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Patient Name: 박인희
Gender: F
Sample ID: N25-53

Primary Tumor Site: Bronchus
Collection Date: 2025.05.30

Sample Cancer Type: Lung Cancer

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Report Highlights
6 Relevant Biomarkers
17 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	***4.77 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: 23.65% Locus: chr7:55242464 Transcript: NM_005228.5	**afatinib** [1, 2 / I, II+] **amivantamab + lazertinib** [1, 2 / I, II+] **bevacizumab† + erlotinib** [2 / I, II+] **dacomitinib** [1, 2 / I, II+] **erlotinib** [2 / I, II+] **erlotinib + ramucirumab** [1, 2 / I, II+] **gefitinib** [1, 2 / I, II+] **osimertinib** [1, 2 / I, II+] **osimertinib + chemotherapy** [1, 2 / I] **amivantamab + chemotherapy** [1, 2 / II+] **BAT1706 + erlotinib** [2] gefitinib + chemotherapy [I] atezolizumab + bevacizumab + chemotherapy [II+]	None*	193

*** 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	*MYC amplification* MYC proto-oncogene, bHLH transcription factor Locus: chr8:128748847	None*	None*	4
IIC	*PTEN deletion* phosphatase and tensin homolog Locus: chr10:89623659	None*	None*	2
IIC	*AKT2 amplification* AKT serine/threonine kinase 2 Locus: chr19:40739751	None*	None*	1
IIC	*RICTOR amplification* RPTOR independent companion of MTOR complex 2 Locus: chr5:38942342	None*	None*	1
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	**patritumab deruxtecan** [1]

Public data sources included in alerts: FDA[1], NCCN, **EMA**[2], ESMO

Prevalent cancer biomarkers without relevant evidence based on included data sources
BRCA1 exon 2 duplication, EZH2 amplification, ARID5B deletion, 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.2235_2249delGGAATTAAGAGAAGC	COSM6223	chr7:55242464	23.65%	NM_005228.5	nonframeshift Deletion
ARHGEF10L	p.(F376L)	c.1126T>C	.	chr1:17949596	54.62%	NM_018125.4	missense
DPYD	p.(Y109N)	c.325T>A	.	chr1:98187224	56.11%	NM_000110.4	missense
BMPR2	p.(E427K)	c.1279G>A	.	chr2:203407036	9.50%	NM_001204.7	missense
HLA-A	p.(E176W)	c.526_527delGAinsTG	.	chr6:29911227	59.43%	NM_001242758.1	missense
TP53	p.(I255V)	c.763A>G	.	chr17:7577518	11.81%	NM_000546.6	missense

Variant Details (continued)

Copy Number Variations

Gene	Locus	Copy Number	CNV Ratio
MYC	chr8:128748847	11.47	3.03
PTEN	chr10:89623659	0.23	0.62
AKT2	chr19:40739751	6.56	1.98
RICTOR	chr5:38942342	6.93	2.06
SMAD4	chr18:48573387	0.49	0.68
BRCA1	chr17:41275964	7	
EZH2	chr7:148506391	10.37	2.8
ARID5B	chr10:63661463	0.49	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[22]. In addition to EGFR/ERBB1/HER1, other members of the ERBB/HER family include ERBB2/HER2, ERBB3/HER3, and ERBB4/HER4[76]. 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 pathways[77]. Activation of these pathways promotes cell proliferation, differentiation, and survival[78,79].

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[9,10,80,81]. 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[82]. These mutations constitutively activate EGFR resulting in downstream signaling, and represent 80% of the EGFR mutations observed in lung cancer[82]. A second group of less prevalent activating mutations includes E709K, G719X, S768I, L861Q, and short in-frame insertion mutations in exon 20[83,84,85,86]. EGFR activating mutations in lung cancer tend to be mutually exclusive to KRAS activating mutations[87]. 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[82,88]. 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[9,10,81,88,89]. 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[90,91,92]. Alterations in EGFR are rare in pediatric cancers[9,10]. 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)[9,10]. 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)[9,10].

Potential relevance: Approved first-generation EGFR tyrosine kinase inhibitors (TKIs) include erlotinib[93] (2004) and gefitinib[94] (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[95]. Second-generation TKIs afatinib[96] (2013) and dacomitinib[97] (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[98,99,100,101]. However, BDTX-189[102] was granted a fast track designation (2020) for the treatment of solid tumors harboring an EGFR exon 20 insertion mutations. In 2022, the FDA granted breakthrough therapy designation to the irreversible EGFR inhibitors, CLN-081 (TPC-064)[103] and sunvozertinib[104], 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

Biomarker Descriptions (continued)

associated with the emergence of drug resistance[105]. The primary resistance mutation that emerges following treatment with first-generation TKI is T790M, accounting for 50-60% of resistant cases[82]. Third generation TKIs were developed to maintain sensitivity in the presence of T790M[105]. Osimertinib[106] (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[105]. 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[107]. T790M and C797S can occur in either cis or trans allelic orientation[107]. 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[107]. 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[107,108]. However, C797S occurring in cis conformation with T790M, confers resistance to first- and third-generation TKIs[107]. Fourth-generation TKIs are in development to overcome acquired resistance mutations after osimertinib treatment, including BDTX-1535[109] (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[110]. The bispecific antibody, amivantamab[111] (2021), targeting EGFR and MET was approved for NSCLC tumors harboring EGFR exon 20 insertion mutations. A small molecule kinase inhibitor, lazertinib[112] (2024), was approved in combination with amivantamab as a first-line treatment for adult patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R mutations. In 2024, a CNS penetrating small molecule, ERAS-801[113] received fast track designation for the treatment of adult patients with EGFR altered glioblastoma. HLX-42[114], 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[115] (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[116] (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[117,118,119].

