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Patient Name: 배영우 Primary Tumor Site: gallbladder (presumed)

Gender: M Collection Date: 2025.07.16

Sample ID: N25-122

Sample Cancer Type: Gallbladder Carcinoma

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Relevant Gallbladder Carcinoma Findings

Gene	Finding	
BRAF	None detected	
ERBB2	None detected	
KRAS	None detected	
NTRK1	None detected	
NTRK2	None detected	
NTRK3	None detected	
RET	None detected	
Genomic Alte	eration	Finding
Tumor Mu	tational Burden	4.75 Mut/Mb measured

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	FGFR2 imbalance fibroblast growth factor receptor 2 Locus: chr10:123246867	None*	futibatinib 1, 2 / II+ pemigatinib 1, 2 / II+ erdafitinib I, II+	9
IIC	TP53 p.(R175H) c.524G>A tumor protein p53 Allele Frequency: 9.45% Locus: chr17:7578406 Transcript: NM_000546.6	None*	None*	3

^{*} Public data sources included in relevant therapies: FDA1, NCCN, EMA2, ESMO

Line of therapy: I: First-line therapy, II+: Other line of therapy

Tier Reference: Li et al. Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists. J Mol Diagn. 2017 Jan;19(1):4-23.

Prevalent cancer biomarkers without relevant evidence based on included data sources

ARID2 p.([Q1575=;Q1576*]) c.4725_4726delGCinsAT, Microsatellite stable, EPHA2 p.(E308*) c.922G>T, LARP4B p.(R716G) c.2146C>G, PTPRT p.(K805*) c.2413A>T, Tumor Mutational Burden

^{*} Public data sources included in prognostic and diagnostic significance: NCCN, ESMO

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Variant Details

DNA	Sequence Variar	nts					
Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
TP53	p.(R175H)	c.524G>A	COSM10648	chr17:7578406	9.45%	NM_000546.6	missense
ARID2	p.([Q1575=;Q1576*])	c.4725_4726delGCinsA T	١.	chr12:46246631	6.92%	NM_152641.4	synonymous, nonsense
EPHA2	p.(E308*)	c.922G>T		chr1:16464827	7.81%	NM_004431.5	nonsense
LARP4B	p.(R716G)	c.2146C>G	COSM4333217	chr10:858937	2.77%	NM_015155.3	missense
PTPRT	p.(K805*)	c.2413A>T		chr20:40828015	2.50%	NM_133170.4	nonsense
OR2L2	p.(T75I)	c.224C>T		chr1:248201793	23.34%	NM_001004686.2	missense
SETD2	p.(K47Q)	c.139A>C		chr3:47165987	4.81%	NM_014159.7	missense
ATR	p.(R2544C)	c.7630C>T		chr3:142176471	45.94%	NM_001184.4	missense
MAML3	p.(Q489Tfs*29)	c.1455_1506delACAGC AACAGCAACAGCAGC AGCAGCAGCAGCAGC AGCAGCAGCAGCAGC AGinsGCAGCAACAGA CAGCCAGCAGCAGCA GCAGCAGCAGCAA).	chr4:140811084	12.73%	NM_018717.5	frameshift Block Substitution
MAML3	p.(Q491Pfs*32)	c.1455_1506delACAGC AACAGCAACAGCAGC AGCAGCAGCAGCAGC AGCAGCAGCAGCAGC AGinsGCAGCAACAGC AACAGCCAGCAGCAG CAGCAGCAGCAGCAA	· .	chr4:140811084	87.27%	NM_018717.5	frameshift Block Substitution
TAP2	p.(D323V)	c.968A>T		chr6:32800579	51.08%	NM_018833.2	missense
LATS1	p.(E718K)	c.2152G>A		chr6:150001452	8.22%	NM_004690.4	missense
POT1	p.(R273Q)	c.818G>A		chr7:124493077	3.00%	NM_015450.3	missense
STK11	p.(R415G)	c.1243C>G		chr19:1226587	46.32%	NM_000455.5	missense

