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Patient Name: 표춘영 Gender: Sample ID: N25-266 **Primary Tumor Site:** 2025.10.14 **Collection Date:**

Sample Cancer Type: Lung Cancer

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Relevant Lung Cancer Findings

Gene	Finding		Gene	Finding
ALK	None detected		NTRK1	None detected
BRAF	None detected		NTRK2	None detected
EGFR	EGFR exon 19	deletion	NTRK3	None detected
ERBB2	None detected		RET	None detected
KRAS	None detected		ROS1	None detected
MET	None detected			
Genomic Alt	eration	Finding		
Tumor Mu	ıtational 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	EGFR exon 19 deletion epidermal growth factor receptor Allele Frequency: 7.88% Locus: chr7:55242464 Transcript: NM_005228.5	afatinib 1,2/I,II+ amivantamab + lazertinib 1,2/I,II+ bevacizumab† + erlotinib 2/I,II+ dacomitinib 1,2/I,II+ erlotinib 2/I,II+ erlotinib + ramucirumab 1,2/I,II+ gefitinib 1,2/I,II+ osimertinib + chemotherapy 1,2/I amivantamab + chemotherapy 1,2/II+ BAT1706 + erlotinib 2 gefitinib + chemotherapy I atezolizumab + bevacizumab + chemotherapy II+	None*	199

^{*} 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.

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

[†] Includes biosimilars/generics

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Relevant Biomarkers (continued)

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	TP53 p.(S106R) c.318C>G tumor protein p53 Allele Frequency: 3.40% Locus: chr17:7579369 Transcript: NM_000546.6	None*	None*	6

^{*} 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.

🔼 Alerts informed by public data sources: 🤣 Contraindicated, 🛡 Resistance, 🗳 Breakthrough, 🗚 Fast Track

EGFR exon 19 deletion

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

Prevalent cancer biomarkers without relevant evidence based on included data sources

Microsatellite stable, UGT1A1 p.(G71R) c.211G>A, ERAP2 deletion, HLA-B deletion, Tumor Mutational Burden

Variant Details

DNA S	Sequence Variar	nts					
Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
EGFR	p.(E746_A750del)	c.2235_2249delGGAAT TAAGAGAAGC	COSM6223	chr7:55242464	7.88%	NM_005228.5	nonframeshift Deletion
TP53	p.(S106R)	c.318C>G	COSM45944	chr17:7579369	3.40%	NM_000546.6	missense
UGT1A1	p.(G71R)	c.211G>A	COSM4415616	chr2:234669144	50.28%	NM_000463.3	missense
MSH3	p.(A57_A62del)	c.162_179delTGCAGC GGCCGCAGCGGC		chr5:79950707	50.95%	NM_002439.5	nonframeshift Deletion
HDAC9	p.(V415L)	c.1243G>T		chr7:18687615	6.86%	NM_178425.3	missense
KMT2D	p.(Q3910_Q3911del)	c.11729_11734delAGC AAC		chr12:49426753	45.60%	NM_003482.4	nonframeshift Deletion

Copy Number Variations					
Gene	Locus	Copy Number	CNV Ratio		
ERAP2	chr5:96219500	0	0.47		
HLA-B	chr6:31322252	0	0.56		

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

[†] Includes biosimilars/generics

Biomarker Descriptions

EGFR exon 19 deletion

epidermal growth factor receptor

Background: The EGFR gene encodes the epidermal growth factor receptor (EGFR), a member of the ERBB/human epidermal growth factor receptor (HER) tyrosine kinase family¹. In addition to EGFR/ERBB1/HER1, other members of the ERBB/HER family include ERBB2/HER2, ERBB3/HER3, and ERBB4/HER4⁵8. EGFR ligand-induced dimerization results in kinase activation and leads to stimulation of oncogenic signaling pathways, including the PI3K/AKT/MTOR and RAS/RAF/MEK/ERK pathways⁵9. Activation of these pathways promotes cell proliferation, differentiation, and survival^{60,61}.

