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Patient Name: 지민주
Gender: Female
Sample ID: N26-18

Primary Tumor Site: Lung
Collection Date: 2026.01.05

Sample Cancer Type: Lung Cancer

Table of Contents

Report Highlights

2 Relevant Biomarkers
18 Therapies Available
199 Clinical Trials

Relevant Lung Cancer Findings

Gene	Finding	Gene	Finding
ALK	None detected	NTRK1	None detected
BRAF	None detected	NTRK2	None detected
EGFR	***EGFR exon 19 deletion***	NTRK3	None detected
ERBB2	None detected	RET	None detected
KRAS	None detected	ROS1	None detected
MET	None detected		

Genomic Alteration	Finding
Tumor Mutational Burden	***2.85 Mut/Mb measured***

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	*EGFR exon 19 deletion* epidermal growth factor receptor Allele Frequency: 25.98% Locus: chr7:55242465 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*	198

*** Public data sources included in relevant therapies: FDA**1, NCCN, **EMA**2, 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	*SMAD4 deletion* SMAD family member 4 Locus: chr18:48573387	None*	None*	1

* **Public data sources included in relevant therapies: FDA**1, NCCN, **EMA**2, 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 exon 19 deletion	Breakthrough: **izalontamab brengitecan** [1], **patritumab deruxtecan** [1], **sacituzumab tirumotecan** [1] Fast Track: **DB-1310** [1], **DB-1418** [1]

Public data sources included in alerts: FDA1, NCCN, **EMA**2, ESMO

Prevalent cancer biomarkers without relevant evidence based on included data sources

Microsatellite stable, UGT1A1 p.(G71R) c.211G>A, 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.(E746_A750del)	c.2236_2250delGAATTAAGAGAAGCA	COSM6225	chr7:55242465	25.98%	NM_005228.5	nonframeshift Deletion
UGT1A1	p.(G71R)	c.211G>A	COSM4415616	chr2:234669144	51.05%	NM_000463.3	missense
NQO1	p.(P187S)	c.559C>T	.	chr16:69745145	32.80%	NM_000903.3	missense
HNF1A	p.(A25E)	c.74C>A	.	chr12:121416645	20.10%	NM_000545.8	missense
RNASEH2A	p.(V143I)	c.427G>A	.	chr19:12920900	53.15%	NM_006397.3	missense

Copy Number Variations

Gene	Locus	Copy Number	CNV Ratio
SMAD4	chr18:48573387	1.19	0.68
HLA-B	chr6:31322252	1.18	0.67
PXDNL	chr8:52233342	1.18	0.67

Biomarker Descriptions

EGFR exon 19 deletion

epidermal growth factor receptor

Background: The EGFR gene encodes the epidermal growth factor receptor (EGFR), a member of the ERBB/human epidermal growth factor receptor (HER) tyrosine kinase family[1]. In addition to EGFR/ERBB1/HER1, other members of the ERBB/HER family include ERBB2/HER2, ERBB3/HER3, and ERBB4/HER4[44]. EGFR ligand-induced dimerization results in kinase activation and leads to stimulation

Biomarker Descriptions (continued)

of oncogenic signaling pathways, including the PI3K/AKT/MTOR and RAS/RAF/MEK/ERK pathways[45]. Activation of these pathways promotes cell proliferation, differentiation, and survival[46,47].

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[8,9,48,49]. 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 21[50]. These mutations constitutively activate EGFR resulting in downstream signaling, and represent 80% of the EGFR mutations observed in lung cancer[50]. A second group of less prevalent activating mutations includes E709K, G719X, S768I, L861Q, and short in-frame insertion mutations in exon 20[51,52,53,54]. EGFR activating mutations in lung cancer tend to be mutually exclusive to KRAS activating mutations[55]. 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[50,56]. 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[8,9,49,56,57]. 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[58,59,60]. 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 erlotinib[61] (2004) and gefitinib[62] (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 mutations[63]. Second-generation TKIs afatinib[64] (2013) and dacomitinib[65] (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[66,67,68,69]. In 2025, the FDA approved the irreversible EGFR inhibitor, sunvozertinib[70], 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)[71] 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 resistance[72]. The primary resistance mutation that emerges following treatment with first-generation TKI is T790M, accounting for 50-60% of resistant cases[50]. Third generation TKIs were developed to maintain sensitivity in the presence of T790M[72]. Osimertinib[73] (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 cases[72]. 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 versa[74]. T790M and C797S can occur in either cis or trans allelic orientation[74]. 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 TKIs[74]. 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[74,75]. However, C797S occurring in cis conformation with T790M, confers resistance to first- and third-generation TKIs[74]. Fourth-generation TKIs are in development to overcome acquired resistance mutations after osimertinib treatment, including BDTX-1535[76] (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 mutations[77]. The bispecific antibody, amivantamab[78] (2021), targeting EGFR and MET was approved for NSCLC tumors harboring EGFR exon 20 insertion mutations. A small molecule kinase inhibitor, lazertinib[79] (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-42[80], an anti-EFGR-antibody-drug conjugate (ADC) consisting of an anti-EGFR monoclonal antibody conjugated with a novel high potency DNA topoisomerase I (topo I) inhibitor, also received fast 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. CPO301[81] (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 ozeplasmid[82] (2020), in combination with osimertinib, received fast track designation from the FDA for NSCLC tumors harboring EGFR mutations that

