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**Patient Name:** 유기운
**Gender:** M
**Sample ID:** N25-344

**Primary Tumor Site:** lung
**Collection Date:** 2025.12.05

## Sample Cancer Type: Lung Cancer

### Table of Contents



### Report Highlights

4 Relevant Biomarkers
61 Therapies Available
81 Clinical Trials

## Relevant Lung Cancer Findings

| Gene | Finding | Gene | Finding |
|---|---|---|---|
| ALK | None detected | NTRK1 | None detected |
| BRAF | None detected | NTRK2 | None detected |
| EGFR | None detected | NTRK3 | None detected |
| ERBB2 | ***ERBB2 amplification*** | RET | None detected |
| KRAS | None detected | ROS1 | None detected |
| MET | None detected | | |

| Genomic Alteration | Finding |
|---|---|
| Tumor Mutational Burden | ***5.68 Mut/Mb measured*** |

## Relevant Biomarkers

| Tier | Genomic Alteration | Relevant Therapies (In this cancer type) | Relevant Therapies (In other cancer type) | Clinical Trials |
|---|---|---|---|---|
| IA | *ERBB2 amplification*<br>erb-b2 receptor tyrosine kinase 2<br>Locus: chr17:37863255 | **trastuzumab deruxtecan** [1 / II+] | **lapatinib + hormone therapy** [1, 2 / I, II+]<br>**lapatinib + trastuzumab** [2 / I, II+]<br>**pertuzumab + trastuzumab + chemotherapy** [1, 2 / I, II+]<br>**trastuzumab + tucatinib** [1 / I, II+]<br>**trastuzumab deruxtecan** [1, 2 / I, II+]<br>**trastuzumab† + chemotherapy** [1, 2 / I, II+]<br>**trastuzumab† + hormone therapy** [2 / I, II+]<br>**pembrolizumab + trastuzumab + chemotherapy** [1, 2 / I]<br>**ado-trastuzumab emtansine** [1, 2 / II+]<br>**lapatinib + chemotherapy** [1, 2 / II+]<br>**margetuximab + chemotherapy** [1 / II+]<br>**neratinib** [1, 2 / II+]<br>**neratinib + chemotherapy** [1 / II+]<br>**trastuzumab + tucatinib + chemotherapy** [1, 2 / II+]<br>**trastuzumab†** [1, 2 / II+]<br>**zanidatamab** [1, 2 / II+]<br>**pembrolizumab + berahyaluronidase alfa + trastuzumab + chemotherapy** [1]<br>**pertuzumab/trastuzumab/ hyaluronidase-zzxf + chemotherapy** [1, 2]<br>**trastuzumab and hyaluronidase-oysk** [1]<br>**trastuzumab and hyaluronidase-oysk + chemotherapy** [1]<br>pertuzumab + trastuzumab [I, II+]<br>pertuzumab + trastuzumab + hormone therapy [I, II+]<br>lapatinib + trastuzumab + hormone therapy [I]<br>abemaciclib + trastuzumab + hormone therapy [II+]<br>ado-trastuzumab emtansine + hormone therapy [II+]<br>hormone therapy [II+]<br>margetuximab [II+]<br>pertuzumab + trastuzumab + hormone therapy + chemotherapy [II+]<br>trastuzumab + hormone therapy + chemotherapy [II+]<br>ado-trastuzumab emtansine + neratinib | 76 |
| IIC | *Microsatellite stable* | None* | **lenvatinib + pembrolizumab + berahyaluronidase alfa** [1] | 0 |
| IIC | *BRCA2 deletion*<br>BRCA2, DNA repair associated<br>Locus: chr13:32890491 | None* | niraparib [II+]<br>olaparib [II+]<br>rucaparib [II+] | 4 |

*** 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 | *RAD52 p.(S346*) c.1037C>A*<br>RAD52 homolog, DNA repair protein<br>Allele Frequency: 56.71%<br>Locus: chr12:1023218<br>Transcript: NM_134424.4 | None* | None* | 3 |

*** 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.

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

*CIC p.(S1104T) c.3310T>A, HLA-B deletion, Tumor Mutational Burden*

## Variant Details

### DNA Sequence Variants

| Gene | Amino Acid Change | Coding | Variant ID | Locus | Allele Frequency | Transcript | Variant Effect |
|---|---|---|---|---|---|---|---|
| RAD52 | p.(S346*) | c.1037C>A | . | chr12:1023218 | 56.71% | NM_134424.4 | nonsense |
| CIC | p.(S1104T) | c.3310T>A | . | chr19:42796852 | 42.69% | NM_015125.5 | missense |
| MSH3 | p.(A61_P63dup) | c.189_190insGCAGCGCCC | . | chr5:79950735 | 63.90% | NM_002439.5 | nonframeshift Insertion |
| HLA-B | p.([T118I;L119I]) | c.353_355delCCCinsTCA | . | chr6:31324208 | 99.18% | NM_005514.8 | missense, missense |
| LATS1 | p.(P531R) | c.1592C>G | . | chr6:150004633 | 18.28% | NM_004690.4 | missense |
| FANCC | p.(G388E) | c.1163G>A | . | chr9:97873911 | 54.54% | NM_000136.3 | missense |
| SUFU | p.(G94C) | c.280G>T | . | chr10:104269023 | 16.72% | NM_016169.4 | missense |
| PPFIA2 | p.(S1195N) | c.3583_3585delTCAinsAAC | . | chr12:81657140 | 6.64% | NM_003625.5 | missense |
| FANCI | p.(L327P) | c.980T>C | . | chr15:89817403 | 49.74% | NM_001113378.2 | missense |
| MAP2K7 | p.(T385M) | c.1154C>T | . | chr19:7977210 | 22.57% | NM_145185.4 | missense |