Alterations and prevalence: Recurrent somatic mutations in the tyrosine kinase domain (TKD) of EGFR are observed in approximately 10-20% of lung adenocarcinoma, and at higher frequencies in never-smoker, female, and Asian populations^{8,9,62,63}. The most common mutations occur near the ATP-binding pocket of the TKD and include short in-frame deletions in exon 19 (EGFR exon 19 deletion) and the L858R amino acid substitution in exon 2164. These mutations constitutively activate EGFR resulting in downstream signaling, and represent 80% of the EGFR mutations observed in lung cancer⁶⁴. A second group of less prevalent activating mutations includes E709K, G719X, S768I, L861Q, and short in-frame insertion mutations in exon 2065,66,67,68. EGFR activating mutations in lung cancer tend to be mutually exclusive to KRAS activating mutations⁶⁹. In contrast, a different set of recurrent activating EGFR mutations in the extracellular domain includes R108K, A289V and G598V and are primarily observed in glioblastoma^{64,70}. Amplification of EGFR is observed in several cancer types including 44% of glioblastoma multiforme, 12% of esophageal adenocarcinoma, 10% of head and neck squamous cell carcinoma, 8% of brain lower grade glioma, 6% of lung squamous cell carcinoma, 5% of bladder urothelial carcinoma cancer, lung adenocarcinoma, and stomach adenocarcinoma, 3% of cholangiocarcinoma, and 2% of cervical squamous cell carcinoma, sarcoma, and breast invasive carcinoma^{8,9,15,63,70}. Deletion of exons 2-7, encoding the extracellular domain of EGFR (EGFRvIII), results in overexpression of a ligand-independent constitutively active protein and is observed in approximately 30% of glioblastoma^{71,72,73}. Alterations in EGFR are rare in pediatric cancers^{8,9}. Somatic mutations are observed in 2% of bone cancer and glioma, 1% of leukemia (4 in 354 cases), and less than 1% of B-lymphoblastic leukemia/lymphoma (2 in 252 cases), peripheral nervous system cancers (1 in 1158 cases), and embryonal tumors (3 in 332 cases)8,9. Amplification of EGFR is observed in 2% of bone cancer and less than 1% of Wilms tumor (1 in 136 cases), B-lymphoblastic leukemia/lymphoma (2 in 731 cases), and leukemia (1 in 250 cases)8,9.

Potential relevance: Approved first-generation EGFR tyrosine kinase inhibitors (TKIs) include erlotinib⁷⁴ (2004) and gefitinib⁷⁵ (2015), which block the activation of downstream signaling by reversible interaction with the ATP-binding site. Although initially approved for advanced lung cancer, the discovery that drug sensitivity was associated with exon 19 and exon 21 activating mutations allowed first-generation TKIs to become subsequently approved for front-line therapy in lung cancer tumors containing exon 19 or exon 21 activating mutations⁷⁶. Second-generation TKIs afatinib⁷⁷ (2013) and dacomitinib⁷⁸ (2018) bind EGFR and other ERBB/HER gene family members irreversibly and were subsequently approved. First- and second-generation TKIs afatinib, dacomitinib, erlotinib, and gefitinib are recommended for the treatment NSCLC harboring EGFR exon 19 insertions, exon 19 deletions, point mutations L861Q, L858R, S768I, and codon 719 mutations, whereas most EGFR exon 20 insertions, except p.A763 Y764insF0EA, confer resistance to the same therapies^{79,80,81,82}. However, BDTX-18983 was granted a fast track designation (2020) for the treatment of solid tumors harboring an EGFR exon 20 insertion mutations. In 2022, the FDA granted breakthrough therapy designation to the irreversible EGFR inhibitors, CLN-081 (TPC-064)84 and sunvozertinib85, for locally advanced or metastatic non-small cell lung cancer harboring EGFR exon 20 insertion mutations. In lung cancer containing EGFR exon 19 or 21 activating mutations, treatment with TKIs is eventually associated with the emergence of drug resistance86. The primary resistance mutation that emerges following treatment with firstgeneration TKI is T790M, accounting for 50-60% of resistant cases⁶⁴. Third generation TKIs were developed to maintain sensitivity in the presence of T790M86. Osimertinib87 (2015) is an irreversible inhibitor indicated for metastatic EGFR T790M positive lung cancer and for the first-line treatment of metastatic NSCLC containing EGFR exon 19 deletions or exon 21 L858R mutations. Like firstgeneration TKIs, treatment with osimertinib is associated with acquired resistance, specifically the C797S mutation, which occurs in 22-44% of cases⁸⁶. The T790M and C797S mutations may be each selected following sequential treatment with a first-generation TKI followed by a third-generation TKI or vice versa⁸⁸. T790M and C797S can occur in either cis or trans allelic orientation⁸⁸. If C797S is observed following progression after treatment with a third-generation TKI in the first-line setting, sensitivity may be retained to first-generation TKIs88. If C797S co-occurs in trans with T790M following sequential treatment with first- and third-generation TKIs, patients may exhibit sensitivity to combination first- and third-generation TKIs, but resistance to third-generation TKIs alone^{88,89}. However, C797S occurring in cis conformation with T790M, confers resistance to first- and third-generation TKIs⁸⁸. Fourth-generation TKIs are in development to overcome acquired resistance mutations after osimertinib treatment, including BDTX-153590 (2024), a CNS-penetrating small molecule inhibitor, that received fast track designation from the FDA for the treatment of patients with EGFR C797S-positive NSCLC who have disease progression on or after a third-generation EGFR TKI. EGFR-targeting antibodies including cetuximab (2004), panitumumab (2006), and necitumumab (2016) are under investigation in combination with EGFR-targeting TKIs for efficacy against EGFR mutations⁹¹. The bispecific antibody, amivantamab⁹² (2021), targeting EGFR and MET was approved for NSCLC tumors harboring EGFR exon 20 insertion mutations. A small molecule kinase inhibitor, lazertinib93 (2024), was approved in combination with amivantamab as a first-line treatment for adult patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R mutations. In 2024, a CNS penetrating small molecule, ERAS-80194 received fast track designation for the treatment of adult patients with EGFR altered glioblastoma. HLX-4295, an anti-EFGR-antibody-drug conjugate (ADC) consisting of an anti-EGFR monoclonal antibody conjugated with a novel high potency DNA topoisomerase I (topo I) inhibitor, also received fast

