Taipei Veterans General Hospital

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Sample Information

Patient Name: 顏秀女
Gender: Female
ID No.: N222266640
History No.: 46768938
Age: 59

Ordering Doctor: DOC3016D 江起陸
Ordering REQ.: D64JFJP
Signing in Date: 2021/04/07

Path No.: S110-98530
MP No.: F21032
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S110-09416B
Percentage of tumor cells: 70%
Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

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Report Highlights

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Relevant Non-Small Cell Lung Cancer Variants

Gene	Finding	Gene	Finding
ALK	Not detected	NTRK1	Not detected
BRAF	Not detected	NTRK2	Not detected
EGFR	***EGFR amplification***	NTRK3	Not detected
ERBB2	***ERBB2 amplification, ERBB2 exon 20 insertion***	RET	Not detected
KRAS	Not detected	ROS1	Not detected
MET	Not detected		

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	*ERBB2 amplification* erb-b2 receptor tyrosine kinase 2	None	**ado-trastuzumab emtansine** [1, 2] **irbinitinib + trastuzumab + chemotherapy** [1] **lapatinib + chemotherapy** [1, 2] **lapatinib + hormone therapy** [1, 2] **lapatinib + trastuzumab** [2] **margetuximab + chemotherapy** [1] **neratinib** [1, 2] **neratinib + chemotherapy** [1] **pertuzumab + trastuzumab + chemotherapy** [1, 2] **pertuzumab/trastuzumab/ hyaluronidase-zzxf + chemotherapy** [1, 2] **trastuzumab deruxtecan** [1, 2] **trastuzumab*** [1, 2] **trastuzumab* + chemotherapy** [1, 2] **trastuzumab* + hormone therapy** [2] hormone therapy lapatinib + trastuzumab + hormone therapy pertuzumab + trastuzumab pertuzumab + trastuzumab + hormone therapy pertuzumab + trastuzumab + hormone therapy + chemotherapy trastuzumab + hormone therapy + chemotherapy trastuzumab containing regimen	40
IA	*ERBB2 exon 20 insertion* erb-b2 receptor tyrosine kinase 2 Allele Frequency: 74.26%	ado-trastuzumab emtansine trastuzumab deruxtecan	None	33
IIC	*EGFR amplification* epidermal growth factor receptor	None	None	8

Public data sources included in relevant therapies: FDA[1], NCCN, **EMA**[2], ESMO
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.
*** Includes biosimilars**

Variants (Exclude variant in Taiwan BioBank with >1% allele frequency)

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
ERBB2	p.(Y772_V773insVMAA)	c.2326_2327insCCGTGATGGCTG	.	chr17:37880986	74.26%	NM_004448.3	nonframeshift Insertion	1966

Copy Number Variations

Gene	Locus	Copy Number
EGFR	chr7:55198956	5.43
ERBB2	chr17:37868126	8.66

Biomarker Descriptions

EGFR (epidermal growth factor receptor)

Background: The EGFR gene encodes the epidermal growth factor receptor (EGFR) tyrosine kinase, a member of the ERBB/human epidermal growth factor receptor (HER) family. In addition to EGFR/ERBB1/HER1, other members of the ERBB/HER family include ERBB2/HER2, ERBB3/HER3, and ERBB4/HER4[1]. 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. Activation of these pathways promote cell proliferation, differentiation, and survival[2,3].

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[4,5,6,7]. 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[8]. These mutations constitutively activate EGFR resulting in downstream signaling, and represent 80% of the EGFR mutations observed in lung cancer. A second group of less prevalent activating mutations include E709K, G719X, S768I, L861Q, and short in-frame insertion mutations in exon 20[9,10,11,12]. EGFR activating mutations in lung cancer tend to be mutually exclusive to KRAS activating mutations[13]. In contrast, a different set of recurrent activating EGFR mutations in the extracellular domain include R108K, A289V and G598V and are primarily observed in glioblastoma[8,14]. Amplification of EGFR is observed in several cancer types including 30% of glioblastoma, 12% of esophageal cancer, 10% of head and neck cancer, 5% of bladder cancer, and 5% of lung squamous cell carcinoma[5,6,7,14,15]. 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[16,17,18].

Potential relevance: Approved first-generation EGFR tyrosine kinase inhibitors (TKIs) include erlotinib[19] (2004) and gefitinib[20] (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. Second-generation TKIs afatinib[21] (2013) and dacomitinib[22] (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[23,24,25,26]. In lung cancer containing EGFR exon 19 or 21 activating mutations, treatment with TKIs is eventually associated with the emergence of drug resistance[27]. The primary resistance mutation that emerges following treatment with first-generation TKI is T790M, accounting for 50-60% of resistant cases[8]. Third generation TKIs were developed to maintain sensitivity in the presence of T790M. Osimertinib[28] (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. In this case, resistance is associated with the C797S mutation, and occurs in 22-44% of cases[27]. 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[29]. T790M and C797S can occur in either cis or trans allelic orientation[29]. 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[29]. 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[29,30]. However, C797S occurring in cis conformation with T790M, confers resistance to first- and third-generation TKIs[29]. Fourth-generation TKIs are in development to overcome acquired C797S and T790M resistance mutations after osimertinib treatment. 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. The bispecific antibody, JNJ-61186372[31], targeting EGFR and MET, and the TKI mobocertinib[32], each received a breakthrough designation from the FDA (2020) for NSCLC tumors harboring EGFR exon 20 insertion mutations. The Oncoprex immunogene therapy CNVN-202[33] in combination with osimertinib received a fast track designation from the FDA (2020) for NSCLC tumors harboring EGFR mutations that progressed on osimertinib alone. BDTX-189[34] was granted a fast track designation (2020) for the treatment of solid tumors harboring an EGFR exon 20 insertion mutation.

