

Patient Name: 김숙희  
Gender: F  
Sample ID: N25-124

Primary Tumor Site: lung  
Collection Date: 20250715

## Sample Cancer Type: Lung Cancer

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## Relevant Lung Cancer Findings

Gene	Finding	Gene	Finding
ALK	None detected	NTRK1	None detected
BRAF	None detected	NTRK2	None detected
EGFR	<b>EGFR exon 19 deletion</b>	NTRK3	None detected
ERBB2	None detected	RET	None detected
KRAS	None detected	ROS1	None detected
MET	None detected		

  

Genomic Alteration	Finding
Tumor Mutational Burden	<b>3.81 Mut/Mb measured</b>

## Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	<b>EGFR exon 19 deletion</b> epidermal growth factor receptor Allele Frequency: 36.00% Locus: chr7:55242466 Transcript: NM_005228.5	<b>afatinib</b> <sup>1, 2 / I, II+</sup> <b>amivantamab + lazertinib</b> <sup>1, 2 / I, II+</sup> <b>bevacizumab† + erlotinib</b> <sup>2 / I, II+</sup> <b>dacomitinib</b> <sup>1, 2 / I, II+</sup> <b>erlotinib</b> <sup>2 / I, II+</sup> <b>erlotinib + ramucirumab</b> <sup>1, 2 / I, II+</sup> <b>gefitinib</b> <sup>1, 2 / I, II+</sup> <b>osimertinib</b> <sup>1, 2 / I, II+</sup> <b>osimertinib + chemotherapy</b> <sup>1, 2 / I</sup> <b>amivantamab + chemotherapy</b> <sup>1, 2 / II+</sup> <b>BAT1706 + erlotinib</b> <sup>2</sup> gefitinib + chemotherapy <sup>I</sup> atezolizumab + bevacizumab + chemotherapy <sup>II+</sup>	None*	194

\* Public data sources included in relevant therapies: FDA<sup>1</sup>, NCCN, EMA<sup>2</sup>, 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	STK11 deletion serine/threonine kinase 11 Locus: chr19:1206847	None*	None*	1

\* Public data sources included in relevant therapies: FDA<sup>1</sup>, NCCN, EMA<sup>2</sup>, 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 <sup>1</sup>

Public data sources included in alerts: FDA<sup>1</sup>, NCCN, EMA<sup>2</sup>, ESMO

Prevalent cancer biomarkers without relevant evidence based on included data sources  
MAP2K7 deletion, MLH1 p.(V384D) c.1151T>A, Microsatellite stable, RAD52 p.(S346\*) c.1037C>A, UGT1A1 p.(G71R) c.211G>A, HLA-B deletion, USP9X p.(Q1476\*) c.4426C>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_A750delinsQP)	c.2236_2248delGAATT AAGAGAAGinsCAAC	COSM13557	chr7:55242466	36.00%	NM_005228.5	nonframeshift Block Substitution
MLH1	p.(V384D)	c.1151T>A	.	chr3:37067240	52.65%	NM_000249.4	missense
RAD52	p.(S346*)	c.1037C>A	.	chr12:1023218	50.30%	NM_134424.4	nonsense
UGT1A1	p.(G71R)	c.211G>A	COSM4415616	chr2:234669144	44.46%	NM_000463.3	missense
USP9X	p.(Q1476*)	c.4426C>T	.	chrX:41057826	13.27%	NM_001039590.3	nonsense
OR2M3	p.(K303E)	c.907A>G	.	chr1:248367276	37.81%	NM_001004689.1	missense
HLA-B	p.([T118L;L119I])	c.353_355delCCCinsT CA	.	chr6:31324208	100.00%	NM_005514.8	missense, missense
MUC19	p.(T2082P)	c.6244A>C	.	chr12:40872998	12.99%	NM_173600.2	missense
FANCM	p.(H1248Q)	c.3744T>A	.	chr14:45645701	7.86%	NM_020937.4	missense

Copy Number Variations			
Gene	Locus	Copy Number	CNV Ratio
STK11	chr19:1206847	0.08	0.61
MAP2K7	chr19:7968792	0	0.58
HLA-B	chr6:31322252	0	0.47
FGFR3	chr4:1801456	0.15	0.63



## 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<sup>12</sup>. In addition to EGFR/ERBB1/HER1, other members of the ERBB/HER family include ERBB2/HER2, ERBB3/HER3, and ERBB4/HER4<sup>58</sup>. 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<sup>59</sup>. Activation of these pathways promotes cell proliferation, differentiation, and survival<sup>60,61</sup>.

