

Patient Name: 이승래  
 Gender: F  
 Sample ID: N25-328

Primary Tumor Site: Lung  
 Collection Date: 2025.11.19

## Sample Cancer Type: Non-Small Cell Lung Cancer

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### Report Highlights

3 Relevant Biomarkers  
 18 Therapies Available  
 204 Clinical Trials

## Relevant Non-Small Cell Lung Cancer Findings

Gene	Finding	Gene	Finding
ALK	None detected	MET	None detected
BRAF	None detected	NRG1	None detected
EGFR	<b>EGFR p.(L858R) c.2573T&gt;G</b>	NTRK1	None detected
ERBB2	None detected	NTRK2	None detected
FGFR1	None detected	NTRK3	None detected
FGFR2	None detected	RET	None detected
FGFR3	None detected	ROS1	None detected
KRAS	None detected		

Genomic Alteration	Finding
Tumor Mutational Burden	<b>2.84 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 p.(L858R) c.2573T&gt;G</b>  epidermal growth factor receptor Allele Frequency: 20.79% Locus: chr7:55259515 Transcript: NM_005228.5	afatinib <sup>1, 2 / I, II+</sup> amivantamab + lazertinib <sup>1, 2 / I, II+</sup> bevacizumab <sup>†</sup> + erlotinib <sup>2 / I, II+</sup> dacomitinib <sup>1, 2 / I, II+</sup> erlotinib <sup>2 / I, II+</sup> erlotinib + ramucirumab <sup>1, 2 / I, II+</sup> gefitinib <sup>1, 2 / I, II+</sup> osimertinib <sup>1, 2 / I, II+</sup> osimertinib + chemotherapy <sup>1, 2 / I</sup> amivantamab + chemotherapy <sup>1, 2 / II+</sup> datopotamab deruxtecan-dlnk <sup>1 / II+</sup> BAT1706 + erlotinib <sup>2</sup> gefitinib + chemotherapy <sup>1</sup>	None*	201

\* Public data sources included in relevant therapies: FDA1, NCCN, EMA2, ESMO

\* Public data sources included in prognostic and diagnostic significance: NCCN, ESMO

† Includes biosimilars/generics

Line of therapy: I: First-line therapy, II+: Other line of therapy

Tier Reference: Li et al. Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists. J Mol Diagn. 2017 Jan;19(1):4-23.

## Relevant Biomarkers (continued)

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
		atezolizumab + bevacizumab + chemotherapy <sup>II+</sup>		
IIC	<b>TP53 p.(Q136E) c.406C&gt;G</b>  tumor protein p53 Allele Frequency: 37.22% Locus: chr17:7578524 Transcript: NM_000546.6	None*	None*	6
IIC	<b>KIT amplification</b>  KIT proto-oncogene receptor tyrosine kinase Locus: chr4:55589693	None*	None*	3

\* Public data sources included in relevant therapies: FDA1, NCCN, EMA2, ESMO

\* Public data sources included in prognostic and diagnostic significance: NCCN, ESMO

† Includes biosimilars/generics

Line of therapy: I: First-line therapy, II+: Other line of therapy

Tier Reference: Li et al. *Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists*. J Mol Diagn. 2017 Jan;19(1):4-23.

**⚠ Alerts informed by public data sources:** 🚫 Contraindicated, ⚠ Resistance, ↗ Breakthrough, ⚠ Fast Track

**EGFR p.(L858R) c.2573T>G** ↗ **azalontamab brengitecan<sup>1</sup>, patritumab deruxtecan<sup>1</sup>**  
⚠ **DB-1310<sup>1</sup>**

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

### Prevalent cancer biomarkers without relevant evidence based on included data sources

*Microsatellite stable, PARP1 p.(R340\*) c.1018C>T, NQO1 p.(P187S) c.559C>T, Tumor Mutational Burden*