ERBB2 (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. Along with ERBB2/HER2, EGFR/ERBB1/HER1, ERBB3/HER3, and ERBB4/HER4 make up the HER protein family[1]. All ERBB/HER proteins encode transmembrane receptor tyrosine kinases. However, ERBB2/HER2 is an orphan receptor with no known ligand. ERBB2 preferentially binds other ligand bound ERBB/HER family members to form hetero-dimers 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[3]. Recurrent focal amplification of the ERBB2 gene leads to increased expression in several cancer types. ERBB2 overexpression in immortalized cell lines is oncogenic and leads to ERBB2 homo-dimerization and activation without ligand binding[35,36,37].

Biomarker Descriptions (continued)

Alterations and prevalence: ERBB2 gene amplification occurs in 10-20% of breast, esophageal, and gastric cancers, 5-10% of bladder, cervical, pancreas, and uterine cancers, and 1-5% of colorectal, lung, and ovarian cancers[5,6,7,38,39,40,41,42]. Recurrent somatic activating mutations in ERBB2/HER2 occur at low frequencies (<1%) in diverse cancer types[7,43,44]. 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[45,46]. Trastuzumab[47] 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[48] (2012), a humanized monoclonal antibody that inhibits HER2 dimerization, and ado-trastuzumab emtansine[49] (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[50]. In addition to monoclonal antibodies, the small molecule inhibitor lapatinib[51], 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[52], 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[52] 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[53] was FDA approved for HER2 overexpressing or amplified breast cancer in combination with trastuzumab and capecitabine. The vaccine, nelipepimut-S[54], was granted fast-track designation by the FDA (2016) in patients with low to intermediate HER2 expressing (IHC score 1+ or 2+) breast cancer. In 2018 fast-track designation was granted to the monoclonal antibody margetuximab[55] in patients with ERBB2 positive breast cancer previously treated with an anti-HER2 therapy. In 2019, the novel bispecific antibody ZW25[56] received fast-track designation for patients with HER2-amplified biliary tract cancer or in combination with standard chemotherapy for patients with HER2-overexpressing gastroesophageal adenocarcinoma (GEA). In 2020, BDTX-189[34] received fast-track designation for adult patients with solid tumors harboring an allosteric human ERBB2 mutation or exon 20 insertion, and the humanized anti-HER2 antibody drug conjugate disitamab vedotin received breakthrough designation for adult patients with HER2-positive urothelial cancer after previous platinum-chemotherapy treatment[57]. In 2021, the antibody-drug conjugate ARX788[58] received fast-track designation as a monothreapy 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[59,60,61,62,63]. ERBB2 kinase domain mutations R896G and V659E both showed response to afatinib in two NSCLC case studies[64,65]. Additionally, acquired HER2 mutations in estrogen receptor-positive (ER +) breast cancer have been shown to confer resistance to hormone therapy[66]. However, this was shown to be overcome by neratinib in combination with therapies targeting ER[66].

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*
ado-trastuzumab emtansine	○	○	○	○	● (II)
pertuzumab + trastuzumab + chemotherapy	○	○	○	○	✖
pertuzumab + trastuzumab + docetaxel	○	○	○	○	✖
trastuzumab + capecitabine + cisplatin	○	○	○	○	✖
trastuzumab + cisplatin + fluorouracil	○	○	○	○	✖
trastuzumab deruxtecan	○	○	○	○	✖
trastuzumab	○	○	○	✖	● (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*
lapatinib + capecitabine	○	○	○	✖	✖
neratinib	○	○	○	✖	✖
trastuzumab + carboplatin + docetaxel	○	○	○	✖	✖
trastuzumab + docetaxel	○	○	○	✖	✖
trastuzumab + paclitaxel	○	○	○	✖	✖
irbinitinib + trastuzumab + capecitabine	○	○	✖	✖	✖
neratinib + capecitabine	○	○	✖	✖	✖
lapatinib + letrozole	○	✖	○	✖	✖
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 (Pfizer)	○	✖	○	✖	✖
trastuzumab (Pfizer) + capecitabine + cisplatin	○	✖	○	✖	✖
trastuzumab (Pfizer) + carboplatin + docetaxel	○	✖	○	✖	✖
trastuzumab (Pfizer) + cisplatin + fluorouracil	○	✖	○	✖	✖
trastuzumab (Pfizer) + docetaxel	○	✖	○	✖	✖
trastuzumab (Pfizer) + paclitaxel	○	✖	○	✖	✖