### Copy Number Variations

| Gene | Locus | Copy Number | CNV Ratio |
|---|---|---|---|
| ERBB2 | chr17:37863255 | 52.09 | 18.53 |
| BRCA2 | chr13:32890491 | 1 | 0.93 |
| HLA-B | chr6:31322252 | 1.01 | 0.65 |

## Biomarker Descriptions

**ERBB2 amplification**

*erb-b2 receptor tyrosine kinase 2*

Background: The ERBB2 gene encodes the erb-b2 receptor tyrosine kinase 2, a member of the human epidermal growth factor receptor (HER) family[1]. Along with ERBB2/HER2, EGFR/ERBB1/HER1, ERBB3/HER3, and ERBB4/HER4 make up the HER protein family[64]. All ERBB/HER proteins encode transmembrane receptor tyrosine kinases[65]. However, ERBB2/HER2 is an orphan receptor with no known ligand[65]. ERBB2 preferentially binds other ligand-bound ERBB/HER family members to form heterodimers resulting in the activation of ERBB2 tyrosine kinase activity and subsequent activation of the PI3K/AKT/MTOR and RAS/RAF/MAPK/ERK signaling pathways which promote cell proliferation, differentiation, and survival[66]. Recurrent focal amplification of the ERBB2 gene leads to increased expression in several cancer types[66]. ERBB2 overexpression in immortalized cell lines is oncogenic and leads to ERBB2 homo-dimerization and activation without ligand binding[67,68,69].

Alterations and prevalence: ERBB2 gene amplification occurs in 10-25% of breast, esophageal, and gastric cancers, 5-10% of bladder, cervical, pancreas, and uterine cancers, and 1-5% of colorectal, lung, and ovarian cancers[8,9,70,71,72,73,74,75]. ERBB2 gene amplification in pediatric population is observed in 2% of peripheral nervous system cancers (2 in 91 patients) and less than 1% of leukemia (1 in 250 cases)[9]. Recurrent somatic activating mutations in ERBB2/HER2 occur at low frequencies (<1%) in diverse cancer types[9,76,77]. In breast, bladder, and colorectal cancers, the most common recurrent ERBB2 activating mutations include kinase domain mutations L755S and V777L and the extracellular domain mutation S310F. In lung cancer, the most common recurrent ERBB2 activating mutations include in-frame exon 20 insertions, particularly Y772_A775dup.