**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<sup>5,6,7,62</sup>. 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<sup>63</sup>. These mutations constitutively activate EGFR resulting in downstream signaling, and represent 80% of the EGFR mutations observed in lung cancer<sup>63</sup>. A second group of less prevalent activating mutations includes E709K, G719X, S768I, L861Q, and short in-frame insertion mutations in exon 20<sup>64,65,66,67</sup>. EGFR activating mutations in lung cancer tend to be mutually exclusive to KRAS activating mutations<sup>68</sup>. 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<sup>63,69</sup>. 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<sup>5,6,7,69,70</sup>. 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<sup>71,72,73</sup>. Alterations in EGFR are rare in pediatric cancers<sup>6,7</sup>. 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)<sup>6,7</sup>. 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)<sup>6,7</sup>.

**Potential relevance:** Approved first-generation EGFR tyrosine kinase inhibitors (TKIs) include erlotinib<sup>74</sup> (2004) and gefitinib<sup>75</sup> (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<sup>76</sup>. Second-generation TKIs afatinib<sup>77</sup> (2013) and dacomitinib<sup>78</sup> (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<sup>79,80,81,82</sup>. However, BDTX-189<sup>83</sup> 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)<sup>84</sup> and sunvozertinib<sup>85</sup>, 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<sup>86</sup>. The primary resistance mutation that emerges following treatment with first-generation TKI is T790M, accounting for 50-60% of resistant cases<sup>63</sup>. Third generation TKIs were developed to maintain sensitivity in the presence of T790M<sup>86</sup>. Osimertinib<sup>87</sup> (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<sup>86</sup>. 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<sup>88</sup>. T790M and C797S can occur in either cis or trans allelic orientation<sup>88</sup>. 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<sup>88</sup>. 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<sup>88,89</sup>. However, C797S occurring in cis conformation with T790M, confers resistance to first- and third-generation TKIs<sup>88</sup>. Fourth-generation TKIs are in development to overcome acquired resistance mutations after osimertinib treatment, including BDTX-1535<sup>90</sup> (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<sup>91</sup>. The bispecific antibody, amivantamab<sup>92</sup> (2021), targeting EGFR and MET was approved for NSCLC tumors harboring EGFR exon 20 insertion mutations. A small molecule kinase inhibitor, lazertinib<sup>93</sup> (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<sup>94</sup> received fast track designation for the treatment of adult patients with EGFR altered glioblastoma. HLX-42<sup>95</sup>, an anti-EGFR-antibody-drug conjugate (ADC) consisting of an anti-EGFR monoclonal antibody conjugated with a novel high potency DNA topoisomerase I (topo I) inhibitor, also received fast



## Biomarker Descriptions (continued)

track designation (2024) for the treatment of patients with advanced or metastatic EGFR-mutated non-small cell lung cancer whose disease has progressed on a third-generation EGFR tyrosine kinase inhibitor. CPO301<sup>96</sup> (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<sup>97</sup> (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<sup>38,98,99</sup>.

### STK11 deletion

*serine/threonine kinase 11*

**Background:** The STK11 gene, also known as liver kinase B1 (LKB1), encodes the serine/threonine kinase 11 protein. STK11 is a tumor suppressor with multiple substrates including AMP-activated protein kinase (AMPK) that regulates cell metabolism, growth, and tumor suppression<sup>1</sup>. Germline mutations in STK11 are associated with Peutz-Jeghers syndrome, an autosomal dominant disorder, characterized by gastrointestinal polyp formation and elevated risk of neoplastic development<sup>2,3</sup>.

**Alterations and prevalence:** Somatic mutations in STK11 have been reported in 10% of lung cancer, 4% of cervical cancer, and up to 3% of cholangiocarcinoma and uterine cancer<sup>4,5,6,7</sup>. Mutations in STK11 are found to co-occur with KEAP1 and KRAS mutations in lung cancer<sup>6,7</sup>. Copy number deletion leads to inactivation of STK11 in cervical, ovarian, and lung cancers, among others<sup>2,5,6,7,8</sup>.