## Variant Details

### DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
EGFR	p.(L858R)	c.2573T>G	COSM6224	chr7:55259515	20.79%	NM_005228.5	missense
TP53	p.(Q136E)	c.406C>G	COSM43767	chr17:7578524	37.22%	NM_000546.6	missense
PARP1	p.(R340*)	c.1018C>T	.	chr1:226570878	13.91%	NM_001618.4	nonsense
NQO1	p.(P187S)	c.559C>T	.	chr16:69745145	38.40%	NM_000903.3	missense

### Copy Number Variations

Gene	Locus	Copy Number	CNV Ratio
KIT	chr4:55589693	7.26	2.4
CYLD	chr16:50783549	5.09	1.82
CTCF	chr16:67644720	4.47	1.66
CDH1	chr16:68771249	4.75	1.73
ZFHX3	chr16:72820995	4.38	1.63

## Biomarker Descriptions

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

*epidermal growth factor receptor*

**Background:** The EGFR gene encodes the epidermal growth factor receptor (EGFR), a member of the ERBB/human epidermal growth factor receptor (HER) tyrosine kinase family<sup>19</sup>. In addition to EGFR/ERBB1/HER1, other members of the ERBB/HER family include ERBB2/HER2, ERBB3/HER3, and ERBB4/HER4<sup>66</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>67</sup>. Activation of these pathways promotes cell proliferation, differentiation, and survival<sup>68,69</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>7,24,70,71</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>72</sup>. These mutations constitutively activate EGFR resulting in downstream signaling, and represent 80% of the EGFR mutations observed in lung cancer<sup>72</sup>. A second group of less prevalent activating mutations includes E709K, G719X, S768I, L861Q, and short in-frame insertion mutations in exon 20<sup>73,74,75,76</sup>. EGFR activating mutations in lung cancer tend to be mutually exclusive to KRAS activating mutations<sup>77</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>72,78</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>7,24,26,71,78</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>79,80,81</sup>. Alterations in EGFR are rare in pediatric cancers<sup>7,24</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>7,24</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>7,24</sup>.

**Potential relevance:** Approved first-generation EGFR tyrosine kinase inhibitors (TKIs) include erlotinib<sup>82</sup> (2004) and gefitinib<sup>83</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>84</sup>. Second-generation TKIs afatinib<sup>85</sup> (2013) and dacomitinib<sup>86</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>87,88,89,90</sup>. In 2025, the FDA approved the irreversible EGFR inhibitor, sunozertinib<sup>91</sup>, for the treatment of locally advanced or metastatic non-small cell lung cancer in adult patients with EGFR exon 20 insertion mutations whose disease has progressed on or after platinum-based chemotherapy. In 2022, the FDA granted breakthrough therapy designation to the irreversible EGFR inhibitor, CLN-081 (TPC-064)<sup>92</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>93</sup>. The primary resistance mutation that emerges following treatment with first-generation TKI is T790M, accounting for 50-60% of resistant cases<sup>72</sup>. Third generation TKIs were developed to maintain sensitivity in the presence of T790M<sup>93</sup>. Osimertinib<sup>94</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>93</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>95</sup>. T790M and C797S can occur in either cis or trans allelic orientation<sup>95</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>95</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>95,96</sup>. However, C797S occurring in cis conformation with T790M, confers resistance to first- and third-generation TKIs<sup>95</sup>. Fourth-generation TKIs are in development to overcome acquired resistance mutations after osimertinib treatment, including BDTX-1535<sup>97</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>98</sup>. The bispecific antibody, amivantamab<sup>99</sup> (2021), targeting EGFR and MET was approved for NSCLC tumors harboring EGFR exon 20 insertion mutations. A small molecule kinase inhibitor, lazertinib<sup>100</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. HLX-42<sup>101</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 track designation (2024) for the

## Biomarker Descriptions (continued)

treatment of patients with advanced or metastatic EGFR-mutated non-small cell lung cancer whose disease has progressed on a third-generation EGFR tyrosine kinase inhibitor. CPO301<sup>102</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>103</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>104,105,106</sup>.