Potential relevance: The discovery of ERBB2/HER2 as an important driver of breast cancer in 1987 led to the development of trastuzumab, a humanized monoclonal antibody with specificity to the extracellular domain of HER2[78,79]. Trastuzumab[80] was FDA approved for the treatment of HER2 positive breast cancer in 1998, and subsequently in HER2 positive metastatic gastric and gastroesophageal junction adenocarcinoma in 2010. Additional monoclonal antibody therapies have been approved by the FDA for HER2-positive breast cancer including pertuzumab[81] (2012), a humanized monoclonal antibody that inhibits HER2 dimerization, and ado-trastuzumab emtansine[82] (2013), a conjugate of trastuzumab and a potent antimicrotubule agent. The combination of pertuzumab, trastuzumab, and a taxane is the preferred front-line regimen for HER2-positive metastatic breast cancer[83]. In addition to monoclonal antibodies, the small molecule inhibitor lapatinib[84], with specificity for both EGFR and ERBB2, was FDA approved (2007) for the treatment of patients with advanced HER2-positive breast cancer who have received prior therapy including trastuzumab. In 2017, the FDA approved the use of neratinib[85], an irreversible kinase inhibitor of EGFR, ERBB2/HER2, and ERBB4, for the extended adjuvant treatment of adult patients with early stage HER2-positive breast cancer. In 2020, the FDA approved neratinib[85] in combination with capecitabine for HER2-positive advanced or metastatic patients after two or more prior HER2-directed therapies. Also in 2020, the TKI irbinitinib[86] was FDA approved for HER2 overexpressing or amplified breast cancer in combination with trastuzumab and capecitabine. In 2021, the PD-1 blocking antibody, pembrolizumab, in combination with trastuzumab, fluoropyrimidine- and platinum-based chemotherapy, was approved for HER2 amplified gastric or gastroesophageal (GEJ) adenocarcinoma in the first line[29]. In 2024, a bispecific HER2 antibody, zanidatamab[87], was approved for the treatment of adults with previously treated, unresectable or metastatic ERBB2 overexpressing biliary tract cancer. In 2018 fast track designation was granted to the monoclonal antibody margetuximab[88] in patients with ERBB2 positive breast cancer previously treated with an anti-HER2 therapy. Additionally, in 2019, zanidatamab[89], received fast track designation in combination with standard chemotherapy for patients with HER2-overexpressing gastroesophageal adenocarcinoma (GEA). The humanized anti-HER2 antibody drug conjugate disitamab vedotin[90] (2020) received breakthrough designation for adult patients with HER2-positive urothelial cancer after previous platinum-chemotherapy treatment. In 2021, the antibody-drug conjugate ARX788[91] received fast track designation as a monotherapy for advanced or metastatic HER2-positive breast cancer that have progressed on one or more anti-HER2 regimens. Certain activating mutations have been observed to impart sensitivity to neratinib, afatinib, lapatinib, and trastuzumab, or dacomitinib in early and ongoing clinical studies[92,93,94,95,96]. ERBB2 kinase domain mutations R896G and V659E both showed response to afatinib in two NSCLC case studies[97,98]. Additionally, acquired HER2 mutations in estrogen receptor-positive (ER+) breast cancer have been shown to confer resistance to hormone therapy[99]. However, this was shown to be overcome by neratinib in combination with therapies targeting ER[99]. Additionally, in 2025, FDA approved the kinase inhibitors zongertinib[100] and sevabertinib[101] for the treatment of adult patients with unresectable or metastatic non-squamous non-small cell lung cancer (NSCLC) whose tumors have HER2 tyrosine kinase domain activating mutations. In 2025, a 9 amino acid transmembrane peptide of the HER2/neu protein, GLSI-100 (GP-2)[102], received fast track designation for the prevention of breast cancer recurrence following surgery.

**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[16]. Microsatellite instability (MSI) is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue[17,18]. 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[19]. 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[20]. Tumors with instability in one of the five markers were defined as

## Biomarker Descriptions (continued)

MSI-low (MSI-L) whereas, those with instability in zero markers were defined as MS-stable (MSS)[20]. Tumors classified as MSI-L are often phenotypically indistinguishable from MSS tumors and tend to be grouped with MSS[21,22,23,24,25]. 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[18]. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer[17,18,22,26].

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[17,18,27,28]. 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[27,28].

Potential relevance: Anti-PD-1 immune checkpoint inhibitors including pembrolizumab[29] (2014) and nivolumab[30] (2015) are approved for patients with MSI-H or dMMR colorectal cancer who have progressed following chemotherapy. Pembrolizumab[29] 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[29]. Dostarlimab[31] (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[23,32]. The cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab[33] (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[23,34,35]. 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[35]. 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[36,37]. However, checkpoint blockade with the addition of chemotherapy or targeted therapies have demonstrated response in MSS or pMMR cancers[36,37].

**BRCA2 deletion**

*BRCA2, DNA repair associated*

Background: The breast cancer early onset gene 2 (BRCA2) 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[38,39]. Specifically, BRCA1/2 are required for repair of chromosomal double strand breaks (DSBs) which are highly unstable and compromise genome integrity[38,39]. 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[40,41,42]. 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%[40,43].

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[44,45,46,47,48,49,50,51]. Somatic alterations in BRCA2 are observed in 5-15% of uterine corpus endometrial carcinoma, cutaneous melanoma, bladder urothelial carcinoma, stomach adenocarcinoma, colorectal adenocarcinoma, lung squamous cell carcinoma, lung adenocarcinoma, and uterine carcinosarcoma, 3-4% of cervical squamous cell carcinoma, head and neck squamous cell carcinoma, esophageal adenocarcinoma, ovarian serous cystadenocarcinoma, cholangiocarcinoma, breast invasive carcinoma, renal papillary cell carcinoma, and 2% of renal clear cell carcinoma, hepatocellular carcinoma, thymoma, prostate adenocarcinoma, sarcoma, and glioblastoma multiforme[8,9].

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)[52]. Inhibitors targeting PARP induce synthetic lethality in recombination deficient BRCA1/2 mutant cells[53,54]. Consequently, several PARP inhibitors have been FDA approved for BRCA1/2-mutated cancers. Olaparib[55] (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[55] is approved (2020) for metastatic castration-resistant prostate cancer (mCRPC) with deleterious or suspected deleterious, germline or somatic mutations in HRR genes that includes BRCA2. Rucaparib[56] is also approved (2020) for deleterious gBRCAm or sBRCAm mCRPC and ovarian cancer. Talazoparib[57] (2018) is indicated for the treatment of gBRCAm HER2-negative locally advanced or metastatic breast cancer. Additionally, talazoparib[57] in combination with enzalutamide is approved (2023) for mCRPC with mutations in HRR genes that includes BRCA2. Niraparib[58] (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. Niraparib in combination with abiraterone acetate[59] received FDA approval (2023) for the treatment of deleterious or suspected deleterious BRCA-mutated (BRCAm) mCRPC. In 2019,

## Biomarker Descriptions (continued)

niraparib[60] received breakthrough designation for the treatment of patients with BRCA1/2 gene-mutated mCRPC who have received prior taxane chemotherapy and androgen receptor (AR)-targeted therapy. Despite tolerability and efficacy, acquired resistance to PARP inhibition has been clinically reported[61]. One of the most common mechanisms of resistance includes secondary intragenic mutations that restore BRCA1/2 functionality[62]. 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[63], 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.