**Potential relevance:** Currently, no therapies are approved for STK11 aberrations. However, in 2023, the FDA granted fast track designation to a first-in-class inhibitor of the CoREST complex (Co-repressor of Repressor Element-1 Silencing Transcription), TNG-260<sup>9</sup> in combination with an anti-PD-1 antibody, for advanced non-small cell lung cancer harboring STK11-mutations. The presence of STK11 mutations may be a mechanism of resistance to immunotherapies. Mutations in STK11 are associated with reduced expression of PD-L1, which may contribute to the ineffectiveness of anti-PD-1 immunotherapy in STK11 mutant tumors<sup>10</sup>. In a phase III clinical trial of nivolumab in lung adenocarcinoma, patients with KRAS and STK11 co-mutations demonstrated a worse (0/6) objective response rate (ORR) in comparison to patients with KRAS and TP53 co-mutations (4/7) or KRAS mutations only (2/11) (ORR= 0% vs 57.1% vs 18.25%, respectively)<sup>11</sup>.

### MAP2K7 deletion

*mitogen-activated protein kinase kinase 7*

**Background:** The MAP2K7 gene encodes the mitogen-activated protein kinase kinase 7, also known as MEK7<sup>12</sup>. MAP2K7 is involved in the JNK signaling pathway along with MAP3K4, MAP3K12, MAP2K4, MAPK8, MAPK9, and MAPK10<sup>100,101,102</sup>. Activation of MAPK proteins occurs through a kinase signaling cascade<sup>100,101,103</sup>. Specifically, MAP3Ks are responsible for phosphorylation of MAP2K family members<sup>100,101,103</sup>. Once activated, MAP2Ks are responsible for the phosphorylation of various MAPK proteins whose signaling is involved in several cellular processes including cell proliferation, differentiation, and inflammation<sup>100,101,103</sup>.

**Alterations and prevalence:** Somatic mutations in MAP2K7 are observed in 7% of stomach adenocarcinoma, 4% of colorectal adenocarcinoma, and 2% of skin cutaneous melanoma and uterine corpus endometrial carcinoma<sup>6,7</sup>. Biallelic deletions are observed in 4% of uterine carcinosarcoma, 2% of esophageal adenocarcinoma, and 1% of uveal melanoma<sup>6,7</sup>.

**Potential relevance:** Currently, no therapies are approved for MAP2K7 aberrations.

### MLH1 p.(V384D) c.1151T>A

*mutL homolog 1*

**Background:** The MLH1 gene encodes the mutL homolog 1 protein<sup>12</sup>. MLH1 is a tumor suppressor gene that heterodimerizes with PMS2 to form the MutLα complex, PMS1 to form the MutLβ complex, and MLH3 to form the MutLγ complex<sup>19</sup>. The MutLα complex functions as an endonuclease that is specifically involved in the mismatch repair (MMR) process and mutations in MLH1 result in the inactivation of MutLα and degradation of PMS2<sup>19,20</sup>. Loss of MLH1 protein expression and MLH1 promoter hypermethylation correlates with mutations in these genes and are used to pre-screen colorectal cancer or endometrial hyperplasia<sup>21,22</sup>. MLH1, along with MSH6, MSH2, and PMS2 form the core components of the MMR pathway<sup>19</sup>. The MMR pathway is critical to the repair of mismatch errors which typically occur during DNA replication<sup>19</sup>. Deficiency in MMR (dMMR) is characterized by mutations and loss of expression in these genes<sup>23</sup>. dMMR is associated with microsatellite instability (MSI), which is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue<sup>24,25,26</sup>. MSI-high (MSI-H) is a hallmark of Lynch Syndrome (LS), also known as hereditary non-polyposis colorectal cancer, which is caused by germline mutations in MMR genes<sup>24,27</sup>. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer<sup>25,27,28,29</sup>. Specifically, MLH1 mutations are associated with an increased risk of ovarian and pancreatic cancer<sup>30,31,32,33</sup>.



## Biomarker Descriptions (continued)

**Alterations and prevalence:** Somatic mutations in MLH1 are observed in 6% of uterine corpus endometrial carcinoma, 4% of colorectal adenocarcinoma, and 2-3% of bladder urothelial carcinoma, stomach adenocarcinoma, and melanoma<sup>6,7</sup>. Alterations in MLH1 are observed in pediatric cancers<sup>6,7</sup>. Somatic mutations are observed in 1% of bone cancer and less than 1% of B-lymphoblastic leukemia/lymphoma (2 in 252 cases), embryonal tumor (2 in 332 cases), and leukemia (2 in 311 cases)<sup>6,7</sup>.

