

Patient Name: 조동욱
Gender: F
Sample ID: N26-57

Primary Tumor Site: lung
Collection Date: 2026.01.22

Sample Cancer Type: Lung Cancer

Table of Contents	Page	Report Highlights
Variant Details	2	3 Relevant Biomarkers
Biomarker Descriptions	3	18 Therapies Available
Alert Details	6	204 Clinical Trials
Relevant Therapy Summary	8	

Relevant Lung Cancer Findings

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

Genomic Alteration	Finding
Tumor Mutational Burden	3.79 Mut/Mb measured

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	EGFR p.(L858R) c.2573T>G epidermal growth factor receptor Allele Frequency: 22.81% 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+} datopotamab deruxtecan-dlnk ^{1 / II+} BAT1706 + erlotinib ² gefitinib + chemotherapy ^I atezolizumab + bevacizumab + chemotherapy ^{II+}	None*	199

* 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
IIC	<i>CDKN2A deletion</i> cyclin dependent kinase inhibitor 2A Locus: chr9:21968178	None*	None*	5
IIC	<i>CDKN2B deletion</i> cyclin dependent kinase inhibitor 2B Locus: chr9:22005728	None*	None*	2

* 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 ivalontamab brengitecan¹, patritumab deruxtecan¹, sacituzumab tirumotecan¹
 DB-1310¹, DB-1418¹

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

Prevalent cancer biomarkers without relevant evidence based on included data sources

Microsatellite stable, 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	22.81%	NM_005228.5	missense
NQO1	p.(P187S)	c.559C>T	.	chr16:69745145	45.55%	NM_000903.3	missense
FANCG	p.(Q343E)	c.1027C>G	.	chr9:35076478	6.55%	NM_004629.2	missense
FANCG	p.(L284M)	c.850C>A	.	chr9:35076795	6.21%	NM_004629.2	missense
PAX5	p.(G84R)	c.250G>A	.	chr9:37015154	2.80%	NM_016734.3	missense
FANCM	p.(S1338N)	c.4013G>A	.	chr14:45645970	20.26%	NM_020937.4	missense

Copy Number Variations

Gene	Locus	Copy Number	CNV Ratio
CDKN2A	chr9:21968178	0.13	0.62
CDKN2B	chr9:22005728	0	0.59

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 family²³. In addition to EGFR/ERBB1/HER1, other members of the ERBB/HER family include ERBB2/HER2, ERBB3/HER3, and ERBB4/HER4²⁴. 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 pathways²⁵. Activation of these pathways promotes cell proliferation, differentiation, and survival^{26,27}.

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^{28,29,30,31}. 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 21³². These mutations constitutively activate EGFR resulting in downstream signaling, and represent 80% of the EGFR mutations observed in lung cancer³². A second group of less prevalent activating mutations includes E709K, G719X, S768I, L861Q, and short in-frame insertion mutations in exon 20^{33,34,35,36}. EGFR activating mutations in lung cancer tend to be mutually exclusive to KRAS activating mutations³⁷. 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^{32,38}. 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^{29,30,31,38,39}. 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^{40,41,42}. Alterations in EGFR are rare in pediatric cancers^{30,31}. 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)^{30,31}. 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)^{30,31}.

Potential relevance: Approved first-generation EGFR tyrosine kinase inhibitors (TKIs) include erlotinib⁴³ (2004) and gefitinib⁴⁴ (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 mutations⁴⁵. Second-generation TKIs afatinib⁴⁶ (2013) and dacomitinib⁴⁷ (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^{48,49,50,51}. In 2025, the FDA approved the irreversible EGFR inhibitor, sunvozertinib⁵², for the treatment of locally advanced or metastatic non-small cell lung cancer in adult patients with EGFR exon 20 insertion mutations whose disease has progressed on or after platinum-based chemotherapy. In 2022, the FDA granted breakthrough therapy designation to the irreversible EGFR inhibitor, CLN-081 (TPC-064)⁵³ 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 resistance⁵⁴. The primary resistance mutation that emerges following treatment with first-generation TKI is T790M, accounting for 50-60% of resistant cases³². Third generation TKIs were developed to maintain sensitivity in the presence of T790M⁵⁴. Osimertinib⁵⁵ (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 cases⁵⁴. 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 versa⁵⁶. T790M and C797S can occur in either cis or trans allelic orientation⁵⁶. 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 TKIs⁵⁶. 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^{56,57}. However, C797S occurring in cis conformation with T790M, confers resistance to first- and third-generation TKIs⁵⁶. Fourth-generation TKIs are in development to overcome acquired resistance mutations after osimertinib treatment, including BDTX-1535⁵⁸ (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 mutations⁵⁹. The bispecific antibody, amivantamab⁶⁰ (2021), targeting EGFR and MET was approved for NSCLC tumors harboring EGFR exon 20 insertion mutations. A small molecule kinase inhibitor, lazertinib⁶¹ (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. HLX-42⁶², 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 track designation (2024) for the

Biomarker Descriptions (continued)

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. CPO301⁶³ (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 ozeplasmid⁶⁴ (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^{65,66,67}.