Biomarker Descriptions (continued)

track designation (2024) for the treatment of patients with advanced or metastatic EGFR-mutated non-small cell lung cancer whose disease has progressed on a third-generation EGFR tyrosine kinase inhibitor. CPO301⁹⁶ (2023) received a fast track designation from the FDA for the treatment of EGFR mutations in patients with metastatic NSCLC who are relapsed/refractory or ineligible for EGFR targeting therapy such as 3rd-generation EGFR inhibitors, including osimertinib. The Oncoprex immunogene therapy quaratusugene ozeplasmid⁹⁷ (2020), in combination with osimertinib, received fast track designation from the FDA for NSCLC tumors harboring EGFR mutations that progressed on osimertinib alone. Amplification and mutations of EGFR commonly occur in H3-wild type IDH-wild type diffuse pediatric high-grade glioma^{98,99,100}.

TP53 p.(S106R) c.318C>G

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 proteolysis¹⁰. Alterations in TP53 are required for oncogenesis as they result in loss of protein function and gain of transforming potential¹¹. Germline mutations in TP53 are the underlying cause of Li-Fraumeni syndrome, a complex hereditary cancer predisposition disorder associated with early-onset cancers^{12,13}.

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%)^{8,9,14,15,16,17}. 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 R2828,⁹. Invariably, recurrent missense mutations in TP53 inactivate its ability to bind DNA and activate transcription of target genes^{18,19,20,21}. Alterations in TP53 are also observed in pediatric cancers^{8,9}. 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)^{8,9}. 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)^{8,9}.

Potential relevance: The small molecule p53 reactivator, PC14586²² (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, eprenetapopt²³, (2019) and breakthrough designation²⁴ (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^{25,26}. TP53 mutation are a diagnostic marker of SHH-activated, TP53-mutant medulloblastoma²⁷. 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)^{28,29,30,31,32,33}. In mantle cell lymphoma, TP53 mutations are associated with poor prognosis when treated with conventional therapy including hematopoietic cell transplant³⁴. Mono- and bi-allelic mutations in TP53 confer unique 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 system³⁵.