**Potential relevance:** The PARP inhibitor, talazoparib<sup>34</sup> in combination with enzalutamide is approved (2023) for metastatic castration-resistant prostate cancer (mCRPC) with mutations in HRR genes that includes MLH1. Additionally, pembrolizumab (2014) is an anti-PD-1 immune checkpoint inhibitor that is approved for patients with MSI-H or dMMR solid tumors that have progressed on prior therapies<sup>35</sup>. Nivolumab (2015), an anti-PD-1 immune checkpoint inhibitor, is approved alone or in combination with the cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab (2011), for patients with dMMR colorectal cancer that have progressed on prior treatment<sup>36,37</sup>. MLH1 mutations are consistent with high grade in pediatric diffuse gliomas<sup>38,39</sup>.

### 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<sup>44</sup>. Microsatellite instability (MSI) is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue<sup>25,27</sup>. 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<sup>26</sup>. 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<sup>45</sup>. 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)<sup>45</sup>. Tumors classified as MSI-L are often phenotypically indistinguishable from MSS tumors and tend to be grouped with MSS<sup>28,46,47,48,49</sup>. 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<sup>27</sup>. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer<sup>25,27,28,29</sup>.

**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<sup>25,27,50,51</sup>. 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<sup>50,51</sup>.

**Potential relevance:** Anti-PD-1 immune checkpoint inhibitors including pembrolizumab<sup>35</sup> (2014) and nivolumab<sup>36</sup> (2015) are approved for patients with MSI-H or dMMR colorectal cancer who have progressed following chemotherapy. Pembrolizumab<sup>35</sup> 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<sup>35</sup>. Dostarlimab<sup>52</sup> (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<sup>47,53</sup>. The cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab<sup>37</sup> (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<sup>47,54,55</sup>. 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<sup>55</sup>. 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<sup>56,57</sup>. However, checkpoint blockade with the addition of chemotherapy or targeted therapies have demonstrated response in MSS or pMMR cancers<sup>56,57</sup>.

### RAD52 p.(S346\*) c.1037C>A

*RAD52 homolog, DNA repair protein*

**Background:** The RAD52 gene encodes the RAD52 homolog, DNA repair protein<sup>12</sup>. RAD52 binds to single- and double-stranded DNA and enables strand exchange for double-strand break (DSB) repair by binding to RAD51<sup>40</sup>. RAD52 also promotes DSB repair through homologous recombination repair (HRR) by recruiting BRCA1 to sites of DSBs, which leads to the removal of TP53BP1 and prevents DSB repair by non-homologous end joining (NHEJ)<sup>41</sup>.

**Alterations and prevalence:** Somatic mutations in RAD52 are observed in 2% of uterine corpus endometrial carcinoma, uterine carcinosarcoma, and skin cutaneous melanoma<sup>6,7</sup>.

**Potential relevance:** Currently, no therapies are approved for RAD52 aberrations.



## 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<sup>12,104</sup>. UGTs are microsomal membrane-bound enzymes that catalyze the glucuronidation of endogenous and xenobiotic compounds and transform the lipophilic molecules into excretable, hydrophilic metabolites<sup>104,105</sup>. 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<sup>106</sup>. 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<sup>106,107,108,109</sup>. 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<sup>110</sup>.

**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<sup>6,7</sup>.

**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<sup>12</sup>. 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<sup>13</sup>. MHC class I molecules are heterodimers composed of two polypeptide chains,  $\alpha$  and B2M<sup>14</sup>. The classical MHC class I genes include HLA-A, HLA-B, and HLA-C and encode the  $\alpha$  polypeptide chains, which present short polypeptide chains, of 7 to 11 amino acids, to the immune system to distinguish self from non-self<sup>15,16,17</sup>. Downregulation of MHC class I promotes tumor evasion of the immune system, suggesting a tumor suppressor role for HLA-B<sup>18</sup>.

**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<sup>6,7</sup>. Biallelic loss of HLA-B is observed in 5% of DLBCL<sup>6,7</sup>.

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

### USP9X p.(Q1476\*) c.4426C>T

*ubiquitin specific peptidase 9 X-linked*

**Background:** The USP9X gene encodes the ubiquitin specific peptidase 9 X-linked protein<sup>12</sup>. USP9X is a deubiquitinating enzyme (DUB) and a member of the ubiquitin-specific protease (USP) subclass of cysteine proteases<sup>42</sup>. DUBs are responsible for protein deubiquitination, thereby counter-regulating post-transcriptional ubiquitin modification of proteins within the cell<sup>42,43</sup>. USP9X has many substrates and is commonly upregulated in several solid tumor types, supporting an oncogenic role for USP9X<sup>43</sup>. Conversely, in some cancer types, USP9X has been observed to function as a tumor suppressor, suggesting its exact role in cancer may be dependent on its substrates<sup>43</sup>. In breast cancer, USP9X has been shown to stabilize BRCA1 by inhibiting its ubiquitination, thereby influencing the regulation of homologous recombination and repair<sup>43</sup>.

