

Patient Name: 고보라
 Gender: F
 Sample ID: N25-325

Primary Tumor Site: unknown
 Collection Date: 20251027

Sample Cancer Type: Unknown Primary Origin

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Report Highlights

1 Relevant Biomarkers
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 54 Clinical Trials

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	EML4::ALK fusion echinoderm microtubule associated protein like 4 - ALK receptor tyrosine kinase Locus: chr2:42491871 - chr2:29446394	None*	alecitinib 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+	54

* 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.

Prevalent cancer biomarkers without relevant evidence based on included data sources

DYPD p.(M166V) c.496A>G, Microsatellite stable, HLA-B deletion, NQO1 p.(P187S) c.559C>T, Tumor Mutational Burden

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
DYPD	p.(M166V)	c.496A>G	.	chr1:98165091	51.58%	NM_000110.4	missense
NQO1	p.(P187S)	c.559C>T	.	chr16:69745145	50.00%	NM_000903.3	missense
MSH3	p.(A57_A62del)	c.162_179delTGCAGC GGCCGCAGCGGC	.	chr5:79950707	50.48%	NM_002439.5	nonframeshift Deletion
HLA-B	p.([T118I;L119I])	c.353_355delCCCinsT CA	.	chr6:31324208	99.18%	NM_005514.8	missense, missense
DAXX	p.(S65L)	c.194C>T	.	chr6:33289545	51.20%	NM_001141970.2	missense
ASXL1	p.(T254I)	c.761C>T	.	chr20:31019166	5.87%	NM_015338.6	missense

Variant Details (continued)

Gene Fusions

Genes	Variant ID	Locus
EML4::ALK	EML4-ALK.E6aA20.AB374361.1	chr2:42491871 - chr2:29446394
EML4::ALK	EML4-ALK.E6bA20.AB374362.1	chr2:42492091 - chr2:29446394

Copy Number Variations

Gene	Locus	Copy Number	CNV Ratio
HLA-B	chr6:31322252	0	0.55

Biomarker Descriptions

EML4::ALK fusion

ALK receptor tyrosine kinase, echinoderm microtubule associated protein like 4

Background: The ALK gene encodes the ALK receptor tyrosine kinase (RTK), which has sequence similarity to the insulin receptor subfamily of kinases³⁴. 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 genes³⁵. ALK fusion kinases are constitutively activated and drive oncogenic transformation via activation of downstream STAT3, PI3K/AKT/MTOR, and RAS/RAF/MEK/ERK pathways^{35,36,37,38}.

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^{34,39,40}. In contrast, about 5% of non-small cell lung cancer (NSCLC) cases generate recurrent ALK fusions with EML4, KIF5B, and HIP1^{41,42,43}. Notably, ALK F1174L, F1245C, and R1275Q mutations are found in over 80% of ALK-mutated neuroblastoma⁴⁴. 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^{4,5}.

Potential relevance: The first-generation small molecule tyrosine kinase inhibitor (TKI), crizotinib⁴⁵, 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 renal cell carcinoma^{46,47,48}. 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^{49,50,51,52}. 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 IGF1R⁵³. In order to overcome acquired resistance, second- and third-generation ALK inhibitors including ceritinib⁵⁴ (2014), alectinib⁵⁵ (2015), brigatinib⁵⁶ (2017), lorlatinib⁵⁷ (2018), and ensartinib⁵⁸ (2024) were developed and approved for adults by the FDA. The FDA granted breakthrough therapy designation (2024) to NVL-655⁵⁹ for locally advanced or metastatic ALK-positive NSCLC patients who have been previously treated with two or more ALK TKIs.

DPYD p.(M166V) c.496A>G

dihydropyrimidine dehydrogenase

Background: The DPYD gene (also known as DPD) encodes dihydropyrimidine dehydrogenase, the initial and rate-limiting enzyme that catalyzes the reduction of uracil and thymidine in the pyrimidine catabolism pathway^{1,2}. DPYD is responsible for the inactivation and liver clearance of fluoropyrimidines (fluorouracil, capecitabine, and other analogs), which are the core chemotherapies used in the treatment of solid tumors, such as colorectal, pancreatic, gastric, breast, and head and neck cancers³. Inherited DPYD polymorphisms, including DPYD*2A, DPYD*13, DPYD c.2846A>T, and DPYD c.1129-5923T>G, can result in DPD deficiency, which is characterized by impaired enzymatic activity and confers an increased risk of severe toxicity to fluoropyrimidine drugs due to an increase in systemic drug exposure³.

Alterations and prevalence: Somatic mutations in DPYD have been observed in 20% of skin cutaneous melanoma, 9% of uterine corpus endometrial carcinoma, 6% of stomach adenocarcinoma, 5% of diffuse large B-cell lymphoma and colorectal adenocarcinoma, 4% of lung adenocarcinoma, 3% of bladder urothelial carcinoma, head and neck squamous cell carcinoma, and lung squamous cell carcinoma, and 2% of adrenocortical carcinoma, cervical squamous cell carcinoma, uterine carcinosarcoma, pancreatic adenocarcinoma, esophageal adenocarcinoma, liver hepatocellular carcinoma, and sarcoma^{4,5}. Biallelic loss of DPYD has been

Biomarker Descriptions (continued)

observed in 4% of pheochromocytoma and paraganglioma and 2% of esophageal adenocarcinoma and lung squamous cell carcinoma^{4,5}.

Potential relevance: Currently, no therapies are approved for DPYD.