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 genome³⁶. Microsatellite instability (MSI) is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue^{37,38}. MSI is closely tied to the status of the mismatch repair (MMR) genes. In humans, the core MMR genes include MLH1, MSH2, MSH6, and PMS2³⁹. 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 D17S250⁴⁰. 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)⁴⁰. Tumors classified as MSI-L are often phenotypically indistinguishable from MSS tumors and tend to be grouped with MSS^{41,42,43,44,45}. 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 genes³⁸. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer^{37,38,42,46}.

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^{37,38,47,48}. 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^{47,48}.

Biomarker Descriptions (continued)

Potential relevance: Anti-PD-1 immune checkpoint inhibitors including pembrolizumab⁴⁹ (2014) and nivolumab⁵⁰ (2015) are approved for patients with MSI-H or dMMR colorectal cancer who have progressed following chemotherapy. Pembrolizumab⁴⁹ 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 indication⁴⁹. Dostarlimab⁵¹ (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^{43,52}. The cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab⁵³ (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^{43,54,55}. 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 patients⁵⁵. 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^{56,57}. However, checkpoint blockade with the addition of chemotherapy or targeted therapies have demonstrated response in MSS or pMMR cancers^{56,57}.

UGT1A1 p.(G71R) c.211G>A

UDP glucuronosyltransferase family 1 member A1

Background: The UGT1A1 gene encodes UDP glucuronosyltransferase family 1 member A1, a member of the UDP-glucuronosyltransferase 1A (UGT1A) subfamily of the UGT protein superfamily^{1,104}. UGTs are microsomal membrane-bound enzymes that catalyze the glucuronidation of endogenous and xenobiotic compounds and transform the lipophilic molecules into excretable, hydrophilic metabolites^{104,105}. UGTs play an important role in drug metabolism, detoxification, and metabolite homeostasis. Differential expression of UGTs can promote cancer development, disease progression, as well as drug resistance¹⁰⁶. Specifically, elevated expression of UGT1As are associated with resistance to many anti-cancer drugs due to drug inactivation and lower active drug concentrations. However, reduced expression and downregulation of UGT1As are implicated in bladder and hepatocellular tumorigenesis and progression due to toxin accumulation^{106,107,108,109}. Furthermore, UGT1A1 polymorphisms, such as UGT1A1*28, UGT1A1*93, and UGT1A1*6, confer an increased risk of severe toxicity to irinotecan-based chemotherapy treatment of solid tumors, due to reduced glucuronidation of the irinotecan metabolite, SN-38¹¹⁰.

Alterations and prevalence: Biallelic deletion of UGT1A1 has been observed in 6% of sarcoma, 3% of brain lower grade glioma and uveal melanoma, and 2% of thymoma, cervical squamous cell carcinoma, bladder urothelial carcinoma, head and neck squamous cell carcinoma, and esophageal adenocarcinoma^{8,9}.

Potential relevance: Currently, no therapies are approved for UGT1A1 aberrations.

ERAP2 deletion

endoplasmic reticulum aminopeptidase 2

<u>Background</u>: The ERAP2 gene encodes the endoplasmic reticulum aminopeptidase 2 protein. ERAP2, and structurally related ERAP1, are zinc metallopeptidases which play a role in antigen processing within the immune response pathway^{101,102}. Upon uptake by an immune cell, antigens are first processed by the proteasome and then transported into the endoplasmic reticulum where ERAP1 and ERAP2 excise peptide N-terminal extensions to generate mature antigen peptides for presentation on MHC class I molecules^{101,103}. The polymorphic variability in ERAP2 is hypothesized to affect the severity of cytotoxic responses to transformed cells and potentially influence their chances to gain mutations that evade the immune system and become tumorigenic¹⁰¹.

Alterations and prevalence: Somatic mutations in ERAP2 are observed in 7% of uterine corpus endometrial carcinoma and skin cutaneous melanoma, and 2% of colorectal adenocarcinoma, uterine carcinosarcoma, head and neck squamous cell carcinoma, and stomach adenocarcinoma^{8,9}. Deletions are observed in 2% of ovarian serous cystadenocarcinoma, prostate adenocarcinoma, and 1% of colorectal adenocarcinoma, mesothelioma, esophageal adenocarcinoma, and lung squamous cell carcinoma^{8,9}.

Potential relevance: Currently, no therapies are approved for ERAP2 aberrations.