### TP53 p.(Q136E) c.406C>G

*tumor protein p53*

**Background:** The TP53 gene encodes the tumor suppressor protein p53, which binds to DNA and activates transcription in response to diverse cellular stresses to induce cell cycle arrest, apoptosis, or DNA repair<sup>19</sup>. In unstressed cells, TP53 is kept inactive by targeted degradation via MDM2, a substrate recognition factor for ubiquitin-dependent proteolysis<sup>20</sup>. Alterations in TP53 are required for oncogenesis as they result in loss of protein function and gain of transforming potential<sup>21</sup>. Germline mutations in TP53 are the underlying cause of Li-Fraumeni syndrome, a complex hereditary cancer predisposition disorder associated with early-onset cancers<sup>22,23</sup>.

**Alterations and prevalence:** TP53 is the most frequently mutated gene in the cancer genome with approximately half of all cancers experiencing TP53 mutations. Ovarian, head and neck, esophageal, and lung squamous cancers have particularly high TP53 mutation rates (60-90%)<sup>7,24,25,26,27,28</sup>. Approximately two-thirds of TP53 mutations are missense mutations and several recurrent missense mutations are common, including substitutions at codons R158, R175, Y220, R248, R273, and R282<sup>7,24</sup>. Invariably, recurrent missense mutations in TP53 inactivate its ability to bind DNA and activate transcription of target genes<sup>29,30,31,32</sup>. Alterations in TP53 are also observed in pediatric cancers<sup>7,24</sup>. Somatic mutations are observed in 53% of non-Hodgkin lymphoma, 24% of soft tissue sarcoma, 19% of glioma, 13% of bone cancer, 9% of B-lymphoblastic leukemia/lymphoma, 4% of embryonal tumors, 3% of Wilms tumor and leukemia, 2% of T-lymphoblastic leukemia/lymphoma, and less than 1% of peripheral nervous system cancers (5 in 1158 cases)<sup>7,24</sup>. Biallelic loss of TP53 is observed in 10% of bone cancer, 2% of Wilms tumor, and less than 1% of B-lymphoblastic leukemia/lymphoma (2 in 731 cases) and leukemia (1 in 250 cases)<sup>7,24</sup>.

**Potential relevance:** The small molecule p53 reactivator, PC14586<sup>33</sup> (2020), received a fast track designation by the FDA for advanced tumors harboring a TP53 Y220C mutation. In addition to investigational therapies aimed at restoring wild-type TP53 activity, compounds that induce synthetic lethality are also under clinical evaluation<sup>34,35</sup>. TP53 mutation are a diagnostic marker of SHH-activated, TP53-mutant medulloblastoma<sup>36</sup>. TP53 mutations confer poor prognosis and poor risk in multiple blood cancers including AML, MDS, myeloproliferative neoplasms (MPN), and chronic lymphocytic leukemia (CLL), and acute lymphoblastic leukemia (ALL)<sup>37,38,39,40,41</sup>. In mantle cell lymphoma, TP53 mutations are associated with poor prognosis when treated with conventional therapy including hematopoietic cell transplant<sup>42</sup>. Mono- and bi-allelic mutations in TP53 confer unique characteristics in MDS, with multi-hit patients also experiencing associations with complex karyotype, few co-occurring mutations, and high-risk disease presentation as well as predicted death and leukemic transformation independent of the IPSS-R staging system<sup>43</sup>.

### KIT amplification

*KIT proto-oncogene receptor tyrosine kinase*

**Background:** The KIT gene, also known as CD117, encodes the KIT proto-oncogene receptor tyrosine kinase (c-KIT), a member of the PDGF receptor type III receptor tyrosine kinase family, which includes PDGFRA, PDGFRB, CSF1R, FLT1, FLT3, FLT4 and KDR<sup>1,2</sup>. KIT is a receptor for stem cell factor, important in regulating growth and development of hematopoietic cells<sup>3</sup>. The KIT gene is flanked by the PDGFRA and KDR genes on chromosome 4q12. Ligand binding to KIT results in kinase activation and stimulation of downstream pathways including the RAS/RAF/MEK/ERK and PI3K/AKT/MTOR pathways, promoting cell proliferation and survival<sup>4</sup>.