CDKN2A deletion

cyclin dependent kinase inhibitor 2A

Background: CDKN2A encodes cyclin dependent kinase inhibitor 2A, a cell cycle regulator that controls G1/S progression²³. CDKN2A, also known as p16/INK4A, belongs to a family of INK4 cyclin-dependent kinase inhibitors, which also includes CDKN2B (p15/INK4B), CDKN2C (p18/INK4C), and CDKN2D (p19/INK4D)⁶⁸. The INK4 family regulates cell cycle progression by inhibiting CDK4 or CDK6, thereby preventing the phosphorylation of Rb^{69,70,71}. CDKN2A encodes two alternative transcript variants, namely p16 and p14ARF, both of which exhibit differential tumor suppressor functions⁷². Specifically, the CDKN2A/p16 transcript inhibits cell cycle kinases CDK4 and CDK6, whereas the CDKN2A/p14ARF transcript stabilizes the tumor suppressor protein p53 to prevent its degradation^{23,72,73}. CDKN2A aberrations commonly co-occur with CDKN2B⁶⁸. Loss of CDKN2A/p16 results in downstream inactivation of the Rb and p53 pathways, leading to uncontrolled cell proliferation⁷⁴. Germline mutations of CDKN2A are known to confer a predisposition to melanoma and pancreatic cancer^{75,76}.

Alterations and prevalence: Somatic alterations in CDKN2A often result in loss of function (LOF) which is attributed to copy number loss, truncating, or missense mutations⁷⁷. Somatic mutations in CDKN2A are observed in 20% of head and neck squamous cell carcinoma and pancreatic adenocarcinoma, 15% of lung squamous cell carcinoma, 13% of skin cutaneous melanoma, 8% of esophageal adenocarcinoma, 7% of bladder urothelial carcinoma, 6% of cholangiocarcinoma, 4% of lung adenocarcinoma and stomach adenocarcinoma, and 2% of liver hepatocellular carcinoma, uterine carcinosarcoma, and cervical squamous cell carcinoma^{30,31}. Biallelic deletion of CDKN2A is observed in 56% of glioblastoma multiforme, 45% of mesothelioma, 39% of esophageal adenocarcinoma, 32% of bladder urothelial carcinoma, 31% of skin cutaneous melanoma and head and neck squamous cell carcinoma, 28% of pancreatic adenocarcinoma, 27% of diffuse large B-cell lymphoma, 26% of lung squamous cell carcinoma, 17% of lung adenocarcinoma and cholangiocarcinoma, 15% of sarcoma, 11% of stomach adenocarcinoma and of brain lower grade glioma, 7% of adrenocortical carcinoma, 6% of liver hepatocellular carcinoma, 4% of breast invasive carcinoma, kidney renal papillary cell carcinoma and thymoma, 3% of ovarian serous cystadenocarcinoma and kidney renal clear cell carcinoma, and 2% of uterine carcinosarcoma and kidney chromophobe^{30,31}. Alterations in CDKN2A are also observed in pediatric cancers³¹. Biallelic deletion of CDKN2A is observed in 68% of T-lymphoblastic leukemia/lymphoma, 40% of B-lymphoblastic leukemia/lymphoma, 25% of glioma, 19% of bone cancer, and 6% of embryonal tumors³¹. Somatic mutations in CDKN2A are observed in less than 1.5% of bone cancer (5 in 327 cases), B-lymphoblastic leukemia/lymphoma (3 in 252 cases), and leukemia (1 in 354 cases)³¹.

Potential relevance: Loss of CDKN2A can be useful in the diagnosis of mesothelioma, and mutations in CDKN2A are ancillary diagnostic markers of malignant peripheral nerve sheath tumors^{78,79,80}. Additionally, deletion of CDKN2B is a molecular marker used in staging Grade 4 pediatric IDH-mutant astrocytoma⁶⁷. Currently, no therapies are approved for CDKN2A aberrations. However, CDKN2A LOF leading to CDK4/6 activation may confer sensitivity to CDK inhibitors such as palbociclib and abemaciclib^{81,82,83}. Alternatively, CDKN2A expression and Rb inactivation demonstrate resistance to palbociclib in cases of glioblastoma multiforme⁸⁴. CDKN2A (p16) expression is associated with a favorable prognosis for progression-free survival (PFS) and overall survival (OS) in p16/HPV positive head and neck cancer^{85,86,87,88}.

CDKN2B deletion

cyclin dependent kinase inhibitor 2B

Background: CDKN2B encodes cyclin dependent kinase inhibitor 2B, a cell cycle regulator that controls G1/S progression^{23,68}. CDKN2B, also known as p15/INK4B, belongs to a family of INK4 cyclin-dependent kinase inhibitors, which also includes CDKN2A (p16/INK4A), CDKN2C (p18/INK4C), and CDKN2D (p19/INK4D)⁶⁸. The INK4 family regulates cell cycle progression by inhibiting CDK4 or CDK6, thereby preventing the phosphorylation of Rb^{69,70,71}. CDKN2B is a tumor suppressor and aberrations in this gene commonly co-occur with CDKN2A⁶⁸. Germline mutations in CDKN2B are linked to pancreatic cancer predisposition and familial renal cell carcinoma^{23,89,90}.

