEL), dermatofibrosarcoma protuberans, and malignant gastrointestinal stromal tumors (GIST). It inhibits proliferation and induces apoptosis in Bcr-Abl positive cell lines as well as fresh leukemic cells from Philadelphia chromosome positive chronic myeloid leukemia. Imatinib also inhibits the receptor tyrosine kinases for platelet derived growth factor (PDGF) and stem cell factor (SCF) - called c-kit.

Dasatinib

Dasatinib is an oral dual BCR-ABL and Src family tyrosine kinase inhibitor approved for use in patients with CML, ALL, and MPN. The main targets of Dasatinib are BCR-ABL, SRC, Ephrins and GFR. Dasatinib, at nanomolar concentrations, inhibits the following kinases: BCR-ABL, SRC family (SRC, LCK, YES, FYN), c-KIT, EPHA2, and PDGFRA. Based on modeling studies, dasatinib is predicted to bind to multiple conformations of the ABL kinase. In vitro, dasatinib was active in leukemic cell lines representing variants of imatinib mesylate sensitive and resistant disease. Dasatinib inhibited the growth of chronic myeloid leukemia (CML) and acute lymphoblastic leukemia (ALL) cell lines overexpressing BCR-ABL.

SUZ12	NP_056170.2:p. Arg555Ter	NM_015355.2:c. 1663A>T	R/*	Aga/Tga	stop_gained	40.86	1050	0
LYN	0	NM_001111097. 2:c.321-5C>T	0	0	*splice_region_varia nt,intron_variant*	29.67	1109	0
DDX11	NP_001244073. 1:p.Tyr202Cys	NM_001257144. 1:c.605A>G	Y/C	tAc/tGc	missense_variant	10.17	344	deleterious
GALNT12	NP_078918.3:p. Cys10Arg	NM_024642.4:c. 28T>C	C/R	Tgc/Cgc	missense_variant	8.92	213	deleterious - low confidence
ABCG2 (RNA)	NP_004818.2:p. Gln141Lys	NM_004827.2:c. 421C>A	Q/K	Cag/Aag	missense_variant	100.0	126	tolerated
ASTN2 (RNA)	NP_937831.1:p. Ser390Ter	NM_198188.2:c. 1169C>A	S/*	tCa/tAa	stop_gained	89.63	241	0

Methodology and Test Background

This is a next generation sequencing (NGS) test that involves separate analysis of DNA and RNA panels for abnormalities that are reported to be altered in various types of solid tumors. The DNA panel is composed of 434 genes and the RNA panel is composed of >1600 genes. The DNA and RNA components of this assay were developed, validated, and set up as separate workflows, with independent extraction, library preparation, sequencing, and analysis pipelines. The NGS assay also detects several viruses that are important in oncology, including EBV, HPV, HTLV1, and TTV. TTV (torque teno virus) was first discovered in a patient with non-A-E hepatitis and is now regarded as a part of the human virome. In general, TTV does not cause pathology in immunocompetent individuals. TTV is considered as a marker of immune competence in patients with immunological impairment and inflammatory disorders. High TTV load is associated with increased risk of infection. In patients with organ transplant, low TTV load is associated with an increased risk of rejection.

Nucleic acid is isolated from paraffin-embedded tissue. For optimal results neoplastic cells should be greater than 30% of the analyzed cells. H&E-sections are reviewed by a pathologist and tumor-enrichment is performed by macrodissection when possible. Testing is performed using massive parallel sequencing of the coding DNA of the listed genes. This includes sequencing of all the exons as well as approximately 50 nucleotides at the 5' and 3' ends of each coding exon to detect splice site abnormalities. The TERT promoter region, including the hotspots at -124 and -146 bp, is also covered. Our DNA sequencing method has a sensitivity of 3% for detecting hotspot mutations and 5% for detecting single nucleotide variants (SNVs) and small (<60 bp) insertions/deletions (indels). MSI status is inferred by interrogating all available genomic microsatellites covered. Borderline MSI results by NGS are confirmed by fragment analysis. Tumor mutational burden (TMB) is measured by counting all nonsynonymous variants and filter settings as follows: (A) Pass all filters; (B) inside genes; (C) had a mutant allele frequency >5%; (D) not found in the dbSNP (to exclude germline variations). The median for TMB is 10 mutations/Mb based on lung carcinoma analysis. The cut off for other types of tumors is not well-established at this time. Significant gene amplification and deletion (copy number variants) are also reported. Targeted RNA NGS is performed by hybrid capture and duplicates are excluded for levels measurements. The Universal Human Reference (UHR) RNA is used as control. All detected fusion transcripts are reported. While the major focus of the RNA analysis is the detection of fusion mRNA, mutations in the expressed RNA of the analyzed genes, HLA class I genotyping, and Epstein-Barr virus (EBV), human papillomavirus (HPV), human T-lymphotropic virus type-1 (HTLV1), and torque teno virus (TTV) viral RNA are also analyzed and reported. B- and T-cell clonality will be reported, if clonal or clinically relevant. The sensitivity of this assay in detecting fusion mRNA is between 5% and 10%. This test specifically covers translocations that lead to the expression of fusion RNA. Translocations that lead to deregulation of expression can be addressed by this test if compared to the expression proper normal control. Since the clinical relevance of the RNA expression level of most of the genes is not characterized at this time, only a few specific genes will be commented on when abnormalities are detected. CD274 (PD-L1) mRNA levels are reported when they are significantly elevated. This assay is not designed to detect minimal residual disease and should be used for diagnosis. Performance of the assays may vary dependent on the quantity and quality of nucleic acid, sample preparation and sample age. Decalcified specimens have not been validated. Decalcification with strong acids is not recommended and may lead to poor nucleic acid quality and suboptimal results. The testing is not validated to detect germline abnormalities. Potential germline mutations detected incidentally should be confirmed by tests specifically designed for detecting germline abnormalities.

Based on our validation study, the following exonic regions of the genes listed below are not covered appropriately <100X coverage and sequencing by NGS may not be reliable in these regions. The poor coverage is primarily due to the inherent difficulty in obtaining adequate sequencing coverage in regions with high GC content. No well-characterized hotspots are present in these regions. ASXL1 NM_001164603 20:30946620-30946635, ATM NM_000051 11:108186550-108186638, BAP1 NM_004656 3:52443858-52443894, BCR NM_004327 22:23652510-23652620, BRD4 NM_058243 19:15353808-15354193, 5355041-15355411, CCNE1 NM_001238 19:30303463-30303485, CD274 NM_001267706 9:5456109-5456165, CD79A NM_001783 19:42384736-42384805, CSF3R NM_000760 1:36937667-36937740, DDX11 NM_001257144 12:31240872-31240917, ERBB3 NM_001982 12:56492284-56492359, FANCI NM_001113378 15:89835919-89836052, FLT3 NM_004119 13:28674605-28674652, FLT4 NM_002020 5:180035281-180035284, GEN1 NM_001130009 2:17954486-17954525, H3-3A NM_002107 1:226259140-226259180, IRS2 NM_003749 13:110437126-110437363, 110437805-110437899, 110438359-110438400, JAK1 NM_002227 1:65309747-65309771, MAGI2 NM_012301 7:77648719-77649044, MITF NM_000248 3:70005606-70005681, MYCL NM_001033081 1:40367518-40367565, NF1 NM_000267 17:29664837-29664898, NOTCH2 NM_001200001 1:120572528-120572610, PBRM1 NM_018313 3:52677264-52677322, PIK3R2 NM_005027 19:18272089-18272305, PMS2 NM_000535 7:6013024-6013173, RANBP2 NM_006267 2:109363166-109363254, 109367779-109367838, 109367984-109368069, 109369453-109369497, 109378578-109378651, RHEB NM_005614 7:151216546-151216597, SUFU NM_001178133 10:104263911-104264039, TNFRSF14 NM_003820 1:2494304-2494335. Data was annotated against GRCh37 (hg19) reference human genome using Nirvana v3.17.0. This human reference is based on the GRCh37.p6 version of the human genome assembly.

