

Patient Name: 유월순
Gender: Female
Sample ID: N26-6

Primary Tumor Site: Lung
Collection Date: 2025.12.24

Sample Cancer Type: Lung Cancer

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Relevant Lung Cancer Findings

Gene	Finding	Gene	Finding
ALK	KIF5B::ALK fusion	NTRK1	None detected
BRAF	None detected	NTRK2	None detected
EGFR	None detected	NTRK3	None detected
ERBB2	None detected	RET	None detected
KRAS	None detected	ROS1	None detected
MET	None detected		

Genomic Alteration	Finding
Tumor Mutational Burden	3.79 Mut/Mb measured

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	KIF5B::ALK fusion kinesin family member 5B - ALK receptor tyrosine kinase Locus: chr10:32306071 - chr2:29446394	alectinib 1, 2 / I, II+ brigatinib 1, 2 / I, II+ ceritinib 1, 2 / I, II+ crizotinib 1, 2 / I, II+ ensartinib 1 / I, II+ lorlatinib 1, 2 / I, II+ atezolizumab + bevacizumab + chemotherapy II+	crizotinib 1 / I, II+ alectinib I, II+ brigatinib I, II+ ceritinib I, II+ lorlatinib I, II+	53

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

* Public data sources included in prognostic and diagnostic significance: NCCN, 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.

Alerts informed by public data sources: ⛔ Contraindicated, 🛡️ Resistance, 🚀 Breakthrough, 🏎️ Fast Track

KIF5B::ALK fusion 🚀 neladalkib ¹

Public data sources included in alerts: FDA¹, NCCN, EMA², ESMO

Prevalent cancer biomarkers without relevant evidence based on included data sources
MLH1 p.(V384D) c.1151T>A, Microsatellite stable, TPMT p.(Y240C) c.719A>G, NQO1 p.(P187S) c.559C>T, DSC1 deletion, Tumor Mutational Burden

Variant Details

DNA Sequence Variants							
Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
MLH1	p.(V384D)	c.1151T>A	.	chr3:37067240	52.78%	NM_000249.4	missense
TPMT	p.(Y240C)	c.719A>G	COSM4986703	chr6:18130918	47.06%	NM_000367.5	missense
NQO1	p.(P187S)	c.559C>T	.	chr16:69745145	99.40%	NM_000903.3	missense
MTOR	p.(K2496N)	c.7488A>T	.	chr1:11169387	9.98%	NM_004958.4	missense
MSH3	p.(A61_P63dup)	c.189_190insGCAGCG CCC	.	chr5:79950735	43.43%	NM_002439.5	nonframeshift Insertion
MAP3K4	p.(I1447V)	c.4339A>G	.	chr6:161530889	21.22%	NM_005922.4	missense
DMD	p.(D2364N)	c.7090G>A	.	chrX:31893313	9.91%	NM_004006.3	missense

Gene Fusions		
Genes	Variant ID	Locus
KIF5B::ALK	KIF5B-ALK.K24A20.COSF1058.1	chr10:32306071 - chr2:29446394

Copy Number Variations			
Gene	Locus	Copy Number	CNV Ratio
DSC1	chr18:28710424	0.35	0.67
CSMD3	chr8:113237020	4.97	1.59

Biomarker Descriptions

KIF5B::ALK fusion

ALK receptor tyrosine kinase, kinesin family member 5B

Background: The ALK gene encodes the ALK receptor tyrosine kinase (RTK), which has sequence similarity to the insulin receptor subfamily of kinases⁴⁷. ALK is frequently altered in cancer, most commonly through chromosomal rearrangements that generate fusion genes containing the intact ALK tyrosine kinase domain combined with various partner genes⁴⁸. ALK fusion kinases are constitutively activated and drive oncogenic transformation via activation of downstream STAT3, PI3K/AKT/MTOR, and RAS/RAF/MEK/ERK pathways^{48,49,50,51}.