Biomarker Descriptions (continued)

progressed on osimertinib alone. Amplification and mutations of EGFR commonly occur in H3-wild type IDH-wild type diffuse pediatric high-grade glioma[83,84,85].

SMAD4 deletion

SMAD family member 4

Background: The SMAD4 gene encodes the SMAD family member 4, a transcription factor that belongs to a family of 8 SMAD genes that can be divided into three main classes. SMAD4 (also known as DPC4) belongs to the common mediator SMAD (co-SMAD) class while SMAD1, SMAD2, SMAD3, SMAD5, and SMAD8 are part of the regulator SMAD (R-SMAD) class. The inhibitory SMAD (I-SMAD) class includes both SMAD6 and SMAD7[10,11]. SMAD4 is a tumor suppressor gene and functions as a mediator of the TGF-β and BMP signaling pathways that are implicated in cancer initiation and progression[11,12,13]. Loss of SMAD4 does not drive oncogenesis, but is associated with progression of cancers initiated by driver genes such as KRAS and APC[10,11]

Alterations and prevalence: Inactivation of SMAD4 can occur due to mutations, allelic loss, homozygous deletions, and 18q loss of heterozygosity (LOH)[10]. Somatic mutations in SMAD4 occur in up to 20% of pancreatic, 12% of colorectal, and 8% of stomach cancers. Recurrent hotspot mutations including R361 and P356 occur in the mad homology 2 (MH2) domain leading to the disruption of the TGF-β signaling[9,13,14]. Copy number deletions occur in up to 12% of pancreatic, 10% of esophageal, and 13% of stomach cancers[8,9,15].

Potential relevance: Currently, no therapies are approved for SMAD4 aberrations. Clinical studies and meta-analyses have demonstrated that loss of SMAD4 expression confers poor prognosis and poor overall survival (OS) in colorectal and pancreatic cancers[11,13,16,17,18]. Importantly, SMAD4 is a predictive biomarker to fluorouracil based chemotherapy[19,20]. In a retrospective analysis of 241 colorectal cancer patients treated with fluorouracil, 21 patients with SMAD4 loss demonstrated significantly poor median OS when compared to SMAD4 positive patients (31 months vs 89 months)[20]. In another clinical study of 173 newly diagnosed and recurrent head and neck squamous cell carcinoma (HNSCC) patients, SMAD4 loss is correlated with cetuximab resistance in HPV-negative HNSCC tumors[21].

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 genome[22]. Microsatellite instability (MSI) is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue[23,24]. MSI is closely tied to the status of the mismatch repair (MMR) genes. In humans, the core MMR genes include MLH1, MSH2, MSH6, and PMS2[25]. 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 D17S250[26]. 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)[26]. Tumors classified as MSI-L are often phenotypically indistinguishable from MSS tumors and tend to be grouped with MSS[27,28,29,30,31]. 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 genes[24]. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer[23,24,28,32].

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[23,24,33,34]. 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[33,34].