**Alterations and prevalence:** Recurrent somatic KIT alterations are observed in both solid and hematological cancers and include activating mutations such as single nucleotide variants, small duplications, and complex in-frame insertions or deletions (indels). Mutations in KIT exons 8, 9, 11, and 17 disrupt auto-inhibitory mechanisms and lead to constitutive activity<sup>5</sup>. Gain of function mutations are found in up to 70% of mast cell tumors, 17% of nasal T-cell lymphomas, and 9% of dysgerminoma<sup>6</sup>. Somatic mutations in exon 11 occur in 60-70% of all gastrointestinal stromal tumor (GIST), whereas alterations in exons 8 and 17 are more common in myeloid cancers<sup>5,6,7</sup>. A common kinase domain mutation that causes ligand-independent constitutive activation, D816V, occurs in 80-93% of aggressive forms of mastocytosis<sup>8,9</sup>.

**Potential relevance:** Imatinib<sup>10</sup> (2001) is approved for KIT positive unresectable or metastatic GIST and adult patients with aggressive systemic mastocytosis (SM) who do not have the D816V c-Kit mutation or whose c-Kit mutational status is unknown. Imatinib is also recommended for activating mutations, including KIT P577\_W582delinsPYD and KIT V560D in melanoma and exon 9 and 11 sensitizing mutations in GIST<sup>11,12,13,14</sup>. Mutations in exon 17 have been identified to confer resistance to imatinib and sunitinib<sup>15</sup>.

## Biomarker Descriptions (continued)

Additionally, detection of activating mutations in KIT is useful as an ancillary technique in the diagnosis of GIST<sup>13</sup>. Patients with acute myeloid leukemia (AML) that harbor KIT activating mutations with t(8;21) and inv(16) have an increased risk of relapse<sup>16</sup>. KIT D816V mutation is associated with the diagnosis of SM and aggressiveness of the disease<sup>17,18</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>45,46</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>47</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>48</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>48</sup>. Tumors classified as MSI-L are often phenotypically indistinguishable from MSS tumors and tend to be grouped with MSS<sup>49,50,51,52,53</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>46</sup>. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer<sup>45,46,50,54</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>45,46,55,56</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>55,56</sup>.

Potential relevance: Anti-PD-1 immune checkpoint inhibitors including pembrolizumab<sup>57</sup> (2014) and nivolumab<sup>58</sup> (2015) are approved for patients with MSI-H or dMMR colorectal cancer who have progressed following chemotherapy. Pembrolizumab<sup>57</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>57</sup>. Dostarlimab<sup>59</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>51,60</sup>. The cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab<sup>61</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>51,62,63</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>63</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>64,65</sup>. However, checkpoint blockade with the addition of chemotherapy or targeted therapies have demonstrated response in MSS or pMMR cancers<sup>64,65</sup>.

### PARP1 p.(R340\*) c.1018C>T

*poly(ADP-ribose) polymerase 1*

Background: The PARP1 gene encodes the poly(ADP-ribose) polymerase 1 protein<sup>19</sup>. PARP1 belongs to the large PARP protein family that also includes PARP2, PARP3, and PARP4<sup>107</sup>. PARP enzymes are responsible for the transfer of ADP-ribose, known as poly(ADP-ribosyl)ation or PARylation, to a variety of protein targets resulting in the recruitment of proteins involved in DNA repair, DNA synthesis, nucleic acid metabolism, and regulation of chromatin structure<sup>107,108</sup>. PARP enzymes are involved in several DNA repair pathways<sup>107,108</sup>. In base excision repair (BER), PARP1 recognizes DNA single-strand breaks and is capable of auto-PARylation (self-PARylation) which promotes the recruitment of additional BER enzymes<sup>108,109</sup>. PARP1 is also responsible for sensing DNA double-strand breaks (DSBs) and assists in end resection during homologous recombination repair (HRR) through the recruitment MRE11 to DSBs<sup>109</sup>. PARylation of histones H1, H2A, and H2B by PARP1 promotes an open chromatin conformation, which allows DNA repair machinery access to sites of DNA damage<sup>110</sup>.