* 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)	○	✖	○	✖	✖
trastuzumab (Samsung Bioepis) + capecitabine + cisplatin	○	✖	○	✖	✖
trastuzumab (Samsung Bioepis) + carboplatin + docetaxel	○	✖	○	✖	✖
trastuzumab (Samsung Bioepis) + cisplatin + fluorouracil	○	✖	○	✖	✖
trastuzumab (Samsung Bioepis) + docetaxel	○	✖	○	✖	✖
trastuzumab (Samsung Bioepis) + paclitaxel	○	✖	○	✖	✖
margetuximab + chemotherapy	○	✖	✖	✖	✖
trastuzumab (Enhanze)	○	✖	✖	✖	✖
trastuzumab (Enhanze) + carboplatin + docetaxel	○	✖	✖	✖	✖
trastuzumab (Enhanze) + docetaxel	○	✖	✖	✖	✖
trastuzumab (Enhanze) + paclitaxel	○	✖	✖	✖	✖
lapatinib + trastuzumab	✖	○	○	○	✖
pertuzumab + trastuzumab	✖	○	✖	○	● (II)
pertuzumab + trastuzumab + hormone therapy + chemotherapy	✖	○	✖	○	✖
pertuzumab + trastuzumab + paclitaxel	✖	○	✖	○	✖
tamoxifen	✖	○	✖	○	✖
trastuzumab + chemotherapy	✖	○	✖	○	✖
trastuzumab + hormone therapy + chemotherapy	✖	○	✖	○	✖
trastuzumab + vinorelbine	✖	○	✖	○	✖
aromatase inhibitor	✖	○	✖	✖	✖
fulvestrant	✖	○	✖	✖	✖
hormone therapy	✖	○	✖	✖	✖
lapatinib + aromatase inhibitor	✖	○	✖	✖	✖
lapatinib + trastuzumab + aromatase inhibitor	✖	○	✖	✖	✖
neratinib + paclitaxel	✖	○	✖	✖	✖
pertuzumab + 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 + aromatase inhibitor	✖	○	✖	✖	✖
trastuzumab + capecitabine	✖	○	✖	✖	✖
trastuzumab + capecitabine + oxaliplatin	✖	○	✖	✖	✖
trastuzumab + carboplatin + docetaxel + fluorouracil	✖	○	✖	✖	✖
trastuzumab + carboplatin + paclitaxel	✖	○	✖	✖	✖
trastuzumab + chemotherapy (other)	✖	○	✖	✖	✖
trastuzumab + cisplatin + docetaxel	✖	○	✖	✖	✖
trastuzumab + cisplatin + docetaxel + fluorouracil	✖	○	✖	✖	✖
trastuzumab + cisplatin + paclitaxel	✖	○	✖	✖	✖
trastuzumab + cyclophosphamide + docetaxel	✖	○	✖	✖	✖
trastuzumab + docetaxel + fluorouracil + oxaliplatin	✖	○	✖	✖	✖
trastuzumab + fluorouracil	✖	○	✖	✖	✖
trastuzumab + fluorouracil + irinotecan	✖	○	✖	✖	✖
trastuzumab + fluorouracil + oxaliplatin	✖	○	✖	✖	✖
trastuzumab + fulvestrant	✖	○	✖	✖	✖
trastuzumab + tamoxifen	✖	○	✖	✖	✖
trastuzumab (Biocon) + anastrozole	✖	✖	○	✖	✖
trastuzumab (Biocon) + CMF + doxorubicin + paclitaxel	✖	✖	○	✖	✖
trastuzumab (Celltrion) + anastrozole	✖	✖	○	✖	✖
trastuzumab (Celltrion) + CMF + doxorubicin + paclitaxel	✖	✖	○	✖	✖
trastuzumab (Henlius)	✖	✖	○	✖	✖
trastuzumab (Henlius) + anastrozole	✖	✖	○	✖	✖
trastuzumab (Henlius) + capecitabine + cisplatin	✖	✖	○	✖	✖
trastuzumab (Henlius) + carboplatin + docetaxel	✖	✖	○	✖	✖
trastuzumab (Henlius) + cisplatin + fluorouracil	✖	✖	○	✖	✖
trastuzumab (Henlius) + CMF + doxorubicin + paclitaxel	✖	✖	○	✖	✖
trastuzumab (Henlius) + 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 (Henlius) + paclitaxel	✖	✖	○	✖	✖
trastuzumab (Pfizer) + anastrozole	✖	✖	○	✖	✖
trastuzumab (Pfizer) + CMF + doxorubicin + paclitaxel	✖	✖	○	✖	✖
trastuzumab (Samsung Bioepis) + anastrozole	✖	✖	○	✖	✖
trastuzumab (Samsung Bioepis) + CMF + doxorubicin + paclitaxel	✖	✖	○	✖	✖
trastuzumab (Synthon)	✖	✖	○	✖	✖
trastuzumab (Synthon) + anastrozole	✖	✖	○	✖	✖
trastuzumab (Synthon) + capecitabine + cisplatin	✖	✖	○	✖	✖
trastuzumab (Synthon) + carboplatin + docetaxel	✖	✖	○	✖	✖
trastuzumab (Synthon) + cisplatin + fluorouracil	✖	✖	○	✖	✖
trastuzumab (Synthon) + CMF + doxorubicin + paclitaxel	✖	✖	○	✖	✖
trastuzumab (Synthon) + docetaxel	✖	✖	○	✖	✖
trastuzumab (Synthon) + paclitaxel	✖	✖	○	✖	✖
trastuzumab + anastrozole	✖	✖	○	✖	✖
trastuzumab + CMF + doxorubicin + paclitaxel	✖	✖	○	✖	✖
aromatase inhibitor + luteinizing hormone-releasing factor	✖	✖	✖	○	✖
pertuzumab + trastuzumab + capecitabine	✖	✖	✖	○	✖
pertuzumab + trastuzumab + hormone therapy	✖	✖	✖	○	✖
pertuzumab + trastuzumab + nab-paclitaxel	✖	✖	✖	○	✖
pertuzumab + trastuzumab + vinorelbine	✖	✖	✖	○	✖
trastuzumab + hormone therapy	✖	✖	✖	○	✖
trastuzumab + taxane	✖	✖	✖	○	✖
trastuzumab containing regimen	✖	✖	✖	○	✖
ado-trastuzumab emtansine + atezolizumab	✖	✖	✖	✖	● (II)
irbinitinib, trastuzumab	✖	✖	✖	✖	● (II)
pyrotinib, chemotherapy	✖	✖	✖	✖	● (II)
targeted therapy, chemotherapy	✖	✖	✖	✖	● (II)

