

Patient Name: 전재복

Gender: F

Sample ID: N25-159

Primary Tumor Site: Lung

Collection Date: 2025.07.30.

Sample Cancer Type: Non-Small Cell Lung Cancer

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Relevant Non-Small Cell Lung Cancer Findings

Gene	Finding	Gene	Finding
ALK	None detected	MET	None detected
BRAF	BRAF wild type	NRG1	None detected
EGFR	EGFR p.(L858R) c.2573T>G	NTRK1	None detected
ERBB2	None detected	NTRK2	None detected
FGFR1	None detected	NTRK3	None detected
FGFR2	None detected	RET	None detected
FGFR3	None detected	ROS1	None detected
KRAS	None detected		

Genomic Alteration	Finding
Tumor Mutational Burden	1.9 Mut/Mb measured

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	EGFR p.(L858R) c.2573T>G epidermal growth factor receptor Allele Frequency: 9.19% Locus: chr7:55259515 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 ^{1, 2 / I, II+} osimertinib + chemotherapy ^{1, 2 / I} amivantamab + chemotherapy ^{1, 2 / II+} BAT1706 + erlotinib ² gefitinib + chemotherapy ^I	None*	201

* Public data sources included in relevant therapies: FDA¹, NCCN, EMA², ESMO
* Public data sources included in prognostic and diagnostic significance: NCCN, ESMO
† Includes biosimilars/generics
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.

Relevant Biomarkers (continued)

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
		atezolizumab + bevacizumab + chemotherapy ^{II+}		
IIC	TP53 p.(C176F) c.527G>T	None*	None*	6
	tumor protein p53			
	Allele Frequency: 5.26%			
	Locus: chr17:7578403			
	Transcript: NM_000546.6			

* Public data sources included in relevant therapies: FDA¹, NCCN, EMA², ESMO
* Public data sources included in prognostic and diagnostic significance: NCCN, ESMO
† Includes biosimilars/generics
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 p.(L858R) c.2573T>G	 patritumab deruxtecan ¹
BRAF wild type	 binimetinib + encorafenib ² , dabrafenib ^{1, 2} , encorafenib ^{1, 2}

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, ERAP2 deletion, 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
EGFR	p.(L858R)	c.2573T>G	COSM6224	chr7:55259515	9.19%	NM_005228.5	missense
TP53	p.(C176F)	c.527G>T	COSM10645	chr17:7578403	5.26%	NM_000546.6	missense
MLH1	p.(V384D)	c.1151T>A	.	chr3:37067240	52.03%	NM_000249.4	missense
NQO1	p.(P187S)	c.559C>T	.	chr16:69745145	45.67%	NM_000903.3	missense
DICER1	p.(A1508P)	c.4522G>C	.	chr14:95562735	4.83%	NM_030621.4	missense

Copy Number Variations

Gene	Locus	Copy Number	CNV Ratio
ERAP2	chr5:96219500	0	0.49
HLA-B	chr6:31322252	0.43	0.68

Biomarker Descriptions

EGFR p.(L858R) c.2573T>G

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/HER4⁷¹. 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 pathways⁷². Activation of these pathways promotes cell proliferation, differentiation, and survival^{73,74}.