HLA-B deletion

major histocompatibility complex, class I, B

 $\frac{Background:}{I} \label{eq:localization} The HLA-B gene encodes the major histocompatibility complex, class I, B¹. MHC (major histocompatibility complex) class I molecules are located on the cell surface of nucleated cells and present antigens from within the cell for recognition by cytotoxic T cells². MHC class I molecules are heterodimers composed of two polypeptide chains, <math>\alpha$ and B2M³. 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,

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Biomarker Descriptions (continued)

to the immune system to distinguish self from non-self 4,5,6 . Downregulation of MHC class I promotes tumor evasion of the immune system, suggesting a tumor suppressor role for HLA-B 7 .

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^{8,9}. Biallelic loss of HLA-B is observed in 5% of DLBCL^{8,9}.

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

EGFR exon 19 deletion

patritumab deruxtecan

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion or EGFRi sensitizing mutation

Supporting Statement:

The FDA has granted Breakthrough Therapy designation to a potential first-in-class HER3 directed antibody-drug conjugate, patritumab deruxtecan, for metastatic or locally advanced, EGFR-mutant non-small cell lung cancer.

https://www.cancernetwork.com/view/fda-grants-breakthrough-therapy-status-to-patritumab-deruxtecan-for-egfr-metastaticnsclc

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, 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,

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 this cancer type	O In other cancer type	In this cancer type and other cancer types	No evidence
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Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
osimertinib					(III)
afatinib	•	•	•		(II)
dacomitinib	•	•	•	•	(II)
gefitinib	•	•	•	•	(II)
erlotinib + ramucirumab	•	•	•	•	×
amivantamab + carboplatin + pemetrexed	•	•	•	×	×
amivantamab + lazertinib	•	•	•	×	×
osimertinib + chemotherapy + pemetrexed	•	×		×	×
bevacizumab + erlotinib	×	•	•	•	×
erlotinib	×		•		×

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

Relevant Therapy Summary (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
osimertinib + carboplatin + pemetrexed	×		×	×	×
osimertinib + cisplatin + pemetrexed	×	•	×	×	×
BAT1706 + erlotinib	×	×		×	×
bevacizumab (Allergan) + erlotinib	×	×		×	×
bevacizumab (Biocon) + erlotinib	×	×	•	×	×
bevacizumab (Celltrion) + erlotinib	×	×	•	×	×
bevacizumab (Mabxience) + erlotinib	×	×	•	×	×
bevacizumab (Pfizer) + erlotinib	×	×	•	×	×
bevacizumab (Samsung Bioepis) + erlotinib	×	×	•	×	×
bevacizumab (Stada) + erlotinib	×	×	•	×	×
atezolizumab + bevacizumab + carboplatin + paclitaxel	×	×	×	•	×
gefitinib + carboplatin + pemetrexed	×	×	×	•	×
adebrelimab, bevacizumab, chemotherapy	×	×	×	×	(IV)
afatinib, bevacizumab, chemotherapy	×	×	×	×	(IV)
befotertinib	×	×	×	×	(IV)
bevacizumab, almonertinib, chemotherapy	×	×	×	×	(IV)
catequentinib, toripalimab	×	×	×	×	(IV)
EGFR tyrosine kinase inhibitor	×	×	×	×	(IV)
gefitinib, chemotherapy	×	×	×	×	(IV)
gefitinib, endostatin	×	×	×	×	(IV)
natural product, gefitinib, erlotinib, icotinib hydrochloride, osimertinib, almonertinib, furmonertinib	×	×	×	×	● (IV)
almonertinib, apatinib	×	×	×	×	(III)
almonertinib, catequentinib	×	×	×	×	(III)
almonertinib, chemotherapy	×	×	×	×	(III)
almonertinib, radiation therapy	×	×	×	×	(III)
almonertinib, radiation therapy, chemotherapy	×	×	×	×	(III)
befotertinib, icotinib hydrochloride	×	×	×	×	(III)
bevacizumab, osimertinib	×	×	×	×	(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)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
BL-B01D1	×	×	×	×	(III)
BL-B01D1, osimertinib	×	×	×	×	(III)
CK-101, gefitinib	×	×	×	×	(III)
datopotamab deruxtecan, osimertinib	×	×	×	×	(III)
FHND9041, afatinib	×	×	×	×	(III)
furmonertinib	×	×	×	×	(III)
furmonertinib, osimertinib, chemotherapy	×	×	×	×	(III)
gefitinib, afatinib, erlotinib, metformin hydrochloride	×	×	×	×	(III)
icotinib hydrochloride, catequentinib	×	×	×	×	(III)
icotinib hydrochloride, chemotherapy	×	×	×	×	(III)
icotinib hydrochloride, radiation therapy	×	×	×	×	(III)
JMT-101, osimertinib	×	×	×	×	(III)
osimertinib, bevacizumab	×	×	×	×	(III)
osimertinib, chemotherapy	×	×	×	×	(III)
osimertinib, datopotamab deruxtecan	×	×	×	×	(III)
sacituzumab tirumotecan	×	×	×	×	(III)
sacituzumab tirumotecan, osimertinib	×	×	×	×	(III)
savolitinib, osimertinib	×	×	×	×	(III)
SH-1028	×	×	×	×	(III)
targeted therapy	×	×	×	×	(III)
TY-9591, osimertinib	×	×	×	×	(III)
SCTB-14, chemotherapy	×	×	×	×	(/)
ABSK-043, furmonertinib	×	×	×	×	● (II)
almonertinib	×	×	×	×	(II)
almonertinib, adebrelimab, chemotherapy	×	×	×	×	(II)
almonertinib, bevacizumab	×	×	×	×	(II)
almonertinib, chemoradiation therapy	×	×	×	×	(II)
almonertinib, dacomitinib	×	×	×	×	(II)
amivantamab, chemotherapy	×	×	×	×	(II)