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

*RAD52 homolog, DNA repair protein*

Background: The RAD52 gene encodes the RAD52 homolog, DNA repair protein[1]. RAD52 binds to single- and double-stranded DNA and enables strand exchange for double-strand break (DSB) repair by binding to RAD51[14]. 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)[15].

Alterations and prevalence: Somatic mutations in RAD52 are observed in 2% of uterine corpus endometrial carcinoma, uterine carcinosarcoma, and skin cutaneous melanoma[8,9].

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

**CIC p.(S1104T) c.3310T>A**

*capicua transcriptional repressor*

Background: The CIC gene encodes the capicua transcriptional repressor, a member of the high mobility group (HMG)-box superfamily[1,10]. The HMG-box domain mediates CIC binding to an octameric consensus sequence at the promoters of target genes[1,10]. CIC interacts with the HDAC complex and SWI/SNF to transcriptionally repress target genes, which include members of the E-Twenty Six (ETS) oncogene family ETV1, ETV4 and ETV5[10]. CIC aberrations lead to increased RTK/MAPK signaling and oncogenesis, supporting a tumor suppressor role for CIC[10].

Alterations and prevalence: Somatic mutations in CIC are observed in 21% of brain lower grade glioma, 11% of uterine corpus endometrial carcinoma, 8% of skin cutaneous melanoma, 7% of stomach adenocarcinoma, and 6% of colorectal adenocarcinoma[8,9]. Biallelic loss of CIC is observed 2% of prostate adenocarcinoma and diffuse large B-cell lymphoma (DLBCL)[8,9]. Recurrent CIC fusions are found in Ewing-like sarcoma (ELS) (CIC::DUX4 and CIC::FOXO4), angiosarcoma (CIC::LEUTX), peripheral neuroectodermal tumors (CIC::NUTM1) and oligodendroglioma[10,11].

Potential relevance: Currently, no therapies are approved for CIC aberrations. CIC fusions, including CIC::DUX4 fusion, t(10;19)(q26;q13) and t(4;19)(q35;q13), are ancillary diagnostic markers for CIC-Rearranged Sarcoma[12,13].

**HLA-B deletion**

*major histocompatibility complex, class I, B*

Background: The HLA-B gene encodes the major histocompatibility complex, class I, B[1]. MHC (major histocompatibility complex) class I molecules are located on the cell surface of nucleated cells and present antigens from within the cell for recognition by cytotoxic T cells[2]. MHC class I molecules are heterodimers composed of two polypeptide chains, α and B2M[3]. The classical MHC class I genes include HLA-A, HLA-B, and HLA-C and encode the α polypeptide chains, which present short polypeptide chains, of 7 to 11 amino acids, to the immune system to distinguish self from non-self[4,5,6]. Downregulation of MHC class I promotes tumor evasion of the immune system, suggesting a tumor suppressor role for HLA-B[7].

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

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

# Alerts Informed By Public Data Sources

## Current FDA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

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

## ERBB2 amplification

### trastuzumab pamirtecan

**Cancer type:** Endometrial Carcinoma

**Variant class:** ERBB2 overexpression

**Supporting Statement:**
The FDA has granted Breakthrough Therapy designation to antibody-drug conjugate, trastuzumab pamirtecan (DB-1303), for the treatment of patients with HER2-expressing advanced endometrial cancer.

**Reference:**

https://investors.biontech.de//news-releases/news-release-details/biontech-and-dualitybio-receive-fda-breakthrough-therapy

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### disitamab vedotinaide

**Cancer type:** Bladder Urothelial Carcinoma

**Variant class:** ERBB2 positive

**Supporting Statement:**
The FDA has granted Breakthrough Therapy designation to the humanized anti-HER2 antibody drug conjugate (ADC), disitamab vedotin, for the second-line treatment of HER2 positive locally advanced or metastatic urothelial cancer (UC) after previous platinum-containing chemotherapy treatment.

**Reference:**

https://www.prnewswire.com/news-releases/remegen-announces-us-fda-has-granted-breakthrough-therapy-designation-for-disitamab-vedotin-rc48-in-urothelial-cancer-301138315.html

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### zanidatamab + chemotherapy

**Cancer type:** Gastroesophageal Junction Adenocarcinoma

**Variant class:** ERBB2 overexpression

**Supporting Statement:**
The FDA has granted Fast Track designation to the HER2 targeted bispecific antibody, zanidatamab, for HER2-overexpressing gastroesophageal adenocarcinoma (GEA) to be used in combination with standard-of-care chemotherapy.