Gene Fusions		
Genes	Variant ID	Locus
FGFR2	FGFR2	chr10:123246867

Biomarker Descriptions

FGFR2 imbalance

 $fibroblast\ growth\ factor\ receptor\ 2$

Background: The FGFR2 gene encodes fibroblast growth receptor 2, a member of the fibroblast growth factor receptor (FGFR) family that also includes FGFR1, 3, and 4¹. These proteins are single transmembrane receptors composed of three extracellular immunoglobulin (Ig)-type domains and an intracellular kinase domain¹. Upon FGF-mediated stimulation, FGFRs activate several oncogenic signaling pathways, including the RAS/RAF/MEK/ERK, PI3K/AKT/MTOR, PLCγ/PKC, and JAK/STAT pathways influencing cell proliferation, migration, and survival^{40,41,42}.

Biomarker Descriptions (continued)

Alterations and prevalence: Aberrations most common to the FGFR family are amplifications, followed by mutations and fusions. The majority of these aberrations result in gain of function⁴³. Somatic mutations in FGFR2 are observed in 15% of uterine corpus endometrial carcinomas, 10% of skin cutaneous melanoma, 6% of cholangiocarcinoma, 4% of stomach adenocarcinoma, 3% of colorectal adenocarcinoma, and 2% of lung squamous cell carcinoma, bladder urothelial carcinoma, diffuse large B-cell lymphoma, lung adenocarcinoma, uterine carcinosarcoma, and cervical squamous cell carcinoma^{6,7}. In endometrial cancers, missense mutations are the most prevalent alterations in FGFR2⁴⁴. These mutations are predominantly activating, most often involve substitutions at S252 and P253, and confer sensitivity to pan-FGFR2 inhibitors^{44,45}. FGFR2 amplification occurs in up to 4% of stomach adenocarcinoma, and 2% of ovarian serous cystadenocarcinoma, uterine carcinosarcoma, and uterine corpus endometrial carcinoma^{6,7}. FGFR2 fusions have also been reported in up to 14% of cholangiocarcinoma and confer sensitivity to select FGFR inhibitors^{6,46,47}. Aberrations in FGFR2 are rare in pediatric cancers^{6,7}. Somatic mutations in FGFR2 occur in 2% of T-lymphoblastic leukemia/lymphoma and FGFR2 is amplified in 2% of bone cancer^{6,7}.

Potential relevance: Several pan-FGFR inhibitors have been approved for FGFR2 aberrations in cancer. Futibatinib⁴⁸ (2022) is approved for FGFR2 fusion-positive locally advanced or metastatic intrahepatic cholangiocarcinoma and has been granted breakthrough designation⁴⁹ (2022) for FGFR2-fusion positive cholangiocarcinoma. Erdafitinib⁵⁰ (2019) is approved for the treatment of locally advanced or metastatic urothelial cancer with FGFR2 fusions, including FGFR2::BICC1 and FGFR2::CASP7, Pemigatinib⁵¹ (2020) is approved for previously treated, advanced, or unresectable cholangiocarcinoma harboring FGFR2 fusions. The FDA has granted fast track designation to the pan-FGFR inhibitor, KIN-324852 (2023), for unresectable, locally advanced, or metastatic cholangiocarcinoma with FGFR2 fusions or other alterations after receiving at least one prior systemic therapy. The FDA has also granted fast track designation to the FGFR2 inhibitor, 3HP-282753 (2024), for the treatment of patients with cholangiocarcinoma harboring FGFR2 mutations. The FDA has granted breakthrough designation to the FGFR2 inhibitor, lirafugratinib54 (2024), for the treatment of FGFR2driven cholangiocarcinoma and other FGFR2-altered solid tumors. The FDA also granted fast track designation to the small molecule inhibitor, Debio 1347⁵⁵ (2018), for solid tumors harboring FGFR1, FGFR2, or FGFR3 aberrations. The FDA has granted breakthrough designation to bemarituzumab⁵⁶ (2021), in combination with modified FOLFOX6 (fluoropyrimidine, leucovorin, and oxaliplatin), for treating FGFR2b-overexpressing, HER2-negative metastatic and locally advanced gastric and gastroesophageal adenocarcinoma. Additional FGFR inhibitors are under clinical evaluation for FGFR2 aberrations^{57,58}. In a phase II study of patients with FGFR2 fusionpositive intrahepatic cholangiocarcinoma, the pan-kinase inhibitor derazantinib, demonstrated an overall response rate (ORR) of 20.7% with progression-free survival (PFS) of 5.7 months⁵⁷. Likewise, results of a phase II trial testing the pan-FGFR inhibitor, infigratinib (BGJ398) demonstrated an ORR of 14.8% (18.8% FGFR2 fusions only), disease control rate (DCR) of 75.4% (83.3% FGFR2 fusions only), and a median PFS of 5.8 months⁵⁸.