Alterations and prevalence: Somatic mutations in PARP1 are observed in 6% of uterine corpus endometrial carcinoma, 4% of skin cutaneous melanoma, and 3% of adrenocortical carcinoma, stomach adenocarcinoma, bladder urothelial carcinoma, and colorectal adenocarcinoma<sup>7,24</sup>.

Potential relevance: Currently, no therapies are approved for PARP1 aberrations. However, PARP inhibition is known to induce synthetic lethality in certain cancer types that are HRR deficient (HRD) due to mutations in the HRR pathway. This is achieved from PARP inhibitors (PARPi) by promoting the accumulation of DNA damage in cells with HRD, consequently resulting in cell death<sup>111,112</sup>. Although not indicated for specific alterations in PARP1, several PARPis including olaparib, rucaparib, talazoparib, and niraparib have been approved in various cancer types with HRD. Olaparib<sup>113</sup> (2014) was the first PARPi to be approved by the FDA for BRCA1/2

## Biomarker Descriptions (continued)

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<sup>113</sup> 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<sup>114</sup> (2016) was the first PARPi approved for the treatment of patients with either gBRCAm or sBRCAm epithelial ovarian, fallopian tube, or primary peritoneal cancers and is also approved (2020) for deleterious gBRCAm or sBRCAm mCRPC. Talazoparib<sup>115</sup> (2018) is indicated for the treatment of gBRCAm HER2-negative locally advanced or metastatic breast cancer. Niraparib<sup>116</sup> (2017) is another PARPi approved for the treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancers with a deleterious or suspected deleterious BRCA mutation.

## Alerts Informed By Public Data Sources

### Current FDA Information

 Contraindicated

 Not recommended

 Resistance

 Breakthrough

 Fast Track

FDA information is current as of 2025-09-17. For the most up-to-date information, search [www.fda.gov](http://www.fda.gov).

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

##### izalectamab brengitecan

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

**Supporting Statement:**

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

**Reference:**

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

##### patritumab deruxtecan

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation or EGFRi sensitizing mutation

**Supporting Statement:**

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

**Reference:**

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

##### DB-1310

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

**Supporting Statement:**

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

**Reference:**

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

## 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,

## Genes Assayed (continued)

### Genes Assayed for the Detection of DNA Sequence Variants (continued)

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, SNCAP, 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, CBF, 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, 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, TGFBR2, TNFAIP3, TNFRSF14, TOP1, TP53, 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, 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, CBF, 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, TP53, 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 p.(L858R) c.2573T>G

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
osimertinib	●	●	●	●	● (III)
afatinib	●	●	●	●	● (II)
dacomitinib	●	●	●	●	● (II)
gefitinib	●	●	●	●	● (II)
erlotinib + ramucirumab	●	●	●	●	✖
amivantamab + carboplatin + pemetrexed	●	●	●	✖	✖
amivantamab + lazertinib	●	●	●	✖	✖
datopotamab deruxtecan-dlnk	●	●	✖	✖	✖
osimertinib + chemotherapy + pemetrexed	●	✖	●	✖	✖
bevacizumab + erlotinib	✖	●	●	●	✖
erlotinib	✖	●	●	●	✖
osimertinib + carboplatin + pemetrexed	✖	●	✖	✖	✖
osimertinib + cisplatin + pemetrexed	✖	●	✖	✖	✖
BAT1706 + erlotinib	✖	✖	●	✖	✖
bevacizumab (Allergan) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Biocon) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Celltrion) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Mabxience) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Pfizer) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Samsung Bioepis) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Stada) + erlotinib	✖	✖	●	✖	✖
atezolizumab + bevacizumab + carboplatin + paclitaxel	✖	✖	✖	●	✖
gefitinib + carboplatin + pemetrexed	✖	✖	✖	●	✖
adebrelimab, bevacizumab, chemotherapy	✖	✖	✖	✖	● (IV)
afatinib, bevacizumab, chemotherapy	✖	✖	✖	✖	● (IV)
befotertinib	✖	✖	✖	✖	● (IV)
bevacizumab, almonertinib, chemotherapy	✖	✖	✖	✖	● (IV)
catequentinib, toripalimab	✖	✖	✖	✖	● (IV)
EGFR tyrosine kinase inhibitor	✖	✖	✖	✖	● (IV)