The table below may contain a partial list of the tested DNA genes. For a complete list, please go to: <https://genomictestingcooperative.com/genomic-tests/solid-tumor-profile-plus/> (click the DNA tab)

The table below contains a partial list of the tested RNA genes (Fusions/Expression). For a complete list, please go to: <https://genomictestingcooperative.com/genomic-tests/solid-tumor-profile-plus/> (click the RNA tab)

Tested genes

Genes Tested for Abnormalities in Coding Sequence

ABCB7	ATRX	BTX	CDKN2B	DKC1	FANCA	FLI1	GREM1	INPP4B	LIG4	MSH2	NSD2 (WHSC1)	POLE	RAF1	SDHD	STAG2	TP53
ABL1	AURKA	CALR	CDKN2C	DNM2	FANCB	FLT1	GRIN2A	IRF2	LMO1	MSH6	NTRK1	POT1	RANBP2	SEC23B	STAT3	TRAF3
ABL2	AURKB	CARD11	CEBPA	DNMT3A	FANCC	FLT3	GRM3	IRF4	LPIN2	MTOR	NTRK2	PPM1D	RARA	SETBP1	STAT4	TSC1
ABRAXAS1	AURKC	CBFB	CHD2	DOT1L	FANCD2	FLT4	GSK3B	IRS2	LRP1B	MUTYH	NTRK3	PPP2R1A	RB1	SETD2	STAT6	TSC2
ACD	AXIN1	CBL	CHD4	EED	FANCE	FOXJ2	GSKIP	JAGN1	LYN	MVK	NUP93	PRDM1	RBBP6	SF3B1	STK11	TSHR
ACVR1B	AXIN2	CBLB	CHEK1	EGFR	FANCF	FOXPI	H3-3A (H3F3A)	JAK1	LYST	MYC	PAK3	PREX2	RBM10	SLIT2	SUFU	U2AF1
ADA	AXL	CBLG	CHEK2	EGLN1	FANCG	FRS2	H3C2	JAK2	LZTR1	MYCL	PALB2	PRKAR1A	RBM8A	SLX4	SUZ12	U2AF2
ADGRA2	B2M	CCN6 (WISP3)	CIC	ELANE	FANCI	FUBP1	HAX1	JAK3	MAGI2	MYCN	PAX5	PRKCI	REEP5	SMAD2	SYK	VEGFA
AK2	BAP1	CCND1	CREBBP	EMSY	FANCL	G6PC3	HGF	JUN	MAP2K1	MYD88	PBRM1	PRKDC	RET	SMAD3	TAF1	VHL
AKT1	BARD1	CCND2	CRKL	EP300	FANCM	GABRA6	HNF1A	KAT6A	MAP2K2	NBN	PDCD1LG2	PRKN (PARK2)	RHEB	SMAD4	TAL1	WAS
AKT2	BCL2	CCND3	CRLF2	EPAS1	FAS	GALNT12	HOXA11	KDM5A	MAP2K4	NF1	PDGFRA	PRSS1	RHOA	SMAD9	TBX3	WT1
AKT3	BCL2L1	CCNE1	CSF1R	EPCAM	FAT1	GATA1	HOXB13	KDM5C	MAP3K1	NF2	PDGFRB	PRSS8	RICTOR	SMARCA4	TCF3	XP01
ALK	BCL2L2	CD274	CSF3R	EPHA3	FBXW7	GATA2	HRAS	KDM6A	MAP3K14	NFE2L2	PDK1	PSTPIP1	RIT1	SMARCB1	TCIRG1	XRCC2
AMER1	BCL6	CD79A	CTC1	EPHA5	FGF10	GATA3	HSD3B1	KDR	MAPK1	NFKBIA	PHF6	PTCH1	RNF168	SMC1A	TENT5C (FAM46C)	XRCC3
ANKRD26	BCOR	CD79B	CTCF	EPHA7	FGF14	GATA4	HSP90AA1	KEAP1	MCL1	NHP2	PIK3C2B	PTEN	RNF43	SMC3	TERC	ZBTB2
APC	BCORL1	CDAN1	CTNNA1	EPHB1	FGF19	GATA6	ID3	KEL	MDM2	NKX2-1	PIK3CA	PTPN11	ROS1	SMG	TERF1	ZNF217
AR	BCR	CDC73	CTNNA1	EPHB2	FGF23	GEN1	IDH1	KIF23	MDM4	NLRP3	PIK3CB	QKI	RPTOR	SNCAIP	TERF2	ZNF703
ARAF	BIRC3	CDH1	CUL3	ERBB3	FGF3	GFI1	IDH2	KIT	MED12	NME1	PIK3CG	RAB27A	RTEL1	SOC1	TERF2IP	ZRSR2
ARFRP1	BLM	CDIN1 (C15orf41)	CUX1	ERBB4	FGF4	GFI1B	IGF1R	KLF1	MEF2B	NOP10	PIK3R1	RAC1	RUNX1	SOX10	TERT	-
ARID1A	BMPRI1A	CDK12	CXCR4	ERCC4	FGF6	GID4	IGF2	KLHL6	MEFV	NOTCH1	PIK3R2	RAD21	RUNX1T1	SOX2	TET2	-
ARID1B	BRAF	CDK4	CYLD	ERG	FGFR1	GLI1	IKBKE	KLLN	MEN1	NOTCH2	PIM1	RAD50	SAMD9L	SOX9	TGFB2	-



GOVERNMENT OF INDIA
MINISTRY OF DEFENCE

OFFICE OF THE SECRETARY
DEFENCE SECRETARIAT

NEW DELHI

SECRET

TO: THE CHIEF OF THE ARMY STAFF
HEADQUARTERS, NEW DELHI

FROM: THE SECRETARY

REF: [Reference Number]