Alterations and prevalence: CDKN2B copy number loss is a frequently occurring somatic aberration that is observed in 55% of glioblastoma multiforme, 43% of mesothelioma, 35% of esophageal adenocarcinoma, 31% of bladder urothelial carcinoma, 29% of skin cutaneous melanoma, 28% of head and neck squamous cell carcinoma, 27% of pancreatic adenocarcinoma, 26% of lung squamous cell carcinoma, 25% of diffuse large B-cell lymphoma, 16% of lung adenocarcinoma, 15% of sarcoma, 14% of cholangiocarcinoma, 11% of stomach adenocarcinoma and brain lower grade glioma, 5% of liver hepatocellular carcinoma, 4% of adrenocortical carcinoma, breast invasive carcinoma, thymoma, and kidney renal papillary cell carcinoma, 3% of kidney renal clear cell carcinoma and ovarian

Biomarker Descriptions (continued)

serous cystadenocarcinoma, and 2% of uterine carcinosarcoma and kidney chromophobe^{30,31}. Somatic mutations in CDKN2B are observed in 2% of uterine carcinosarcoma^{30,31}. CDKN2B copy number loss is also observed in pediatric cancers, including 64% of childhood T-lymphoblastic leukemia/lymphoma, 37% of pediatric B-lymphoblastic leukemia/lymphoma, 25% of pediatric gliomas, 14% of pediatric bone cancers, 6% of embryonal tumors, and 2% of peripheral nervous system cancers^{30,31}. Somatic mutations in CDKN2B are observed in less than 1% of bone cancer (1 in 327 cases)^{30,31}.

Potential relevance: Currently, no therapies are approved for CDKN2B aberrations. Homozygous deletion of CDKN2B is a molecular marker used in staging grade 4 pediatric IDH-mutant astrocytoma⁶⁷.

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 genome¹. Microsatellite instability (MSI) is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue^{2,3}. MSI is closely tied to the status of the mismatch repair (MMR) genes. In humans, the core MMR genes include MLH1, MSH2, MSH6, and PMS2⁴. 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 D17S250⁵. 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)⁵. Tumors classified as MSI-L are often phenotypically indistinguishable from MSS tumors and tend to be grouped with MSS^{6,7,8,9,10}. 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 genes³. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer^{2,3,7,11}.

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^{2,3,12,13}. 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^{12,13}.

Potential relevance: Anti-PD-1 immune checkpoint inhibitors including pembrolizumab¹⁴ (2014) and nivolumab¹⁵ (2015) are approved for patients with MSI-H or dMMR colorectal cancer who have progressed following chemotherapy. Pembrolizumab¹⁴ 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 indication¹⁴. Dostarlimab¹⁶ (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^{8,17}. The cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab¹⁸ (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^{8,19,20}. 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 patients²⁰. 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^{21,22}. However, checkpoint blockade with the addition of chemotherapy or targeted therapies have demonstrated response in MSS or pMMR cancers^{21,22}.

Alerts Informed By Public Data Sources

Current FDA Information

 Contraindicated  Not recommended  Resistance  Breakthrough  Fast Track

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

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

izationaltamab brengitecan

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

Supporting Statement:

The FDA has granted Breakthrough designation to EGFR/HER3 targeting bispecific antibody-drug conjugate (ADC), izationaltamab brengitecan, for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) harboring EGFR exon 19 deletions or exon 21 L858R substitution mutations who experienced disease progression on or after treatment with an EGFR TKI and platinum-based chemotherapy.

Reference:

<https://www.onclive.com/view/fda-grants-breakthrough-therapy-designation-to-izationaltamab-brengitecan-in-egfr-nsclc>

patritumab deruxtecan

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation 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.

Reference:

<https://www.cancernetwork.com/view/fda-grants-breakthrough-therapy-status-to-patritumab-deruxtecan-for-egfr-metastatic-nsclc>

sacituzumab tirumotecan

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

Supporting Statement:

The FDA has granted Breakthrough designation to the trophoblast cell-surface antigen 2 (TROP2)-directed antibody drug conjugate (ADC), sacituzumab tirumotecan, for the treatment of patients with advanced or metastatic nonsquamous non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) mutations (exon 19 deletion [19del] or exon 21 L858R) whose disease progressed on or after tyrosine kinase inhibitor (TKI) and platinum-based chemotherapy.

Reference:

<https://www.merck.com/news/fda-grants-breakthrough-therapy-designation-to-sacituzumab-tirumotecan-sac-tmt-for-the-treatment-of-certain-patients-with-previously-treated-advanced-or-metastatic-nonsquamous-non-small-cell-lung-ca/>

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

A DB-1310

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

Supporting Statement:

The FDA has granted Fast Track designation to the HER3-targeting antibody-drug conjugate, DB-1310, for the treatment of adult patients with advanced, unresectable or metastatic non-squamous non-small cell lung cancer with EGFR exon 19 deletion or L858R mutation and who have progressed after treatment with a third-generation EGFR tyrosine kinase inhibitor and platinum-based chemotherapy.

Reference:

<https://www.targetedonc.com/view/novel-her3-adc-receives-fda-fast-track-for-refractory-nsclc>

A DB-1418

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

Supporting Statement:

The FDA has granted Fast Track designation to the EGFR/HER3 bispecific antibody-drug conjugate (BsADC), AVZO-1418 (DB-1418), for the treatment of patients with unresectable, locally advanced, or metastatic non-small cell lung cancer (NSCLC) with an epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R mutation, whose disease has progressed on or after therapy with an EGFR tyrosine kinase inhibitor (TKI).