MYC amplification

MYC proto-oncogene, bHLH transcription factor

Background: The MYC gene encodes the MYC proto-oncogene, bHLH transcription factor (c-MYC), a basic helix-loop-helix transcription factor that regulates the expression of numerous genes that control cell cycle progression, apoptosis, metabolic pathways, and cellular transformation[1,2,3,4]. MYC is part of the MYC oncogene family, which includes the related transcription factors, MYCN and MYCL, and regulates transcription in 10-15% of promoter regions[5]. MYC functions as a heterodimer in complex with the transcription factor MAX[2,6].

Alterations and prevalence: Recurrent somatic alterations are observed in both solid and hematological cancers. Recurrent somatic mutations in MYC, including those at codon T58, are infrequent and hypothesized to increase the stability of the MYC protein[7,8]. Amplification of the MYC gene is observed in 15-30% of ovarian serous cystadenocarcinoma, esophageal adenocarcinoma, uterine carcinosarcoma, and breast invasive carcinoma, 10-15% of pancreatic adenocarcinoma, stomach adenocarcinoma, and liver hepatocellular carcinoma, 5-10% of head and neck squamous cell carcinoma, uterine corpus endometrial carcinoma, prostate adenocarcinoma, lung adenocarcinoma, lung squamous cell carcinoma, bladder urothelial carcinoma, and colorectal adenocarcinoma, and 2-5% of skin cutaneous melanoma, brain lower grade glioma, sarcoma, cervical squamous cell carcinoma, uveal melanoma, diffuse B-cell lymphoma, glioblastoma, and kidney chromophobe[9,10]. MYC is the target of the t(8;14)(q24;32) chromosomal translocation in Burkitt lymphoma that places MYC coding sequences adjacent to immunoglobulin region regulatory sequences, resulting in increased MYC expression[11,12]. Overall, MYC translocations are observed in 2% of diffuse large B-cell lymphoma[9,10]. Somatic mutations in MYC are observed in 7% of diffuse large B-cell lymphoma, 4% of uterine carcinosarcoma, 3% of uterine corpus endometrial carcinoma and skin cutaneous melanoma, and 2% of colorectal adenocarcinoma and stomach adenocarcinoma[9,10]. Alterations in MYC are also observed in pediatric cancers[10]. Somatic mutations in MYC have been observed in 59% of non-Hodgkin lymphoma, 2% of leukemia, and less than 1% of bone cancer (2 in 327 cases) and B-lymphoblastic leukemia/lymphoma (1 in 252 cases)[10]. Amplification of MYC is observed in 6% of embryonal tumor, 5% of bone cancer, and less than 1% of B-lymphoblastic leukemia/lymphoma (2 in 731 cases) and MYC translocations are observed in 5% of T-lymphoblastic leukemia/lymphoma[10].

Potential relevance: B-cell lymphoma with MYC translocations that co-occur with BCL2 or BCL6 are referred to as double hit lymphoma, while co-occurrence with BCL2 and BCL6 rearrangements is referred to as triple-hit lymphoma[13,14]. MYC translocations are a diagnostic marker of Burkitt Lymphoma[15,16]. MYC translocations are also indicative of high risk for multiple myeloma and are associated with poor risk in acute lymphoblastic leukemia[17,18]. Currently, no therapies are approved for MYC aberrations. Due to the high frequency of

Biomarker Descriptions (continued)

somatic MYC alterations in cancer, many approaches are being investigated in clinical trials including strategies to disrupt complex formation with MAX, including inhibition of MYC expression and synthetic lethality associated with MYC overexpression[1,19,20,21].

PTEN deletion

phosphatase and tensin homolog

Background: The PTEN gene encodes the phosphatase and tensin homolog, a tumor suppressor protein with lipid and protein phosphatase activities[25]. PTEN antagonizes PI3K/AKT signaling by catalyzing the dephosphorylation of phosphatidylinositol (3,4,5)-trisphosphate (PIP3) to PIP2 at the cell membrane, which inhibits the activation of AKT[26,27]. In addition, PTEN has been proposed to influence RAD51 loading at double strand breaks during homologous recombination repair (HRR) and regulate the G2/M checkpoint by influencing CHEK1 localization through AKT inhibition, thereby regulating HRR efficiency[28]. Germline mutations in PTEN are linked to hamartoma tumor syndromes, including Cowden disease, which are defined by uncontrolled cell growth and benign or malignant tumor formation[29]. PTEN germline mutations are also associated with inherited cancer risk in several cancer types[30].