1. The following information is being furnished for your information:

2. The [Subject] is [Details]

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ARID2	BRCA1	CDK6	DAXX	ERBB1	FGFR2	GLI2	IKZF1	KMT2A	MET	NOTCH3	PLCG1	RAD51	SBDS	SPEN	TNFAIP3	-
ASXL1	BRCA2	CDK8	DDR2	ESR1	FGFR3	GNA11	IKZF3	KMT2B	MITF	NPM1	PLCG2	RAD51B	SBF2	SPOP	TNFRSF14	-
ATG2B	BRD4	CDKN1A	DDX11	ETV6	FGFR4	GNA13	IL2RG	KMT2C	MLH1	NROB1	PMS1	RAD51C	SDHA	SPTA1	TNFRSF1A	-
ATM	BRIP1	CDKN1B	DDX41	EXO1	FN	GNAQ	IL7R	KMT2D	MPL	NRAS	PMS2	RAD51D	SDHB	SRC	TOP1	-
ATR	BTG1	CDKN2A	DICER1	EZH2	FLCN	GNAS	INHBA	KRAS	MRE11	NSD1	POLD1	RAD54L	SDHC	SRSF2	TOP2A	-

RNA Fusions/Expression

Fusion/Expression															
ABL1	BCL6	CD274 (PD-L1)	EGFR	EWSR1	FLI1	IKZF3	MAP3K1	NRG1	NUP98	PML	RET	SS18	THADA		
AKT3	BRAF	CIC	ERG	FGFR1	FOXO1	JAK2	MECOM	NTRK1	PAX8	PPARG	RHOA	STAT6	TMPSR2		
ALK	CAMTA1	CREB1	ETS1	FGFR2	FUS	KIAA1549	MYB	NTRK2	PDGFRA	PRKACA	ROS1	TAL1	YAP1		
AR	CBFB	CREBBP	ETV1	FGFR3	GLI1	KMT2A	MYC	NTRK3	PDGFRB	RAF1	RUNX1	TCF3	YWHAE		
BCL2	CCND1	ERBB2	ETV6	FIP1L1	HMG2	MAML2	NOTCH1	NUP214	PICALM	RARA	RUNX1T1	TFG	ZFTA		

Reference

1. Tumour and microenvironment crosstalk in NSCLC progression and response to therapy. Rahal Z, El Darzi R, Moghaddam SJ, Cascone T, Kadara H. Nat Rev Clin Oncol. 2025 Jul;22(7):463-482. doi: 10.1038/s41571-025-01021-1. Epub 2025 May 16. PMID: 40379986.
2. Recent advances in therapeutic strategies for non-small cell lung cancer. Su PL, Furuya N, Asrar A, Rolfo C, Li Z, Carbone DP, He K. J Hematol Oncol. 2025 Mar 27;18(1):35. doi: 10.1186/s13045-025-01679-1. PMID: 40140911.

Electronic Signature

Ahmad Charifa, M.D.

Genomic Testing Cooperative, LCA serves as the coordinating laboratory for this assay and is responsible for overall test performance and reporting. The test (sample processing, sequencing and data generation) was performed at Genomic Testing Cooperative, LCA, 25371 Commercentre Drive Lake Forest, CA 92630. Medical Director: Maher Albitar, M.D. Analysis of the data was performed by Genomic Testing Cooperative, LCA, 25371 Commercentre Drive, Lake Forest, CA 92630. Medical Director: Maher Albitar, M.D. (CLIA #: 05D2111917 CAP #: 9441574). The signing pathologist is responsible for the accuracy and interpretation of results and the release of this report.

The test was developed and its performance characteristics have been determined by Genomic Testing Cooperative, LCA. This test has not been approved by the FDA. The FDA has determined such clearance or approval is not necessary. This laboratory is CLIA certified to perform high complexity clinical testing.



المستشفى الاستشاري
Istishari Hospital

Patient Name: Samir Hameed Majeed	Exam Date & Time: 6:25 PM 4/11/2026
Patient ID: 425209	Accession: 17192437
Date Of Birth: 4/13/1958	
Gender: M	
Age: 67Y 11M	

BRAIN CT

No evidence of focal parenchymal lesion or acute hemorrhage.

Ventricular system appears normal to the age.

Normal basilar cisterns.

Normal brain stem and cerebellum.

No shift in the midline structures.

No epidural or subdural collections .

After administration of I.V. contrast , a tiny ill-defined non-mass-like patchy enhancement seen in the right parietal lobe superiorly and posteriorly, which could suggest an enhanced vessel, less likely enhanced lesion, for followup.

no evidence of other abnormal leptomeningeal or parenchymal enhancement could be seen .

NECK CT

No evidence of pharyngeal or laryngeal masses .

Intact post nasal and para-pharyngeal spaces .

Unremarkable salivary glands .

No evidence of significant neck lymphadenopathy .

No evidence of soft tissue masses or fluid collections

CHEST CT

Almost total collapse of the left lung, with a few residual air bronchograms seen in the lower lobe, with evidence of an ill-defined area of soft tissue density seen at the infrahilar region on the left side, inseparable from the rest of the collapsed lung, however, it shows a distorted pulmonary architecture, with no obvious traversing vessels and appears slightly hyperdense in comparison with the Adjacent lung tissue, it measures roughly about 4 cm in diameter, after the administration of IV contrast, it shows less enhancement than the rest of the collapsed lung, findings could suggest a tumoral mass , however, the possibility of necrotic pneumonic infiltration could not be ruled out , for followup.

There is evidence of an ill-defined small soft tissue fullness seen at the distal end of the left main bronchus, with resultant abrupt cut-off of the bronchus at the level of the soft tissue density, (endobronchial invasion of the above-mentioned mass? Solitary endobronchial mass? Less likely mucous plug?)

Left-sided pleural effusion is noted.

Shifting of the mediastinal structure toward the left side, secondary to the total left lung collapse.

Multiple peripherally emphysematous bullae with fibrotic changes involving the right lung apex.

Also atelectatic bands with slight patchy opacity seen in the right lung base suggesting mild inflammatory changes.

The rest of the right lung field appears unremarkable with no evidence of obvious masses or lesions.

Few mediastinal and bilateral hilar lymph nodes are noted, the largest one measures about 2cm and located in the right hilum.

No right-sided pleural effusion.

The heart is not enlarged.

ABDOMEN AND PELVIC CT

A small hiatal hernia is noted.

The liver appears normal with no focal lesion or biliary tree dilatation.

Patent spleno-portal venous system.

Normal spleen and pancreas.

Normal both kidneys and supra renal glands.
Unremarkable abdominal aorta and its major branches.
Unremarkable bowel loops.
The prostate appears enlarged.
The urinary bladder shows diffuse wall thickening.
Clear mesenteric fat.
No abdominal or pelvic lymphadenopathy , masses or fluid collections.

No obvious bony lesions could be seen in the obtained bony structures.