Alterations and prevalence: ALK was discovered by positional cloning of translocations involving nucleophosmin 1 (NPM1) on 5q35 with a previously unidentified RTK on 2p23 (ALK), which occur in over 50% of adult and over 80% of pediatric anaplastic large cell lymphoma (ALCL) cases^{47,52,53}. In contrast, about 5% of non-small cell lung cancer (NSCLC) cases generate recurrent ALK fusions with EML4, KIF5B, and HIP1^{54,55,56}. Notably, ALK F1174L, F1245C, and R1275Q mutations are found in over 80% of ALK-mutated neuroblastoma⁵⁷. ALK mutations have also been reported in 5% of pediatric soft tissue sarcomas and less than 1.5% of other solid and hematological malignancies, including peripheral nervous system tumors, gliomas, leukemia, and bone cancer^{17,18}.

Potential relevance: The first-generation small molecule tyrosine kinase inhibitor (TKI), crizotinib⁵⁸, was FDA approved (2011) for the treatment of adults with ALK-positive advanced NSCLC, as well as pediatric and adult populations with ALK-positive ALCL or inflammatory myofibroblastic tumor (IMT). ALK fusions are a diagnostic marker of infant-type hemispheric glioma and ALK-rearranged

Biomarker Descriptions (continued)

renal cell carcinoma^{59,60,61}. Kinase domain mutations including L1196M, G1269A, F1174L, G1202R, as well as other variants, have been shown to confer acquired resistance to crizotinib in ALK-positive NSCLC^{62,63,64,65}. Other mechanisms of acquired resistance involve amplification of the ALK fusion gene and activation of alternate or bypass signaling pathways involving EGFR, KIT, MET, and IGF1R⁶⁶. In order to overcome acquired resistance, second- and third-generation ALK inhibitors including ceritinib⁶⁷ (2014), alectinib⁶⁸ (2015), brigatinib⁶⁹ (2017), lorlatinib⁷⁰ (2018), and ensartinib⁷¹ (2024) were developed and approved for adults by the FDA. The FDA granted breakthrough therapy designation (2024) to NVL-655⁷² for locally advanced or metastatic ALK-positive NSCLC patients who have been previously treated with two or more ALK TKIs.

MLH1 p.(V384D) c.1151T>A

mutL homolog 1

Background: The MLH1 gene encodes the mutL homolog 1 protein¹. MLH1 is a tumor suppressor gene that heterodimerizes with PMS2 to form the MutLa complex, PMS1 to form the MutLβ complex, and MLH3 to form the MutLy complex². The MutLa complex functions as an endonuclease that is specifically involved in the mismatch repair (MMR) process and mutations in MLH1 result in the inactivation of MutLa and degradation of PMS2^{2,3}. Loss of MLH1 protein expression and MLH1 promoter hypermethylation correlates with mutations in these genes and are used to pre-screen colorectal cancer or endometrial hyperplasia^{4,5}. MLH1, along with MSH6, MSH2, and PMS2 form the core components of the MMR pathway². The MMR pathway is critical to the repair of mismatch errors which typically occur during DNA replication². Deficiency in MMR (dMMR) is characterized by mutations and loss of expression in these genes⁶. dMMR is associated with microsatellite instability (MSI), which is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue^{7,8,9}. MSI-high (MSI-H) is a hallmark of Lynch Syndrome (LS), also known as hereditary non-polyposis colorectal cancer, which is caused by germline mutations in MMR genes^{7,10}. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer^{8,10,11,12}. Specifically, MLH1 mutations are associated with an increased risk of ovarian and pancreatic cancer^{13,14,15,16}.

Alterations and prevalence: Somatic mutations in MLH1 are observed in 6% of uterine corpus endometrial carcinoma, 4% of colorectal adenocarcinoma, and 2-3% of bladder urothelial carcinoma, stomach adenocarcinoma, and melanoma^{17,18}. Alterations in MLH1 are observed in pediatric cancers^{17,18}. Somatic mutations are observed in 1% of bone cancer and less than 1% of B-lymphoblastic leukemia/lymphoma (2 in 252 cases), embryonal tumor (2 in 332 cases), and leukemia (2 in 311 cases)^{17,18}.