Alterations and prevalence: PTEN is frequently altered in cancer by inactivating loss-of-function mutations and by gene deletion. PTEN mutations are frequently observed in 50%-60% of uterine cancer[9,10]. Nearly half of somatic mutations in PTEN are stop-gain or frame-shift mutations that result in truncation of the protein reading frame. Recurrent missense or stop-gain mutations at codons R130, R173, and R233 result in loss of phosphatase activity and inhibition of wild-type PTEN[27,31,32,33,34]. PTEN gene deletion is observed in 15% of prostate cancer, 9% of squamous lung cancer, 9% of glioblastoma, and 1-5% of melanoma, sarcoma, and ovarian cancer[9,10].

Potential relevance: Due to the role of PTEN in HRR, poly(ADP-ribose) polymerase inhibitors (PARPi) are being explored as a potential therapeutic strategy in PTEN deficient tumors[35,36]. In 2022, the FDA granted fast track designation to the small molecule inhibitor, pidnarulex[37], for BRCA1/2, PALB2, or other homologous recombination deficiency (HRD) mutations in breast and ovarian cancers. In 2023, the FDA approved the kinase inhibitor, capivasertib[38] in combination with fulvestrant for locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer with one or more PIK3CA/AKT1/PTEN-alterations following progression after endocrine treatment.

AKT2 amplification

AKT serine/threonine kinase 2

Background: The AKT2 gene encodes a serine/threonine kinase that belongs to a family of closely related protein kinases that also includes AKT1 and AKT3. Growth factor signaling leads to the activation of phosphatidylinositol 3-kinase (PI3K), recruitment of AKT to the plasma membrane, and subsequent activation of downstream effectors including MTOR. The PI3K/AKT/MTOR pathway is central to the regulation of cancer cell proliferation, survival, and metabolism[145,146]. Amongst the three AKT isoforms (AKT1, AKT2, and AKT3), AKT2 is implicated in cancer cell invasion and metastasis[147,148,149].

Alterations and prevalence: AKT2 is altered by recurrent activating mutations at amino acid positions homologous to those observed in AKT1 which are found in 1-4% of melanomas, bladder, lung, uterine, and gastric cancers[150]. In AKT2, recurrent activating mutations occur at E17K, L52R, and D324G/H[150]. AKT2 is also subject to gene amplification in ovarian cancer, lung squamous cell carcinoma, and bladder cancer at a prevalence of 3-8%[9]. A BCAM::AKT2 fusion has been identified in ovarian cancer[151].

Potential relevance: Currently, no therapies are approved for AKT2 aberrations. However, the pan-AKT inhibitor capivasertib (AZD5363) is active against all AKT isoforms[152] but clinical evidence in AKT2 aberrant cancers is lacking.

RICTOR amplification

RPTOR independent companion of MTOR complex 2

Background: The RICTOR gene encodes the RPTOR independent companion of MTOR complex 2, a core component of the mTOR complex-2 (mTORC2)[22,135]. RICTOR complexes with MTOR, DEPTOR, mSin1 and Protor1/2 to form the mTORC2 complex, which regulates cell proliferation and survival by phosphorylating members of the PKA/PKG/PKC family of protein kinases[136]. The mTORC2 complex is a downstream effector of the PI3K/AKT/MTOR signaling pathway and facilitates integration of the PI3K/AKT/MTOR and RAS/RAF/MEK/ERK signaling pathways[137,138,139]. Independent of mTORC2, RICTOR can interact with integrin-linked kinases and promote phosphorylation of AKT[136,140]. Aberrations in RICTOR can lead to downstream pathway activation promoting cell proliferation and survival, supporting an oncogenic role for RICTOR[141].

Alterations and prevalence: Amplification of RICTOR is observed in several types of solid tumors and has been observed to correlate with protein overexpression[142]. Specifically, RICTOR amplification is observed in 10% of lung squamous cell carcinoma, 8% of esophageal adenocarcinoma, 7% of lung adenocarcinoma, 6% of stomach adenocarcinoma, 5% of adrenocortical carcinoma, bladder urothelial carcinoma, cervical squamous cell carcinoma, ovarian serous cystadenocarcinoma, and sarcoma[9,10]. Somatic mutations in

Biomarker Descriptions (continued)

RICTOR are observed in 7% of uterine corpus endometrial carcinoma and skin cutaneous melanoma, 5% of stomach adenocarcinoma and bladder urothelial carcinoma, and 3% of lung adenocarcinoma and lung squamous cell carcinoma[9,10].

Potential relevance: Currently, no therapies are approved for RICTOR aberrations. RICTOR overexpression is associated with poor survival in hepatocellular carcinoma and endometrial carcinoma[143,144].

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[39,40]. 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[40,41,42]. Loss of SMAD4 does not drive oncogenesis, but is associated with progression of cancers initiated by driver genes such as KRAS and APC[39,40]

Alterations and prevalence: Inactivation of SMAD4 can occur due to mutations, allelic loss, homozygous deletions, and 18q loss of heterozygosity (LOH)[39]. 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[10,42,43]. Copy number deletions occur in up to 12% of pancreatic, 10% of esophageal, and 13% of stomach cancers[9,10,44].