**Reference:**

https://www.targetedonc.com/view/her2targeted-antibody-zw25-earns-fda-fast-track-designation-in-gea

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### anvatabart opadotin

**Cancer type:** Breast Cancer

**Variant class:** ERBB2 positive

**Supporting Statement:**
The FDA has granted Fast Track designation to the HER2-targeting antibody drug conjugate, anvatabart opadotin (ARX-788), for HER2-positive metastatic breast cancer.

**Reference:**

https://ir.ambrx.com/news/news-details/2023/ACE-Breast-02-Pivotal-Phase-3-Study-of-Ambrxs-ARX788-for-the-Treatment-of-HER2-Positive-Metastatic-Breast-Cancer-Achieves-Positive-Results/default.aspx

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## ERBB2 amplification (continued)

### evorpacept

**Cancer type:** Gastric Cancer, Gastroesophageal Junction Adenocarcinoma

**Variant class:** ERBB2 positive

**Supporting Statement:**
The FDA has granted Fast Track designation to the CD47 checkpoint inhibitor, ALX148, for the second-line treatment of patients with HER2-positive gastric or gastroesophageal junction carcinoma.

**Reference:**

https://www.targetedonc.com/view/two-fda-fast-track-designations-granted-to-alx148-for-hnscc-and-gastricgej-adenocarcinomas

### GLSI-100

**Cancer type:** Breast Cancer

**Variant class:** ERBB2 positive

**Supporting Statement:**
The FDA has granted Fast Track designation to the immunotherapy, GLSI-100, for the treatment of patients with HLA-A*02 genotype and HER2-positive breast cancer who have completed treatment with standard of care HER2/neu targeted therapy to improve invasive breast cancer free survival.

**Reference:**

https://investor.greenwichlifesciences.com/news-events/press-releases/detail/102/us-fda-fast-track-designation

### Current ESMO Information

Contraindicated | Not recommended | Resistance | Breakthrough | Fast Track

ESMO information is current as of 2025-11-03. For the most up-to-date information, search www.esmo.org.

## ERBB2 amplification

### trastuzumab

**Cancer type:** Gastric Cancer

**Variant class:** ERBB2 overexpression

**Summary:**

ESMO Clinical Practice Guidelines include the following supporting statement:

- "Treatment with trastuzumab is not recommended after first-line therapy in HER2-positive advanced gastric cancer [I, D]."

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Gastric Cancer [Ann Oncol (2022), doi: https://doi.org/10.1016/j.annonc.2022.07.004.]

## ERBB2 amplification (continued)

### hormone therapy

**Cancer type:** Breast Cancer **Variant class:** ERBB2 positive

**Other criteria:** Hormone receptor positive

**ESMO Level of Evidence/Grade of Recommendation:** III / C

**Summary:**

ESMO™ Clinical Practice Guidelines include the following supporting statement:

- "The use of single-agent ET without a HER2-targeted therapy is not routinely recommended unless cardiac disease precludes the safe use of HER2-directed therapies [III, C]"

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021) VOLUME 32, ISSUE 12, P1475-1495, DECEMBER 01, 2021; DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

# 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, 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 (continued)

## 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

## ERBB2 amplification

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| trastuzumab deruxtecan | ◑ | ◑ | ○ | ○ | ● (II) |
| zanidatamab | ○ | ○ | ○ | ○ | ● (II) |
| ado-trastuzumab emtansine | ○ | ○ | ○ | ○ | ✖ |
| lapatinib + capecitabine | ○ | ○ | ○ | ○ | ✖ |
| neratinib | ○ | ○ | ○ | ○ | ✖ |
| pertuzumab + trastuzumab + chemotherapy | ○ | ○ | ○ | ○ | ✖ |
| pertuzumab + trastuzumab + docetaxel | ○ | ○ | ○ | ○ | ✖ |
| trastuzumab + docetaxel | ○ | ○ | ○ | ○ | ✖ |
| trastuzumab + paclitaxel | ○ | ○ | ○ | ○ | ✖ |
| trastuzumab + tucatinib + capecitabine | ○ | ○ | ○ | ○ | ✖ |
| trastuzumab | ○ | ○ | ○ | ✖ | ● (II) |
| trastuzumab + capecitabine + cisplatin | ○ | ○ | ○ | ✖ | ✖ |
| trastuzumab + carboplatin + docetaxel | ○ | ○ | ○ | ✖ | ✖ |