Potential relevance: Anti-PD-1 immune checkpoint inhibitors including pembrolizumab[35] (2014) and nivolumab[36] (2015) are approved for patients with MSI-H or dMMR colorectal cancer who have progressed following chemotherapy. Pembrolizumab[35] 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 indication[35]. Dostarlimab[37] (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[29,38]. The cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab[39] (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[29,40,41]. Specifically, MSI-H is a strong prognostic indicator of better overall survival (OS) and relapse free survival (RFS) in stage II as compared to stage III colorectal cancer patients[41]. The majority of patients with tumors classified as either MSS or pMMR do not benefit from treatment with single-agent immune checkpoint inhibitors as compared to those with MSI-H tumors[42,43]. However, checkpoint blockade with the addition of chemotherapy or targeted therapies have demonstrated response in MSS or pMMR cancers[42,43].

Biomarker Descriptions (continued)

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

UDP glucuronosyltransferase family 1 member A1

Background: The UGT1A1 gene encodes UDP glucuronosyltransferase family 1 member A1, a member of the UDP-glucuronosyltransferase 1A (UGT1A) subfamily of the UGT protein superfamily[1,86]. UGTs are microsomal membrane-bound enzymes that catalyze the glucuronidation of endogenous and xenobiotic compounds and transform the lipophilic molecules into excretable, hydrophilic metabolites[86,87]. UGTs play an important role in drug metabolism, detoxification, and metabolite homeostasis. Differential expression of UGTs can promote cancer development, disease progression, as well as drug resistance[88]. Specifically, elevated expression of UGT1As are associated with resistance to many anti-cancer drugs due to drug inactivation and lower active drug concentrations. However, reduced expression and downregulation of UGT1As are implicated in bladder and hepatocellular tumorigenesis and progression due to toxin accumulation[88,89,90,91]. Furthermore, UGT1A1 polymorphisms, such as UGT1A1*28, UGT1A1*93, and UGT1A1*6, confer an increased risk of severe toxicity to irinotecan-based chemotherapy treatment of solid tumors, due to reduced glucuronidation of the irinotecan metabolite, SN-38[92].

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

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

HLA-B deletion

major histocompatibility complex, class I, B

Background: The HLA-B gene encodes the major histocompatibility complex, class I, B[1]. 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 cells[2]. MHC class I molecules are heterodimers composed of two polypeptide chains, α and B2M[3]. 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-B[7].

Alterations and prevalence: Somatic mutations in HLA-B are observed in 10% of diffuse large B-cell lymphoma (DLBCL), 5% of cervical squamous cell carcinoma and stomach adenocarcinoma, 4% of head and neck squamous cell carcinoma and colorectal adenocarcinoma, 3% of uterine cancer, and 2% of esophageal adenocarcinoma and skin cutaneous melanoma[8,9]. Biallelic loss of HLA-B is observed in 5% of DLBCL[8,9].

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

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 exon 19 deletion

izalontamab brengitecan

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

Supporting Statement:
The FDA has granted Breakthrough designation to EGFR/HER3 targeting bispecific antibody-drug conjugate (ADC), izalontamab 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-izalontamab-brengitecan-in-egfr-nsclc

patritumab deruxtecan

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion or EGFRi sensitizing mutation

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

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 exon 19 deletion

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 exon 19 deletion (continued)

DB-1310

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

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

DB-1418

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

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, CTNNB1, CUL1, CYSLTR2, DDR2, DGCR8, DROSHA, E2F1, EGFR, EIF1AX, EPAS1, ERBB2, ERBB3, ERBB4, ESR1, EZH2, FAM135B, FGF7, FGFR1, FGFR2, FGFR3, FGFR4, FLT3, FLT4, FOXA1, FOXL2, FOXO1, GATA2, GLI1, GNA11, GNAQ, GNAS, HIF1A, HRAS, IDH1, IDH2, IKBKB, IL6ST, IL7R, IRF4, IRS4, KCNJ5, KDR, KIT, KLF4, KLF5, KNSTRN, KRAS, MAGOH, MAP2K1, MAP2K2, MAPK1, MAX, MDM4, MECOM, MED12, MEF2B, MET, MITF, MPL, MTOR, MYC, MYCN, MYD88, MYOD1, NFE2L2, NRAS, NSD2, NT5C2, NTRK1, NTRK2, NTRK3, NUP93, PAX5, PCBP1, PDGFRA, PDGFRB, PIK3C2B, PIK3CA, PIK3CB, PIK3CD, PIK3CG, PIK3R2, PIM1, PLCG1, PPP2R1A, PPP6C, PRKACA, PTPN11, PTPRD, PXDNL, RAC1, RAF1, RARA, RET, RGS7, RHEB, RHOA, RICTOR, RIT1, ROS1, RPL10, SETBP1, SF3B1, SIX1, SIX2, SLCO1B3, SMC1A, SMO, SNCAIP, SOS1, SOX2, SPOP, SRC, SRSF2, STAT3, STAT5B, STAT6, TAF1, TERT, TGFBR1, TOP1, TOP2A, TPMT, TRRAP, TSHR, U2AF1, USP8, WAS, XPO1, ZNF217, ZNF429