TP53 p.(R175H) c.524G>A

tumor protein p53

Background: The TP53 gene encodes the tumor suppressor protein p53, which binds to DNA and activates transcription in response to diverse cellular stresses to induce cell cycle arrest, apoptosis, or DNA repair¹. In unstressed cells, TP53 is kept inactive by targeted degradation via MDM2, a substrate recognition factor for ubiquitin-dependent proteolysis¹⁴. Alterations in TP53 are required for oncogenesis as they result in loss of protein function and gain of transforming potential¹⁵. Germline mutations in TP53 are the underlying cause of Li-Fraumeni syndrome, a complex hereditary cancer predisposition disorder associated with early-onset cancers^{16,17}.

Alterations and prevalence: TP53 is the most frequently mutated gene in the cancer genome with approximately half of all cancers experiencing TP53 mutations. Ovarian, head and neck, esophageal, and lung squamous cancers have particularly high TP53 mutation rates (60-90%)^{6,7,18,19,20,21}. Approximately two-thirds of TP53 mutations are missense mutations and several recurrent missense mutations are common, including substitutions at codons R158, R175, Y220, R248, R273, and R282^{6,7}. Invariably, recurrent missense mutations in TP53 inactivate its ability to bind DNA and activate transcription of target genes^{22,23,24,25}. Alterations in TP53 are also observed in pediatric cancers^{6,7}. Somatic mutations are observed in 53% of non-Hodgkin lymphoma, 24% of soft tissue sarcoma, 19% of glioma, 13% of bone cancer, 9% of B-lymphoblastic leukemia/lymphoma, 4% of embryonal tumors, 3% of Wilms tumor and leukemia, 2% of T-lymphoblastic leukemia/lymphoma, and less than 1% of peripheral nervous system cancers (5 in 1158 cases)^{6,7}. Biallelic loss of TP53 is observed in 10% of bone cancer, 2% of Wilms tumor, and less than 1% of B-lymphoblastic leukemia/lymphoma (2 in 731 cases) and leukemia (1 in 250 cases)^{6,7}.

Potential relevance: The small molecule p53 reactivator, PC14586²⁶ (2020), received a fast track designation by the FDA for advanced tumors harboring a TP53 Y220C mutation. The FDA has granted fast track designation to the p53 reactivator, eprenetapopt²⁷, (2019) and breakthrough designation²⁸ (2020) in combination with azacitidine or azacitidine and venetoclax for acute myeloid leukemia patients (AML) and myelodysplastic syndrome (MDS) harboring a TP53 mutation, respectively. In addition to investigational therapies aimed at restoring wild-type TP53 activity, compounds that induce synthetic lethality are also under clinical evaluation^{29,30}. TP53 mutation are a diagnostic marker of SHH-activated, TP53-mutant medulloblastoma³¹. TP53 mutations confer poor prognosis and poor risk in multiple blood cancers including AML, MDS, myeloproliferative neoplasms (MPN), and chronic lymphocytic leukemia (CLL), and acute lymphoblastic leukemia (ALL)^{32,33,34,35,36,37}. In mantle cell lymphoma, TP53 mutations are associated with poor prognosis when treated with conventional therapy including hematopoietic cell transplant³⁸. Mono- and bi-allelic mutations in TP53 confer unique

Biomarker Descriptions (continued)

characteristics in MDS, with multi-hit patients also experiencing associations with complex karyotype, few co-occurring mutations, and high-risk disease presentation as well as predicted death and leukemic transformation independent of the IPSS-R staging system³⁹.