* 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

### ERBB2 amplification (continued)

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| trastuzumab + cisplatin + fluorouracil | ○ | ○ | ○ | ✖ | ✖ |
| neratinib + capecitabine | ○ | ○ | ✖ | ✖ | ✖ |
| trastuzumab + tucatinib | ○ | ○ | ✖ | ✖ | ✖ |
| lapatinib + letrozole | ○ | ✖ | ○ | ✖ | ✖ |
| pembrolizumab + trastuzumab + chemotherapy + fluoropyrimidine | ○ | ✖ | ○ | ✖ | ✖ |
| pertuzumab/trastuzumab/hyaluronidase-zzxf + cyclophosphamide + doxorubicin | ○ | ✖ | ○ | ✖ | ✖ |
| pertuzumab/trastuzumab/hyaluronidase-zzxf + docetaxel | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Biocon) | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Biocon) + capecitabine + cisplatin | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Biocon) + carboplatin + docetaxel | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Biocon) + cisplatin + fluorouracil | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Biocon) + docetaxel | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Biocon) + paclitaxel | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Celltrion) | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Celltrion) + capecitabine + cisplatin | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Celltrion) + carboplatin + docetaxel | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Celltrion) + cisplatin + fluorouracil | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Celltrion) + docetaxel | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Celltrion) + paclitaxel | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Henlius) | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Pfizer) | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Pfizer) + capecitabine + cisplatin | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Pfizer) + carboplatin + docetaxel | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Pfizer) + cisplatin + fluorouracil | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Pfizer) + docetaxel | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Pfizer) + paclitaxel | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Samsung Bioepis) | ○ | ✖ | ○ | ✖ | ✖ |

* 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

### ERBB2 amplification (continued)

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| trastuzumab (Samsung Bioepis) + capecitabine + cisplatin | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Samsung Bioepis) + carboplatin + docetaxel | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Samsung Bioepis) + cisplatin + fluorouracil | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Samsung Bioepis) + docetaxel | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Samsung Bioepis) + paclitaxel | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Synthon) | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Synthon) + capecitabine + cisplatin | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Synthon) + carboplatin + docetaxel | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Synthon) + cisplatin + fluorouracil | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Synthon) + docetaxel | ○ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Synthon) + paclitaxel | ○ | ✖ | ○ | ✖ | ✖ |
| margetuximab + chemotherapy | ○ | ✖ | ✖ | ○ | ✖ |
| pembrolizumab + berahyaluronidase alfa + trastuzumab + chemotherapy | ○ | ✖ | ✖ | ✖ | ✖ |
| trastuzumab and hyaluronidase-oysk | ○ | ✖ | ✖ | ✖ | ✖ |
| trastuzumab and hyaluronidase-oysk + carboplatin + docetaxel | ○ | ✖ | ✖ | ✖ | ✖ |
| trastuzumab and hyaluronidase-oysk + docetaxel | ○ | ✖ | ✖ | ✖ | ✖ |
| trastuzumab and hyaluronidase-oysk + paclitaxel | ○ | ✖ | ✖ | ✖ | ✖ |
| lapatinib + trastuzumab | ✖ | ○ | ○ | ○ | ✖ |
| pertuzumab + trastuzumab | ✖ | ○ | ✖ | ○ | ● (II/III) |
| pertuzumab + trastuzumab + hormone therapy | ✖ | ○ | ✖ | ○ | ✖ |
| pertuzumab + trastuzumab + paclitaxel | ✖ | ○ | ✖ | ○ | ✖ |
| trastuzumab + chemotherapy | ✖ | ○ | ✖ | ○ | ✖ |
| trastuzumab + hormone therapy | ✖ | ○ | ✖ | ○ | ✖ |
| abemaciclib + trastuzumab + fulvestrant | ✖ | ○ | ✖ | ✖ | ✖ |
| ado-trastuzumab emtansine + neratinib | ✖ | ○ | ✖ | ✖ | ✖ |
| aromatase inhibitor | ✖ | ○ | ✖ | ✖ | ✖ |