**Alterations and prevalence:** Somatic mutations are observed in 16% of uterine corpus endometrial carcinoma, 11% of skin cutaneous melanoma, 7% of colorectal adenocarcinoma, 6% of cholangiocarcinoma, 5% of stomach adenocarcinoma, lung squamous cell carcinoma, diffuse large B-cell lymphoma (DLBCL), and head and neck squamous cell carcinoma<sup>6,7</sup>. Biallelic deletions are observed in 4% of esophageal adenocarcinoma, 3% of head and neck squamous cell carcinoma, 2% of mesothelioma, uterine carcinosarcoma, and lung squamous cell carcinoma<sup>6,7</sup>.

**Potential relevance:** Currently, no therapies are approved for USP9X aberrations.



Alerts Informed By Public Data Sources

Current FDA Information

Contraindicated   Not recommended   Resistance   Breakthrough   Fast Track

FDA information is current as of 2025-05-14. For the most up-to-date information, search [www.fda.gov](https://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-nsccl>

Genes Assayed

Genes Assayed for the Detection of DNA Sequence Variants

ABL1, ABL2, ACVR1, AKT1, AKT2, AKT3, ALK, AR, ARAF, ATP1A1, AURKA, AURKB, AURKC, AXL, BCL2, BCL2L12, BCL6, BCR, BMP5, BRAF, BTK, CACNA1D, CARD11, CBL, CCND1, CCND2, CCND3, CCNE1, CD79B, CDK4, CDK6, CHD4, CSF1R, CTNNB1, CUL1, CYSLTR2, DDR2, DGCR8, DROSHA, E2F1, EGFR, EIF1AX, EPAS1, ERBB2, ERBB3, ERBB4, ESR1, EZH2, FAM135B, FGF7, FGFR1, FGFR2, FGFR3, FGFR4, FLT3, FLT4, FOXA1, FOXL2, FOXO1, GATA2, GLI1, GNA11, GNAQ, GNAS, HIF1A, HRAS, IDH1, IDH2, IKBKB, IL6ST, IL7R, IRF4, IRS4, KCNJ5, KDR, KIT, KLF4, KLF5, KNSTRN, KRAS, MAGOH, MAP2K1, MAP2K2, MAPK1, MAX, MDM4, MECOM, MED12, MEF2B, MET, MITF, MPL, MTOR, MYC, MYCN, MYD88, MYOD1, NFE2L2, NRAS, NSD2, NT5C2, NTRK1, NTRK2, NTRK3, NUP93, PAX5, PCBP1, PDGFRA, PDGFRB, PIK3C2B, PIK3CA, PIK3CB, PIK3CD, PIK3CG, PIK3R2, PIM1, PLCG1, PPP2R1A, PPP6C, PRKACA, PTPN11, PTPRD, PXDNL, RAC1, RAF1, RARA, RET, RGS7, RHEB, RHOA, RICTOR, RIT1, ROS1, RPL10, SETBP1, SF3B1, SIX1, SIX2, SLC01B3, SMC1A, SMO, SNCAIP, SOS1, SOX2, SPOP, SRC, SRSF2, STAT3, STAT5B, STAT6, TAF1, TERT, TGFBF1, 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, ERFFI1, ESR1, ETV6, EZH2, FAM135B, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, FAT1, FBXW7, FGF19, FGF23, FGF3, FGF4, FGF9, FGFR1, FGFR2, FGFR3, FGFR4, FLT3, FLT4, FOXA1, FUBP1, FYN, GATA2, GATA3, GLI3, GNA13, GNAS, GPS2, HDAC2, HDAC9, HLA-A, HLA-B, HNF1A, IDH2, IGF1R, IKBKB, IL7R, INPP4B, JAK1, JAK2, JAK3, KDM5C, KDM6A, KDR, KEAP1, KIT, KLF5, KMT2A, KMT2B, KMT2C, KMT2D, KRAS, LARP4B, LATS1, LATS2, MAGOH, MAP2K1, MAP2K4, MAP2K7, MAP3K1, MAP3K4, MAPK1, MAPK8, MAX, MCL1, MDM2, MDM4, MECOM, MEF2B, MEN1, MET, MGA, MITF, MLH1, MLH3, MPL, MRE11, MSH2, MSH3, MSH6, MTAP, MTOR, MUTYH, MYC, MYCL, MYCN, MYD88, NBN, NCOR1, NF1, NF2, NFE2L2, NOTCH1, NOTCH2, NOTCH3, NOTCH4, NRAS, NTRK1, NTRK3, PALB2, PARP1, PARP2, PARP3, PARP4, PBRM1, PCBP1, PDCD1, PDCD1LG2, PDGFRA, PDGFRB, PDIA3, PGD, PHF6, PIK3C2B, PIK3CA, PIK3CB, PIK3R1, PIK3R2, PIM1, PLCG1, PMS1, PMS2, POLD1, POLE, POT1, PPM1D, PPP2R1A, PPP2R2A, PPP6C, PRDM1, PRDM9, PRKACA, PRKAR1A, PTCH1, PTEN, PTPN11, PTPRT, PXDNL, RAC1, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD52, RAD54L, RAF1, RARA, RASA1, RASA2, RB1, RBM10, RECQL4, RET, RHEB, RICTOR, RIT1, RNASEH2A, RNASEH2B, RNF43, ROS1, RPA1, RPS6KB1, RPTOR, RUNX1, SDHA, SDHB, SDHD, SETBP1, SETD2, SF3B1, SLC01B3, SLX4, SMAD2, SMAD4, SMARCA4, SMARCB1, SMC1A, SMO, SOX9, SPEN, SPOP, SRC, STAG2, STAT3, STAT6, STK11, SUFU, TAP1, TAP2, TBX3, TCF7L2, TERT, TET2, TGFBF2,