ARID2 p.([Q1575=;Q1576*]) c.4725_4726delGCinsAT

AT-rich interaction domain 2

Background: The ARID2 gene encodes the AT-rich interaction domain 2 protein¹. ARID2, also known as BAF200, belongs to the ARID superfamily that also includes ARID1A, ARID1B, and ARID5B⁸. ARID2 is an essential member of the PBAF complex, a SWI/SNF chromatin-remodeling complex^{8,9}. The PBAF complex is a multisubunit protein complex that consists of ARID2, SMARCA4A/BRG1, BRD7, ACTL6A/BAF53A, PHF10/BAF45A, PBRM1/BAF180, SMARCC2/BAF170, SMARCC1/BAF155, SMARCB1/BAF47, SMARCD1/BAF60A, and SMARCE1/BAF57^{9,10}. ARID2 may alter the expression of IFN responsive genes, which suppress cell proliferation⁸. Loss of function mutations in ARID2 may promote cell proliferation, suggesting a tumor suppressor role of ARID2⁸.

Alterations and prevalence: Mutations in SWI/SNF complex subunits are the most commonly mutated chromatin modulators in cancer and have been observed in 20% of all tumors¹¹. Somatic mutations in ARID2 are observed in 17% of skin cutaneous melanoma, 11% of uterine corpus endometrial carcinoma, 8% of bladder urothelial carcinoma and stomach adenocarcinoma, 7% of colorectal adenocarcinoma, and 5% of liver hepatocellular carcinoma, lung adenocarcinoma, and lung squamous cell carcinoma^{6,7}. ARID2 biallelic deletions are observed in 2% of mesothelioma^{6,7}.

Potential relevance: Currently, no therapies are approved for ARID2 aberrations.

Microsatellite stable

Background: Microsatellites are short tandem repeats (STR) of 1 to 6 bases of DNA between 5 to 50 repeat units in length. There are approximately 0.5 million STRs that occupy 3% of the human genome⁵⁹. Microsatellite instability (MSI) is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue^{60,61}. MSI is closely tied to the status of the mismatch repair (MMR) genes. In humans, the core MMR genes include MLH1, MSH2, MSH6, and PMS2⁶². Mutations and loss of expression in MMR genes, known as defective MMR (dMMR), lead to MSI. In contrast, when MMR genes lack alterations, they are referred to as MMR proficient (pMMR). Consensus criteria were first described in 1998 and defined MSI-high (MSI-H) as instability in two or more of the following five markers: BAT25, BAT26, D5S346, D2S123, and D17S250⁶³. Tumors with instability in one of the five markers were defined as MSI-low (MSI-L) whereas, those with instability in zero markers were defined as MS-stable (MSS)⁶³. Tumors classified as MSI-L are often phenotypically indistinguishable from MSS tumors and tend to be grouped with MSS^{64,65,66,67,68}. MSI-H is a hallmark of Lynch syndrome (LS), also known as hereditary non-polyposis colorectal cancer, which is caused by germline mutations in the MMR genes⁶¹. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer^{60,61,65,69}.

Alterations and prevalence: The MSI-H phenotype is observed in 30% of uterine corpus endothelial carcinoma, 20% of stomach adenocarcinoma, 15-20% of colon adenocarcinoma, and 5-10% of rectal adenocarcinoma^{60,61,70,71}. MSI-H is also observed in 5% of adrenal cortical carcinoma and at lower frequencies in other cancers such as esophageal, liver, and ovarian cancers^{70,71}.