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

(II)

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(II)

Relevant Therapy Summary (continued)

EGFR exon 19 deletion (continued)

furmonertinib, icotinib hydrochloride

gefitinib, bevacizumab, chemotherapy

icotinib hydrochloride, autologous RAK cell

gefitinib, icotinib hydrochloride

icotinib hydrochloride, osimertinib

ivonescimab, chemotherapy

gefitinib, thalidomide

icotinib hydrochloride

lazertinib

In this cancer type

O In other cancer type

In this cancer type and other cancer types

X No evidence

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials
amivantamab, lazertinib, chemotherapy	×	×	×	×	(II)
atezolizumab, bevacizumab, tiragolumab	×	×	×	×	(II)
befotertinib, bevacizumab, chemotherapy	×	×	×	×	(II)
bevacizumab, afatinib	×	×	×	×	(II)
bevacizumab, furmonertinib	×	×	×	×	(II)
cadonilimab, chemotherapy, catequentinib	×	×	×	×	(II)
camrelizumab, apatinib	×	×	×	×	(II)
capmatinib, osimertinib, ramucirumab	×	×	×	×	(II)
catequentinib, almonertinib	×	×	×	×	(II)
chemotherapy, atezolizumab, bevacizumab	×	×	×	×	(II)
dacomitinib, osimertinib	×	×	×	×	(II)
EGFR tyrosine kinase inhibitor, osimertinib, chemotherapy	×	×	×	×	(II)
EGFR tyrosine kinase inhibitor, radiation therapy	×	×	×	×	(II)
erlotinib, chemotherapy	×	×	×	×	(II)
erlotinib, OBI-833	×	×	×	×	(II)
furmonertinib, bevacizumab	×	×	×	×	(II)
furmonertinib, bevacizumab, chemotherapy	×	×	×	×	(II)
furmonertinib, catequentinib	×	×	×	×	(II)
furmonertinib, chemotherapy	×	×	×	×	(II)
furmonertinib, chemotherapy, bevacizumab	×	×	×	×	(II)