Reference:

<https://avenzotx.com/press-releases/avenzo-therapeutics-granted-fast-track-designation-for-avzo-1418-a-potential-best-in-class-egfr-her3-bispecific-adc-for-the-treatment-of-patients-with-egfr-mutated-tki-pretreated-nsclc/>

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, CTNNA1, 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, MYO10, 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, PXDN, RAC1, RAF1, RARA, RET, RGS7, RHEB, RHOA, RICTOR, RIT1, ROS1, RPL10, SETBP1, SF3B1, SIX1, SIX2, SLC1B3, 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, BMP2, BRAF, BRCA1, BRCA2, BRIP1, CARD11, CASP8, CEBF, 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, 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,

Genes Assayed (continued)

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

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, PLOG1, 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, TGFBR2, TNFAIP3, TNFRSF14, TOP1, TP53, TP63, TPMT, TPP2, TSC1, TSC2, U2AF1, USP8, USP9X, VHL, WT1, XPO1, XRCC2, XRCC3, YAP1, YES1, ZFH3, ZMYM3, ZNF217, ZNF429, ZRSR2

Genes Assayed for the Detection of Fusions

AKT2, ALK, AR, AXL, BRAF, BRCA1, BRCA2, CDKN2A, EGFR, ERBB2, ERBB4, ERG, ESR1, ETV1, ETV4, ETV5, FGFR1, FGFR2, FGFR3, FGR, FLT3, JAK2, KRAS, MDM4, MET, MYB, MYBL1, NF1, NOTCH1, NOTCH4, NRG1, NTRK1, NTRK2, NTRK3, NUTM1, PDGFRA, PDGFRB, PIK3CA, PPARG, PRKACA, PRKACB, PTEN, RAD51B, RAF1, RB1, RELA, RET, ROS1, 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, CBF3, CD274, CD276, CDC73, CDH1, CDH10, CDK12, CDKN1A, CDKN1B, CDKN2A, CDKN2B, CDKN2C, CHEK1, CHEK2, CIC, CIITA, CREBBP, CSMD3, CTCF, CTLA4, CUL3, CUL4A, CUL4B, CYLD, CYP2C9, CYP2D6, DAXX, DDX3X, DICER1, DNMT3A, DOCK3, DPYD, DSC1, DSC3, ELF3, ENO1, EP300, EPCAM, EPHA2, ERAP1, ERAP2, ERCC2, ERCC4, ERCC5, 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, 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	●	●	●	×	×

* 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

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
amivantamab + lazertinib	●	●	●	✕	✕
datopotamab deruxtecan-dlnk	●	●	✕	✕	✕
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	✕	✕	●	✕	✕
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)
furmonertinib, chemotherapy	✕	✕	✕	✕	● (IV)
gefitinib, chemotherapy	✕	✕	✕	✕	● (IV)
gefitinib, endostatin	✕	✕	✕	✕	● (IV)
natural product, gefitinib, erlotinib, icotinib hydrochloride, osimertinib, almonertinib, furmonertinib	✕	✕	✕	✕	● (IV)
almonertinib, apatinib	✕	✕	✕	✕	● (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*
almonertinib, chemotherapy	✕	✕	✕	✕	● (III)
almonertinib, radiation therapy	✕	✕	✕	✕	● (III)
asandeutertinib, osimertinib	✕	✕	✕	✕	● (III)
ASKC-202, limertinib	✕	✕	✕	✕	● (III)
befotertinib, icotinib hydrochloride	✕	✕	✕	✕	● (III)
bevacizumab, osimertinib	✕	✕	✕	✕	● (III)
CK-101, gefitinib	✕	✕	✕	✕	● (III)
furmonertinib	✕	✕	✕	✕	● (III)
furmonertinib, osimertinib, chemotherapy	✕	✕	✕	✕	● (III)
gefitinib, afatinib, erlotinib, metformin hydrochloride	✕	✕	✕	✕	● (III)
glumetinib, osimertinib	✕	✕	✕	✕	● (III)
icotinib hydrochloride, catequentinib	✕	✕	✕	✕	● (III)
icotinib hydrochloride, chemotherapy	✕	✕	✕	✕	● (III)
icotinib hydrochloride, radiation therapy	✕	✕	✕	✕	● (III)
izalontamab brengitecan, osimertinib	✕	✕	✕	✕	● (III)
JMT-101, osimertinib	✕	✕	✕	✕	● (III)
osimertinib, bevacizumab	✕	✕	✕	✕	● (III)
osimertinib, chemotherapy	✕	✕	✕	✕	● (III)
osimertinib, datopotamab deruxtecan-dlnk	✕	✕	✕	✕	● (III)
osimertinib, gefitinib, chemotherapy	✕	✕	✕	✕	● (III)
sacituzumab tirumotecan	✕	✕	✕	✕	● (III)
sacituzumab tirumotecan, osimertinib	✕	✕	✕	✕	● (III)
SH-1028	✕	✕	✕	✕	● (III)
PM-1080, almonertinib	✕	✕	✕	✕	● (II/III)
SCTB-14, chemotherapy	✕	✕	✕	✕	● (II/III)
ABSK-043, furmonertinib	✕	✕	✕	✕	● (II)
afatinib, chemotherapy	✕	✕	✕	✕	● (II)
almonertinib	✕	✕	✕	✕	● (II)
almonertinib, adbrelimab, chemotherapy	✕	✕	✕	✕	● (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 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*
almonertinib, bevacizumab	✕	✕	✕	✕	● (II)
almonertinib, chemoradiation therapy	✕	✕	✕	✕	● (II)
almonertinib, chemotherapy, radiation therapy	✕	✕	✕	✕	● (II)
almonertinib, dacomitinib	✕	✕	✕	✕	● (II)
amivantamab, chemotherapy	✕	✕	✕	✕	● (II)
amivantamab, lazertinib, chemotherapy	✕	✕	✕	✕	● (II)
asandeutertinib, chemotherapy	✕	✕	✕	✕	● (II)
befotertinib, bevacizumab, chemotherapy	✕	✕	✕	✕	● (II)
befotertinib, chemotherapy	✕	✕	✕	✕	● (II)
bevacizumab, afatinib	✕	✕	✕	✕	● (II)
bevacizumab, furmonertinib	✕	✕	✕	✕	● (II)
cadonilimab, chemotherapy, catequentinib	✕	✕	✕	✕	● (II)
camrelizumab, apatinib	✕	✕	✕	✕	● (II)
capmatinib, osimertinib, ramucirumab	✕	✕	✕	✕	● (II)
catequentinib, almonertinib	✕	✕	✕	✕	● (II)
catequentinib, chemotherapy	✕	✕	✕	✕	● (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, bevacizumab	✕	✕	✕	✕	● (II)
furmonertinib, icotinib hydrochloride	✕	✕	✕	✕	● (II)
gefitinib, bevacizumab, chemotherapy	✕	✕	✕	✕	● (II)
gefitinib, icotinib hydrochloride	✕	✕	✕	✕	● (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*
gefitinib, thalidomide	✕	✕	✕	✕	● (II)
IBI-318, lenvatinib	✕	✕	✕	✕	● (II)
icotinib hydrochloride	✕	✕	✕	✕	● (II)
icotinib hydrochloride, autologous RAK cell	✕	✕	✕	✕	● (II)
icotinib hydrochloride, osimertinib	✕	✕	✕	✕	● (II)
ivonescimab, chemotherapy	✕	✕	✕	✕	● (II)
izalontamab brengitecan, almonertinib	✕	✕	✕	✕	● (II)
JS-207, chemotherapy	✕	✕	✕	✕	● (II)
JSKN-016	✕	✕	✕	✕	● (II)
lazertinib	✕	✕	✕	✕	● (II)
lazertinib, bevacizumab	✕	✕	✕	✕	● (II)
lazertinib, chemotherapy	✕	✕	✕	✕	● (II)
osimertinib, radiation therapy	✕	✕	✕	✕	● (II)
PLB-1004, bozitinib, osimertinib	✕	✕	✕	✕	● (II)
ramucirumab, erlotinib	✕	✕	✕	✕	● (II)
sunvozertinib	✕	✕	✕	✕	● (II)
sunvozertinib, catequentinib	✕	✕	✕	✕	● (II)
sunvozertinib, golidocitinib	✕	✕	✕	✕	● (II)
tislelizumab, chemotherapy, bevacizumab	✕	✕	✕	✕	● (II)
toripalimab	✕	✕	✕	✕	● (II)
toripalimab, bevacizumab, Clostridium butyricum, chemotherapy	✕	✕	✕	✕	● (II)
toripalimab, chemotherapy	✕	✕	✕	✕	● (II)
vabametkib, lazertinib	✕	✕	✕	✕	● (II)
YL-202	✕	✕	✕	✕	● (II)
zipalertinib	✕	✕	✕	✕	● (II)
zorifertinib, pirotinib	✕	✕	✕	✕	● (II)
AP-L1898	✕	✕	✕	✕	● (I/II)
BH-30643	✕	✕	✕	✕	● (I/II)
bozitinib, 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)