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

Relevant Therapy Summary (continued)

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

ERBB2 amplification (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
trastuzumab, pertuzumab, ado-trastuzumab emtansine, lapatinib	✖	✖	✖	✖	● (II)
A-166	✖	✖	✖	✖	● (I/II)
BAT 1306, BAT-8001	✖	✖	✖	✖	● (I/II)
BDC-1001, pembrolizumab	✖	✖	✖	✖	● (I/II)
BDTX-189	✖	✖	✖	✖	● (I/II)
zotatifin	✖	✖	✖	✖	● (I/II)
AC-101 (AbClon)	✖	✖	✖	✖	● (I)
ado-trastuzumab (Shanghai Fosun Pharma)	✖	✖	✖	✖	● (I)
AMX-3009	✖	✖	✖	✖	● (I)
ARX-788	✖	✖	✖	✖	● (I)
BAY-2701439	✖	✖	✖	✖	● (I)
CART	✖	✖	✖	✖	● (I)
CART-HER2	✖	✖	✖	✖	● (I)
disitamab vedotin	✖	✖	✖	✖	● (I)
KN026	✖	✖	✖	✖	● (I)
M802	✖	✖	✖	✖	● (I)
MBS301	✖	✖	✖	✖	● (I)
MT-5111	✖	✖	✖	✖	● (I)
neratinib, palbociclib, everolimus, trametinib	✖	✖	✖	✖	● (I)
pirotinib	✖	✖	✖	✖	● (I)
pivotinib	✖	✖	✖	✖	● (I)
PRS-343	✖	✖	✖	✖	● (I)
SBT6050, pembrolizumab	✖	✖	✖	✖	● (I)
SHR-A1811	✖	✖	✖	✖	● (I)
tebotelimab, margetuximab	✖	✖	✖	✖	● (I)
trastuzumab deruxtecan, durvalumab, chemotherapy	✖	✖	✖	✖	● (I)
trastuzumab deruxtecan, pembrolizumab	✖	✖	✖	✖	● (I)
zanidatamab	✖	✖	✖	✖	● (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*
ZN-A-1041	✖	✖	✖	✖	● (I)

ERBB2 exon 20 insertion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
ado-trastuzumab emtansine	✖	●	✖	✖	● (II)
trastuzumab deruxtecan	✖	●	✖	✖	✖
pyrotinib	✖	✖	✖	✖	● (III)
ado-trastuzumab emtansine + atezolizumab	✖	✖	✖	✖	● (II)
afatinib	✖	✖	✖	✖	● (II)
anti-PD-L1 antibody, pyrotinib	✖	✖	✖	✖	● (II)
irbinitinib, trastuzumab	✖	✖	✖	✖	● (II)
neratinib	✖	✖	✖	✖	● (II)
pertuzumab + trastuzumab	✖	✖	✖	✖	● (II)
poziotinib	✖	✖	✖	✖	● (II)
pyrotinib, chemotherapy	✖	✖	✖	✖	● (II)
pyrotinib, thalidomide	✖	✖	✖	✖	● (II)
sintilimab	✖	✖	✖	✖	● (II)
targeted therapy, chemotherapy	✖	✖	✖	✖	● (II)
tarloxotinib	✖	✖	✖	✖	● (II)
trastuzumab, pertuzumab, ado-trastuzumab emtansine, lapatinib	✖	✖	✖	✖	● (II)
BDTX-189	✖	✖	✖	✖	● (I/II)
CBT-502, anlotinib hydrochloride	✖	✖	✖	✖	● (I/II)
DZD-9008	✖	✖	✖	✖	● (I/II)
mobocertinib	✖	✖	✖	✖	● (I/II)
zotatifin	✖	✖	✖	✖	● (I/II)
disitamab vedotin	✖	✖	✖	✖	● (I)
neratinib, palbociclib, everolimus, trametinib	✖	✖	✖	✖	● (I)
pirotinib	✖	✖	✖	✖	● (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 exon 20 insertion (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
SHR-A1811	✖	✖	✖	✖	● (I)
trastuzumab deruxtecan, pembrolizumab	✖	✖	✖	✖	● (I)

EGFR amplification

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
apatinib, gefitinib	✖	✖	✖	✖	● (IV)
crizotinib	✖	✖	✖	✖	● (II)
erlotinib	✖	✖	✖	✖	● (II)
gefitinib	✖	✖	✖	✖	● (II)
nimotuzumab + chemotherapy	✖	✖	✖	✖	● (II)
BCA101	✖	✖	✖	✖	● (I)
FT500, nivolumab, pembrolizumab, atezolizumab	✖	✖	✖	✖	● (I)
neratinib, palbociclib, everolimus, trametinib	✖	✖	✖	✖	● (I)

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

Relevant Therapy Details

Current FDA Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

FDA information is current as of 2021-02-17. For the most up-to-date information, search www.fda.gov.

ERBB2 amplification

○ ado-trastuzumab emtansine

Cancer type: Breast Cancer **Label as of:** 2020-09-27 **Variant class:** ERBB2 amplification or ERBB2 overexpression

Indications and usage:

KADCYLA® is a HER2-targeted antibody and microtubule inhibitor conjugate indicated, as a single agent, for:

- the treatment of patients with HER2-positive, metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:
  - received prior therapy for metastatic disease, or
  - developed disease recurrence during or within six months of completing adjuvant therapy.
- the adjuvant treatment of patients with HER2-positive early breast cancer who have residual invasive disease after neoadjuvant taxane and trastuzumab-based treatment.