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^{*} 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)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials
lazertinib, bevacizumab	×	×	×	×	(II)
lazertinib, chemotherapy	×	×	×	×	(II)
lenvatinib, pembrolizumab	×	×	×	×	(II)
osimertinib, bevacizumab, chemotherapy	×	×	×	×	(II)
osimertinib, chemoradiation therapy	×	×	×	×	(II)
osimertinib, radiation therapy	×	×	×	×	(II)
PLB-1004, bozitinib, osimertinib	×	×	×	×	(II)
ramucirumab, erlotinib	×	×	×	×	(II)
sacituzumab govitecan	×	×	×	×	(II)
sacituzumab tirumotecan, chemotherapy, osimertinib	×	×	×	×	(II)
sunvozertinib	×	×	×	×	(II)
sunvozertinib, catequentinib	×	×	×	×	(II)
sunvozertinib, golidocitinib	×	×	×	×	(II)
tislelizumab, chemotherapy, bevacizumab	×	×	×	×	(II)
toripalimab	×	×	×	×	(II)
toripalimab, bevacizumab, Clostridium butyricum, chemotherapy	×	×	×	×	(II)
toripalimab, chemotherapy	×	×	×	×	(II)
TY-9591, chemotherapy	×	×	×	×	(II)
zorifertinib, pirotinib	×	×	×	×	(II)
AFM-24_I, atezolizumab	×	×	×	×	(I/II)
almonertinib, icotinib hydrochloride	×	×	×	×	(I/II)
benmelstobart, catequentinib	×	×	×	×	(I/II)
BH-30643	×	×	×	×	(1/11)
bozitinib, osimertinib	×	×	×	×	(I/II)
BPI-361175	×	×	×	×	(I/II)
cetrelimab, amivantamab	×	×	×	×	(I/II)
dacomitinib, catequentinib	×	×	×	×	(1/11)
DAJH-1050766	×	×	×	×	(I/II)
DB-1310, osimertinib	×	×	×	×	(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)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
dositinib	×	×	×	×	(/)
FWD-1509	×	×	×	×	(1/11)
H-002	×	×	×	×	(1/11)
ifebemtinib, furmonertinib	×	×	×	×	(I/II)
MRTX0902	×	×	×	×	(I/II)
necitumumab, osimertinib	×	×	×	×	(I/II)
quaratusugene ozeplasmid, osimertinib	×	×	×	×	(I/II)
RC-108, furmonertinib, toripalimab	×	×	×	×	(I/II)
sotiburafusp alfa, HB-0030	×	×	×	×	(/)
sunvozertinib, chemotherapy	×	×	×	×	(/)
TAS-3351	×	×	×	×	(/)
TQ-B3525, osimertinib	×	×	×	×	(/)
TRX-221	×	×	×	×	(/)
WSD-0922	×	×	×	×	(/)
afatinib, chemotherapy	×	×	×	×	(I)
almonertinib, midazolam	×	×	×	×	(I)
ASKC-202	×	×	×	×	(I)
AZD-9592	×	×	×	×	(I)
BG-60366	×	×	×	×	(I)
BPI-1178, osimertinib	×	×	×	×	(I)
catequentinib, gefitinib, metformin hydrochloride	×	×	×	×	(I)
DZD-6008	×	×	×	×	(I)
EGFR tyrosine kinase inhibitor, catequentinib	×	×	×	×	(I)
genolimzumab, fruquintinib	×	×	×	×	(I)
IBI-318, lenvatinib	×	×	×	×	(I)
KQB-198, osimertinib	×	×	×	×	(I)
LAVA-1223	×	×	×	×	(I)
MRX-2843, osimertinib	×	×	×	×	(I)

^{*} 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)

■ In this cancer type
O In other cancer type
In this cancer type and other cancer types
X No evidence

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials
osimertinib, Minnelide	×	×	×	×	(I)
osimertinib, tegatrabetan	×	×	×	×	(l)
patritumab deruxtecan	×	×	×	×	(l)
PB-101 (Precision Biotech Taiwan Corp), EGFR tyrosine kinase inhibitor	×	×	×	×	(l)
repotrectinib, osimertinib	×	×	×	×	(1)
VIC-1911, osimertinib	×	×	×	×	(I)
WJ13404	×	×	×	×	(l)
WTS-004	×	×	×	×	(l)
YH-013	×	×	×	×	(I)
YL-202	×	×	×	×	(I)

TP53 p.(S106R) c.318C>G					
Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
almonertinib, catequentinib	×	×	×	×	(III)
osimertinib, chemotherapy	×	×	×	×	(III)
osimertinib, bevacizumab, chemotherapy	×	×	×	×	(II)
sunvozertinib, catequentinib	×	×	×	×	(II)

^{*} 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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