Potential relevance: The PARP inhibitor, talazoparib¹⁹ in combination with enzalutamide is approved (2023) for metastatic castration-resistant prostate cancer (mCRPC) with mutations in HRR genes that includes MLH1. Additionally, pembrolizumab (2014) is an anti-PD-1 immune checkpoint inhibitor that is approved for patients with MSI-H or dMMR solid tumors that have progressed on prior therapies²⁰. Nivolumab (2015), an anti-PD-1 immune checkpoint inhibitor, is approved alone or in combination with the cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab (2011), for patients with dMMR colorectal cancer that have progressed on prior treatment^{21,22}. MLH1 mutations are consistent with high grade in pediatric diffuse gliomas^{23,24}.

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 genome³⁰. Microsatellite instability (MSI) is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue^{8,10}. MSI is closely tied to the status of the mismatch repair (MMR) genes. In humans, the core MMR genes include MLH1, MSH2, MSH6, and PMS2⁹. 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 D17S250³¹. 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)³¹. Tumors classified as MSI-L are often phenotypically indistinguishable from MSS tumors and tend to be grouped with MSS^{11,32,33,34,35}. 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 genes¹⁰. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer^{8,10,11,12}.

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^{8,10,36,37}. 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^{36,37}.

Potential relevance: Anti-PD-1 immune checkpoint inhibitors including pembrolizumab²⁰ (2014) and nivolumab²¹ (2015) are approved for patients with MSI-H or dMMR colorectal cancer who have progressed following chemotherapy. Pembrolizumab²⁰ 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 indication²⁰. Dostarlimab³⁸ (2021) is also approved for dMMR recurrent or advanced endometrial

Biomarker Descriptions (continued)

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^{33,39}. The cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab²² (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^{33,40,41}. 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 patients⁴¹. 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^{42,43}. However, checkpoint blockade with the addition of chemotherapy or targeted therapies have demonstrated response in MSS or pMMR cancers^{42,43}.

TPMT p.(Y240C) c.719A>G

thiopurine S-methyltransferase

Background: The TPMT gene encodes thiopurine S-methyltransferase, a cytosolic enzyme that methylates aromatic and heterocyclic sulfhydryl compounds such as thiopurines^{1,44,45}. TPMT is the major enzyme responsible for the metabolic inactivation of thiopurine chemotherapeutic drugs used in the treatment of acute lymphoblastic leukemia (ALL), including, 6-mercaptopurine, 6-thioguanine, and azathioprine^{44,45,46}. Inherited TPMT polymorphisms, including TPMT*2, TPMT*3A, TPMT*3B, TPMT*3C, and TPMT*8, can result in TPMT deficiency, which is characterized by impaired enzymatic activity and confers an increased risk of severe toxicity to thiopurine drugs due to an increase in systemic drug exposure^{44,46}.

Alterations and prevalence: Somatic mutations in TPMT are observed in 2% of uterine corpus endometrial carcinoma and colorectal adenocarcinoma^{17,18}. Biallelic loss of TPMT is observed in 1% of stomach adenocarcinoma, esophageal adenocarcinoma, and adrenocortical carcinoma^{17,18}. Amplification of TPMT is observed in 7% of ovarian serous cystadenocarcinoma, 6% of bladder urothelial carcinoma, 4% of diffuse large B-cell lymphoma, uveal melanoma, uterine carcinosarcoma, and skin cutaneous melanoma, 3% of cholangiocarcinoma, and 2% of breast invasive carcinoma, uterine corpus endometrial carcinoma, and liver hepatocellular carcinoma^{17,18}. Alterations in TPMT are also observed in pediatric cancers¹⁸. Somatic mutations are observed in less than 1% of peripheral nervous system tumors (1 in 1158 cases)¹⁸. Amplification of TPMT is observed in 1% of peripheral nervous system tumors (1 in 91 cases)¹⁸.

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

DSC1 deletion

desmocollin 1

Background: The DSC1 gene encodes desmocollin 1, a member of the desmocollin (DSC) subfamily of the cadherin superfamily, which also includes DSC2 and DSC3¹. DSCs along with desmogleins (DSGs) function as membrane-spanning constituents of the desmosomes²⁵. Desmosomes are protein complexes in the intracellular junctions that confer stability and strengthen cell-cell adhesion²⁶. Deregulation of DSC expression is suggested to impact β -catenin signaling and has been observed in a number of cancer types, supporting a potential role for DSC1 in tumorigenesis^{25,27,28,29}.