Select patients for therapy based on an FDA-approved companion diagnostic for KADCYLA®

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/125427s108lbl.pdf

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○ irbinitinib + trastuzumab + capecitabine

Cancer type: Breast Cancer **Label as of:** 2020-04-17 **Variant class:** ERBB2 amplification or ERBB2 overexpression

Indications and usage:
TUKYSA™ is a kinase inhibitor indicated in combination with trastuzumab and capecitabine for treatment of adult patients with advanced unresectable or metastatic HER2-positive breast cancer, including patients with brain metastases, who have received one or more prior anti-HER2-based regimens in the metastatic setting.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213411s000lbl.pdf

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ERBB2 amplification (continued)

lapatinib + capecitabine, lapatinib + letrozole

Cancer type: Breast Cancer **Label as of:** 2018-12-06 **Variant class:** ERBB2 overexpression

Other criteria: ER positive, PR positive

Indications and usage:

TYKERB® is a kinase inhibitor indicated in combination with:

- capecitabine for the treatment of patients with advanced or metastatic breast cancer whose tumors overexpress human epidermal growth factor receptor 2 (HER2) and who have received prior therapy including an anthracycline, a taxane, and trastuzumab.
- Limitations of Use: Patients should have disease progression on trastuzumab prior to initiation of treatment with TYKERB® in combination with capecitabine.
- letrozole for the treatment of postmenopausal women with hormone receptor-positive metastatic breast cancer that overexpresses the HER2 receptor for whom hormonal therapy is indicated.

TYKERB® in combination with an aromatase inhibitor has not been compared to a trastuzumab-containing chemotherapy regimen for the treatment of metastatic breast cancer.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/022059s024lbl.pdf

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margetuximab + chemotherapy

Cancer type: Breast Cancer **Label as of:** 2020-12-16 **Variant class:** ERBB2 overexpression or ERBB2 amplification

Indications and usage:
MARGENZA™ is a HER2/neu receptor antagonist indicated, in combination with chemotherapy, for the treatment of adult patients with metastatic HER2 positive breast cancer who have received two or more prior anti-HER2 regimens, at least one of which was for metastatic disease.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761150s000lbl.pdf

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neratinib, neratinib + capecitabine

Cancer type: Breast Cancer **Label as of:** 2020-07-29 **Variant class:** ERBB2 overexpression

Indications and usage:

NERLYNX® is a kinase inhibitor indicated:

- As a single agent, for the extended adjuvant treatment of adult patients with early stage HER2-positive breast cancer, to follow adjuvant trastuzumab-based therapy.
- In combination with capecitabine, for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 based regimens in the metastatic setting.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/208051s007lbl.pdf

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ERBB2 amplification (continued)

pertuzumab + trastuzumab + chemotherapy, pertuzumab + trastuzumab + docetaxel

Cancer type: Breast Cancer **Label as of:** 2020-01-16 **Variant class:** ERBB2 amplification or ERBB2 overexpression

Indications and usage:

PERJETA® is a HER2/neu receptor antagonist indicated for:

- Use in combination with trastuzumab and docetaxel for treatment of patients with HER2-positive metastatic breast cancer (MBC) who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.
- Use in combination with trastuzumab and chemotherapy as
  - neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive) as part of a complete treatment regimen for early breast cancer.
  - adjuvant treatment of patients with HER2-positive early breast cancer at high risk of recurrence

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/125409s124lbl.pdf

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pertuzumab/trastuzumab/hyaluronidase-zzxf + cyclophosphamide + doxorubicin

Cancer type: Breast Cancer **Label as of:** 2020-06-29 **Variant class:** ERBB2 amplification

Indications and usage:

PHESGO™ is a combination of pertuzumab and trastuzumab, HER2/neu receptor antagonists, and hyaluronidase, an endoglycosidase, indicated for:

- Use in combination with chemotherapy as:
  - neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive) as part of a complete treatment regimen for early breast cancer.
  - adjuvant treatment of patients with HER2-positive early breast cancer at high risk of recurrence
- Use in combination with docetaxel for treatment of patients with HER2 positive metastatic breast cancer (MBC) who have not received prioranti-HER2 therapy or chemotherapy for metastatic disease.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761170s000lbl.pdf

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pertuzumab/trastuzumab/hyaluronidase-zzxf + docetaxel, pertuzumab/trastuzumab/hyaluronidase-zzxf + cyclophosphamide + doxorubicin

Cancer type: Breast Cancer **Label as of:** 2020-06-29 **Variant class:** ERBB2 overexpression

Indications and usage:

PHESGO™ is a combination of pertuzumab and trastuzumab, HER2/neu receptor antagonists, and hyaluronidase, an endoglycosidase, indicated for:

- Use in combination with chemotherapy as:
  - neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive) as part of a complete treatment regimen for early breast cancer.
  - adjuvant treatment of patients with HER2-positive early breast cancer at high risk of recurrence
- Use in combination with docetaxel for treatment of patients with HER2 positive metastatic breast cancer (MBC) who have not received prioranti-HER2 therapy or chemotherapy for metastatic disease.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761170s000lbl.pdf

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ERBB2 amplification (continued)

trastuzumab (Biocon), trastuzumab (Biocon) + docetaxel, trastuzumab (Biocon) + paclitaxel, trastuzumab (Biocon) + capecitabine + cisplatin, trastuzumab (Biocon) + carboplatin + docetaxel, trastuzumab (Biocon) + cisplatin + fluorouracil

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

Label as of: 2019-04-17

Variant class: ERBB2 overexpression or ERBB2 amplification

Indications and usage:

OGIVRI™ is a HER2/neu receptor antagonist indicated for:

- The treatment of HER2-overexpressing breast cancer.
- The treatment of HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma.