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[40,42,45,46,47]. Importantly, SMAD4 is a predictive biomarker to fluorouracil based chemotherapy[48,49]. 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)[49]. 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[50].

BRCA1 exon 2 duplication

BRCA1, DNA repair associated

Background: The breast cancer early onset gene 1 (BRCA1) encodes one of two BRCA proteins (BRCA1 and BRCA2) initially discovered as major hereditary breast cancer genes. Although structurally unrelated, both BRCA1 and BRCA2 exhibit tumor suppressor function and are integrally involved in the homologous recombination repair (HRR) pathway, a pathway critical in the repair of damaged DNA[51,52]. Specifically, BRCA1/2 are required for the repair of chromosomal double strand breaks (DSBs) which are highly unstable and compromise genome integrity[51,52]. Inherited pathogenic mutations in BRCA1/2 are known to confer increased risk in women for breast and ovarian cancer and in men for breast and prostate cancer[53,54,55]. For individuals diagnosed with inherited pathogenic or likely pathogenic BRCA1/2 variants, the cumulative risk of breast cancer by 80 years of age was 69-72% and the cumulative risk of ovarian cancer by 70 years was 20-48%[53,56].

Alterations and prevalence: Inherited BRCA1/2 mutations occur in 1:400 to 1:500 individuals and are observed in 10-15% of ovarian cancer, 5-10% of breast cancer, and 1-4% of prostate cancer[57,58,59,60,61,62,63,64]. Somatic alterations in BRCA1 are observed in 5-10% of uterine corpus endometrial carcinoma, cutaneous melanoma, bladder urothelial carcinoma, diffuse large B-cell lymphoma, and cervical squamous cell carcinoma, 3-4% of lung squamous cell carcinoma, lung adenocarcinoma, stomach adenocarcinoma, ovarian serous cystadenocarcinoma, colorectal adenocarcinoma, and breast invasive carcinoma, and 2% of head and neck squamous cell carcinoma and glioblastoma multiforme[9,10].

Potential relevance: Individuals possessing BRCA1/2 pathogenic germline or somatic mutations are shown to exhibit sensitivity to platinum based chemotherapy as well as treatment with poly (ADP-ribose) polymerase inhibitors (PARPi)[65]. Inhibitors targeting PARP induce synthetic lethality in recombination deficient BRCA1/2 mutant cells[66,67]. Consequently, several PARP inhibitors have been FDA approved for BRCA1/2-mutated cancers. Olaparib[68] (2014) was the first PARPi to be approved by the FDA for BRCA1/2 aberrations. Originally approved for the treatment of germline variants, olaparib is now indicated (2018) for the maintenance treatment of both germline BRCA1/2-mutated (gBRCAm) and somatic BRCA1/2-mutated (sBRCAm) epithelial ovarian, fallopian tube, or primary peritoneal cancers that are responsive to platinum-based chemotherapy. Olaparib is also indicated for the treatment of patients with gBRCAm HER2-negative metastatic breast cancer and metastatic pancreatic adenocarcinoma. Additionally, olaparib[68] is approved (2020) for metastatic castration-resistant prostate cancer (mCRPC) with deleterious or suspected deleterious, germline or somatic mutations in HRR genes that includes BRCA1. Rucaparib[69] is also approved (2020) for deleterious gBRCAm or sBRCAm mCRPC and ovarian cancer. Talazoparib[70] (2018) is indicated for the treatment of gBRCAm HER2-negative locally advanced or metastatic breast cancer. Additionally, talazoparib[70] in combination with enzalutamide is approved (2023) for metastatic castration-resistant prostate cancer (mCRPC) with mutations in HRR genes that includes BRCA1. Niraparib[71] (2017) is another PARPi approved for the treatment of

Biomarker Descriptions (continued)

epithelial ovarian, fallopian tube, or primary peritoneal cancers with a deleterious or suspected deleterious BRCA mutation. Niraparib in combination with abiraterone acetate[72] received FDA approval (2023) for the treatment of deleterious or suspected deleterious BRCA-mutated (BRCAm) mCRPC. Despite tolerability and efficacy, acquired resistance to PARP inhibition has been clinically reported[73]. One of the most common mechanisms of resistance includes secondary intragenic mutations that restore BRCA1/2 functionality[74]. In addition to PARP inhibitors, other drugs which promote synthetic lethality have been investigated for BRCA mutations. In 2022, the FDA granted fast track designation to the small molecule inhibitor, pidnarulex[37], for BRCA1/2, PALB2, or other homologous recombination deficiency (HRD) mutations in breast and ovarian cancers. Like PARPi, pidnarulex promotes synthetic lethality but through an alternative mechanism which involves stabilization of G-quadruplexes at the replication fork leading to DNA breaks and genomic instability. In 2024, the FDA granted fast track designation to TNG-348[75], a USP1 inhibitor, for the treatment of BRCA1/2 mutated breast and ovarian cancer.