Potential relevance: Anti-PD-1 immune checkpoint inhibitors including pembrolizumab⁷² (2014) and nivolumab⁷³ (2015) are approved for patients with MSI-H or dMMR colorectal cancer who have progressed following chemotherapy. Pembrolizumab⁷² is also approved as a single agent, for the treatment of patients with advanced endometrial carcinoma that is MSI-H or dMMR with disease progression on prior therapy who are not candidates for surgery or radiation. Importantly, pembrolizumab is approved for the treatment of MSI-H or dMMR solid tumors that have progressed following treatment, with no alternative option and is the first anti-PD-1 inhibitor to be approved with a tumor agnostic indication⁷². Dostarlimab⁷⁴ (2021) is also approved for dMMR recurrent or advanced endometrial carcinoma or solid tumors that have progressed on prior treatment and is recommended as a subsequent therapy option in dMMR/MSI-H advanced or metastatic colon or rectal cancer^{66,75}. The cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab⁷⁶ (2011), is approved alone or in combination with nivolumab in MSI-H or dMMR colorectal cancer that has progressed following treatment with chemotherapy. MSI-H may confer a favorable prognosis in colorectal cancer although outcomes vary depending on stage and tumor location^{66,77,78}. Specifically, MSI-H is a strong prognostic indicator of better overall survival (OS) and relapse free survival (RFS) in stage II as compared to stage III colorectal cancer patients⁷⁸. The majority of patients with tumors classified as either MSS or pMMR do not benefit from treatment with single-agent immune checkpoint inhibitors as compared to those with MSI-H tumors^{79,80}. However, checkpoint blockade with the addition of chemotherapy or targeted therapies have demonstrated response in MSS or pMMR cancers^{79,80}.

EPHA2 p.(E308*) c.922G>T

EPH receptor A2

Background: The EPHA2 gene encodes the EPH receptor A2¹. EPHA2 is a member of the erythropoietin-producing hepatocellular carcinoma (Eph) receptors, a group of receptor tyrosine kinases divided into EPHA (EphA1-10) and EPHB (EphB1-6) classes of

Biomarker Descriptions (continued)

proteins^{81,82}. Like classical tyrosine kinase receptors, Eph activation is initiated by ligand binding resulting downstream signaling involved in various cellular processes including cell growth, differentiation, and apoptosis⁸². Specifically, Eph-EphrinA ligand interaction regulates pathways critical for malignant transformation and key downstream target proteins including PI3K, SRC, Rho and Rac1 GTPases, MAPK, and integrins^{81,82}.

<u>Alterations and prevalence</u>: Somatic mutations in EPHA2 are observed in 11% of cholangiocarcinoma, 7% of uterine corpus endometrial carcinoma, stomach adenocarcinoma, and skin cutaneous melanoma, 6% of bladder urothelial carcinoma, and 5% of diffuse large B-cell lymphoma (DLBCL) and cervical squamous cell carcinoma^{6,7}.

Potential relevance: Currently, no therapies are approved for EPHA2 aberrations.

LARP4B p.(R716G) c.2146C>G

La ribonucleoprotein domain family member 4B

Background: The LARP4B gene encodes the La ribonucleoprotein 4B protein¹. La-related proteins (LARPs) are RNA binding proteins and can be split into 5 families, LARP1, La, LARP4, LARP6, and LARP7¹². Along with LARP4, LARP4B is part of the LARP4 family and is observed to bind AU-rich regions in the 3' untranslated regions of mRNAs¹². In glioma, LARP4B has been observed to induce mitotic arrest and apoptosis in vitro, supporting a tumor suppressor role for LARP4B¹³.

Alterations and prevalence: Somatic mutations in LARP4B are observed in 8% of uterine corpus endometrial carcinoma, 7% of stomach adenocarcinoma, 5% of colorectal adenocarcinoma and skin cutaneous melanoma, 4% of uterine carcinosarcoma, and 2% of lung adenocarcinoma, lung squamous cell carcinoma, esophageal adenocarcinoma, and bladder urothelial carcinoma^{6,7}. Biallelic deletions in LARP4B are observed in 4% of diffuse large B-cell lymphoma (DLBCL), 3% of sarcoma and testicular germ cell tumors, and 2% of mesothelioma, stomach adenocarcinoma, and lung squamous cell carcinoma^{6,7}.

Potential relevance: Currently, no therapies are approved for LARP4B aberrations.

PTPRT p.(K805*) c.2413A>T

protein tyrosine phosphatase, receptor type T

Background: PTPRT encodes protein tyrosine phosphatase receptor type T, part of the protein tyrosine phosphatase (PTP) family which consists of 125 members^{1,2,3}. PTPs are responsible for protein dephosphorylation of tyrosine residues and are involved in several cellular processes including proliferation, differentiation, adhesion, and survival^{4,5}. Aberrant tyrosine phosphorylation resulting from PTP dysfunction has been linked to cancer progression^{4,5}.