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 genome¹². Microsatellite instability (MSI) is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue^{13,14}. MSI is closely tied to the status of the mismatch repair (MMR) genes. In humans, the core MMR genes include MLH1, MSH2, MSH6, and PMS2¹⁵. 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 D17S250¹⁶. 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)¹⁶. Tumors classified as MSI-L are often phenotypically indistinguishable from MSS tumors and tend to be grouped with MSS^{17,18,19,20,21}. 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 genes¹⁴. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer^{13,14,18,22}.

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^{13,14,23,24}. 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^{23,24}.

Potential relevance: Anti-PD-1 immune checkpoint inhibitors including pembrolizumab²⁵ (2014) and nivolumab²⁶ (2015) are approved for patients with MSI-H or dMMR colorectal cancer who have progressed following chemotherapy. Pembrolizumab²⁵ 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 indication²⁵. Dostarlimab²⁷ (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^{19,28}. The cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab²⁹ (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^{19,30,31}. 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 patients³¹. 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^{32,33}. However, checkpoint blockade with the addition of chemotherapy or targeted therapies have demonstrated response in MSS or pMMR cancers^{32,33}.

HLA-B deletion

major histocompatibility complex, class I, B

Background: The HLA-B gene encodes the major histocompatibility complex, class I, B¹. MHC (major histocompatibility complex) class I molecules are located on the cell surface of nucleated cells and present antigens from within the cell for recognition by cytotoxic T cells⁶. MHC class I molecules are heterodimers composed of two polypeptide chains, α and B2M⁷. The classical MHC class I genes include HLA-A, HLA-B, and HLA-C and encode the α polypeptide chains, which present short polypeptide chains, of 7 to 11 amino acids, to the immune system to distinguish self from non-self^{8,9,10}. Downregulation of MHC class I promotes tumor evasion of the immune system, suggesting a tumor suppressor role for HLA-B¹¹.

Alterations and prevalence: Somatic mutations in HLA-B are observed in 10% of diffuse large B-cell lymphoma (DLBCL), 5% of cervical squamous cell carcinoma and stomach adenocarcinoma, 4% of head and neck squamous cell carcinoma and colorectal adenocarcinoma, 3% of uterine cancer, and 2% of esophageal adenocarcinoma and skin cutaneous melanoma^{4,5}. Biallelic loss of HLA-B is observed in 5% of DLBCL^{4,5}.

Potential relevance: Currently, no therapies are approved for HLA-B aberrations.

Alerts Informed By Public Data Sources

Current FDA Information

 Contraindicated

 Not recommended

 Resistance

 Breakthrough

 Fast Track

FDA information is current as of 2025-09-17. For the most up-to-date information, search www.fda.gov.

EML4::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-Received-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, MYD88L, 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, SNCAP, SOS1, SOX2, SPOP, SRC, SRSF2, STAT3, STAT5B, STAT6, TAF1, TERT, TGFBR1, 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, 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, ERF1, 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, 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, RBBM10, 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, 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, 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, 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, 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, ERRF1, 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, TGFBR2, TMEM132D, TNFAIP3, TNFRSF14, TP53, TP63, TPP2, TSC1, TSC2, UGT1A1, USP9X, VHL, WT1, XRCC2, XRCC3, ZBTB20, ZFHX3, ZMYM3, ZRSR2

Relevant Therapy Summary

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

EML4::ALK fusion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
alectinib	○	○	○	○	● (IV)
brigatinib	○	○	○	○	● (II)
crizotinib	○	○	○	○	● (I)
lorlatinib	○	○	○	○	○ (II)
ceritinib	○	○	○	○	✗
ensartinib	○	○	✗	✗	○ (II)
atezolizumab + bevacizumab + carboplatin + paclitaxel	✗	✗	✗	○	✗
alectinib, crizotinib	✗	✗	✗	✗	● (II)
furetinib	✗	✗	✗	✗	● (I/II)
neladalkib	✗	✗	✗	✗	● (I/II)

* 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

EML4::ALK fusion (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
LZ-001	✖	✖	✖	✖	● (I)
talazoparib, crizotinib	✖	✖	✖	✖	● (I)
alectinib, chemotherapy	✖	✖	✖	✖	○ (III)
alectinib, durvalumab	✖	✖	✖	✖	○ (III)
neladalkib, alectinib	✖	✖	✖	✖	○ (III)
alectinib, lorlatinib	✖	✖	✖	✖	○ (II)
avutometinib, defactinib	✖	✖	✖	✖	○ (II)
brigatinib, chemotherapy	✖	✖	✖	✖	○ (II)
chemotherapy, lorlatinib	✖	✖	✖	✖	○ (II)
ensartinib, radiation therapy, bevacizumab	✖	✖	✖	✖	○ (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)
ramucirumab, lorlatinib	✖	✖	✖	✖	○ (I/II)
soturafusp alfa, chemotherapy	✖	✖	✖	✖	○ (I/II)
soturafusp alfa, HB-0030	✖	✖	✖	✖	○ (I/II)
ACR-246	✖	✖	✖	✖	○ (I)
APG-2449	✖	✖	✖	✖	○ (I)
CGT-9475	✖	✖	✖	✖	○ (I)
gilteritinib	✖	✖	✖	✖	○ (I)
IBI-318, lenvatinib	✖	✖	✖	✖	○ (I)
IBI-363, IBI-325, lenvatinib	✖	✖	✖	✖	○ (I)
mesothelin-targeted CAR-T cells	✖	✖	✖	✖	○ (I)
SYS-6023	✖	✖	✖	✖	○ (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 2025.10(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 2025-09-17. NCCN information was sourced from www.nccn.org and is current as of 2025-09-02. EMA information was sourced from www.ema.europa.eu and is current as of 2025-09-17. ESMO information was sourced from www.esmo.org and is current as of 2025-09-02. Clinical Trials information is current as of 2025-09-02. 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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