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

## Relevant Therapy Summary (continued)

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

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

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
furmonertinib, chemotherapy	×	×	×	×	● (IV)
gefitinib, chemotherapy	×	×	×	×	● (IV)
gefitinib, endostatin	×	×	×	×	● (IV)
natural product, gefitinib, erlotinib, icotinib hydrochloride, osimertinib, almonertinib, furmonertinib	×	×	×	×	● (IV)
almonertinib, apatinib	×	×	×	×	● (III)
almonertinib, catequentinib	×	×	×	×	● (III)
almonertinib, chemotherapy	×	×	×	×	● (III)
almonertinib, radiation therapy	×	×	×	×	● (III)
befotertinib, icotinib hydrochloride	×	×	×	×	● (III)
bevacizumab, osimertinib	×	×	×	×	● (III)
CK-101, gefitinib	×	×	×	×	● (III)
datopotamab deruxtecan-dlnk, osimertinib	×	×	×	×	● (III)
furmonertinib	×	×	×	×	● (III)
furmonertinib, osimertinib, chemotherapy	×	×	×	×	● (III)
gefitinib, afatinib, erlotinib, metformin hydrochloride	×	×	×	×	● (III)
glumetinib, osimertinib	×	×	×	×	● (III)
icotinib hydrochloride, catequentinib	×	×	×	×	● (III)
icotinib hydrochloride, chemotherapy	×	×	×	×	● (III)
icotinib hydrochloride, radiation therapy	×	×	×	×	● (III)
izalontamab brengitecan	×	×	×	×	● (III)
izalontamab brengitecan, osimertinib	×	×	×	×	● (III)
JMT-101, osimertinib	×	×	×	×	● (III)
osimertinib, bevacizumab	×	×	×	×	● (III)
osimertinib, chemotherapy	×	×	×	×	● (III)
osimertinib, datopotamab deruxtecan-dlnk	×	×	×	×	● (III)
sacituzumab tirumotecan	×	×	×	×	● (III)
sacituzumab tirumotecan, osimertinib	×	×	×	×	● (III)
savolitinib, osimertinib	×	×	×	×	● (III)

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

## Relevant Therapy Summary (continued)

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

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

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
SH-1028	✖	✖	✖	✖	● (III)
TY-9591, osimertinib	✖	✖	✖	✖	● (III)
PM-1080, almonertinib	✖	✖	✖	✖	● (II/III)
SCTB-14, chemotherapy	✖	✖	✖	✖	● (II/III)
ABSK-043, furmonertinib	✖	✖	✖	✖	● (II)
afatinib, chemotherapy	✖	✖	✖	✖	● (II)
almonertinib	✖	✖	✖	✖	● (II)
almonertinib, adebrelimab, chemotherapy	✖	✖	✖	✖	● (II)
almonertinib, bevacizumab	✖	✖	✖	✖	● (II)
almonertinib, chemoradiation therapy	✖	✖	✖	✖	● (II)
almonertinib, dacomitinib	✖	✖	✖	✖	● (II)
amivantamab, chemotherapy	✖	✖	✖	✖	● (II)
amivantamab, lazertinib, chemotherapy	✖	✖	✖	✖	● (II)
atezolizumab, bevacizumab, tiragolumab	✖	✖	✖	✖	● (II)
befotertinib, bevacizumab, chemotherapy	✖	✖	✖	✖	● (II)
bevacizumab, afatinib	✖	✖	✖	✖	● (II)
bevacizumab, furmonertinib	✖	✖	✖	✖	● (II)
cadonilimab, chemotherapy, cetequentinib	✖	✖	✖	✖	● (II)
camrelizumab, apatinib	✖	✖	✖	✖	● (II)
capmatinib, osimertinib, ramucirumab	✖	✖	✖	✖	● (II)
cetequentinib, almonertinib	✖	✖	✖	✖	● (II)
cetequentinib, chemotherapy	✖	✖	✖	✖	● (II)
chemotherapy, atezolizumab, bevacizumab	✖	✖	✖	✖	● (II)
dacomitinib, osimertinib	✖	✖	✖	✖	● (II)
EGFR tyrosine kinase inhibitor, osimertinib, chemotherapy	✖	✖	✖	✖	● (II)
EGFR tyrosine kinase inhibitor, radiation therapy	✖	✖	✖	✖	● (II)
erlotinib, chemotherapy	✖	✖	✖	✖	● (II)
erlotinib, OBI-833	✖	✖	✖	✖	● (II)
furmonertinib, bevacizumab	✖	✖	✖	✖	● (II)