Alterations and prevalence: Somatic mutations in PTPRT are observed in 29% of skin cutaneous melanoma, 12% of stomach adenocarcinoma and uterine corpus endometrial carcinoma, 10% of colorectal adenocarcinoma and lung adenocarcinoma, 7% of esophageal adenocarcinoma and lung squamous cell carcinoma, 5% of uterine carcinosarcoma and bladder urothelial carcinoma, 4% of head and neck squamous cell carcinoma and cervical squamous cell carcinoma, 3% of glioblastoma multiforme and liver hepatocellular carcinoma, and 2% of diffuse large B-cell lymphoma, pancreatic adenocarcinoma, adrenocortical carcinoma, kidney renal clear cell carcinoma, and ovarian serous cystadenocarcinoma^{6,7}. Biallelic loss of PTPRT is observed in about 1% of mesothelioma, prostate adenocarcinoma, and acute myeloid leukemia.^{6,7}.

Potential relevance: Currently, no therapies are approved for PTPRT aberrations.

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Alerts Informed By Public Data Sources

Current FDA Information

Contraindicated

Not recommended

Resistance Breakthrough

Fast Track

FDA information is current as of 2025-05-14. For the most up-to-date information, search www.fda.gov.

FGFR2 imbalance

A KIN-3248

Cancer type: Cholangiocarcinoma

Variant class: FGFR2 fusion

Supporting Statement:

The FDA has granted Fast Track designation to the pan-FGFR inhibitor, KIN-3248, for unresectable, locally advanced or metastatic cholangiocarcinoma with FGFR2 fusions or other alterations after receiving at least one prior systemic therapy.

Reference:

https://www.globenewswire.com/news-release/2023/02/14/2608131/0/en/Kinnate-Biopharma-Inc-Receives-Fast-Track-Designation-from-the-U-S-Food-and-Drug-Administration-for-KIN-3248-an-Investigational-Pan-FGFR-Inhibitor.html

Genes Assayed

Genes Assayed for the Detection of DNA Sequence Variants

ABL1, ABL2, ACVR1, AKT1, AKT2, AKT3, ALK, AR, ARAF, ATP1A1, AURKA, AURKB, AURKC, AXL, BCL2, BCL2L12, BCL6, BCR, BMP5, BRAF, BTK, CACNA1D, CARD11, CBL, CCND1, CCND2, CCND3, CCNE1, CD79B, CDK4, CDK6, CHD4, CSF1R, CTNNB1, CUL1, CYSLTR2, DDR2, DGCR8, DROSHA, E2F1, EGFR, EIF1AX, EPAS1, ERBB2, ERBB3, ERBB4, ESR1, EZH2, FAM135B, FGF7, FGFR1, FGFR2, FGFR3, FGFR4, FLT3, FLT4, FOXA1, FOXL2, FOXO1, GATA2, GLI1, GNA11, GNAQ, GNAS, HIF1A, HRAS, IDH1, IDH2, IKBKB, IL6ST, IL7R, IRF4, IRS4, KCNJ5, KDR, KIT, KLF4, KLF5, KNSTRN, KRAS, MAGOH, MAP2K1, MAP2K2, MAPK1, MAX, MDM4, MECOM, MED12, MEF2B, MET, MITF, MPL, MTOR, MYC, MYCN, MYD88, MYOD1, NFE2L2, NRAS, NSD2, NT5C2, NTRK1, NTRK2, NTRK3, NUP93, PAX5, PCBP1, PDGFRA, PDGFRB, PIK3C2B, PIK3CB, PIK3CB, PIK3CD, PIK3CG, PIK3R2, PIM1, PLCG1, PPP2R1A, PPP6C, PRKACA, PTPN11, PTPRD, PXDNL, RAC1, RAF1, RARA, RET, RGS7, RHEB, RHOA, RICTOR, RIT1, ROS1, RPL10, SETBP1, SF3B1, SIX1, SIX2, SLC01B3, SMC1A, SMO. SNCAIP, SOS1, SOX2, SPOP, SRC, SRSF2, STAT3, STAT5B, STAT6, TAF1, TERT, TGFBR1, TOP1, TOP2A, TPMT, TRRAP, TSHR, U2AF1, USP8, WAS, XP01, ZNF217, ZNF429