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^{8,9,75,76}. 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 21⁷⁷. These mutations constitutively activate EGFR resulting in downstream signaling, and represent 80% of the EGFR mutations observed in lung cancer⁷⁷. A second group of less prevalent activating mutations includes E709K, G719X, S768I, L861Q, and short in-frame insertion mutations in exon 20^{78,79,80,81}. EGFR activating mutations in lung cancer tend to be mutually exclusive to KRAS activating mutations⁸². 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^{77,83}. 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^{8,9,36,76,83}. 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^{84,85,86}. 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 erlotinib⁸⁷ (2004) and gefitinib⁸⁸ (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 mutations⁸⁹. Second-generation TKIs afatinib⁹⁰ (2013) and dacomitinib⁹¹ (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_Y764insFQEA, confer resistance to the same therapies^{92,93,94,95}. However, BDTX-189⁹⁶ 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)⁹⁷ and sunvozertinib⁹⁸, 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 resistance⁹⁹. The primary resistance mutation that emerges following treatment with first-generation TKI is T790M, accounting for 50-60% of resistant cases⁷⁷. Third generation TKIs were developed to maintain sensitivity in the presence of T790M⁹⁹. Osimertinib¹⁰⁰ (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 first-generation TKIs, treatment with osimertinib is associated with acquired resistance, specifically the C797S mutation, which occurs in 22-44% of cases⁹⁹. 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 versa¹⁰¹. T790M and C797S can occur in either cis or trans allelic orientation¹⁰¹. 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 TKIs¹⁰¹. 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^{101,102}. However, C797S occurring in cis conformation with T790M, confers resistance to first- and third-generation TKIs¹⁰¹. Fourth-generation TKIs are in development to overcome acquired resistance mutations after osimertinib treatment, including BDTX-1535¹⁰³ (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 mutations¹⁰⁴. The bispecific antibody, amivantamab¹⁰⁵ (2021), targeting EGFR and MET was approved for NSCLC tumors harboring EGFR exon 20 insertion mutations. A small molecule kinase inhibitor, lazertinib¹⁰⁶ (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-801¹⁰⁷ received fast track designation for the treatment of adult patients with EGFR altered glioblastoma. HLX-42¹⁰⁸, an anti-EGFR-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. CPO301¹⁰⁹ (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 ozeplasmid¹¹⁰ (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^{29,111,112}.

TP53 p.(C176F) c.527G>T

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 proteolysis³¹. Alterations in TP53 are required for oncogenesis as they result in loss of protein function and gain of transforming potential³². Germline mutations in TP53 are the underlying cause of Li-Fraumeni syndrome, a complex hereditary cancer predisposition disorder associated with early-onset cancers^{33,34}.

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%)^{8,9,35,36,37,38}. 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^{8,9}. Invariably, recurrent missense mutations in TP53 inactivate its ability to bind DNA and activate transcription of target genes^{39,40,41,42}. 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, PC14586⁴³ (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, eprenetapopt⁴⁴, (2019) and breakthrough designation⁴⁵ (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^{46,47}. TP53 mutation are a diagnostic marker of SHH-activated, TP53-mutant medulloblastoma⁴⁸. 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)^{49,50,51,52,53,54}. In mantle cell lymphoma, TP53 mutations are associated with poor prognosis when treated with conventional therapy including hematopoietic cell transplant⁵⁵. 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 system⁵⁶.

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 MutLα complex, PMS1 to form the MutLβ complex, and MLH3 to form the MutLγ complex¹⁰. The MutLα complex functions as an endonuclease that is specifically involved in the mismatch repair (MMR) process and mutations in MLH1 result in the inactivation of MutLα and degradation of PMS2^{10,11}. 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^{12,13}. MLH1, along with MSH6, MSH2, and PMS2 form the core components of the MMR pathway¹⁰. The MMR pathway is critical to the repair of mismatch errors which typically occur during DNA replication¹⁰. Deficiency in MMR (dMMR) is characterized by mutations and loss of expression in these genes¹⁴. 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^{15,16,17}. 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^{15,18}. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer^{16,18,19,20}. Specifically, MLH1 mutations are associated with an increased risk of ovarian and pancreatic cancer^{21,22,23,24}.

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^{8,9}. Alterations in MLH1 are

Biomarker Descriptions (continued)

observed in pediatric cancers^{8,9}. 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)^{8,9}.

Potential relevance: The PARP inhibitor, talazoparib²⁵ 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 therapies²⁶. 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^{27,28}. MLH1 mutations are consistent with high grade in pediatric diffuse gliomas^{29,30}.