Alterations and prevalence: Somatic mutations in DSC1 are observed in 17% of skin cutaneous melanoma, 8% of uterine corpus endometrial carcinoma, 4% of uterine carcinosarcoma, and 3% of lung adenocarcinoma, lung squamous cell carcinoma, and colorectal adenocarcinoma^{17,18}. Biallelic deletion of DSC1 is observed in 2% of pancreatic adenocarcinoma and esophageal adenocarcinoma^{17,18}.

Potential relevance: Currently, no therapies are approved for DSC1 aberrations.

Alerts Informed By Public Data Sources

Current FDA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

FDA information is current as of 2025-11-25. For the most up-to-date information, search www.fda.gov.

KIF5B::ALK fusion

neladalkib

Cancer type: Non-Small Cell Lung Cancer Variant class: ALK fusion

Supporting Statement:
The FDA has granted Breakthrough Therapy designation to a brain-penetrant ALK-selective tyrosine kinase inhibitor (TKI), NVL-655, for the treatment of patients with locally advanced or metastatic ALK-positive non-small cell lung cancer (NSCLC) who have been previously treated with two or more ALK TKIs.

Reference:
<https://investors.nuvalent.com/2024-05-16-Nuvalent-Receives-U-S-FDA-Breakthrough-Therapy-Designation-for-NVL-655>

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, PIK3CA, 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, TGFB1, TOP1, TOP2A, TPMT, TRRAP, TSHR, U2AF1, USP8, WAS, XPO1, 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, ERFF1, ESR1, ETV6, EZH2, FAM135B, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, FAT1, FBXW7, FGF19, FGF23, FGF3, 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, SLC01B3, SLX4, SMAD2, SMAD4, SMARCA4, SMARCB1, SMC1A, SMO, SOX9, SPEN, SPOP, SRC, STAG2, STAT3, STAT6, STK11, SUFU, TAP1, TAP2, TBX3, TCF7L2, TERT, TET2, TGFB1, TGFBR2

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, ZFH3, 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, PRKACA, PRKACB, PTEN, RAD51B, RAF1, RB1, RELA, RET, ROS1, RSP02, RSP03, 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, CBF3, 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, ERFF1, ETV6, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, FAS, FAT1, FBXW7, FUBP1, GATA3, GNA13, GPS2, HDAC2, HDAC9, HLA-A, HLA-B, HNF1A, ID3, INPP4B, JAK1, JAK2, JAK3, KDM5C, KDM6A, KEAP1, KLHL13, KMT2A, KMT2B, KMT2C, KMT2D, LARP4B, LATS1, LATS2, MAP2K4, MAP2K7, MAP3K1, MAP3K4, MAPK8, MEN1, MGA, MLH1, MLH3, MRE11, MSH2, MSH3, MSH6, MTAP, MTUS2, MUTYH, NBN, NCOR1, NF1, NF2, NOTCH1, NOTCH2, NOTCH3, NOTCH4, PALB2, PARP1, PARP2, PARP3, PARP4, PBRM1, PDCD1, PDCD1LG2, PDIA3, PGD, PHF6, PIK3R1, PMS1, PMS2, POLD1, POLE, POT1, PPM1D, PPP2R2A, PRDM1, PRDM9, PRKAR1A, PSMB10, PSMB8, PSMB9, PTCH1, PTEN, PTPRT, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD52, RAD54L, RASA1, RASA2, RB1, RBM10, RECQL4, RNASEH2A, RNASEH2B, RNASEH2C, RNF43, RPA1, RPL22, RPL5, RUNX1, RUNX1T1, SDHA, SDHB, SDHC, SDHD, SETD2, SLX4, SMAD2, SMAD4, SMARCA4, SMARCB1, SOCS1, SOX9, SPEN, STAG2, STAT1, STK11, SUFU, TAP1, TAP2, TBX3, TCF7L2, TET2, TGFB2, TMEM132D, TNFAIP3, TNFRSF14, TP53, TP63, TPP2, TSC1, TSC2, UGT1A1, USP9X, VHL, WT1, XRCC2, XRCC3, ZBTB20, ZFH3, ZMYM3, ZRSR2