Solid Tumor Profile Plus

Patient Name: Hameed Majeed Majeed, Sameer Ordering Physician: Omar Al Rawi
Date of Birth: 01/01/1958 Accession #: 209933
Gender (M/F): M Specimen Type: TISSUE
Client: Tahleel Laboratories Technical Cons LLC Specimen ID: H26-613
Case #: NGS26-008215
Body Site: LUNG

MRN: 1794053 Tumor Type: small cell lung cancer
Collected Date: 04/25/2026 Time: 12:00 AM
Received Date: 04/30/2026 Time: 12:20 PM
Reported Date: 05/15/2026 Time: 05:06 PM

Detected Genomic Alterations

Level 1 (FDA-Approved)	Level 2 (Standard of Care)	Level 3 (Clinical Evidence)	Level 4 (Biological Evidence)	Other
Tumor Mutation Burden High: 12 Mut/Mb	-Homologous recombination deficiency (HRD): Positive-High -No evidence of microsatellite instability	TP53, APC, SETD2, SUZ12, LYN	NKX2-1, DDX11, GALNT12, ABCG2 (?Germline), ASTN2 (?Germline)	-t(17;17)(q21;q21) LSM12::ETV4 fusion mRNA -Autosomal chromosomal structural analysis shows 3p-, 3q+, -4, 5q-, +8, -9, -10, -11, 13q-, 15q-, 19p- (distal)

Results Summary

- Somatic mutations in TP53, APC, SETD2, NKX2-1, SUZ12, LYN, DDX11, and GALNT12 genes
- Possible germline mutation in ABCG2 and ASTN2 gene, heterozygous
- Tumor Mutation Burden High: 12 Mut/Mb
- Homologous recombination deficiency (HRD): Positive-High
- No evidence of microsatellite instability
- No evidence of EGFR, KRAS, BRAF, MET, ALK or ERBB2 mutations
- No evidence of fusion mRNA involving ALK, RET, ROS1, or NTRK
- EBV, HPV, TTV, and HTLV1 viral mRNA: Not detected
- HLA Genotyping:
 - HLA-A: A*24:03-A*24:03
 - HLA-B: B*44:02-B*18:01
 - HLA-C: C*16:04-C*12:03
- Autosomal chromosomal structural analysis shows 3p-, 3q+, -4, 5q-, +8, -9, -10, -11, 13q-, 15q-, 19p- (distal)
- Increased CK, MET mRNA
- High TMB suggests response to immune checkpoint inhibitors.

- Positive homologous recombination deficiency (HRD) suggests response to platinum-based chemotherapy and PARP inhibitors.
- APC mutation activates beta-catenin and WNT signaling pathway and suggests possible response to WNT and COX-2 inhibitors.
- SETD2 mutation suggests response to wee1 inhibitors.
- TP53 mutation suggests possible response to eprenetapopt (APR-246), Aurora kinase A and Wee1 inhibitors.
- The ABCG2 mutation is detected at high level raising the possibility of a germline abnormality. This gene is involved in membrane transport and possibly associated with drug response.
- The ASTN2 mutation is detected at high level, raising the possibility of a germline mutation. This mutation leads to early termination (loss of function). However, there is no data on its clinical relevance and should be classified as of "uncertain significance" at this time.
- See additional report information at the end of the report**

Tumor Heterogeneity

There are dominant abnormal clones with TP53, APC, SETD2, and NKX2-1 mutations. The SUZ12 and LYN mutations are detected in subclones. There are abnormal low-level clones with DDX11 and GALNT12 mutations.
 The ABCG2 and ASTN2 mutations are detected at high levels, possible germline abnormalities.

Expression

Increased CK, MET mRNA

Diagnostic Implications

TP53, APC, SETD2,
 NKX2-1, SUZ12, LYN,
 DDX11, GALNT12,
 ABCG2, ASTN2

The findings are consistent with aggressive neoplasm.
 The ABCG2 and ASTN2 mutations are likely germline variants.

FDA-Approved Therapeutics

TMB-High	Pembrolizumab
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FDA-Approved Therapeutics in Other Tumor Types

HRD Positive	Niraparib + platinum-based chemotherapy
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Relevant Alteration Associated with Resistance

TP53 mutation is associated with resistance to therapy.

Levels 2, 3 & 4 (Standard of Care and Clinical/Biological Evidence)

TP53	Aurora kinase A inhibitors, Wee1 inhibitors, Chk1 inhibitors, kevetrin, APR-246, nutlins, gene therapy
APC	WNT, beta-catenin, and COX-2 inhibitors
SETD2	SETD2 mutation suggests response to WEE1 inhibitors
SUZ12	SUZ12 mutation may suggest sensitivity to bromodomain inhibitors.
LYN	Src family kinase inhibitors
TMB-High	Immunotherapy with checkpoint inhibitor
HRD Positive	PARP Inhibitors & Platinum based chemotherapy

Relevant Genes with NO Alteration

-No evidence of mutation in KRAS, NRAS, EGFR, BRAF, or BRCA 1/2 -No specific mutation in DPYD gene, associated with enzymatic deficiency	No evidence of fusion mRNA involving ALK, RET, ROS1, or NTRK	-No evidence of METex14 skipping or EGFRvIII -No evidence of ERBB2 (HER2) amplification
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Test Description:

This is a comprehensive molecular profile which uses next generation sequencing (NGS) to identify molecular abnormalities, including single nucleotide variants (SNVs), insertions/deletions (indels), copy number variants (CNVs), fusions, tumor mutational burden (TMB), microsatellite instability (MSI), homologous recombination deficiency (HRD), B- and T-cell clonality, and viruses (HPV, EBV, HTLV1, and TTV), in DNA of 434 genes and RNA in greater than 1600 genes implicated in solid tumors. Whenever possible, clinical relevance and implications of detected abnormalities are described below.

Biological relevance of detected Alterations

- TP53. This gene encodes a tumor suppressor protein containing transcriptional activation, DNA binding, and oligomerization domains. The encoded protein responds to diverse cellular stresses to regulate expression of target genes, thereby inducing cell cycle arrest, apoptosis, senescence, DNA repair, or changes in metabolism. Mutations in this gene are associated with a variety of human cancers, including hereditary cancers such as Li-Fraumeni syndrome. Alternative splicing of this gene and the use of alternate promoters result in multiple transcript variants and isoforms. Additional isoforms have also been shown to result from the use of alternate translation initiation codons from identical transcript variants (PMIDs: 12032546, 20937277). [provided by RefSeq, Dec 2016]
- APC. This gene encodes a tumor suppressor protein that acts as an antagonist of the Wnt signaling pathway. It is also involved in other processes including cell migration and adhesion, transcriptional activation, and apoptosis. Defects in this gene cause familial adenomatous polyposis (FAP), an autosomal dominant pre-malignant disease that usually progresses to malignancy. Mutations in the APC gene have been found to occur in most colorectal cancers. Disease-associated mutations tend to be clustered in a small region designated the mutation cluster region (MCR) and result in a truncated protein product. [provided by RefSeq, Dec 2019]
- SETD2. Huntington's disease (HD), a neurodegenerative disorder characterized by loss of striatal neurons, is caused by an expansion of a polyglutamine tract in the HD protein huntingtin. This gene encodes a protein belonging to a class of huntingtin interacting proteins characterized by WW motifs. This protein is a histone methyltransferase that is specific for lysine-36 of histone H3, and methylation of this residue is associated with active chromatin. This protein also contains a novel transcriptional activation domain and has been found associated with hyperphosphorylated RNA polymerase II. [provided by RefSeq, Aug 2008]