Genes Assayed for the Detection of Copy Number Variations

ABCB1, ABL1, ABL2, ABRAXAS1, ACVR1B, ACVR2A, ADAMTS12, ADAMTS2, AKT1, AKT2, AKT3, ALK, AMER1, APC, AR, ARAF, ARHGAP35, ARID1A, ARID1B, ARID2, ARID5B, ASXL1, ASXL2, ATM, ATR, ATRX, AURKA, AURKC, AXIN1, AXIN2, AXL, B2M, BAP1, BARD1, BCL2, BCL2L12, BCL6, BCOR, BLM, BMPR2, BRAF, BRCA1, BRCA2, BRIP1, CARD11, CASP8, CBFB, CBL, CCND1, CCND2, CCND3, CCNE1, CD274, CD276, CDC73, CDH1, CDH10, CDK12, CDK4, CDK6, CDKN1A, CDKN1B, CDKN2A, CDKN2B, CDKN2C, CHD4, CHEK1, CHEK2, CIC, CREBBP, CSMD3, CTCF, CTLA4, CTNND2, CUL3, CUL4A, CUL4B, CYLD, CYP2C9, DAXX, DDR1, DDR2, DDX3X, DICER1, DNMT3A, DOCK3, DPYD, DSC1, DSC3, EGFR, EIF1AX, ELF3, EMSY, ENO1, EP300, EPCAM, EPHA2, ERAP1, ERAP2, ERBB2, ERBB3, ERBB4, ERCC2, ERCC4, ERRFI1, ESR1, ETV6, EZH2, FAM135B, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, 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, PLCG1, PMS1, PMS2, POLD1, POLE, POT1, PPM1D, PPP2R1A, PPP2R2A, PPP6C, PRDM1, PRDM9, PRKACA, PRKAR1A, PTCH1, PTEN, PTPN11, PTPRT, PXDNL, RAC1, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD52, RAD54L, RAF1, RARA, RASA1, RASA2, RB1, RBM10, RECQL4, RET, RHEB, RICTOR, RIT1, RNASEH2A, RNASEH2B, RNF43, ROS1, RPA1, RPS6KB1, RPTOR, RUNX1, SDHA, SDHB, SDHD, SETBP1, SETD2, SF3B1, SLCO1B3, SLX4, SMAD2, SMAD4, SMARCA4, SMARCB1, SMC1A, SMO, SOX9, SPEN, SPOP, SRC, STAG2, STAT3, STAT6, STK11, SUFU, TAP1, TAP2, TBX3, TCF7L2, TERT, TET2, TGFBR2, TNFAIP3, TNFRSF14, TOP1, TP53, TP63, TPMT, TPP2, TSC1, TSC2, U2AF1, USP8, USP9X, VHL, WT1, XPO1, XRCC2, XRCC3, YAP1, YES1, ZFHX3, ZMYM3, ZNF217, ZNF429, ZRSR2

Genes Assayed for the Detection of Fusions

AKT2, ALK, AR, AXL, BRAF, BRCA1, BRCA2, CDKN2A, EGFR, ERBB2, ERBB4, ERG, ESR1, ETV1, ETV4, ETV5, FGFR1, FGFR2, FGFR3, FGR, FLT3, JAK2, KRAS, MDM4, MET, MYB, MYBL1, NF1, NOTCH1, NOTCH4, NRG1, NTRK1, NTRK2, NTRK3, NUTM1, PDGFRA, PDGFRB, PIK3CA, PPARG, PRKACA, PRKACB, PTEN, RAD51B, RAF1, RB1, RELA, RET, ROS1, RSPO2, RSPO3, TERT