EZH2 amplification

enhancer of zeste 2 polycomb repressive complex 2 subunit

Background: The EZH2 gene encodes the enhancer of zeste homolog 2 protein, a histone methyltransferase that functions as both a transcriptional suppressor and co-activator[120]. EZH2 mediates methylation of histone H3 at Lys 27 (H3K27me3) and promotes tumor growth and metastasis through regulation of the cell cycle[120,121]. Since EZH2 loss-of-function is associated with the development of cancer, it is considered a tumor suppressor. EZH2 is overexpressed in various cancer types, consequently, it can also function as an oncogene[120].

Alterations and prevalence: Diverse EZH2 alterations including missense, nonsense, frameshift mutations, and inactivating deletions are observed in 18-25% of T-cell acute lymphocytic leukemia (T-ALL), 3-13% of myeloproliferative neoplasms (MPN), 8-12% of myelodysplastic/myeloproliferative neoplasms overlap disorders (MDS/MPN), and 6% of diverse MDS[121,122]. Heterozygous gain-of-function mutations at tyrosine 641 (Y641) are observed in 22% of germinal center B-cell (GBC) and diffuse large B-cell lymphoma (DLBCL), and 7-17% of follicular lymphoma (FL)[121,123]. In solid tumors, EZH2 mutations are observed in up to 8% of uterine corpus endometrial carcinoma, 5% of skin cutaneous melanoma, and 3% of cholangiocarcinoma[9,10]. Amplifications are observed in up to 7% of ovarian carcinoma[9,10]. Increased EZH2 copy number corresponds with enhanced protein expression and is observed in over 50% of hormone-refractory prostate cancers[124].

Potential relevance: The methyltransferase inhibitor tazemetostat[125] was FDA approved (2020) for EZH2 mutated relapsed or refractory follicular lymphoma after at least 2 prior systemic therapies. Tazemetostat was also granted FDA fast track designation in 2016 for DLBCL harboring EZH2 activating mutations[126]. Somatic mutation in EZH2 is one of the possible molecular abnormality requirements for the diagnosis of myelodysplasia-related AML (AML-MR)[127]. EZH2 nonsense or frameshift mutations are independently associated with poor prognosis in MDS and MDS/MPN[128]. EZH2 mutations also confer poor prognosis in essential thrombocythemia (ET), primary myelofibrosis (PMF), and AML[129,130,131]. EZH2 overexpression correlates with malignancy, poor prognosis, and poor survival, and has been detected in MDS and acute myeloid leukemia (AML)[120,132]. Several studies have shown that EZH2 overexpression enhances chemoresistance in solid tumor types[133,134].

ARID5B deletion

AT-rich interaction domain 5B

Background: The ARID5B gene encodes the AT-rich interaction domain 5B protein[22]. ARID5B, also known as MRF2, belongs to the ARID superfamily that also includes ARID1A, ARID1B, and ARID2[23,24]. ARID5B forms a complex with PHF2, which is capable of histone demethylation leading to transcriptional activation of target genes[24]. ARID5B is known to be essential for the development of hematopoietic cells[24]. Several single-nucleotide polymorphisms (SNPs) in ARID5B have been associated with susceptibility of acute lymphoblastic leukemia (ALL)[24].

Alterations and prevalence: Somatic mutations in ARID5B are observed in 15% of uterine corpus endometrial carcinoma, 6% of skin cutaneous melanoma, 5% of diffuse large B-cell lymphoma, 4% of stomach adenocarcinoma[9,10]. Biallelic loss of ARID5B is observed in 1% of kidney chromophobe, lung squamous cell carcinoma, and skin cutaneous melanoma[9,10].

Potential relevance: Currently, no therapies are approved for ARID5B aberrations.

Alerts Informed By Public Data Sources

Current FDA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

FDA information is current as of 2025-04-16. For the most up-to-date information, search www.fda.gov.

EGFR exon 19 deletion

patritumab deruxtecan

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion or EGFRi sensitizing mutation

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

Reference:

https://www.cancernetwork.com/view/fda-grants-breakthrough-therapy-status-to-patritumab-deruxtecan-for-egfr-metastatic-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, MTAP, MTOR, MUTYH, MYC, MYCL, MYCN, MYD88, NBN, NCOR1, NF1, NF2, NFE2L2, NOTCH1, NOTCH2, NOTCH3, NOTCH4, NRAS, NTRK1, NTRK3, PALB2, PARP1, PARP2, PARP3, PARP4, PBRM1, PCBP1, PDCD1, PDCD1LG2, PDGFRA, PDGFRB, PDIA3, PGD, PHF6, PIK3C2B, PIK3CA, PIK3CB, PIK3R1, PIK3R2, PIM1, PLCG1, PMS1, PMS2, POLD1, POLE, POT1, PPM1D, PPP2R1A, PPP2R2A, PPP6C, PRDM1, PRDM9, PRKACA, PRKAR1A, PTCH1, PTEN, PTPN11, PTPRT, PXDNL, RAC1, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD52, RAD54L, RAF1, RARA, RASA1, RASA2, RB1, RBM10, RECQL4, RET, RHEB, RICTOR, RIT1, RNASEH2A, RNASEH2B, RNF43, ROS1, RPA1, RPS6KB1, RPTOR, RUNX1, SDHA, SDHB, SDHD, SETBP1, SETD2, SF3B1, SLCO1B3, SLX4, SMAD2, SMAD4, SMARCA4, SMARCB1, SMC1A, SMO, SOX9, SPEN, SPOP, SRC, STAG2, STAT3, STAT6, STK11, SUFU, TAP1, TAP2, TBX3, TCF7L2, TERT, TET2, TGFBR2,