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 genome⁵⁷. Microsatellite instability (MSI) is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue^{16,18}. MSI is closely tied to the status of the mismatch repair (MMR) genes. In humans, the core MMR genes include MLH1, MSH2, MSH6, and PMS2¹⁷. 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 D17S250⁵⁸. 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)⁵⁸. Tumors classified as MSI-L are often phenotypically indistinguishable from MSS tumors and tend to be grouped with MSS^{19,59,60,61,62}. 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 genes¹⁸. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer^{16,18,19,20}.

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^{16,18,63,64}. 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^{63,64}.

Potential relevance: Anti-PD-1 immune checkpoint inhibitors including pembrolizumab²⁶ (2014) and nivolumab²⁷ (2015) are approved for patients with MSI-H or dMMR colorectal cancer who have progressed following chemotherapy. Pembrolizumab²⁶ 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 indication²⁶. Dostarlimab⁶⁵ (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^{60,66}. The cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab²⁸ (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^{60,67,68}. 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 patients⁶⁸. 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^{69,70}. However, checkpoint blockade with the addition of chemotherapy or targeted therapies have demonstrated response in MSS or pMMR cancers^{69,70}.

ERAP2 deletion

endoplasmic reticulum aminopeptidase 2

Background: 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^{113,114}. 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^{113,115}. 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 tumorigenic¹¹³.

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.

Biomarker Descriptions (continued)

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 cells². MHC class I molecules are heterodimers composed of two polypeptide chains, α 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, 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-B⁷.

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.

BRAF wild type (continued)

encorafenib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2025-03-12

Variant class: BRAF wild type

Indications and usage:

BRAFTOVI® is a kinase inhibitor indicated:

Melanoma

- in combination with binimetinib, for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test.

Colorectal Cancer (CRC)

- in combination with cetuximab and mFOLFOX6, for the treatment of patients with metastatic colorectal cancer (mCRC) with a BRAF V600E mutation, as detected by an FDA-approved test.

This indication is approved under accelerated approval based on response rate and durability of response.

Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

- in combination with cetuximab, for the treatment of adult patients with metastatic CRC with a BRAF V600E mutation, as detected by an FDA-approved test, after prior therapy.

Non-Small Cell Lung Cancer (NSCLC)

- in combination with binimetinib, for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) with a BRAF V600E mutation, as detected by an FDA-approved test.

Limitations of Use:

BRAFTOVI® is not indicated for treatment of patients with wild-type BRAF melanoma, wild-type BRAF CRC, or wild-type BRAF NSCLC.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/210496s018lbl.pdf

Current EMA Information

 Contraindicated

 Not recommended

 Resistance

 Breakthrough

 Fast Track

EMA information is current as of 2025-05-14. For the most up-to-date information, search www.ema.europa.eu.

BRAF wild type

binimetinib + encorafenib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2024-12-10

Variant class: BRAF wild type

Reference:

https://www.ema.europa.eu/en/documents/product-information/mektovi-epar-product-information_en.pdf

dabrafenib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2024-12-05

Variant class: BRAF wild type

Reference:

https://www.ema.europa.eu/en/documents/product-information/tafinlar-epar-product-information_en.pdf

BRAF wild type (continued)

encorafenib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2024-12-10

Variant class: BRAF wild type

Reference:

https://www.ema.europa.eu/en/documents/product-information/braftovi-epar-product-information_en.pdf

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, MYO1, 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, 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, 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, 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, REL, 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,

Genes Assayed (continued)

Genes Assayed with Full Exon Coverage (continued)

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

EGFR p.(L858R) c.2573T>G

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	×	●	●	●	×
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	×	×	●	×	×

* 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
 ① In this cancer type and other cancer types
 ✕ No evidence

EGFR p.(L858R) c.2573T>G (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
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)
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)