Genes Assayed for the Detection of Copy Number Variations

ABCB1, ABL1, ABL2, ABRAXAS1, ACVR1B, ACVR2A, ADAMTS12, ADAMTS2, AKT1, AKT2, AKT3, ALK, AMER1, APC, AR, ARAF, ARHGAP35, ARID1A, ARID1B, ARID2, ARID5B, ASXL1, ASXL2, ATM, ATR, ATRX, AURKA, AURKC, AXIN1, AXIN2, AXL, B2M, BAP1, BARD1, BCL2, BCL2L12, BCL6, BCOR, BLM, BMPR2, BRAF, BRCA1, BRCA2, BRIP1, CARD11, CASP8, CBFB, CBL, CCND1, CCND2, CCND3, CCNE1, CD274, CD276, CDC73, CDH1, CDH10, CDK12, CDK4, CDK6, CDKN1A, CDKN1B, CDKN2A, CDKN2B, CDKN2C, CHD4, CHEK1, CHEK2, CIC, CREBBP, CSMD3, CTCF, CTLA4, CTNND2, CUL3, CUL4A, CUL4B, CYLD, CYP2C9, DAXX, DDR1, DDR2, DDX3X, DICER1, DNMT3A, DOCK3, DPYD, DSC1, DSC3, EGFR, EIF1AX, ELF3, EMSY, ENO1, EP300, EPCAM, EPHA2, ERAP1, ERAP2, ERBB2, ERBB3, ERBB4, ERCC2, ERCC4, ERRFI1, ESR1, ETV6, EZH2, FAM135B, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCI, FANCM, FAT1, FBXW7, FGF19, FGF23, FGF4, FGF9, FGFR1, FGFR2, FGFR3, FGFR4, FLT3, FLT4, FOXA1, FUBP1, FYN, GATA2, GATA3, GLI3, GNA13, GNAS, GPS2, HDAC2, HDAC9, HLA-A, HLA-B, HNF1A, IDH2, IGF1R, IKBKB, IL7R, INPP4B, JAK1, JAK2, JAK3, KDM5C, KDM6A, KDR, KEAP1, KIT, KLF5, KMT2A, KMT2B, KMT2C, KMT2D, KRAS, LARP4B, LATS1, LATS2, MAGOH, MAP2K1, MAP2K4, MAP2K7, MAP3K1, MAP3K4, MAPK1, MAPK8, MAX, MCL1, MDM2, MDM4, MECOM, MEF2B, MEN1, MET, MGA, MITF, MLH1, MLH3, MPL, MRE11, MSH2, MSH3, MSH6, MTAP, MTOR, MUTYH, MYC, MYCL, MYCN, MYD88, NBN, NCOR1, NF1, NF2, NFE2L2, NOTCH1, NOTCH2, NOTCH3, NOTCH4, NRAS, NTRK1, NTRK3, PALB2, PARP1, PARP2, PARP3, PARP4, PBRM1, PCBP1, PDCD1, PDCD1LG2, PDGFRA, PDGFRB, PDIA3, PGD, PHF6, PIK3C2B, PIK3CA, PIK3CB, PIK3R1, PIK3R2, PIM1, PLCG1, PMS1, PMS2, POLD1, POLE, POT1, PPM1D, PPP2R1A, PPP2R2A, PPP6C, PRDM1, PRDM9, PRKACA, PRKAR1A, PTCH1, PTEN, PTPN11, PTPRT, PXDNL, RAC1, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD52, RAD54L, RAF1, RARA, RASA1, RASA2, RB1, RBM10, RECQL4, RET, RHEB, RICTOR, RIT1, RNASEH2A, RNASEH2B, RNF43, ROS1, RPA1, RPS6KB1, RPTOR, RUNX1, SDHA, SDHB, SDHD, SETBP1, SETD2, SF3B1, SLCO1B3, SLX4, SMAD2, SMAD4, SMARCA4, SMARCB1, SMC1A, SMO, SOX9, SPEN, SPOP, SRC, STAG2, STAT3, STAT6, STK11, SUFU, TAP1, TAP2, TBX3, TCF7L2, TERT, TET2, TGFBR2,

X No evidence

Genes Assayed (continued)