- **NKX2-1.** This gene encodes a protein initially identified as a thyroid-specific transcription factor. The encoded protein binds to the thyroglobulin promoter and regulates the expression of thyroid-specific genes but has also been shown to regulate the expression of genes involved in morphogenesis. Mutations and deletions in this gene are associated with benign hereditary chorea, choreoathetosis, congenital hypothyroidism, and neonatal respiratory distress, and may be associated with thyroid cancer. Multiple transcript variants encoding different isoforms have been found for this gene. This gene shares the symbol/alias 'TTF1' with another gene, transcription termination factor 1, which plays a role in ribosomal gene transcription. [provided by RefSeq, Feb 2014]
- **SUZ12.** This zinc finger gene has been identified at the breakpoints of a recurrent chromosomal translocation reported in endometrial stromal sarcoma. Recombination of these breakpoints results in the fusion of this gene and JAZF1. The protein encoded by this gene contains a zinc finger domain in the C terminus of the coding region. [provided by RefSeq, Jul 2009]
- **LYN.** This gene encodes a tyrosine protein kinase, which maybe involved in the regulation of mast cell degranulation, and erythroid differentiation. Alternatively spliced transcript variants encoding different isoforms have been found for this gene. [provided by RefSeq, Jul 2011]
- **DDX11.** DEAD box proteins, characterized by the conserved motif Asp-Glu-Ala-Asp (DEAD), are putative RNA helicases. They are implicated in a number of cellular processes involving alteration of RNA secondary structure such as translation initiation, nuclear and mitochondrial splicing, and ribosome and spliceosome assembly. Based on their distribution patterns, some members of this family are believed to be involved in embryogenesis, spermatogenesis, and cellular growth and division. This gene encodes a DEAD box protein, which is an enzyme that possesses both ATPase and DNA helicase activities. This gene is a homolog of the yeast CHL1 gene, and may function to maintain chromosome transmission fidelity and genome stability. Alternative splicing results in multiple transcript variants encoding distinct isoforms. [provided by RefSeq, Jul 2008]
- **GALNT12.** This gene encodes a member of a family of UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferases, which catalyze the transfer of N-acetylgalactosamine (GalNAc) from UDP-GalNAc to a serine or threonine residue on a polypeptide acceptor in the initial step of O-linked protein glycosylation. Mutations in this gene are associated with an increased susceptibility to colorectal cancer. [provided by RefSeq, Mar 2011]
- **ABCG2.** The membrane-associated protein encoded by this gene is included in the superfamily of ATP-binding cassette (ABC) transporters. ABC proteins transport various molecules across extra- and intra-cellular membranes. ABC genes are divided into seven distinct subfamilies (ABCI, MDR/TAP, MRP, ALD, OABP, GCN20, White). This protein is a member of the White subfamily. Alternatively referred to as a breast cancer resistance protein, this protein functions as a xenobiotic transporter which may play a major role in multi-drug resistance. It likely serves as a cellular defense mechanism in response to mitoxantrone and anthracycline exposure. Significant expression of this protein has been observed in the placenta, which may suggest a potential role for this molecule in placenta tissue. Multiple transcript variants encoding different isoforms have been found for this gene. [provided by RefSeq, Apr 2012]
- **ASTN2.** This gene encodes a protein that is expressed in the brain and may function in neuronal migration, based on functional studies of the related astrotactin 1 gene in human and mouse. A deletion at this locus has been associated with schizophrenia. Multiple transcript variants encoding different proteins have been found for this locus. [provided by RefSeq, May 2010]

Drug Information

Pembrolizumab (Keytruda)

Pembrolizumab is a highly selective IgG4-kappa humanized monoclonal antibody against PD-1 receptor. It was generated by grafting the variable sequences of a very high-affinity mouse antihuman PD-1 antibody onto a human IgG4-kappa isotype with the containing a stabilizing S228P Fc mutation.

Olaparib (Lynparza)

Olaparib (Lynparza) is an antineoplastic agent, Poly(ADP-ribose) Polymerase 1;2;3 inhibitor. (PARP1;2;3 inhibitor).

Lynparza is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated for the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza.

Talazoparib

Talazoparib is a poly(ADP-ribose) Polymerase 1, 2 (PARP 1;2 inhibitor).

Talazoparib was approved by the FDA for use in germline BRCA mutated, HER2 negative, locally advanced or metastatic breast cancer on October 16, 2018 under the trade name Talzenna. Talazoparib prevents PARP-mediated repair of DNA damage in cancer cells, allowing accumulation of damage and PARP-DNA complexes. Repair related errors by error prone secondary repair pathways may also contribute to the cytotoxicity of Talazoparib. Talazoparib is indicated for the treatment of deleterious or suspected deleterious germline BRCA mutated, HER2 negative locally advanced or metastatic breast cancer in adults.

Niraparib (Zejula)

Niraparib (ZEJULA) is an inhibitor of poly (ADP-ribose) polymerase (PARP) with potential antineoplastic activity. PARP Inhibitor MK4827 inhibits PARP activity, enhancing the accumulation of DNA strand breaks and promoting genomic instability and apoptosis. The PARP family of proteins detect and repair single strand DNA breaks by the base-excision repair (BER) pathway. The specific PARP family member target for PARP inhibitor MK4827 is unknown. (NCI Thesaurus)

ZEJULA is a poly(ADP-ribose) polymerase (PARP) inhibitor indicated for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.

Rucaparib (Rubraca)

Rucaparib is a potent mammalian poly(ADP-ribose) polymerase 1, 2 and 3 inhibitor with anticancer properties (PARP 1;2;3 inhibitor).

Rucaparib is an inhibitor of PARP-1, PARP-2, and PARP-3. Via an inhibitory effect on the PARP enzymatic activity, rucaparib decreases the formation of PARP-DNA complexes resulting in DNA damage, apoptosis, and cell death. It is proposed that PARP inhibition specifically targets tumor cells with preexisting HRD, such as those cells possessing mutations in the BRCA1 or BRCA2 genes.

APR-246

APR-246 is a first-in-class agent targeting mutant p53. In vitro and in vivo preclinical models have demonstrated that APR-246 has excellent efficacy in OC (both adenocarcinoma and squamous cell carcinoma) and potentially synergises with chemotherapies used in the treatment of OC, restoring sensitivity to chemotherapy-resistant tumours. An initial phase I clinical trial has shown APR-246 to be safe in humans and early results from a currently running phase Ib/II trial of APR-246 with carboplatin and liposomal doxorubicin in ovarian cancer have been promising. Together, these data provide a strong rationale for investigating the efficacy of APR-246 in OC.

APR-246 has been used in trials studying the treatment of Prostatic Neoplasms, Hematologic Neoplasms, and Platinum Sensitive Recurrent High-grade Serous Ovarian Cancer With Mutated p53.

APR-246 is an analogue of PRIMA-1, which modifies the core domain of mutant p53, resulting in restoration of wild-type p53 conformation and reactivation of normal p53 function, leading to increased cell cycle arrest and tumor cell death (PMID: 20498645).

Sulindac

Sulindac is a COX-1/COX-2 inhibitor. It is being evaluated as a potential cancer chemo-preventive and therapeutic drug in clinical trials for a variety of malignancies.