Genes Assayed (continued)

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

TNFAIP3, TNFRSF14, TOP1, TP53, TP63, TPMT, TPP2, TSC1, TSC2, U2AF1, USP8, USP9X, VHL, WT1, XPO1, XRCC2, XRCC3, YAP1, YES1, ZFHX3, ZMYM3, ZNF217, ZNF429, ZRSR2

Genes Assayed for the Detection of Fusions

AKT2, ALK, AR, AXL, BRAF, BRCA1, BRCA2, CDKN2A, EGFR, ERBB2, ERBB4, ERG, ESR1, ETV1, ETV4, ETV5, FGFR1, FGFR2, FGFR3, FGR, FLT3, JAK2, KRAS, MDM4, MET, MYB, MYBL1, NF1, NOTCH1, NOTCH4, NRG1, NTRK1, NTRK2, NTRK3, NUTM1, PDGFRA, PDGFRB, PIK3CA, PPARG, 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	●	●	●	✖	✖
amivantamab + lazertinib	●	●	●	✖	✖
osimertinib + chemotherapy + pemetrexed	●	✖	●	✖	✖
bevacizumab + erlotinib	✖	●	●	●	✖
erlotinib	✖	●	●	●	✖

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

Relevant Therapy Summary (continued)

● 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*
osimertinib + carboplatin + pemetrexed	✖	●	✖	✖	✖
osimertinib + cisplatin + pemetrexed	✖	●	✖	✖	✖
BAT1706 + erlotinib	✖	✖	●	✖	✖
bevacizumab (Allergan) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Biocon) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Celltrion) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Mabxience) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Pfizer) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Samsung Bioepis) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Stada) + erlotinib	✖	✖	●	✖	✖
atezolizumab + bevacizumab + carboplatin + paclitaxel	✖	✖	✖	●	✖
gefitinib + carboplatin + pemetrexed	✖	✖	✖	●	✖
adebrelimab, bevacizumab, chemotherapy	✖	✖	✖	✖	● (IV)
afatinib, bevacizumab, chemotherapy	✖	✖	✖	✖	● (IV)
befotertinib	✖	✖	✖	✖	● (IV)
bevacizumab, almonertinib, chemotherapy	✖	✖	✖	✖	● (IV)
catequentinib, toripalimab	✖	✖	✖	✖	● (IV)
EGFR tyrosine kinase inhibitor	✖	✖	✖	✖	● (IV)
gefitinib, chemotherapy	✖	✖	✖	✖	● (IV)
gefitinib, endostatin	✖	✖	✖	✖	● (IV)
natural product, gefitinib, erlotinib, icotinib hydrochloride, osimertinib, almonertinib, furmonertinib	✖	✖	✖	✖	● (IV)
almonertinib, apatinib	✖	✖	✖	✖	● (III)
almonertinib, chemotherapy	✖	✖	✖	✖	● (III)
almonertinib, radiation therapy	✖	✖	✖	✖	● (III)
almonertinib, radiation therapy, chemotherapy	✖	✖	✖	✖	● (III)
befotertinib, icotinib hydrochloride	✖	✖	✖	✖	● (III)
bevacizumab, osimertinib	✖	✖	✖	✖	● (III)
BL-B01D1	✖	✖	✖	✖	● (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*
BL-B01D1, osimertinib	✖	✖	✖	✖	● (III)
CK-101, gefitinib	✖	✖	✖	✖	● (III)
datopotamab deruxtecan, osimertinib	✖	✖	✖	✖	● (III)
FHND9041, afatinib	✖	✖	✖	✖	● (III)
furmonertinib	✖	✖	✖	✖	● (III)
furmonertinib, osimertinib, chemotherapy	✖	✖	✖	✖	● (III)
gefitinib, afatinib, erlotinib, metformin hydrochloride	✖	✖	✖	✖	● (III)
icotinib hydrochloride, catequentinib	✖	✖	✖	✖	● (III)
icotinib hydrochloride, chemotherapy	✖	✖	✖	✖	● (III)
icotinib hydrochloride, radiation therapy	✖	✖	✖	✖	● (III)
JMT-101, osimertinib	✖	✖	✖	✖	● (III)
osimertinib, bevacizumab	✖	✖	✖	✖	● (III)
osimertinib, chemotherapy	✖	✖	✖	✖	● (III)
osimertinib, datopotamab deruxtecan	✖	✖	✖	✖	● (III)
sacituzumab tirumotecan	✖	✖	✖	✖	● (III)
sacituzumab tirumotecan, osimertinib	✖	✖	✖	✖	● (III)
savolitinib, osimertinib	✖	✖	✖	✖	● (III)
SH-1028	✖	✖	✖	✖	● (III)
targeted therapy	✖	✖	✖	✖	● (III)
TY-9591, osimertinib	✖	✖	✖	✖	● (III)
ABSK-043, furmonertinib	✖	✖	✖	✖	● (II)
almonertinib	✖	✖	✖	✖	● (II)
almonertinib, adebrelimab, chemotherapy	✖	✖	✖	✖	● (II)
almonertinib, bevacizumab	✖	✖	✖	✖	● (II)
almonertinib, chemoradiation therapy	✖	✖	✖	✖	● (II)
almonertinib, dacomitinib	✖	✖	✖	✖	● (II)
amivantamab, chemotherapy	✖	✖	✖	✖	● (II)
amivantamab, lazertinib, chemotherapy	✖	✖	✖	✖	● (II)
atezolizumab, bevacizumab, tiragolumab	✖	✖	✖	✖	● (II)