Relevant Therapy Summary

☒ In this cancer type ☐ In other cancer type ☒ In this cancer type and other cancer types ☒ No evidence

KIF5B::ALK fusion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
crizotinib	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/> (I)
alectinib	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/> (IV)
brigatinib	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/> (II)
lorlatinib	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/> (II)
ceritinib	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="checkbox"/>
ensartinib	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="radio"/> (II)
atezolizumab + bevacizumab + carboplatin + paclitaxel	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="radio"/>	<input checked="" type="checkbox"/>
alectinib, durvalumab	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="radio"/> (III)
ASKC-202, limertinib	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="radio"/> (III)
neladalkib, alectinib	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="radio"/> (III)

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

Relevant Therapy Summary (continued)

● In this cancer type
 ○ In other cancer type
 ● In this cancer type and other cancer types
 ✕ No evidence

KIF5B::ALK fusion (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
alectinib, crizotinib	✕	✕	✕	✕	● (II)
alectinib, lorlatinib	✕	✕	✕	✕	● (II)
brigatinib, chemotherapy	✕	✕	✕	✕	● (II)
chemotherapy, lorlatinib	✕	✕	✕	✕	● (II)
ensartinib, radiation therapy, bevacizumab	✕	✕	✕	✕	● (II)
IBI-318, lenvatinib	✕	✕	✕	✕	● (II)
IBI323, bevacizumab, chemotherapy	✕	✕	✕	✕	● (II)
iruplinalkib	✕	✕	✕	✕	● (II)
JS-207, chemotherapy	✕	✕	✕	✕	● (II)
pembrolizumab, bevacizumab, chemotherapy	✕	✕	✕	✕	● (II)
SY-3505	✕	✕	✕	✕	● (II)
alectinib, radiation therapy	✕	✕	✕	✕	● (I/II)
amivantamab, alectinib, brigatinib, lorlatinib	✕	✕	✕	✕	● (I/II)
DAJH-1050766	✕	✕	✕	✕	● (I/II)
furetinib	✕	✕	✕	✕	● (I/II)
neladalkib	✕	✕	✕	✕	● (I/II)
ramucirumab, lorlatinib	✕	✕	✕	✕	● (I/II)
sotiburafusp alfa, chemotherapy	✕	✕	✕	✕	● (I/II)
sotiburafusp alfa, HB-0030	✕	✕	✕	✕	● (I/II)
ACR-246	✕	✕	✕	✕	● (I)
APG-2449	✕	✕	✕	✕	● (I)
CGT-9475	✕	✕	✕	✕	● (I)
gilteritinib	✕	✕	✕	✕	● (I)
IBI-363, IBI-325, lenvatinib	✕	✕	✕	✕	● (I)
LZ-001	✕	✕	✕	✕	● (I)
SYS-6023	✕	✕	✕	✕	● (I)
talazoparib, crizotinib	✕	✕	✕	✕	● (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	29.69%
BRCA2	LOH, 13q13.1(32890491-32972932)x2
BARD1	LOH, 2q35(215593375-215674382)x3
CHEK2	LOH, 22q12.1(29083868-29130729)x2
FANCL	LOH, 2p16.1(58386886-58468467)x3
PALB2	LOH, 16p12.2(23614759-23652528)x3

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 OncoPrint Reporter software was used in generation of this report. Software was developed and designed internally by Thermo Fisher Scientific. The analysis was based on OncoPrint Reporter (6.2.4 data version 2025.12(007)). 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 2025-11-25. NCCN information was sourced from www.nccn.org and is current as of 2025-11-03. EMA information was sourced from www.ema.europa.eu and is current as of 2025-11-25. ESMO information was sourced from www.esmo.org and is current as of 2025-11-03. Clinical Trials information is current as of 2025-11-03. 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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