Celecoxib

Celecoxib is a selective cyclooxygenase-2 (COX-2) inhibitor, is a nonsteroidal anti-inflammatory drug (NSAID). It is used to manage symptoms of various types of arthritis pain and in familial adenomatous polyposis (FAP) to reduce precancerous polyps in the colon. It is marketed by Pfizer under the brand name Celebrex, and was initially granted FDA approval in 1998. Interestingly, selective COX-2 inhibitors (especially celecoxib), have been evaluated as potential cancer chemopreventive and therapeutic drugs in clinical trials for a variety of malignancies.

Birabresib

Birabresib (OTX015 or MK-8628) is a potent BET bromodomain inhibitor, which targets the BET bromodomain proteins 2, 3, and 4 (BRD2/3/4). BRDs 2, 3, and 4 are considered potential cancer targets because of their pivotal role in regulating the transcription of growth-promoting genes and cell cycle regulators. OTX015 is the first BRD2/3/4 inhibitor to enter clinical trials. Upon administration, birabresib binds to the acetylated lysine recognition motifs on the bromodomain of BET proteins, thereby preventing the interaction between the BET proteins and acetylated histone peptides. This disrupts chromatin remodeling and gene expression.

Imatinib

Imatinib is indicated treatment of Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML), Ph+ acute lymphoblastic leukaemia, myelodysplastic/myeloproliferative diseases, aggressive systemic mastocytosis, hypereosinophilic syndrome and/or chronic eosinophilic leukemia (CEL), dermatofibrosarcoma protuberans, and malignant gastrointestinal stromal tumors (GIST). It inhibits proliferation and induces apoptosis in Bcr-Abl positive cell lines as well as fresh leukemic cells from Philadelphia chromosome positive chronic myeloid leukemia. Imatinib also inhibits the receptor tyrosine kinases for platelet derived growth factor (PDGF) and stem cell factor (SCF) - called c-kit.

Dasatinib

Dasatinib is an oral dual BCR-ABL and Src family tyrosine kinase inhibitor approved for use in patients with CML, ALL, and MPN. The main targets of Dasatinib are BCR-ABL, SRC, Ephrins and GFR. Dasatinib, at nanomolar concentrations, inhibits the following kinases: BCR-ABL, SRC family (SRC, LCK, YES, FYN), c-KIT, EPHA2, and PDGFRA. Based on modeling studies, dasatinib is predicted to bind to multiple conformations of the ABL kinase. In vitro, dasatinib was active in leukemic cell lines representing variants of imatinib mesylate sensitive and resistant disease. Dasatinib inhibited the growth of chronic myeloid leukemia (CML) and acute lymphoblastic leukemia (ALL) cell lines overexpressing BCR-ABL.

Nilotinib

Nilotinib is a transduction inhibitor that targets BCR-ABL, c-kit and PDGF, for the potential treatment of various leukemias, including chronic myeloid leukemia (CML).

Bosutinib

Bosutinib is a tyrosine kinase inhibitor. Although it is able to inhibit several tyrosine kinases such as Src, Lyn, and Hck, which are members of the Src-family of kinases, its primary target is the Bcr-Abl kinase.

The Bcr-Abl gene is a chimeric oncogene created from the fusion of the breakpoint-cluster (Bcr) gene and Abelson (Abl) tyrosine gene. This chromosomal abnormality results in the formation of what is commonly known as the Philadelphia chromosome or Philadelphia translocation. The Bcr-Abl gene expresses a particular kinase that promotes the progression of CML. A decrease in the growth and size of the CML tumour has been observed following administration of bosutinib. Bosutinib did not inhibit the T315I and V299L mutant cells.

Potential Clinical Trials

Trial URL	Status	Title	Disease	Drug	Sites
https://clinicaltrials.gov/study/NCT05902988	Recruiting	A Phase I/II Study of VLS-1488 (an Oral KIF18A Inhibitor) in Subjects With Advanced Cancer	Lung Cancer	VLS-1488	Memorial Sloan Kettering Cancer Center, New York, New York 10065
https://clinicaltrials.gov/study/NCT07444814	Recruiting	A Phase 1 First-in-Human Study of PTK7-Directed Antibody Drug Conjugate HWK-007 in Participants With Advanced Solid Tumors	Lung Cancer	HWK-007	Hackensack University Medical Center - John Theurer Cancer Center, Hackensack, New Jersey 07601
https://clinicaltrials.gov/study/NCT07397338	Recruiting	A Phase 1/2 Open-Label, Multicenter Study of RAS(ON) Inhibitors in Combination With Ivonescimab With or Without Other Anti-Cancer Agents in Patients With Solid Tumors	Lung Cancer	Daraxonrasib, Elironrasib, Zoldonrasib, Ivonescimab, Carboplatin/Cisplatin + Pemetrexed (Dose Expansion Only), cetuximab (Cohort C2 Only), Carboplatin/Cisplatin + Pemetrexed (Cohort B2 Only), Daraxonrasib (Cohort B1 only)	NEXT Virginia, Fairfax, Virginia 22031

Detailed Results

Single Nucleotide Variant (SNV) and Insertions-Deletions (INDELS)								
Gene name	Hgvsp	Hgvsc	Amino acids	Codons	Consequence	Allele frequency	Read depth	Predicted effect on protein
TP53	0	NM_000546.5:c.375+1G>A	0	0	splice_donor_variant	85.66	244	0
APC	NP_000029.2:p.Ser1344Ter	NM_000038.5:c.4031C>A	S/*	tCa/tAa	stop_gained	74.42	473	0
SETD2	NP_054878.5:p.Ser185Ter	NM_014159.6:c.554C>G	S/*	tCa/tGa	stop_gained	64.96	234	0
NKX2-1	NP_001073136.1:p.Ala146Val	NM_001079668.2:c.437C>T	A/V	gCc/gTc	missense_variant	62.07	29	deleterious

SUZ12	NP_056170.2:p. Arg555Ter	NM_015355.2:c. 1663A>T	R/*	Aga/Tga	stop_gained	40.86	1050	0
LYN	0	NM_001111097. 2:c.321-5C>T	0	0	"splice_region_varia nt,intron_variant"	29.67	1109	0
DDX11	NP_001244073. 1:p.Tyr202Cys	NM_001257144. 1:c.605A>G	Y/C	tAc/tGc	missense_variant	10.17	344	deleterious
GALNT12	NP_078918.3:p. Cys10Arg	NM_024642.4:c. 28T>C	C/R	Tgc/Cgc	missense_variant	8.92	213	deleterious - low confidence
ABCG2 (RNA)	NP_004818.2:p. Gln141Lys	NM_004827.2:c. 421C>A	Q/K	Cag/Aag	missense_variant	100.0	126	tolerated
ASTN2 (RNA)	NP_937831.1:p. Ser390Ter	NM_198188.2:c. 1169C>A	S/*	tCa/tAa	stop_gained	89.63	241	0

Methodology and Test Background

This is a next generation sequencing (NGS) test that involves separate analysis of DNA and RNA panels for abnormalities that are reported to be altered in various types of solid tumors. The DNA panel is composed of 434 genes and the RNA panel is composed of >1600 genes. The DNA and RNA components of this assay were developed, validated, and set up as separate workflows, with independent extraction, library preparation, sequencing, and analysis pipelines. The NGS assay also detects several viruses that are important in oncology, including EBV, HPV, HTLV1, and TTV. TTV (torque teno virus) was first discovered in a patient with non-A-E hepatitis and is now regarded as a part of the human virome. In general, TTV does not cause pathology in immunocompetent individuals. TTV is considered as a marker of immune competence in patients with immunological impairment and inflammatory disorders. High TTV load is associated with increased risk of infection. In patients with organ transplant, low TTV load is associated with an increased risk of rejection.