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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*
befotertinib, bevacizumab, chemotherapy	✖	✖	✖	✖	● (II)
bevacizumab, afatinib	✖	✖	✖	✖	● (II)
bevacizumab, furmonertinib	✖	✖	✖	✖	● (II)
cadonilimab, chemotherapy, catequentinib	✖	✖	✖	✖	● (II)
camrelizumab, apatinib	✖	✖	✖	✖	● (II)
capmatinib, osimertinib, ramucirumab	✖	✖	✖	✖	● (II)
catequentinib, almonertinib	✖	✖	✖	✖	● (II)
chemotherapy, atezolizumab, bevacizumab	✖	✖	✖	✖	● (II)
dacomitinib, osimertinib	✖	✖	✖	✖	● (II)
EGFR tyrosine kinase inhibitor, osimertinib, chemotherapy	✖	✖	✖	✖	● (II)
EGFR tyrosine kinase inhibitor, radiation therapy	✖	✖	✖	✖	● (II)
erlotinib, chemotherapy	✖	✖	✖	✖	● (II)
erlotinib, OBI-833	✖	✖	✖	✖	● (II)
furmonertinib, bevacizumab	✖	✖	✖	✖	● (II)
furmonertinib, bevacizumab, chemotherapy	✖	✖	✖	✖	● (II)
furmonertinib, chemotherapy	✖	✖	✖	✖	● (II)
furmonertinib, chemotherapy, bevacizumab	✖	✖	✖	✖	● (II)
furmonertinib, icotinib hydrochloride	✖	✖	✖	✖	● (II)
gefitinib, bevacizumab, chemotherapy	✖	✖	✖	✖	● (II)
gefitinib, icotinib hydrochloride	✖	✖	✖	✖	● (II)
gefitinib, thalidomide	✖	✖	✖	✖	● (II)
icotinib hydrochloride	✖	✖	✖	✖	● (II)
icotinib hydrochloride, autologous RAK cell	✖	✖	✖	✖	● (II)
icotinib hydrochloride, osimertinib	✖	✖	✖	✖	● (II)
ivonescimab, chemotherapy	✖	✖	✖	✖	● (II)
lazertinib	✖	✖	✖	✖	● (II)
lazertinib, bevacizumab	✖	✖	✖	✖	● (II)
lazertinib, chemotherapy	✖	✖	✖	✖	● (II)
lenvatinib, pembrolizumab	✖	✖	✖	✖	● (II)

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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*
osimertinib, chemoradiation therapy	✖	✖	✖	✖	● (II)
osimertinib, radiation therapy	✖	✖	✖	✖	● (II)
PLB-1004, bozitinib, osimertinib	✖	✖	✖	✖	● (II)
ramucirumab, erlotinib	✖	✖	✖	✖	● (II)
sacituzumab govitecan	✖	✖	✖	✖	● (II)
sacituzumab tirumotecan, chemotherapy, osimertinib	✖	✖	✖	✖	● (II)
sunvozertinib	✖	✖	✖	✖	● (II)
sunvozertinib, catequentinib	✖	✖	✖	✖	● (II)
sunvozertinib, golidocitinib	✖	✖	✖	✖	● (II)
tislelizumab, chemotherapy, bevacizumab	✖	✖	✖	✖	● (II)
toripalimab	✖	✖	✖	✖	● (II)
toripalimab, bevacizumab, Clostridium butyricum, chemotherapy	✖	✖	✖	✖	● (II)
toripalimab, chemotherapy	✖	✖	✖	✖	● (II)
zorifertinib, pirotinib	✖	✖	✖	✖	● (II)
AFM-24_I, atezolizumab	✖	✖	✖	✖	● (I/II)
almonertinib, icotinib hydrochloride	✖	✖	✖	✖	● (I/II)
BEBT-908, BEBT-109	✖	✖	✖	✖	● (I/II)
benmelstobart, catequentinib	✖	✖	✖	✖	● (I/II)
BH-30643	✖	✖	✖	✖	● (I/II)
bozitinib, osimertinib	✖	✖	✖	✖	● (I/II)
bozitinib, PLB-1004	✖	✖	✖	✖	● (I/II)
BPI-361175	✖	✖	✖	✖	● (I/II)
cetrelimab, amivantamab	✖	✖	✖	✖	● (I/II)
dacomitinib, catequentinib	✖	✖	✖	✖	● (I/II)
DAJH-1050766	✖	✖	✖	✖	● (I/II)
DB-1310, osimertinib	✖	✖	✖	✖	● (I/II)
dositinib	✖	✖	✖	✖	● (I/II)
FWD-1509	✖	✖	✖	✖	● (I/II)
H-002	✖	✖	✖	✖	● (I/II)