Select patients for therapy based on an FDA-approved companion diagnostic for a trastuzumab product.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761074s004lbl.pdf

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trastuzumab (Celltrion), trastuzumab (Celltrion) + docetaxel, trastuzumab (Celltrion) + paclitaxel, trastuzumab (Celltrion) + capecitabine + cisplatin, trastuzumab (Celltrion) + carboplatin + docetaxel, trastuzumab (Celltrion) + cisplatin + fluorouracil

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

Label as of: 2019-05-16

Variant class: ERBB2 overexpression or ERBB2 amplification

Indications and usage:

HERZUMA® is a HER2/neu receptor antagonist indicated for:

- the treatment of HER2-overexpressing breast cancer.
- the treatment of HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma.

Select patients for therapy based on an FDA-approved companion diagnostic for a trastuzumab product.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761091s001s002lbl.pdf

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trastuzumab (Enhanze), trastuzumab (Enhanze) + docetaxel, trastuzumab (Enhanze) + paclitaxel, trastuzumab (Enhanze) + carboplatin + docetaxel

Cancer type: Breast Cancer

Label as of: 2019-02-28

Variant class: ERBB2 overexpression or ERBB2 amplification

Indications and usage:

HERCEPTIN HYLECTA™ is a combination of trastuzumab, a HER2/neu receptor antagonist, and hyaluronidase, an endoglycosidase, indicated in adults for:

- The treatment of HER2-overexpressing breast cancer.

Select patients for therapy based on an FDA-approved companion diagnostic for trastuzumab.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761106Orig1s000lbl.pdf

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ERBB2 amplification (continued)

trastuzumab (Pfizer), trastuzumab (Pfizer) + docetaxel, trastuzumab (Pfizer) + paclitaxel, trastuzumab (Pfizer) + capecitabine + cisplatin, trastuzumab (Pfizer) + carboplatin + docetaxel, trastuzumab (Pfizer) + cisplatin + fluorouracil

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

Label as of: 2019-03-11

Variant class: ERBB2 amplification or ERBB2 overexpression

Indications and usage:

TRAZIMERA™ is a HER2/neu receptor antagonist indicated for:

- The treatment of HER2-overexpressing breast cancer.
- The treatment of HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma.

Select patients for therapy based on an FDA-approved companion diagnostic for a trastuzumab product.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761081s000lbl.pdf

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trastuzumab (Samsung Bioepis), trastuzumab (Samsung Bioepis) + docetaxel, trastuzumab (Samsung Bioepis) + paclitaxel, trastuzumab (Samsung Bioepis) + capecitabine + cisplatin, trastuzumab (Samsung Bioepis) + carboplatin + docetaxel, trastuzumab (Samsung Bioepis) + cisplatin + fluorouracil

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

Label as of: 2019-01-18

Variant class: ERBB2 amplification or ERBB2 overexpression

Indications and usage:

Ontruzant® is a HER2/neu receptor antagonist indicated for:

- The treatment of HER2-overexpressing breast cancer.
- The treatment of HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma.

Select patients for therapy based on an FDA-approved companion diagnostic for a trastuzumab product.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761100s000lbl.pdf

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trastuzumab deruxtecan

Cancer type: Breast Cancer

Label as of: 2021-01-15

Variant class: ERBB2 amplification

Indications and usage:

ENHERTU® is a HER2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of:

- adult patients with unresectable or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting.
  - This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
- adult patients with locally advanced or metastatic HER2-positive gastric or gastroesophageal junction adenocarcinoma who have received a prior trastuzumab-based regimen.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761139s011lbl.pdf

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ERBB2 amplification (continued)

trastuzumab deruxtecan

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

Label as of: 2021-01-15

Variant class: ERBB2 overexpression

Indications and usage:

ENHERTU® is a HER2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of:

- adult patients with unresectable or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting.
  - This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
- adult patients with locally advanced or metastatic HER2-positive gastric or gastroesophageal junction adenocarcinoma who have received a prior trastuzumab-based regimen.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761139s011lbl.pdf

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trastuzumab, trastuzumab + docetaxel, trastuzumab + paclitaxel, trastuzumab + capecitabine + cisplatin, trastuzumab + carboplatin + docetaxel, trastuzumab + cisplatin + fluorouracil

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

Label as of: 2018-11-29

Variant class: ERBB2 overexpression or ERBB2 amplification

Indications and usage:

HERCEPTIN® is a HER2/neu receptor antagonist indicated for:

- The treatment of HER2-overexpressing breast cancer.
- The treatment of HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma.