Genes Assayed with Full Exon Coverage

ABRAXAS1, ACVR1B, ACVR2A, ADAMTS12, ADAMTS2, AMER1, APC, ARHGAP35, ARID1A, ARID1B, ARID2, ARID5B, ASXL1, ASXL2, ATM, ATR, ATRX, AXIN1, AXIN2, B2M, BAP1, BARD1, BCOR, BLM, BMPR2, BRCA1, BRCA2, BRIP1, CALR, CASP8, CBFB, CD274, CD276, CDC73, CDH1, CDH10, CDK12, CDKN1A, CDKN1B, CDKN2A, CDKN2B, CDKN2C, CHEK1, CHEK2, CIC, CIITA, CREBBP, CSMD3, CTCF, CTLA4, CUL3, CUL4A, CUL4B, CYLD, CYP2C9, CYP2D6, DAXX, DDX3X, DICER1, DNMT3A, DOCK3, DPYD, DSC1, DSC3, ELF3, ENO1, EP300, EPCAM, EPHA2, ERAP1, ERAP2, ERCC2, ERCC4, ERCC5, ERRFI1, ETV6, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, FAS, FAT1, FBXW7, FUBP1, GATA3, GNA13, GPS2, HDAC2, HDAC9, HLA-A, HLA-B, HNF1A, ID3, INPP4B, JAK1, JAK2, JAK3, KDM5C, KDM6A, KEAP1, KLHL13, KMT2A, KMT2B, KMT2C, KMT2D, LARP4B, LATS1, LATS2, MAP2K4, MAP2K7, MAP3K1, MAP3K4, MAPK8, MEN1, MGA, MLH1, MLH3, MRE11, MSH2, MSH3, MSH6, MTAP, MTUS2, MUTYH, NBN, NCOR1, NF1, NF2, NOTCH1, NOTCH2, NOTCH3, NOTCH4, PALB2, PARP1, PARP2, PARP3, PARP4, PBRM1, PDCD1, PDCD1LG2, PDIA3, PGD, PHF6, PIK3R1, PMS1, PMS2, POLD1, POLE, POT1, PPM1D, PPP2R2A, PRDM1, PRDM9, PRKAR1A, PSMB10, PSMB8, PSMB9, PTCH1, PTEN, PTPRT, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD52, RAD54L, RASA1, RASA2, RB1, RBM10, RECQL4, RNASEH2A, RNASEH2B, RNASEH2C, RNF43, RPA1, RPL22, RPL5, RUNX1, RUNX1T1, SDHA, SDHB, SDHC, SDHD, SETD2, SLX4, SMAD2, SMAD4, SMARCA4, SMARCB1, SOCS1, SOX9, SPEN, STAG2, STAT1, STK11, SUFU, TAP1, TAP2, TBX3, TCF7L2, TET2, TGFBR2, TMEM132D, TNFAIP3, TNFRSF14, TP53, TP63, TPP2, TSC1, TSC2, UGT1A1, USP9X, VHL, WT1, XRCC2, XRCC3, ZBTB20, ZFHX3, ZMYM3, ZRSR2

Relevant Therapy Summary

● In this cancer type ○ In other cancer type ◐ In this cancer type and other cancer types ✖ No evidence

EGFR exon 19 deletion

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

EGFR exon 19 deletion (continued)

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 exon 19 deletion (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, adebrelimab, 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 ◐ In this cancer type and other cancer types ✖ No evidence

EGFR exon 19 deletion (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 exon 19 deletion (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

EGFR exon 19 deletion (continued)

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 exon 19 deletion (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)
PB-101 (Precision Biotech Taiwan Corp), EGFR tyrosine kinase inhibitor	✖	✖	✖	✖	● (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)

SMAD4 deletion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
regorafenib	✖	✖	✖	✖	● (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	***10.47%***
BRCA2	***LOH, 13q13.1(32890491-32972932)x2***