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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*
ifebemtinib, furmonertinib	✖	✖	✖	✖	● (I/II)
MRTX0902	✖	✖	✖	✖	● (I/II)
necitumumab, osimertinib	✖	✖	✖	✖	● (I/II)
quaratusugene ozeplasmid, osimertinib	✖	✖	✖	✖	● (I/II)
RC-108, furmonertinib, toripalimab	✖	✖	✖	✖	● (I/II)
sotiburafusp alfa, HB-0030	✖	✖	✖	✖	● (I/II)
sunvozertinib, chemotherapy	✖	✖	✖	✖	● (I/II)
TAS-3351	✖	✖	✖	✖	● (I/II)
TQ-B3525, osimertinib	✖	✖	✖	✖	● (I/II)
TRX-221	✖	✖	✖	✖	● (I/II)
WSD-0922	✖	✖	✖	✖	● (I/II)
afatinib, chemotherapy	✖	✖	✖	✖	● (I)
alisertib, osimertinib	✖	✖	✖	✖	● (I)
AZD-9592	✖	✖	✖	✖	● (I)
BG-60366	✖	✖	✖	✖	● (I)
BPI-1178, osimertinib	✖	✖	✖	✖	● (I)
catequentinib, gefitinib, metformin hydrochloride	✖	✖	✖	✖	● (I)
cemiplimab, sarilumab	✖	✖	✖	✖	● (I)
DZD-6008	✖	✖	✖	✖	● (I)
EGFR tyrosine kinase inhibitor, catequentinib	✖	✖	✖	✖	● (I)
genolimzumab, fruquintinib	✖	✖	✖	✖	● (I)
IBI-318, lenvatinib	✖	✖	✖	✖	● (I)
KQB-198, osimertinib	✖	✖	✖	✖	● (I)
LAVA-1223	✖	✖	✖	✖	● (I)
MRX-2843, osimertinib	✖	✖	✖	✖	● (I)
osimertinib, carotuximab	✖	✖	✖	✖	● (I)
osimertinib, Minnelide	✖	✖	✖	✖	● (I)
osimertinib, tegatrabetan	✖	✖	✖	✖	● (I)
patritumab deruxtecan	✖	✖	✖	✖	● (I)

* 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*
PB-101 (Precision Biotech Taiwan Corp), EGFR tyrosine kinase inhibitor	✖	✖	✖	✖	● (I)
repotrectinib, osimertinib	✖	✖	✖	✖	● (I)
VIC-1911, osimertinib	✖	✖	✖	✖	● (I)
WJ13404	✖	✖	✖	✖	● (I)
WTS-004	✖	✖	✖	✖	● (I)
YH-013	✖	✖	✖	✖	● (I)
YL-202	✖	✖	✖	✖	● (I)

MYC amplification

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
CCS-1477	✖	✖	✖	✖	● (I/II)
entinostat, nivolumab	✖	✖	✖	✖	● (I/II)
nedisertib, tuvusertib	✖	✖	✖	✖	● (I)
talazoparib, palbociclib	✖	✖	✖	✖	● (I)

PTEN deletion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
TQ-B3525, osimertinib	✖	✖	✖	✖	● (I/II)
palbociclib, gedatolisib	✖	✖	✖	✖	● (I)

AKT2 amplification

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
TQ-B3525, osimertinib	✖	✖	✖	✖	● (I/II)

RICTOR amplification

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
TQ-B3525, 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

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.

Thermo Fisher Scientific's Ion Torrent Oncomine Reporter software was used in generation of this report. Software was developed and designed internally by Thermo Fisher Scientific. The analysis was based on Oncomine Reporter (6.1.1 data version 2025.05(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 2025-04-16. NCCN information was sourced from www.nccn.org and is current as of 2025-04-01. EMA information was sourced from www.ema.europa.eu and is current as of 2025-04-16. ESMO information was sourced from www.esmo.org and is current as of 2025-04-01. Clinical Trials information is current as of 2025-04-01. For the most up-to-date information regarding a particular trial, search www.clinicaltrials.gov by NCT ID or search local clinical trials authority website by local identifier listed in 'Other identifiers.' Variants are reported according to HGVS nomenclature and classified following AMP/ASCO/CAP guidelines (Li et al. 2017). Based on the data sources selected, variants, therapies, and trials listed in this report are listed in order of potential clinical significance but not for predicted efficacy of the therapies.

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