Select patients for therapy based on an FDA-approved companion diagnostic for HERCEPTIN®.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/103792s5345lbl.pdf

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Current NCCN Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

NCCN information is current as of 2021-02-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

ERBB2 amplification

○ ado-trastuzumab emtansine

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

○ irbinitinib + trastuzumab + capecitabine

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

○ pertuzumab + trastuzumab + docetaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Line of therapy not specified); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

○ trastuzumab + capecitabine + cisplatin

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 5.2020]

ERBB2 amplification (continued)

trastuzumab + capecitabine + cisplatin

Cancer type: Gastric Cancer **Variant class:** ERBB2 overexpression

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2020]

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trastuzumab + chemotherapy

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor negative

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Ductal, Lobular, Mixed, Micropapillary; Invasive (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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trastuzumab + chemotherapy

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Ductal, Lobular, Mixed, Micropapillary; Invasive (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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trastuzumab + cisplatin + fluorouracil

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma **Variant class:** ERBB2 overexpression

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 5.2020]

ERBB2 amplification (continued)

trastuzumab + cisplatin + fluorouracil

Cancer type: Gastric Cancer **Variant class:** ERBB2 overexpression

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2020]

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aromatase inhibitor

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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fulvestrant

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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hormone therapy

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Ductal, Lobular, Mixed, Micropapillary; Invasive (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

ERBB2 amplification (continued)

lapatinib + aromatase inhibitor

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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lapatinib + capecitabine

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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lapatinib + trastuzumab

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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lapatinib + trastuzumab

Cancer type: Colon Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: BRAF wild type, RAS wild type

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Advanced, Metastatic (First-line therapy)
- Advanced, Metastatic, Progression (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 2.2021]

ERBB2 amplification (continued)

lapatinib + trastuzumab

Cancer type: Rectal Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: BRAF wild type, RAS wild type

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Advanced, Metastatic (First-line therapy)
- Advanced, Metastatic, Progression (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 1.2021]

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lapatinib + trastuzumab + aromatase inhibitor

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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neratinib

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Ductal, Lobular, Mixed, Micropapillary; Invasive (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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neratinib + capecitabine

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

ERBB2 amplification (continued)

pertuzumab + trastuzumab

Cancer type: Colon Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: BRAF wild type, RAS wild type

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Advanced, Metastatic (First-line therapy)
- Advanced, Metastatic, Progression (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 2.2021]

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pertuzumab + trastuzumab

Cancer type: Rectal Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: BRAF wild type, RAS wild type

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Advanced, Metastatic (First-line therapy)
- Advanced, Metastatic, Progression (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 1.2021]

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pertuzumab + trastuzumab + carboplatin + docetaxel

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Adjuvant therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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pertuzumab + trastuzumab + chemotherapy

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Ductal, Lobular, Mixed, Micropapillary; Invasive (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

ERBB2 amplification (continued)

pertuzumab + trastuzumab + hormone therapy + chemotherapy

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Ductal, Lobular, Mixed, Micropapillary; Invasive (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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pertuzumab + trastuzumab + paclitaxel

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Line of therapy not specified); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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tamoxifen

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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trastuzumab + aromatase inhibitor

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

ERBB2 amplification (continued)

trastuzumab + capecitabine

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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trastuzumab + capecitabine

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 5.2020]

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trastuzumab + capecitabine

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2020]

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trastuzumab + capecitabine + oxaliplatin

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 5.2020]

ERBB2 amplification (continued)

trastuzumab + capecitabine + oxaliplatin

Cancer type: Gastric Cancer **Variant class:** ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2020]

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trastuzumab + carboplatin + docetaxel

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Adjuvant therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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trastuzumab + carboplatin + paclitaxel

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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trastuzumab + carboplatin + paclitaxel

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma **Variant class:** ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 5.2020]

ERBB2 amplification (continued)

trastuzumab + carboplatin + paclitaxel

Cancer type: Gastric Cancer **Variant class:** ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2020]

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trastuzumab + carboplatin + paclitaxel

Cancer type: Endometrial Cancer **Variant class:** ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Uterine Serous Carcinoma; Stage III/IV; Recurrent (Adjuvant therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Uterine Neoplasms [Version 1.2021]

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trastuzumab + chemotherapy

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Ductal, Lobular, Mixed, Micropapillary; Invasive (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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trastuzumab + chemotherapy (other)

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

ERBB2 amplification (continued)

trastuzumab + cisplatin + docetaxel

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 5.2020]

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trastuzumab + cisplatin + docetaxel

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2020]

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trastuzumab + cisplatin + docetaxel + fluorouracil

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 5.2020]

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trastuzumab + cisplatin + docetaxel + fluorouracil

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2020]

ERBB2 amplification (continued)

trastuzumab + cisplatin + paclitaxel

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 5.2020]

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trastuzumab + cisplatin + paclitaxel

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2020]

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trastuzumab + cyclophosphamide + docetaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Adjuvant therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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trastuzumab + docetaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

ERBB2 amplification (continued)

trastuzumab + docetaxel

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 5.2020]

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trastuzumab + docetaxel

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2020]

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trastuzumab + docetaxel + fluorouracil + oxaliplatin

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 5.2020]

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trastuzumab + docetaxel + fluorouracil + oxaliplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2020]

ERBB2 amplification (continued)

trastuzumab + fluorouracil

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 5.2020]

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trastuzumab + fluorouracil

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2020]

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trastuzumab + fluorouracil + irinotecan

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 5.2020]

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trastuzumab + fluorouracil + irinotecan

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2020]

ERBB2 amplification (continued)

trastuzumab + fluorouracil + oxaliplatin

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 5.2020]

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trastuzumab + fluorouracil + oxaliplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2020]

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trastuzumab + fulvestrant

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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trastuzumab + hormone therapy + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Ductal, Lobular, Mixed, Micropapillary; Invasive (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

ERBB2 amplification (continued)

trastuzumab + paclitaxel

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Ductal, Lobular, Mixed, Micropapillary; Invasive (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

---

trastuzumab + paclitaxel

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Adjuvant therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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trastuzumab + paclitaxel

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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trastuzumab + paclitaxel

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma **Variant class:** ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 5.2020]