* 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

### ERBB2 amplification (continued)

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| fulvestrant | ✖ | ○ | ✖ | ✖ | ✖ |
| hormone therapy | ✖ | ○ | ✖ | ✖ | ✖ |
| lapatinib + aromatase inhibitor | ✖ | ○ | ✖ | ✖ | ✖ |
| lapatinib + trastuzumab + aromatase inhibitor | ✖ | ○ | ✖ | ✖ | ✖ |
| margetuximab + capecitabine | ✖ | ○ | ✖ | ✖ | ✖ |
| margetuximab + eribulin | ✖ | ○ | ✖ | ✖ | ✖ |
| margetuximab + gemcitabine | ✖ | ○ | ✖ | ✖ | ✖ |
| margetuximab + vinorelbine | ✖ | ○ | ✖ | ✖ | ✖ |
| neratinib + paclitaxel | ✖ | ○ | ✖ | ✖ | ✖ |
| pembrolizumab + trastuzumab + capecitabine + cisplatin | ✖ | ○ | ✖ | ✖ | ✖ |
| pembrolizumab + trastuzumab + capecitabine + oxaliplatin | ✖ | ○ | ✖ | ✖ | ✖ |
| pembrolizumab + trastuzumab + cisplatin + fluorouracil | ✖ | ○ | ✖ | ✖ | ✖ |
| pembrolizumab + trastuzumab + fluorouracil + oxaliplatin | ✖ | ○ | ✖ | ✖ | ✖ |
| pertuzumab + trastuzumab + carboplatin + docetaxel | ✖ | ○ | ✖ | ✖ | ✖ |
| pertuzumab + trastuzumab + carboplatin + paclitaxel | ✖ | ○ | ✖ | ✖ | ✖ |
| pertuzumab + trastuzumab + hormone therapy + chemotherapy | ✖ | ○ | ✖ | ✖ | ✖ |
| tamoxifen | ✖ | ○ | ✖ | ✖ | ✖ |
| trastuzumab + aromatase inhibitor | ✖ | ○ | ✖ | ✖ | ✖ |
| trastuzumab + capecitabine | ✖ | ○ | ✖ | ✖ | ✖ |
| trastuzumab + capecitabine + oxaliplatin | ✖ | ○ | ✖ | ✖ | ✖ |
| trastuzumab + carboplatin + paclitaxel | ✖ | ○ | ✖ | ✖ | ✖ |
| trastuzumab + chemotherapy (non-anthracycline) | ✖ | ○ | ✖ | ✖ | ✖ |
| trastuzumab + cisplatin + docetaxel | ✖ | ○ | ✖ | ✖ | ✖ |
| trastuzumab + cisplatin + docetaxel + fluorouracil | ✖ | ○ | ✖ | ✖ | ✖ |
| trastuzumab + cisplatin + paclitaxel | ✖ | ○ | ✖ | ✖ | ✖ |
| trastuzumab + cyclophosphamide + docetaxel | ✖ | ○ | ✖ | ✖ | ✖ |

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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

### ERBB2 amplification (continued)

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| trastuzumab + docetaxel + fluorouracil + oxaliplatin | ✖ | ○ | ✖ | ✖ | ✖ |
| trastuzumab + fluorouracil | ✖ | ○ | ✖ | ✖ | ✖ |
| trastuzumab + fluorouracil + irinotecan | ✖ | ○ | ✖ | ✖ | ✖ |
| trastuzumab + fluorouracil + oxaliplatin | ✖ | ○ | ✖ | ✖ | ✖ |
| trastuzumab + fulvestrant | ✖ | ○ | ✖ | ✖ | ✖ |
| trastuzumab + hormone therapy + chemotherapy | ✖ | ○ | ✖ | ✖ | ✖ |
| trastuzumab + tamoxifen | ✖ | ○ | ✖ | ✖ | ✖ |
| trastuzumab + vinorelbine | ✖ | ○ | ✖ | ✖ | ✖ |
| pertuzumab/trastuzumab/hyaluronidase-zzxf + carboplatin + docetaxel | ✖ | ✖ | ○ | ✖ | ✖ |
| pertuzumab/trastuzumab/hyaluronidase-zzxf + cyclophosphamide + doxorubicin + fluorouracil | ✖ | ✖ | ○ | ✖ | ✖ |
| pertuzumab/trastuzumab/hyaluronidase-zzxf + cyclophosphamide + epirubicin | ✖ | ✖ | ○ | ✖ | ✖ |
| pertuzumab/trastuzumab/hyaluronidase-zzxf + paclitaxel | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Biocon) + anastrozole | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Celltrion) + anastrozole | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (CuraTeQ Biologics) | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (CuraTeQ Biologics) + anastrozole | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (CuraTeQ Biologics) + capecitabine + cisplatin | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (CuraTeQ Biologics) + carboplatin + docetaxel | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (CuraTeQ Biologics) + cisplatin + fluorouracil | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (CuraTeQ Biologics) + docetaxel | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (CuraTeQ Biologics) + paclitaxel | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (EirGenix) | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (EirGenix) + anastrozole | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (EirGenix) + capecitabine + cisplatin | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (EirGenix) + carboplatin + docetaxel | ✖ | ✖ | ○ | ✖ | ✖ |

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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

### ERBB2 amplification (continued)

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| trastuzumab (EirGenix) + cisplatin + fluorouracil | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (EirGenix) + docetaxel | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (EirGenix) + paclitaxel | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Henlius) + anastrozole | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Henlius) + capecitabine + cisplatin | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Henlius) + carboplatin + docetaxel | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Henlius) + cisplatin + fluorouracil | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Henlius) + docetaxel | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Henlius) + paclitaxel | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Pfizer) + anastrozole | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Prestige BioPharma) | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Prestige BioPharma) + anastrozole | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Prestige BioPharma) + capecitabine + cisplatin | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Prestige BioPharma) + carboplatin + docetaxel | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Prestige BioPharma) + cisplatin + fluorouracil | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Prestige BioPharma) + docetaxel | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Prestige BioPharma) + paclitaxel | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Samsung Bioepis) + anastrozole | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab (Synthon) + anastrozole | ✖ | ✖ | ○ | ✖ | ✖ |
| trastuzumab + anastrozole | ✖ | ✖ | ○ | ✖ | ✖ |
| ado-trastuzumab emtansine + hormone therapy | ✖ | ✖ | ✖ | ○ | ✖ |
| lapatinib + hormone therapy | ✖ | ✖ | ✖ | ○ | ✖ |
| lapatinib + trastuzumab + hormone therapy | ✖ | ✖ | ✖ | ○ | ✖ |
| margetuximab | ✖ | ✖ | ✖ | ○ | ✖ |
| neratinib + chemotherapy | ✖ | ✖ | ✖ | ○ | ✖ |
| pertuzumab + trastuzumab + nab-paclitaxel | ✖ | ✖ | ✖ | ○ | ✖ |
| pyrotinib | ✖ | ✖ | ✖ | ✖ | ● (IV) |
| IAH-0968, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (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