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

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
BPI-361175	✕	✕	✕	✕	● (I/II)
chemotherapy, DZD-6008	✕	✕	✕	✕	● (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)
necitumumab, osimertinib	✕	✕	✕	✕	● (I/II)
PLB-1004, chemotherapy	✕	✕	✕	✕	● (I/II)
quaratusugene ozeplasmid, osimertinib	✕	✕	✕	✕	● (I/II)
RC-108, furmonertinib, toripalimab	✕	✕	✕	✕	● (I/II)
sotiburafusp alfa, chemotherapy	✕	✕	✕	✕	● (I/II)
sotiburafusp alfa, HB-0030	✕	✕	✕	✕	● (I/II)
sunvozertinib, chemotherapy	✕	✕	✕	✕	● (I/II)
TRX-221	✕	✕	✕	✕	● (I/II)
WSD-0922	✕	✕	✕	✕	● (I/II)
YL-202, pumitamig	✕	✕	✕	✕	● (I/II)
alisertib, osimertinib	✕	✕	✕	✕	● (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)

* 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*
izalontamab brengitecan	✕	✕	✕	✕	● (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)
VT-3989, osimertinib, nivolumab, ipilimumab	✕	✕	✕	✕	● (I)
WTS-004	✕	✕	✕	✕	● (I)
YH-013	✕	✕	✕	✕	● (I)
zipalertinib, chemotherapy, glumetinib, pimitespib, quemliclustat	✕	✕	✕	✕	● (I)

CDKN2A deletion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
palbociclib	✕	✕	✕	✕	● (II)
palbociclib, abemaciclib	✕	✕	✕	✕	● (II)
AMG 193	✕	✕	✕	✕	● (I/II)
ABSK-131	✕	✕	✕	✕	● (I)
CID-078	✕	✕	✕	✕	● (I)

CDKN2B deletion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
palbociclib, abemaciclib	✕	✕	✕	✕	● (II)
CID-078	✕	✕	✕	✕	● (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	11.87%
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 OncoPrint Reporter software was used in generation of this report. Software was developed and designed internally by Thermo Fisher Scientific. The analysis was based on OncoPrint Reporter (6.2.4 data version 2025.12(007)). The data presented here are from a curated knowledge base of publicly available information, but may not be exhaustive. FDA information was sourced from www.fda.gov and is current as of 2025-11-25. NCCN information was sourced from www.nccn.org and is current as of 2025-11-03. EMA information was sourced from www.ema.europa.eu and is current as of 2025-11-25. ESMO information was sourced from www.esmo.org and is current as of 2025-11-03. Clinical Trials information is current as of 2025-11-03. For the most up-to-date information regarding a particular trial, search www.clinicaltrials.gov by NCT ID or search local clinical trials authority website by local identifier listed in 'Other identifiers.' Variants are reported according to HGVS nomenclature and classified following AMP/ASCO/CAP guidelines (Li et al. 2017). Based on the data sources selected, variants, therapies, and trials listed in this report are listed in order of potential clinical significance but not for predicted efficacy of the therapies.