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, ZFH3, ZMYM3, ZNF217, ZNF429, ZRSR2

Genes Assayed for the Detection of Fusions

AKT2, ALK, AR, AXL, BRAF, BRCA1, BRCA2, CDKN2A, EGFR, ERBB2, ERBB4, ERG, ESR1, ETV1, ETV4, ETV5, FGFR1, FGFR2, FGFR3, FGR, FLT3, JAK2, KRAS, MDM4, MET, MYB, MYBL1, NF1, NOTCH1, NOTCH4, NRG1, NTRK1, NTRK2, NTRK3, NUTM1, PDGFRA, PDGFRB, PIK3CA, PPARG, PRKACA, PRKACB, PTEN, RAD51B, RAF1, RB1, RELA, RET, ROS1, RSP02, RSP03, TERT

Genes Assayed with Full Exon Coverage

ABRAXAS1, ACVR1B, ACVR2A, ADAMTS12, ADAMTS2, AMER1, APC, ARHGAP35, ARID1A, ARID1B, ARID2, ARID5B, ASXL1, ASXL2, ATM, ATR, ATRX, AXIN1, AXIN2, B2M, BAP1, BARD1, BCOR, BLM, BMPR2, BRCA1, BRCA2, BRIP1, CALR, CASP8, CBF3, CD274, CD276, CDC73, CDH1, CDH10, CDK12, CDKN1A, CDKN1B, CDKN2A, CDKN2B, CDKN2C, CHEK1, CHEK2, CIC, CIITA, CREBBP, CSMD3, CTCF, CTLA4, CUL3, CUL4A, CUL4B, CYLD, CYP2C9, CYP2D6, DAXX, DDX3X, DICER1, DNMT3A, DOCK3, DPYD, DSC1, DSC3, ELF3, ENO1, EP300, EPCAM, EPHA2, ERAP1, ERAP2, ERCC2, ERCC4, ERCC5, ERFF1, ETV6, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, FAS, FAT1, FBXW7, FUBP1, GATA3, GNA13, GPS2, HDAC2, HDAC9, HLA-A, HLA-B, HNF1A, ID3, INPP4B, JAK1, JAK2, JAK3, KDM5C, KDM6A, KEAP1, KLHL13, KMT2A, KMT2B, KMT2C, KMT2D, LARP4B, LATS1, LATS2, MAP2K4, MAP2K7, MAP3K1, MAP3K4, MAPK8, MEN1, MGA, MLH1, MLH3, MRE11, MSH2, MSH3, MSH6, MTAP, MTUS2, MUTYH, NBN, NCOR1, NF1, NF2, NOTCH1, NOTCH2, NOTCH3, NOTCH4, PALB2, PARP1, PARP2, PARP3, PARP4, PBRM1, PDCD1, PDCD1LG2, PDIA3, PGD, PHF6, PIK3R1, PMS1, PMS2, POLD1, POLE, POT1, PPM1D, PPP2R2A, PRDM1, PRDM9, PRKAR1A, PSMB10, PSMB8, PSMB9, PTCH1, PTEN, PTPRT, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD52, RAD54L, RASA1, RASA2, RB1, RBM10, RECQL4, RNASEH2A, RNASEH2B, RNASEH2C, RNF43, RPA1, RPL22, RPL5, RUNX1, RUNX1T1, SDHA, SDHB, SDHC, SDHD, SETD2, SLX4, SMAD2, SMAD4, SMARCA4, SMARCB1, SOCS1, SOX9, SPEN, STAG2, STAT1, STK11, SUFU, TAP1, TAP2, TBX3, TCF7L2, TET2, TGFB2, TMEM132D, TNFAIP3, TNFRSF14, TP53, TP63, TPP2, TSC1, TSC2, UGT1A1, USP9X, VHL, WT1, XRCC2, XRCC3, ZBTB20, ZFH3, ZMYM3, ZRSR2