### ERBB2 amplification (continued)

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| trastuzumab deruxtecan, pembrolizumab, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (III) |
| allitinib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| CART-HER2, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (II) |
| disitamab vedotinaide, tislelizumab, bevacizumab | ✖ | ✖ | ✖ | ✖ | ● (II) |
| FDA022-BB05 | ✖ | ✖ | ✖ | ✖ | ● (II) |
| neratinib, neratinib + palbociclib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| pertuzumab + trastuzumab, atezolizumab + pertuzumab/trastuzumab/hyaluronidase-zzxf, trastuzumab + tucatinib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| pyrotinib, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (II) |
| TQB-2102, benmelstobart | ✖ | ✖ | ✖ | ✖ | ● (II) |
| trastuzumab (Samsung Bioepis), chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (II) |
| tucatinib, ado-trastuzumab emtansine | ✖ | ✖ | ✖ | ✖ | ● (II) |
| tucatinib, trastuzumab | ✖ | ✖ | ✖ | ✖ | ● (II) |
| zongertinib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| AP-402 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| AZD-9574, trastuzumab deruxtecan | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| BAT-8010, BAT-1006 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| BL-M07D1 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| DF-1001, nivolumab | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| disitamab vedotinaide, catequentinib | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| E01001 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| HypoSti.CART-HER2, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| IAH-0968 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| IBI-354 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| JIN-A-04 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| ST-1703 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| trastuzumab deruxtecan, neratinib | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| trastuzumab pamirtecan, pertuzumab | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| YH32367 | ✖ | ✖ | ✖ | ✖ | ● (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

### ERBB2 amplification (continued)

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| YL-202, pumitamig | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| ZV-0203 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| 177Lu-RAD202 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| ado-trastuzumab emtansine (Shanghai Fosun Pharma) | ✖ | ✖ | ✖ | ✖ | ● (I) |
| anti-HER-2 MAb (Anke Biotechnology) | ✖ | ✖ | ✖ | ✖ | ● (I) |
| BC004 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| BL-M17D1 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| BM-230 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| CART-HER2 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| CART-HER2/PD-L1 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| ceralasertib, trastuzumab deruxtecan | ✖ | ✖ | ✖ | ✖ | ● (I) |
| D3L-001 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| doxorubicin (Hangzhou HighField Biopharma) | ✖ | ✖ | ✖ | ✖ | ● (I) |
| DX126-262 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| ENT-H-1, trastuzumab | ✖ | ✖ | ✖ | ✖ | ● (I) |
| GQ-1005 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| GQ1001 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| HF-50 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| KJ-015 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| MBS301 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| NC-18 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| NVL-330 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| SPH5030 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| TAS0728 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| TL-938 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| trastuzumab deruxtecan, azenosertib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| trastuzumab deruxtecan, durvalumab, chemotherapy, volrustomig | ✖ | ✖ | ✖ | ✖ | ● (I) |
| VRN-10 | ✖ | ✖ | ✖ | ✖ | ● (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

### ERBB2 amplification (continued)

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| VVD-159642 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| XMT-2056 | ✖ | ✖ | ✖ | ✖ | ● (I) |

### Microsatellite stable

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| lenvatinib + pembrolizumab + berahyaluronidase alfa | ○ | ✖ | ✖ | ✖ | ✖ |

### BRCA2 deletion

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| olaparib | ✖ | ○ | ✖ | ✖ | ● (II) |
| niraparib | ✖ | ○ | ✖ | ✖ | ✖ |
| rucaparib | ✖ | ○ | ✖ | ✖ | ✖ |
| pamiparib, tislelizumab | ✖ | ✖ | ✖ | ✖ | ● (II) |
| SYN-608 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| SYN-818, olaparib | ✖ | ✖ | ✖ | ✖ | ● (I) |

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

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| SNV-1521, trastuzumab deruxtecan | ✖ | ✖ | ✖ | ✖ | ● (I) |
| SYN-608 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| SYN-818, olaparib | ✖ | ✖ | ✖ | ✖ | ● (I) |

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

## HRR Details

| Gene/Genomic Alteration | Finding |
|---|---|
| LOH percentage | ***14.83%*** |
| BRCA2 | ***CNV, CN:1.0*** |
| BRCA2 | ***LOH, 13q13.1(32890491-32972932)x1*** |

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

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

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