References

1. Lander et al. Initial sequencing and analysis of the human genome. *Nature*. 2001 Feb 15;409(6822):860-921. PMID: 11237011
2. Baudrin et al. Molecular and Computational Methods for the Detection of Microsatellite Instability in Cancer. *Front Oncol*. 2018 Dec 12;8:621. doi: 10.3389/fonc.2018.00621. eCollection 2018. PMID: 30631754
3. Nojadeh et al. Microsatellite instability in colorectal cancer. *EXCLI J*. 2018;17:159-168. PMID: 29743854
4. Saeed et al. Microsatellites in Pursuit of Microbial Genome Evolution. *Front Microbiol*. 2016 Jan 5;6:1462. doi: 10.3389/fmicb.2015.01462. eCollection 2015. PMID: 26779133
5. Boland et al. A National Cancer Institute Workshop on Microsatellite Instability for cancer detection and familial predisposition: development of international criteria for the determination of microsatellite instability in colorectal cancer. *Cancer Res*. 1998 Nov 15;58(22):5248-57. PMID: 9823339
6. Halford et al. Low-level microsatellite instability occurs in most colorectal cancers and is a nonrandomly distributed quantitative trait. *Cancer Res*. 2002 Jan 1;62(1):53-7. PMID: 11782358
7. Imai et al. Carcinogenesis and microsatellite instability: the interrelationship between genetics and epigenetics. *Carcinogenesis*. 2008 Apr;29(4):673-80. PMID: 17942460
8. NCCN Guidelines® - NCCN-Colon Cancer [Version 5.2025]
9. Pawlik et al. Colorectal carcinogenesis: MSI-H versus MSI-L. *Dis. Markers*. 2004;20(4-5):199-206. PMID: 15528785
10. Lee et al. Low-Level Microsatellite Instability as a Potential Prognostic Factor in Sporadic Colorectal Cancer. *Medicine (Baltimore)*. 2015 Dec;94(50):e2260. PMID: 26683947
11. Latham et al. Microsatellite Instability Is Associated With the Presence of Lynch Syndrome Pan-Cancer. *J. Clin. Oncol*. 2019 Feb 1;37(4):286-295. PMID: 30376427
12. Cortes-Ciriano et al. A molecular portrait of microsatellite instability across multiple cancers. *Nat Commun*. 2017 Jun 6;8:15180. doi: 10.1038/ncomms15180. PMID: 28585546
13. Bonneville et al. Landscape of Microsatellite Instability Across 39 Cancer Types. *JCO Precis Oncol*. 2017;2017. PMID: 29850653
14. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125514s178lbl.pdf
15. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125554s131lbl.pdf
16. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761174s009lbl.pdf
17. NCCN Guidelines® - NCCN-Rectal Cancer [Version 4.2025]
18. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125377s136lbl.pdf
19. Ribic et al. Tumor microsatellite-instability status as a predictor of benefit from fluorouracil-based adjuvant chemotherapy for colon cancer. *N. Engl. J. Med*. 2003 Jul 17;349(3):247-57. PMID: 12867608
20. Klingbiel et al. Prognosis of stage II and III colon cancer treated with adjuvant 5-fluorouracil or FOLFIRI in relation to microsatellite status: results of the PETACC-3 trial. *Ann. Oncol*. 2015 Jan;26(1):126-32. PMID: 25361982
21. Hermel et al. The Emerging Role of Checkpoint Inhibition in Microsatellite Stable Colorectal Cancer. *J Pers Med*. 2019 Jan 16;9(1). PMID: 30654522
22. Ciardiello et al. Immunotherapy of colorectal cancer: Challenges for therapeutic efficacy. *Cancer Treat. Rev*. 2019 Jun;76:22-32. PMID: 31079031
23. O'Leary et al. Reference sequence (RefSeq) database at NCBI: current status, taxonomic expansion, and functional annotation. *Nucleic Acids Res*. 2016 Jan 4;44(D1):D733-45. PMID: 26553804
24. King et al. Amplification of a novel v-erbB-related gene in a human mammary carcinoma. *Science*. 1985 Sep 6;229(4717):974-6. PMID: 2992089
25. Liu et al. EGFR-TKIs resistance via EGFR-independent signaling pathways. *Mol Cancer*. 2018 Feb 19;17(1):53. PMID: 29455669
26. Zhixiang. ErbB Receptors and Cancer. *Methods Mol. Biol*. 2017;1652:3-35. PMID: 28791631
27. Gutierrez et al. HER2: biology, detection, and clinical implications. *Arch. Pathol. Lab. Med*. 2011 Jan;135(1):55-62. PMID: 21204711
28. Pines et al. Oncogenic mutant forms of EGFR: lessons in signal transduction and targets for cancer therapy. *FEBS Lett*. 2010 Jun 18;584(12):2699-706. PMID: 20388509
29. Cancer Genome Atlas Research Network. Comprehensive molecular profiling of lung adenocarcinoma. *Nature*. 2014 Jul 31;511(7511):543-50. doi: 10.1038/nature13385. Epub 2014 Jul 9. PMID: 25079552
30. Weinstein et al. The Cancer Genome Atlas Pan-Cancer analysis project. *Nat. Genet*. 2013 Oct;45(10):1113-20. PMID: 24071849
31. Cerami et al. The cBio cancer genomics portal: an open platform for exploring multidimensional cancer genomics data. *Cancer Discov*. 2012 May;2(5):401-4. PMID: 22588877