Nucleic acid is isolated from paraffin-embedded tissue. For optimal results neoplastic cells should be greater than 30% of the analyzed cells. H&E-sections are reviewed by a pathologist and tumor-enrichment is performed by macrodissection when possible. Testing is performed using massive parallel sequencing of the coding DNA of the listed genes. This includes sequencing of all the exons as well as approximately 50 nucleotides at the 5' and 3' ends of each coding exon to detect splice site abnormalities. The TERT promoter region, including the hotspots at -124 and -146 bp, is also covered. Our DNA sequencing method has a sensitivity of 3% for detecting hotspot mutations and 5% for detecting single nucleotide variants (SNVs) and small (<60 bp) insertions/ deletions (indels). MSI status is inferred by interrogating all available genomic microsatellites covered. Borderline MSI results by NGS are confirmed by fragment analysis. Tumor mutational burden (TMB) is measured by counting all nonsynonymous variants and filter settings as follows: (A) Pass all filters; (B) inside genes; (C) had a mutant allele frequency >5%; (D) not found in the dbSNP (to exclude germline variations). The median for TMB is 10 mutations/Mb based on lung carcinoma analysis. The cut off for other types of tumors is not well-established at this time. Significant gene amplification and deletion (copy number variants) are also reported. Targeted RNA NGS is performed by hybrid capture and duplicates are excluded for levels measurements. The Universal Human Reference (UHR) RNA is used as control. All detected fusion transcripts are reported. While the major focus of the RNA analysis is the detection of fusion mRNA, mutations in the expressed RNA of the analyzed genes, HLA class I genotyping, and Epstein-Barr virus (EBV), human papillomavirus (HPV), human T-lymphotropic virus type-1 (HTLV1), and torque teno virus (TTV) viral RNA are also analyzed and reported. B- and T-cell clonality will be reported, if clonal or clinically relevant. The sensitivity of this assay in detecting fusion mRNA is between 5% and 10%. This test specifically covers translocations that lead to the expression of fusion RNA. Translocations that lead to deregulation of expression can be addressed by this test if compared to the expression proper normal control. Since the clinical relevance of the RNA expression level of most of the genes is not characterized at this time, only a few specific genes will be commented on when abnormalities are detected. CD274 (PD-L1) mRNA levels are reported when they are significantly elevated. This assay is not designed to detect minimal residual disease and should be used for diagnosis. Performance of the assays may vary dependent on the quantity and quality of nucleic acid, sample preparation and sample age. Decalcified specimens have not been validated. Decalcification with strong acids is not recommended and may lead to poor nucleic acid quality and suboptimal results. The testing is not validated to detect germline abnormalities. Potential germline mutations detected incidentally should be confirmed by tests specifically designed for detecting germline abnormalities.

Based on our validation study, the following exonic regions of the genes listed below are not covered appropriately <100X coverage and sequencing by NGS may not be reliable in these regions. The poor coverage is primarily due to the inherent difficulty in obtaining adequate sequencing coverage in regions with high GC content. No well-characterized hotspots are present in these regions. ASXL1 NM_001164603 20:30946620-30946635, ATM NM_000051 11:108186550-108186638, BAP1 NM_004656 3:52443858-52443894, BCR NM_004327 22:23652510-23652620, BRD4 NM_058243 19:15353808-15354193,5355041-15355411, CCNE1 NM_001238 19:30303463-30303485, CD274 NM_001267706 9:5456109-5456165, CD79A NM_001783 19:42384736-42384805, CSF3R NM_000760 1:36937667-36937740, DDX11 NM_001257144 12:31240872-31240917, ERBB3 NM_001982 12:56492284-56492359, FANCI NM_001113378 15:89835919-89836052, FLT3 NM_004119 13:28674605-28674652, FLT4 NM_002020 5:180035281-180035284, GEN1 NM_001130009 2:17954486-17954525, H3-3A NM_002107 1:226259140-226259180, IRS2 NM_003749 13:110437126-110437363, 110437805-110437899, 110438359-110438400, JAK1 NM_002227 1:65309747-65309771, MAGI2 NM_012301 7:77648719-77649044, MITF NM_000248 3:70005606-70005681, MYCL NM_001033081 1:40367518-40367565, NF1 NM_000267 17:29664837-29664898, NOTCH2 NM_001200001 1:120572528-120572610, PBRM1 NM_018313 3:52677264-52677322, PIK3R2 NM_005027 19:18272089-18272305, PMS2 NM_000535 7:6013024-6013173, RANBP2 NM_006267 2:109363166-109363254, 109367779-109367838, 109367984-109368069, 109369453-109369497, 109378578-109378651, RHEB NM_005614 7:151216546-151216597, SUFU NM_001178133 10:104263911-104264039, TNFRSF14 NM_003820 1:2494304-2494335. Data was annotated against GRCh37 (hg19) reference human genome using Nirvana v3.17.0. This human reference is based on the GRCh37.p6 version of the human genome assembly.

The table below may contain a partial list of the tested DNA genes. For a complete list, please go to:

<https://genomictestingcooperative.com/genomic-tests/solid-tumor-profile-plus/> (click the DNA tab)

The table below contains a partial list of the tested RNA genes (Fusions/Expression). For a complete list, please go to:

<https://genomictestingcooperative.com/genomic-tests/solid-tumor-profile-plus/> (click the RNA tab)