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 (6.2.4 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. 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
2. Hulpke et al. The MHC I loading complex: a multitasking machinery in adaptive immunity. Trends Biochem Sci. PMID: 23849087
3. Adams et al. The adaptable major histocompatibility complex (MHC) fold: structure and function of nonclassical and MHC class I-like molecules. Annu Rev Immunol. 2013;31:529-61. PMID: 23298204
4. Rossjohn et al. T cell antigen receptor recognition of antigen-presenting molecules. Annu Rev Immunol. 2015;33:169-200. PMID: 25493333
5. Parham. MHC class I molecules and KIRs in human history, health and survival. Nat Rev Immunol. 2005 Mar;5(3):201-14. PMID: 15719024
6. Sidney et al. HLA class I supertypes: a revised and updated classification. BMC Immunol. 2008 Jan 22;9:1. PMID: 18211710
7. Cornel et al. MHC Class I Downregulation in Cancer: Underlying Mechanisms and Potential Targets for Cancer Immunotherapy. Cancers (Basel). 2020 Jul 2;12(7). PMID: 32630675
8. Weinstein et al. The Cancer Genome Atlas Pan-Cancer analysis project. Nat. Genet. 2013 Oct;45(10):1113-20. PMID: 24071849
9. 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
10. Ahmed et al. The TGF-β/Smad4 Signaling Pathway in Pancreatic Carcinogenesis and Its Clinical Significance. J Clin Med. 2017 Jan 5;6(1). PMID: 28067794
11. Zhao et al. The role of TGF-β/SMAD4 signaling in cancer. Int. J. Biol. Sci. 2018;14(2):111-123. PMID: 29483830
12. Cicenas et al. KRAS, TP53, CDKN2A, SMAD4, BRCA1, and BRCA2 Mutations in Pancreatic Cancer. Cancers (Basel). 2017 Apr 28;9(5). PMID: 28452926
13. Miyaki et al. Role of Smad4 (DPC4) inactivation in human cancer. Biochem. Biophys. Res. Commun. 2003 Jul 11;306(4):799-804. PMID: 12821112
14. Mehrvarz Sarshekeh et al. Association of SMAD4 mutation with patient demographics, tumor characteristics, and clinical outcomes in colorectal cancer. PLoS ONE. 2017;12(3):e0173345. PMID: 28267766
15. Cancer Genome Atlas Research Network. Comprehensive molecular characterization of gastric adenocarcinoma. Nature. 2014 Sep 11;513(7517):202-9. doi: 10.1038/nature13480. Epub 2014 Jul 23. PMID: 25079317
16. Yan et al. Reduced Expression of SMAD4 Is Associated with Poor Survival in Colon Cancer. Clin. Cancer Res. 2016 Jun 15;22(12):3037-47. PMID: 26861460
17. Voorneveld et al. A Meta-Analysis of SMAD4 Immunohistochemistry as a Prognostic Marker in Colorectal Cancer. Transl Oncol. 2015 Feb;8(1):18-24. PMID: 25749173
18. Shugang et al. Prognostic Value of SMAD4 in Pancreatic Cancer: A Meta-Analysis. Transl Oncol. 2016 Feb;9(1):1-7. PMID: 26947875
19. Boulay et al. SMAD4 is a predictive marker for 5-fluorouracil-based chemotherapy in patients with colorectal cancer. Br. J. Cancer. 2002 Sep 9;87(6):630-4. PMID: 12237773
20. Kozak et al. Smad4 inactivation predicts for worse prognosis and response to fluorouracil-based treatment in colorectal cancer. J. Clin. Pathol. 2015 May;68(5):341-5. PMID: 25681512
21. Ozawa et al. SMAD4 Loss Is Associated with Cetuximab Resistance and Induction of MAPK/JNK Activation in Head and Neck Cancer Cells. Clin. Cancer Res. 2017 Sep 1;23(17):5162-5175. PMID: 28522603
22. Lander et al. Initial sequencing and analysis of the human genome. Nature. 2001 Feb 15;409(6822):860-921. PMID: 11237011
23. 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
24. Nojadeh et al. Microsatellite instability in colorectal cancer. EXCLI J. 2018;17:159-168. PMID: 29743854
25. 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
26. 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
27. 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
28. Imai et al. Carcinogenesis and microsatellite instability: the interrelationship between genetics and epigenetics. Carcinogenesis. 2008 Apr;29(4):673-80. PMID: 17942460

References (continued)