* 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

EGFR p.(L858R) c.2573T>G (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
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	✕	✕	✕	✕	● (II/III)
ABSK-043, furmonertinib	✕	✕	✕	✕	● (II)
almonertinib	✕	✕	✕	✕	● (II)
almonertinib, adebrelimab, chemotherapy	✕	✕	✕	✕	● (II)
almonertinib, bevacizumab	✕	✕	✕	✕	● (II)
almonertinib, chemoradiation therapy	✕	✕	✕	✕	● (II)
almonertinib, dacomitinib	✕	✕	✕	✕	● (II)
amivantamab, chemotherapy	✕	✕	✕	✕	● (II)
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)

* 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

EGFR p.(L858R) c.2573T>G (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
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)
furmonertinib, icotinib hydrochloride	×	×	×	×	● (II)
gefitinib, bevacizumab, chemotherapy	×	×	×	×	● (II)
gefitinib, icotinib hydrochloride	×	×	×	×	● (II)
gefitinib, thalidomide	×	×	×	×	● (II)
icotinib hydrochloride	×	×	×	×	● (II)
icotinib hydrochloride, autologous RAK cell	×	×	×	×	● (II)
icotinib hydrochloride, osimertinib	×	×	×	×	● (II)
ivonescimab, chemotherapy	×	×	×	×	● (II)
lazertinib	×	×	×	×	● (II)
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)

* 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

EGFR p.(L858R) c.2573T>G (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
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)
BDTX-1535	×	×	×	×	● (I/II)
benmelstobart, catequentinib	×	×	×	×	● (I/II)
BH-30643	×	×	×	×	● (I/II)
bozitinib, osimertinib	×	×	×	×	● (I/II)
BPI-361175	×	×	×	×	● (I/II)
cetrelimab, amivantamab	×	×	×	×	● (I/II)
dacomitinib, catequentinib	×	×	×	×	● (I/II)
DAJH-1050766	×	×	×	×	● (I/II)
DB-1310, osimertinib	×	×	×	×	● (I/II)
dositinib	×	×	×	×	● (I/II)
FWD-1509	×	×	×	×	● (I/II)
H-002	×	×	×	×	● (I/II)
ifebemtinib, furmonertinib	×	×	×	×	● (I/II)
MRTX0902	×	×	×	×	● (I/II)
necitumumab, osimertinib	×	×	×	×	● (I/II)
quaratusugene ozeplasmid, osimertinib	×	×	×	×	● (I/II)
RC-108, furmonertinib, toripalimab	×	×	×	×	● (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

EGFR p.(L858R) c.2573T>G (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
sotiburafusp alfa, HB-0030	✕	✕	✕	✕	● (I/II)
sunvozertinib, chemotherapy	✕	✕	✕	✕	● (I/II)
TAS-3351	✕	✕	✕	✕	● (I/II)
TQ-B3525, osimertinib	✕	✕	✕	✕	● (I/II)
TRX-221	✕	✕	✕	✕	● (I/II)
WSD-0922	✕	✕	✕	✕	● (I/II)
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)
osimertinib, carotuximab	✕	✕	✕	✕	● (I)
osimertinib, Minnelide	✕	✕	✕	✕	● (I)
osimertinib, tegatrabetan	✕	✕	✕	✕	● (I)
patritumab deruxtecan	✕	✕	✕	✕	● (I)
repotrectinib, osimertinib	✕	✕	✕	✕	● (I)
VIC-1911, osimertinib	✕	✕	✕	✕	● (I)
WJ13404	✕	✕	✕	✕	● (I)
WTS-004	✕	✕	✕	✕	● (I)
YH-013	✕	✕	✕	✕	● (I)

* 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

EGFR p.(L858R) c.2573T>G (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
YL-202	×	×	×	×	<div></div> (I)

TP53 p.(C176F) c.527G>T

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
almonertinib, catequentinib	×	×	×	×	<div></div> (III)
osimertinib, chemotherapy	×	×	×	×	<div></div> (III)
osimertinib, bevacizumab, chemotherapy	×	×	×	×	<div></div> (II)
sunvozertinib, catequentinib	×	×	×	×	<div></div> (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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