Genes Assayed for the Detection of Copy Number Variations (continued)

TNFAIP3, TNFRSF14, TOP1, TP53, TP63, TPMT, TPP2, TSC1, TSC2, U2AF1, USP8, USP9X, VHL, WT1, XPO1, XRCC2, XRCC3, YAP1, YES1, ZFHX3, ZMYM3, ZNF217, ZNF429, ZRSR2

Genes Assayed for the Detection of Fusions

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, PRKACB, PTEN, RAD51B, RAF1, RB1, RELA, RET, ROS1, RSPO2, RSPO3, TERT

Genes Assayed with Full Exon Coverage

ABRAXAS1, ACVR1B, ACVR2A, ADAMTS12, ADAMTS2, AMER1, APC, ARHGAP35, ARID1A, ARID1B, ARID2, ARID5B, ASXL1, ASXL2, ATM, ATR, ATRX, AXIN1, AXIN2, B2M, BAP1, BARD1, BCOR, BLM, BMPR2, BRCA1, BRCA2, BRIP1, CALR, CASP8, CBFB, CD274, CD276, CDC73, CDH1, CDH10, CDK12, CDKN1A, CDKN1B, CDKN2A, CDKN2B, CDKN2C, CHEK1, CHEK2, CIC, CIITA, CREBBP, CSMD3, CTCF, CTLA4, CUL3, CUL4A, CUL4B, CYLD, CYP2C9, CYP2D6, DAXX, DDX3X, DICER1, DNMT3A, DOCK3, DPYD, DSC1, DSC3, ELF3, ENO1, EP300, EPCAM, EPHA2, ERAP1, ERAP2, ERCC2, ERCC4, ERCC5, ERRF11, ETV6, FANCA, FANCC, FANCD2, FANCE, FANCE, FANCG, FANCI, FANCI, FANCH, FA

Relevant Therapy Summary

In other cancer type

In this cancer type

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials
futibatinib	0	0	0	0	(II)
pemigatinib	0	0	0	0	(II)
erdafitinib	×	0	×	×	×
ABSK061, ABSK-043	×	×	×	×	(II)
immune checkpoint inhibitor, pemigatinib	×	×	×	×	(II)
ICP-192	×	×	×	×	(I/II)
ABSK-121	×	×	×	×	(l)
afatinib, pemigatinib	×	×	×	×	(I)
TYRA-200	×	×	×	×	(I)

In this cancer type and other cancer types

^{*} Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

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Relevant Therapy Summary (continued)

TP53 p.(R175H) c.524G>A					
Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
CLSP-1025	×	×	×	×	(l)
NT-175, chemotherapy, aldesleukin	×	×	×	×	(I)
TP53-EphA-2-CAR-DC, anti-PD-1	×	×	×	×	(I)

^{*} Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

HRR Details

Gene/Genomic Alteration	Finding
LOH percentage	0.0%
Not Detected	Not Applicable

Homologous recombination repair (HRR) genes were defined from published evidence in relevant therapies, clinical guidelines, as well as clinical trials, and include - BRCA1, BRCA2, ATM, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, and RAD54L.

Thermo Fisher Scientific's Ion Torrent Oncomine Reporter software was used in generation of this report. Software was developed and designed internally by Thermo Fisher Scientific. The analysis was based on Oncomine Reporter (6.1.1 data version 2025.06(006)). The data presented here are from a curated knowledge base of publicly available information, but may not be exhaustive. FDA information was sourced from www.fda.gov and is current as of 2025-05-14. NCCN information was sourced from www.nccn.org and is current as of 2025-05-01. EMA information was sourced from www.ema.europa.eu and is current as of 2025-05-14. ESMO information was sourced from www.esmo.org and is current as of 2025-05-01. Clinical Trials information is current as of 2025-05-01. For the most up-to-date information regarding a particular trial, search www.clinicaltrials.gov by NCT ID or search local clinical trials authority website by local identifier listed in 'Other identifiers.' Variants are reported according to HGVS nomenclature and classified following AMP/ASCO/CAP guidelines (Li et al. 2017). Based on the data sources selected, variants, therapies, and trials listed in this report are listed in order of potential clinical significance but not for predicted efficacy of the therapies.

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