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

## Relevant Therapy Summary (continued)

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

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

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
furmonertinib, bevacizumab, chemotherapy	✗	✗	✗	✗	● (II)
furmonertinib, catequentinib	✗	✗	✗	✗	● (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)
izalontamab brengitecan, almonertinib	✗	✗	✗	✗	● (II)
JS-207, chemotherapy	✗	✗	✗	✗	● (II)
lazertinib	✗	✗	✗	✗	● (II)
lazertinib, bevacizumab	✗	✗	✗	✗	● (II)
lazertinib, chemotherapy	✗	✗	✗	✗	● (II)
osimertinib, bevacizumab, chemotherapy	✗	✗	✗	✗	● (II)
osimertinib, radiation therapy	✗	✗	✗	✗	● (II)
PLB-1004, bozitinib, osimertinib	✗	✗	✗	✗	● (II)
ramucirumab, erlotinib	✗	✗	✗	✗	● (II)
sunvozertinib	✗	✗	✗	✗	● (II)
sunvozertinib, catequentinib	✗	✗	✗	✗	● (II)
sunvozertinib, golidocitinib	✗	✗	✗	✗	● (II)
tislelizumab, chemotherapy, bevacizumab	✗	✗	✗	✗	● (II)
toripalimab	✗	✗	✗	✗	● (II)
toripalimab, bevacizumab, Clostridium butyricum, chemotherapy	✗	✗	✗	✗	● (II)
toripalimab, chemotherapy	✗	✗	✗	✗	● (II)
TY-9591, chemotherapy	✗	✗	✗	✗	● (II)
vabametkib, lazertinib	✗	✗	✗	✗	● (II)

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

## Relevant Therapy Summary (continued)

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

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

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
YL-202	✖	✖	✖	✖	● (II)
zorifertinib, pirotinib	✖	✖	✖	✖	● (II)
AP-L1898	✖	✖	✖	✖	● (I/II)
BH-30643	✖	✖	✖	✖	● (I/II)
bozitinib, osimertinib	✖	✖	✖	✖	● (I/II)
BPI-361175	✖	✖	✖	✖	● (I/II)
chemotherapy, DZD-6008	✖	✖	✖	✖	● (I/II)
dacomitinib, cetequentinib	✖	✖	✖	✖	● (I/II)
DAJH-1050766	✖	✖	✖	✖	● (I/II)
DB-1310, osimertinib	✖	✖	✖	✖	● (I/II)
dostinib	✖	✖	✖	✖	● (I/II)
FWD-1509	✖	✖	✖	✖	● (I/II)
H-002	✖	✖	✖	✖	● (I/II)
ifebemtinib, furmonertinib	✖	✖	✖	✖	● (I/II)
MRTX0902	✖	✖	✖	✖	● (I/II)
necitumumab, osimertinib	✖	✖	✖	✖	● (I/II)
quaratusugene ozeplasmid, osimertinib	✖	✖	✖	✖	● (I/II)
RC-108, furmonertinib, toripalimab	✖	✖	✖	✖	● (I/II)
soturafusp alfa, chemotherapy	✖	✖	✖	✖	● (I/II)
soturafusp alfa, HB-0030	✖	✖	✖	✖	● (I/II)
sunvozertinib, chemotherapy	✖	✖	✖	✖	● (I/II)
TRX-221	✖	✖	✖	✖	● (I/II)
WSD-0922	✖	✖	✖	✖	● (I/II)
almonertinib, midazolam	✖	✖	✖	✖	● (I)
ASKC-202	✖	✖	✖	✖	● (I)
AZD-9592	✖	✖	✖	✖	● (I)
BG-60366	✖	✖	✖	✖	● (I)
BPI-1178, osimertinib	✖	✖	✖	✖	● (I)
cetequentinib, gefitinib, metformin hydrochloride	✖	✖	✖	✖	● (I)