29. NCCN Guidelines® - NCCN-Colon Cancer [Version 5.2025]
30. Pawlik et al. Colorectal carcinogenesis: MSI-H versus MSI-L. Dis. Markers. 2004;20(4-5):199-206. PMID: 15528785
31. 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
32. 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
33. 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
34. Bonneville et al. Landscape of Microsatellite Instability Across 39 Cancer Types. JCO Precis Oncol. 2017;2017. PMID: 29850653
35. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125514s178lbl.pdf
36. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125554s131lbl.pdf
37. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761174s009lbl.pdf
38. NCCN Guidelines® - NCCN-Rectal Cancer [Version 4.2025]
39. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125377s136lbl.pdf
40. 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
41. 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
42. Hermel et al. The Emerging Role of Checkpoint Inhibition in Microsatellite Stable Colorectal Cancer. J Pers Med. 2019 Jan 16;9(1). PMID: 30654522
43. Ciardiello et al. Immunotherapy of colorectal cancer: Challenges for therapeutic efficacy. Cancer Treat. Rev. 2019 Jun;76:22-32. PMID: 31079031
44. 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
45. Liu et al. EGFR-TKIs resistance via EGFR-independent signaling pathways. Mol Cancer. 2018 Feb 19;17(1):53. PMID: 29455669
46. Zhixiang. ErbB Receptors and Cancer. Methods Mol. Biol. 2017;1652:3-35. PMID: 28791631
47. Gutierrez et al. HER2: biology, detection, and clinical implications. Arch. Pathol. Lab. Med. 2011 Jan;135(1):55-62. PMID: 21204711
48. 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
49. 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
50. 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
51. 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
52. 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
53. 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
54. 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
55. Karachaliou et al. KRAS mutations in lung cancer. Clin Lung Cancer. 2013 May;14(3):205-14. PMID: 23122493
56. Brennan et al. The somatic genomic landscape of glioblastoma. Cell. 2013 Oct 10;155(2):462-77. PMID: 24120142
57. Cancer Genome Atlas Network. Comprehensive genomic characterization of head and neck squamous cell carcinomas. Nature. 2015 Jan 29;517(7536):576-82. PMID: 25631445
58. 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

References (continued)

59. 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
60. Gan et al. The EGFRvIII variant in glioblastoma multiforme. J Clin Neurosci. 2009 Jun;16(6):748-54. PMID: 19324552
61. https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/021743s025lbl.pdf
62. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/206995s004lbl.pdf
63. 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
64. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/201292s017lbl.pdf
65. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/211288s003lbl.pdf
66. NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2025]
67. 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
68. Vyse et al. Targeting EGFR exon 20 insertion mutations in non-small cell lung cancer. Signal Transduct Target Ther. 2019;4:5. PMID: 30854234
69. 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
70. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219839s000lbl.pdf
71. https://investors.cullinanoncology.com/news-releases/news-release-details/fda-grants-breakthrough-therapy-designation-cullinan-oncologys
72. 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
73. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/208065s033lbl.pdf
74. 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
75. 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
76. https://investors.blackdiamondtherapeutics.com//news-releases/news-release-details/black-diamond-therapeutics-announces-corporate-update-and
77. 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
78. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761210s011lbl.pdf
79. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219008s003lbl.pdf
80. https://iis.aastocks.com/20231227/11015917-0.PDF
81. https://www1.hkexnews.hk/listedco/listconews/sehk/2024/1008/2024100800433.pdf
82. https://www.genprex.com/news/genprex-receives-u-s-fda-fast-track-designation-for-gene-therapy-that-targets-lung-cancer/
83. NCCN Guidelines® - NCCN-Pediatric Central Nervous System Cancers [Version 3.2025]
84. 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
85. 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
86. Ouzzine et al. The UDP-glucuronosyltransferases of the blood-brain barrier: their role in drug metabolism and detoxication. Front Cell Neurosci. 2014;8:349. PMID: 25389387
87. Nagar et al. Uridine diphosphoglucuronosyltransferase pharmacogenetics and cancer. Oncogene. 2006 Mar 13;25(11):1659-72. PMID: 16550166
88. Allain et al. Emerging roles for UDP-glucuronosyltransferases in drug resistance and cancer progression. Br J Cancer. 2020 Apr;122(9):1277-1287. PMID: 32047295
89. Izumi et al. Expression of UDP-glucuronosyltransferase 1A in bladder cancer: association with prognosis and regulation by estrogen. Mol Carcinog. 2014 Apr;53(4):314-24. PMID: 23143693

References (continued)

90. Sundararaghavan et al. Glucuronidation and UGT isozymes in bladder: new targets for the treatment of uroepithelial carcinomas?. Oncotarget. 2017 Jan 10;8(2):3640-3648. PMID: 27690298
91. Lu et al. Drug-Metabolizing Activity, Protein and Gene Expression of UDP-Glucuronosyltransferases Are Significantly Altered in Hepatocellular Carcinoma Patients. PLoS One. 2015;10(5):e0127524. PMID: 26010150
92. Karas et al. JCO Oncol Pract. 2021 Dec 3:OP2100624. PMID: 34860573