Relevant Therapy Summary

In this cancer type

In other cancer type

In this cancer type and other cancer types

No evidence

EGFR 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	✕	✕	✕	●	✕
adebreliumab, 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)
SCTB-14, chemotherapy	×	×	×	×	● (II/III)
ABSK-043, furmonertinib	×	×	×	×	● (II)
almonertinib	×	×	×	×	● (II)
almonertinib, adbrelimab, chemotherapy	×	×	×	×	● (II)
almonertinib, bevacizumab	×	×	×	×	● (II)
almonertinib, chemoradiation therapy	×	×	×	×	● (II)
almonertinib, dacomitinib	×	×	×	×	● (II)
amivantamab, chemotherapy	×	×	×	×	● (II)
amivantamab, lazertinib, 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*
atezolizumab, bevacizumab, tiragolumab	✕	✕	✕	✕	● (II)
befotertinib, bevacizumab, chemotherapy	✕	✕	✕	✕	● (II)
bevacizumab, afatinib	✕	✕	✕	✕	● (II)
bevacizumab, furmonertinib	✕	✕	✕	✕	● (II)
cadonilimab, chemotherapy, catequentinib	✕	✕	✕	✕	● (II)
camrelizumab, apatinib	✕	✕	✕	✕	● (II)
capmatinib, osimertinib, ramucirumab	✕	✕	✕	✕	● (II)
catequentinib, almonertinib	✕	✕	✕	✕	● (II)
chemotherapy, atezolizumab, bevacizumab	✕	✕	✕	✕	● (II)
dacomitinib, osimertinib	✕	✕	✕	✕	● (II)
EGFR tyrosine kinase inhibitor, osimertinib, chemotherapy	✕	✕	✕	✕	● (II)
EGFR tyrosine kinase inhibitor, radiation therapy	✕	✕	✕	✕	● (II)
erlotinib, chemotherapy	✕	✕	✕	✕	● (II)
erlotinib, OBI-833	✕	✕	✕	✕	● (II)
furmonertinib, bevacizumab	✕	✕	✕	✕	● (II)
furmonertinib, bevacizumab, chemotherapy	✕	✕	✕	✕	● (II)
furmonertinib, catequentinib	✕	✕	✕	✕	● (II)
furmonertinib, chemotherapy	✕	✕	✕	✕	● (II)
furmonertinib, chemotherapy, bevacizumab	✕	✕	✕	✕	● (II)
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)

\* 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*
lazertinib, chemotherapy	✕	✕	✕	✕	● (II)
lenvatinib, pembrolizumab	✕	✕	✕	✕	● (II)
osimertinib, chemoradiation therapy	✕	✕	✕	✕	● (II)
osimertinib, radiation therapy	✕	✕	✕	✕	● (II)
PLB-1004, bozitinib, osimertinib	✕	✕	✕	✕	● (II)
ramucirumab, erlotinib	✕	✕	✕	✕	● (II)
sacituzumab govitecan	✕	✕	✕	✕	● (II)
sacituzumab tirumotecan, chemotherapy, osimertinib	✕	✕	✕	✕	● (II)
sunvozertinib	✕	✕	✕	✕	● (II)
sunvozertinib, catequentinib	✕	✕	✕	✕	● (II)
sunvozertinib, golidocitinib	✕	✕	✕	✕	● (II)
tislelizumab, chemotherapy, bevacizumab	✕	✕	✕	✕	● (II)
toripalimab	✕	✕	✕	✕	● (II)
toripalimab, bevacizumab, Clostridium butyricum, chemotherapy	✕	✕	✕	✕	● (II)
toripalimab, chemotherapy	✕	✕	✕	✕	● (II)
TY-9591, chemotherapy	✕	✕	✕	✕	● (II)
zorifertinib, pirotinib	✕	✕	✕	✕	● (II)
AFM-24_I, atezolizumab	✕	✕	✕	✕	● (I/II)
almonertinib, icotinib hydrochloride	✕	✕	✕	✕	● (I/II)
benmelstobart, catequentinib	✕	✕	✕	✕	● (I/II)
BH-30643	✕	✕	✕	✕	● (I/II)
bozitinib, osimertinib	✕	✕	✕	✕	● (I/II)
BPI-361175	✕	✕	✕	✕	● (I/II)
cetrelimab, amivantamab	✕	✕	✕	✕	● (I/II)
dacomitinib, catequentinib	✕	✕	✕	✕	● (I/II)
DAJH-1050766	✕	✕	✕	✕	● (I/II)
DB-1310, osimertinib	✕	✕	✕	✕	● (I/II)
dositinib	✕	✕	✕	✕	● (I/II)
FWD-1509	✕	✕	✕	✕	● (I/II)