References (continued)

32. da Cunha Santos et al. EGFR mutations and lung cancer. *Annu Rev Pathol.* 2011;6:49-69. doi: 10.1146/annurev-pathol-011110-130206. PMID: 20887192
33. Arcila et al. EGFR exon 20 insertion mutations in lung adenocarcinomas: prevalence, molecular heterogeneity, and clinicopathologic characteristics. *Mol. Cancer Ther.* 2013 Feb;12(2):220-9. PMID: 23371856
34. Kobayashi et al. EGFR Exon 18 Mutations in Lung Cancer: Molecular Predictors of Augmented Sensitivity to Afatinib or Neratinib as Compared with First- or Third-Generation TKIs. *Clin Cancer Res.* 2015 Dec 1;21(23):5305-13. doi: 10.1158/1078-0432.CCR-15-1046. Epub 2015 Jul 23. PMID: 26206867
35. Yasuda et al. Structural, biochemical, and clinical characterization of epidermal growth factor receptor (EGFR) exon 20 insertion mutations in lung cancer. *Sci Transl Med.* 2013 Dec 18;5(216):216ra177. PMID: 24353160
36. Chiu et al. Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor Treatment Response in Advanced Lung Adenocarcinomas with G719X/L861Q/S768I Mutations. *J Thorac Oncol.* 2015 May;10(5):793-9. PMID: 25668120
37. Karachaliou et al. KRAS mutations in lung cancer. *Clin Lung Cancer.* 2013 May;14(3):205-14. PMID: 23122493
38. Brennan et al. The somatic genomic landscape of glioblastoma. *Cell.* 2013 Oct 10;155(2):462-77. PMID: 24120142
39. Cancer Genome Atlas Network. Comprehensive genomic characterization of head and neck squamous cell carcinomas. *Nature.* 2015 Jan 29;517(7536):576-82. PMID: 25631445
40. Mitsudomi et al. Epidermal growth factor receptor in relation to tumor development: EGFR gene and cancer. *FEBS J.* 2010 Jan;277(2):301-8. PMID: 19922469
41. Gazdar. Activating and resistance mutations of EGFR in non-small-cell lung cancer: role in clinical response to EGFR tyrosine kinase inhibitors. *Oncogene.* 2009 Aug;28 Suppl 1:S24-31. PMID: 19680293
42. Gan et al. The EGFRvIII variant in glioblastoma multiforme. *J Clin Neurosci.* 2009 Jun;16(6):748-54. PMID: 19324552
43. https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/021743s025lbl.pdf
44. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/206995s004lbl.pdf
45. Riely et al. Clinical course of patients with non-small cell lung cancer and epidermal growth factor receptor exon 19 and exon 21 mutations treated with gefitinib or erlotinib. *Clin Cancer Res.* 2006 Feb 1;12(3 Pt 1):839-44. PMID: 16467097
46. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/201292s017lbl.pdf
47. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/211288s003lbl.pdf
48. NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2025]
49. Naidoo et al. Epidermal growth factor receptor exon 20 insertions in advanced lung adenocarcinomas: Clinical outcomes and response to erlotinib. *Cancer.* 2015 Sep 15;121(18):3212-3220. PMID: 26096453
50. Vyse et al. Targeting EGFR exon 20 insertion mutations in non-small cell lung cancer. *Signal Transduct Target Ther.* 2019;4:5. PMID: 30854234
51. Yi et al. A comparison of epidermal growth factor receptor mutation testing methods in different tissue types in non-small cell lung cancer. *Int J Mol Med.* 2014 Aug;34(2):464-74. PMID: 24891042
52. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219839s000lbl.pdf
53. <https://investors.cullinanoncology.com/news-releases/news-release-details/fda-grants-breakthrough-therapy-designation-cullinan-oncologys>
54. Madic et al. EGFR C797S, EGFR T790M and EGFR sensitizing mutations in non-small cell lung cancer revealed by six-color crystal digital PCR. *Oncotarget.* 2018 Dec 21;9(100):37393-37406. PMID: 30647840
55. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/208065s033lbl.pdf
56. Niederst et al. The Allelic Context of the C797S Mutation Acquired upon Treatment with Third-Generation EGFR Inhibitors Impacts Sensitivity to Subsequent Treatment Strategies. *Clin. Cancer Res.* 2015 Sep 1;21(17):3924-33. PMID: 25964297
57. Wang et al. Lung Adenocarcinoma Harboring EGFR T790M and In Trans C797S Responds to Combination Therapy of First- and Third-Generation EGFR TKIs and Shifts Allelic Configuration at Resistance. *J Thorac Oncol.* 2017 Nov;12(11):1723-1727. PMID: 28662863
58. <https://investors.blackdiamondtherapeutics.com/news-releases/news-release-details/black-diamond-therapeutics-announces-corporate-update-and>
59. Ciardiello et al. The role of anti-EGFR therapies in EGFR-TKI-resistant advanced non-small cell lung cancer. *Cancer Treat Rev.* 2024 Jan;122:102664. PMID: 38064878
60. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761210s011lbl.pdf
61. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219008s003lbl.pdf

References (continued)