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

## Relevant Therapy Summary (continued)

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

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

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
DZD-6008	✗	✗	✗	✗	● (I)
EGFR tyrosine kinase inhibitor, cetequentinib	✗	✗	✗	✗	● (I)
genolimzumab, fruquintinib	✗	✗	✗	✗	● (I)
IBI-318, lenvatinib	✗	✗	✗	✗	● (I)
KQB-198, osimertinib	✗	✗	✗	✗	● (I)
LAVA-1223	✗	✗	✗	✗	● (I)
MRX-2843, osimertinib	✗	✗	✗	✗	● (I)
osimertinib, carotuximab	✗	✗	✗	✗	● (I)
osimertinib, Minnelide	✗	✗	✗	✗	● (I)
osimertinib, tegatrabetan	✗	✗	✗	✗	● (I)
patritumab deruxtecan	✗	✗	✗	✗	● (I)
repotrectinib, osimertinib	✗	✗	✗	✗	● (I)
VIC-1911, osimertinib	✗	✗	✗	✗	● (I)
WTS-004	✗	✗	✗	✗	● (I)
YH-013	✗	✗	✗	✗	● (I)
zipalertinib, chemotherapy, glumetinib, pimtespib, quemliclustat	✗	✗	✗	✗	● (I)

### TP53 p.(Q136E) c.406C>G

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
almonertinib, cetequentinib	✗	✗	✗	✗	● (III)
osimertinib, chemotherapy	✗	✗	✗	✗	● (III)
osimertinib, bevacizumab, chemotherapy	✗	✗	✗	✗	● (II)
sunvozertinib, cetequentinib	✗	✗	✗	✗	● (II)

### KIT amplification

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
nilotinib, pazopanib	✗	✗	✗	✗	● (II)
regorafenib	✗	✗	✗	✗	● (II)
sunitinib, regorafenib	✗	✗	✗	✗	● (II)

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

## HRR Details

Gene/Genomic Alteration	Finding
LOH percentage	<b>17.63%</b>
BRCA2	<b>LOH, 13q13.1(32890491-32972932)x2</b>

Homologous recombination repair (HRR) genes were defined from published evidence in relevant therapies, clinical guidelines, as well as clinical trials, and include - BRCA1, BRCA2, ATM, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, and RAD54L.

Thermo Fisher Scientific's Ion Torrent Oncomine Reporter software was used in generation of this report. Software was developed and designed internally by Thermo Fisher Scientific. The analysis was based on Oncomine Reporter (6.1.1 data version 2025.10(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 2025-09-17. NCCN information was sourced from [www.nccn.org](http://www.nccn.org) and is current as of 2025-09-02. EMA information was sourced from [www.ema.europa.eu](http://www.ema.europa.eu) and is current as of 2025-09-17. ESMO information was sourced from [www.esmo.org](http://www.esmo.org) and is current as of 2025-09-02. Clinical Trials information is current as of 2025-09-02. 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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