\* 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*
H-002	✕	✕	✕	✕	● (I/II)
ifebemtiniib, furmonertiniib	✕	✕	✕	✕	● (I/II)
MRTX0902	✕	✕	✕	✕	● (I/II)
necitumumab, osimertiniib	✕	✕	✕	✕	● (I/II)
quaratusugene ozeplasmid, osimertiniib	✕	✕	✕	✕	● (I/II)
RC-108, furmonertiniib, toripalimab	✕	✕	✕	✕	● (I/II)
sotiburafusp alfa, HB-0030	✕	✕	✕	✕	● (I/II)
sunvozertiniib, chemotherapy	✕	✕	✕	✕	● (I/II)
TAS-3351	✕	✕	✕	✕	● (I/II)
TQ-B3525, osimertiniib	✕	✕	✕	✕	● (I/II)
TRX-221	✕	✕	✕	✕	● (I/II)
WSD-0922	✕	✕	✕	✕	● (I/II)
afatinib, chemotherapy	✕	✕	✕	✕	● (I)
alisertib, osimertiniib	✕	✕	✕	✕	● (I)
almonertiniib, midazolam	✕	✕	✕	✕	● (I)
ASKC-202	✕	✕	✕	✕	● (I)
AZD-9592	✕	✕	✕	✕	● (I)
BG-60366	✕	✕	✕	✕	● (I)
BPI-1178, osimertiniib	✕	✕	✕	✕	● (I)
catequentiniib, gefitinib, metformin hydrochloride	✕	✕	✕	✕	● (I)
DZD-6008	✕	✕	✕	✕	● (I)
EGFR tyrosine kinase inhibitor, catequentiniib	✕	✕	✕	✕	● (I)
genolimzumab, fruquintiniib	✕	✕	✕	✕	● (I)
IBI-318, lenvatinib	✕	✕	✕	✕	● (I)
KQB-198, osimertiniib	✕	✕	✕	✕	● (I)
LAVA-1223	✕	✕	✕	✕	● (I)
MRX-2843, osimertiniib	✕	✕	✕	✕	● (I)
osimertiniib, carotuximab	✕	✕	✕	✕	● (I)
osimertiniib, Minnelide	✕	✕	✕	✕	● (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*
osimertinib, tegatrabetan	✕	✕	✕	✕	● (I)
patritumab deruxtecan	✕	✕	✕	✕	● (I)
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)

STK11 deletion

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.

HRR Details

Gene/Genomic Alteration	Finding
LOH percentage	4.45%
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 OncoPrint Reporter software was used in generation of this report. Software was developed and designed internally by Thermo Fisher Scientific. The analysis was based on OncoPrint Reporter (6.1.1 data version 2025.06(006)). The data presented here are from a curated knowledge base of publicly available information, but may not be exhaustive. FDA information was sourced from [www.fda.gov](http://www.fda.gov) and is current as of 2025-05-14. NCCN information was sourced from [www.nccn.org](http://www.nccn.org) and is current as of 2025-05-01. EMA information was sourced from [www.ema.europa.eu](http://www.ema.europa.eu) and is current as of 2025-05-14. ESMO information was sourced from [www.esmo.org](http://www.esmo.org) and is current as of 2025-05-01. Clinical Trials information is current as of 2025-05-01. For the most up-to-date information regarding a particular trial, search [www.clinicaltrials.gov](http://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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