62. <https://iis.aastocks.com/20231227/11015917-0.PDF>
63. <https://www1.hkexnews.hk/listedco/listconews/sehk/2024/1008/2024100800433.pdf>
64. <https://www.genprex.com/news/genprex-receives-u-s-fda-fast-track-designation-for-gene-therapy-that-targets-lung-cancer/>
65. NCCN Guidelines® - NCCN-Pediatric Central Nervous System Cancers [Version 3.2025]
66. Buccoliero et al. Pediatric High Grade Glioma Classification Criteria and Molecular Features of a Case Series. *Genes (Basel)*. 2022 Mar 31;13(4). PMID: 35456430
67. Louis et al. cIMPACT-NOW update 6: new entity and diagnostic principle recommendations of the cIMPACT-Utrecht meeting on future CNS tumor classification and grading. *Brain Pathol*. 2020 Jul;30(4):844-856. PMID: 32307792
68. Xia et al. Dominant role of CDKN2B/p15INK4B of 9p21.3 tumor suppressor hub in inhibition of cell-cycle and glycolysis. *Nat Commun*. 2021 Apr 6;12(1):2047. PMID: 33824349
69. Scruggs et al. Loss of CDKN2B Promotes Fibrosis via Increased Fibroblast Differentiation Rather Than Proliferation. *Am. J. Respir. Cell Mol. Biol*. 2018 Aug;59(2):200-214. PMID: 29420051
70. Roussel. The INK4 family of cell cycle inhibitors in cancer. *Oncogene*. 1999 Sep 20;18(38):5311-7. PMID: 10498883
71. Aytac et al. Rb independent inhibition of cell growth by p15(INK4B). *Biochem. Biophys. Res. Commun*. 1999 Aug 27;262(2):534-8. PMID: 10462509
72. Hill et al. The genetics of melanoma: recent advances. *Annu Rev Genomics Hum Genet*. 2013;14:257-79. PMID: 23875803
73. Kim et al. The regulation of INK4/ARF in cancer and aging. *Cell*. 2006 Oct 20;127(2):265-75. PMID: 17055429
74. Sekulic et al. Malignant melanoma in the 21st century: the emerging molecular landscape. *Mayo Clin. Proc*. 2008 Jul;83(7):825-46. PMID: 18613999
75. Orlow et al. CDKN2A germline mutations in individuals with cutaneous malignant melanoma. *J. Invest. Dermatol*. 2007 May;127(5):1234-43. PMID: 17218939
76. Bartsch et al. CDKN2A germline mutations in familial pancreatic cancer. *Ann. Surg*. 2002 Dec;236(6):730-7. PMID: 12454511
77. Adib et al. CDKN2A Alterations and Response to Immunotherapy in Solid Tumors. *Clin Cancer Res*. 2021 Jul 15;27(14):4025-4035. PMID: 34074656
78. NCCN Guidelines® - NCCN-Mesothelioma: Peritoneal [Version 2.2026]
79. NCCN Guidelines® - NCCN-Mesothelioma: Pleural [Version 2.2026]
80. NCCN Guidelines® - NCCN-Soft Tissue Sarcoma [Version 1.2025]
81. Longwen et al. Frequent genetic aberrations in the cell cycle related genes in mucosal melanoma indicate the potential for targeted therapy. *J Transl Med*. 2019 Jul 29;17(1):245. PMID: 31358010
82. Logan et al. PD-0332991, a potent and selective inhibitor of cyclin-dependent kinase 4/6, demonstrates inhibition of proliferation in renal cell carcinoma at nanomolar concentrations and molecular markers predict for sensitivity. *Anticancer Res*. 2013 Aug;33(8):2997-3004. PMID: 23898052
83. von Witzleben et al. Preclinical Characterization of Novel Chordoma Cell Systems and Their Targeting by Pharmacological Inhibitors of the CDK4/6 Cell-Cycle Pathway. *Cancer Res*. 2015 Sep 15;75(18):3823-31. PMID: 26183925
84. Cen et al. p16-Cdk4-Rb axis controls sensitivity to a cyclin-dependent kinase inhibitor PD0332991 in glioblastoma xenograft cells. *Neuro-oncology*. 2012 Jul;14(7):870-81. PMID: 22711607
85. Vitzthum et al. The role of p16 as a biomarker in nonoropharyngeal head and neck cancer. *Oncotarget*. 2018 Sep 7;9(70):33247-33248. PMID: 30279955
86. Chung et al. p16 protein expression and human papillomavirus status as prognostic biomarkers of nonoropharyngeal head and neck squamous cell carcinoma. *J. Clin. Oncol*. 2014 Dec 10;32(35):3930-8. PMID: 25267748
87. Bryant et al. Prognostic Role of p16 in Nonoropharyngeal Head and Neck Cancer. *J. Natl. Cancer Inst*. 2018 Dec 1;110(12):1393-1399. PMID: 29878161
88. Stephen et al. Significance of p16 in Site-specific HPV Positive and HPV Negative Head and Neck Squamous Cell Carcinoma. *Cancer Clin Oncol*. 2013;2(1):51-61. PMID: 23935769
89. Jafri et al. Germline Mutations in the CDKN2B Tumor Suppressor Gene Predispose to Renal Cell Carcinoma. *Cancer Discov*. 2015 Jul;5(7):723-9. PMID: 25873077
90. Tu et al. CDKN2B deletion is essential for pancreatic cancer development instead of unmeaningful co-deletion due to juxtaposition to CDKN2A. *Oncogene*. 2018 Jan 4;37(1):128-138. PMID: 28892048