Tested genes

Genes Tested for Abnormalities in Coding Sequence

ABCB7	ATRX	BTK	CDKN2B	DKC1	FANCA	FLT1	GREM1	INPP4B	LIG4	MSH2	NSD2 (WHSC1)	POLE	RAF1	SDHD	STAG2	TP53
ABL1	AURKA	CALR	CDKN2C	DNM2	FANCB	FLT1	GRIN2A	IRF2	LMO1	MSH6	NTRK1	POT1	RANBP2	SEC23B	STAT3	TRAF3
ABL2	AURKB	CARD11	CEBPA	DNMT3A	FANCC	FLT3	GRM3	IRF4	LPIN2	MTOR	NTRK2	PPM1D	RARA	SETBP1	STAT4	TSC1
ABRAXAS1	AURKC	CBFB	CHD2	DOT1L	FANCD2	FLT4	GSK3B	IRS2	LRP1B	MUTYH	NTRK3	PPP2R1A	RBT1	SETD2	STAT6	TSC2
ACD	AXIN1	CBL	CHD4	EED	FANCE	FOXL2	GSKIP	JAGN1	LYN	MVK	NUP93	PRDM1	RBBP6	SF3B1	STK11	TSHR
ACVR1B	AXIN2	CBLB	CHEK1	EGFR	FANCF	FOXP1	H3-3A (H3F3A)	JAK1	LYST	MYC	PAK3	PREX2	RBM10	SLIT2	SUFU	U2AF1
ADA	AXL	CBLC	CHEK2	EGLN1	FANCG	FRS2	H3C2	JAK2	LZTR1	MYCL	PALB2	PRKAR1A	RBM8A	SLX4	SUZ12	U2AF2
ADGRA2	B2M	CCN6 (WISP3)	CIC	ELANE	FANCI	FUBP1	HAX1	JAK3	MAGI2	MYCN	PAX5	PRKCI	REEP5	SMAD2	SYK	VEGFA
AK2	BAP1	CCND1	CREBBP	EMSY	FANCL	G6PC3	HGF	JUN	MAP2K1	MYD88	PBRM1	PRKDC	RET	SMAD3	TAF1	VHL
AKT1	BARD1	CCND2	CRKL	EP300	FANCM	GABRA6	HNF1A	KAT6A	MAP2K2	NBN	POCD1LG2	PRKN (PARK2)	RHEB	SMAD4	TAL1	WAS
AKT2	BCL2	CCND3	CRLF2	EPAS1	FAS	GALNT12	HOXA11	KDM5A	MAP2K4	NF1	PDGFRA	PRSS1	RHOA	SMAD9	TBX3	WT1
AKT3	BCL2L1	CCNE1	CSF1R	EPCAM	FAT1	GATA1	HOXB13	KDM5C	MAP3K1	NF2	PDGFRB	PRSS8	RICTOR	SMARCA4	TCF3	XP01
ALK	BCL2L2	CD274	CSF3R	EPHA3	FBXW7	GATA2	HRAS	KDM6A	MAP3K14	NFE2L2	POK1	PSTPIP1	RIT1	SMARCB1	TCIRG1	XRCC2
AMER1	BCL6	CD79A	CTC1	EPHA5	FGF10	GATA3	HSO3B1	KDR	MAPK1	NFKBIA	PHF6	PTCH1	RNF168	SMC1A	TENT5C (FAM46C)	XRCC3
ANKRD26	BCOR	CD79B	CTCF	EPHA7	FGF14	GATA4	HSP90AA1	KEAP1	MCL1	NHP2	PIK3C2B	PTEN	RNF43	SMC3	TERC	ZBTB2
APC	BCORL1	CDAN1	CTNNA1	EPHB1	FGF19	GATA6	ID3	KEL	MDM2	NKX2-1	PIK3CA	PTPN11	ROS1	SMO	TERF1	ZNF217
AR	BCR	CDC73	CTNNA1	ERBB2	FGF23	GEN1	IDH1	KIF23	MDM4	NLRP3	PIK3CB	QKI	RPTOR	SNCAIP	TERF2	ZNF703
ARAF	BIRC3	CDH1	CUL3	ERBB3	FGF3	GF11	IDH2	KIT	MED12	NME1	PIK3CG	RAB27A	RTEL1	SOC1	TERF2IP	ZRSR2
ARFRP1	BLM	CDIN1 (C1orf41)	CUX1	ERBB4	FGF4	GF11B	IGF1R	KLF1	MEF2B	NOP10	PIK3R1	RAC1	RUNX1	SOX10	TERT	-
ARID1A	BMPRIA	CDK12	CXCR4	ERCC4	FGF6	GID4	IGF2	KLHL6	MEFV	NOTCH1	PIK3R2	RAD21	RUNX1T1	SOX2	TET2	-
ARID1B	BRAF	CDK4	CYLD	ERG	FGFR1	GLI1	IKBKE	KLLN	MEN1	NOTCH2	PIM1	RAD50	SAMD9L	SOX9	TGFBR2	-

ARID2	BRCA1	CDK6	DAXX	ERRF1	FGFR2	GLI2	IKZF1	KMT2A	MET	NOTCH3	PLCG1	RAD51	SBS	SPEN	TNFAIP3	-
ASXL1	BRCA2	CDK8	DDR2	ESR1	FGFR3	GNA11	IKZF3	KMT2B	MITF	NPM1	PLCG2	RAD51B	SBF2	SPOP	TNFRSF14	-
ATG2B	BRD4	CDKN1A	DDX11	ETV6	FGFR4	GNA13	IL2RG	KMT2C	MLH1	NR0B1	PMS1	RAD51C	SDHA	SPTA1	TNFRSF1A	-
ATM	BRIP1	CDKN1B	DDX41	EXO1	FH	GNAQ	IL7R	KMT2D	MPL	NRAS	PMS2	RAD51D	SDHB	SRC	TOP1	-
ATR	BTG1	CDKN2A	DICER1	EZH2	FLCN	GNAS	INHBA	KRAS	MRE11	NSD1	POLD1	RAD54L	SDHC	SRSF2	TOP2A	-

RNA Fusions/Expression

Fusion/Expression													
ABL1	BCL6	CD274 (PD-L1)	EGFR	EWSR1	FLI1	IKZF3	MAP3K1	NRG1	NUP98	PML	RET	SS18	THADA
AKT3	BRAF	CIC	ERG	FGFR1	FOXO1	JAK2	MECOM	NTRK1	PAX8	PPARG	RHOA	STAT6	TMPRSS2
ALK	CAMTA1	CREB1	ETS1	FGFR2	FUS	KIAA1549	MYB	NTRK2	PDGFRA	PRKACA	ROS1	TAL1	YAP1
AR	CBFB	CREBBP	ETV1	FGFR3	GLI1	KMT2A	MYC	NTRK3	PDGFRB	RAF1	RUNX1	TCF3	YWHAE
BCL2	CCND1	ERBB2	ETV6	FIP1L1	HMG2	MAML2	NOTCH1	NUP214	PICALM	RARA	RUNX1T1	TFG	ZFTA

Reference

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2. Recent advances in therapeutic strategies for non-small cell lung cancer. Su PL, Furuya N, Asrar A, Rolfo C, Li Z, Carbone DP, He K. J Hematol Oncol. 2025 Mar 27;18(1):35. doi: 10.1186/s13045-025-01679-1. PMID: 40140911.

Electronic Signature

Ahmad Charifa, M.D.

Genomic Testing Cooperative, LCA serves as the coordinating laboratory for this assay and is responsible for overall test performance and reporting. The test (sample processing, sequencing and data generation) was performed at Genomic Testing Cooperative, LCA, 25371 Commercentre Drive Lake Forest, CA 92630. Medical Director: Maher Albitar, M.D. Analysis of the data was performed by Genomic Testing Cooperative, LCA, 25371 Commercentre Drive, Lake Forest, CA 92630. Medical Director: Maher Albitar, M.D. (CLIA #: 05D2111917 CAP #: 9441574). The signing pathologist is responsible for the accuracy and interpretation of results and the release of this report.

The test was developed and its performance characteristics have been determined by Genomic Testing Cooperative, LCA. This test has not been approved by the FDA. The FDA has determined such clearance or approval is not necessary. This laboratory is CLIA certified to perform high complexity clinical testing.