ERBB2 amplification (continued)

trastuzumab + paclitaxel

Cancer type: Gastric Cancer **Variant class:** ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2020]

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trastuzumab + tamoxifen

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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trastuzumab + vinorelbine

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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trastuzumab deruxtecan

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

ERBB2 amplification (continued)

trastuzumab deruxtecan

Cancer type: Colon Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: BRAF wild type, RAS wild type

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Advanced, Metastatic (First-line therapy)
- Advanced, Metastatic, Progression (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 2.2021]

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trastuzumab deruxtecan

Cancer type: Rectal Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: BRAF wild type, RAS wild type

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Advanced, Metastatic (First-line therapy)
- Advanced, Metastatic, Progression (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 1.2021]

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hormone therapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Ductal, Lobular, Mixed, Micropapillary; Invasive (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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trastuzumab + carboplatin + docetaxel + fluorouracil

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 5.2020]

ERBB2 amplification (continued)

trastuzumab + carboplatin + docetaxel + fluorouracil

Cancer type: Gastric Cancer **Variant class:** ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Adenocarcinoma; Unresectable, Locally Advanced, Recurrent, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2020]

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trastuzumab + chemotherapy

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor negative

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Ductal, Lobular, Mixed, Micropapillary; Invasive (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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trastuzumab + hormone therapy + chemotherapy

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Ductal, Lobular, Mixed, Micropapillary; Invasive (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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trastuzumab + paclitaxel

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor negative

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Ductal, Lobular, Mixed, Micropapillary; Invasive (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

ERBB2 amplification (continued)

ado-trastuzumab emtansine

Cancer type: Head and Neck Cancer **Variant class:** ERBB2 positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Salivary Gland Neoplasm; Recurrent, Unresectable, Metastatic (Line of therapy not specified); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 1.2021]

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irbinitinib + trastuzumab + capecitabine

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Brain Metastases (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2020]

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lapatinib + capecitabine

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Brain Metastases (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2020]

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neratinib + capecitabine

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Brain Metastases (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2020]

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pertuzumab + trastuzumab

Cancer type: Head and Neck Cancer **Variant class:** ERBB2 positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Salivary Gland Neoplasm; Recurrent, Unresectable, Metastatic (Line of therapy not specified); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 1.2021]

ERBB2 amplification (continued)

trastuzumab

Cancer type: Head and Neck Cancer **Variant class:** ERBB2 positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Salivary Gland Neoplasm; Recurrent, Unresectable, Metastatic (Line of therapy not specified); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 1.2021]

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trastuzumab + chemotherapy

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Leptomeningeal Metastases, Spine Metastases (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2020]

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trastuzumab + docetaxel

Cancer type: Head and Neck Cancer **Variant class:** ERBB2 positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Salivary Gland Neoplasm; Recurrent, Unresectable, Metastatic (Line of therapy not specified); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 1.2021]

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neratinib + paclitaxel

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

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Brain Metastases (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2020]

ERBB2 exon 20 insertion

ado-trastuzumab emtansine

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ERBB2 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2021]

trastuzumab deruxtecan

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ERBB2 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2021]

Current EMA Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

EMA information is current as of 2021-02-17. For the most up-to-date information, search www.ema.europa.eu/ema.

ERBB2 amplification

○ ado-trastuzumab emtansine

Cancer type: Breast Cancer **Label as of:** 2020-01-20 **Variant class:** ERBB2 overexpression or ERBB2 amplification

Reference:
https://www.ema.europa.eu/en/documents/product-information/kadcyla-epar-product-information_en.pdf

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○ lapatinib + capecitabine, lapatinib + letrozole, lapatinib + trastuzumab

Cancer type: Breast Cancer **Label as of:** 2021-01-15 **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive or Hormone receptor negative

Reference:
https://www.ema.europa.eu/en/documents/product-information/tyverb-epar-product-information_en.pdf

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○ neratinib

Cancer type: Breast Cancer **Label as of:** 2020-11-13 **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

Reference:
https://www.ema.europa.eu/en/documents/product-information/nerlynx-epar-product-information_en.pdf

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○ pertuzumab + trastuzumab + chemotherapy, pertuzumab + trastuzumab + docetaxel

Cancer type: Breast Cancer **Label as of:** 2020-06-08 **Variant class:** ERBB2 amplification or ERBB2 overexpression

Reference:
https://www.ema.europa.eu/en/documents/product-information/perjeta-epar-product-information_en.pdf

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○ pertuzumab/trastuzumab/hyaluronidase-zzxf + cyclophosphamide + doxorubicin

Cancer type: Breast Cancer **Label as of:** 2021-01-13 **Variant class:** ERBB2 amplification

Reference:
https://www.ema.europa.eu/en/documents/product-information/phesgo-epar-product-information_en.pdf

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ERBB2 amplification (continued)

pertuzumab/trastuzumab/hyaluronidase-zzxf + docetaxel, pertuzumab/trastuzumab/hyaluronidase-zzxf + cyclophosphamide + doxorubicin

Cancer type: Breast Cancer **Label as of:** 2021-01-13 **Variant class:** ERBB2 overexpression

Reference:

https://www.ema.europa.eu/en/documents/product-information/phesgo-epar-product-information_en.pdf

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trastuzumab (Biocon), trastuzumab (Biocon) + anastrozole, trastuzumab (Biocon) + docetaxel, trastuzumab (Biocon) + paclitaxel, trastuzumab (Biocon) + capecitabine + cisplatin, trastuzumab (Biocon) + carboplatin + docetaxel, trastuzumab (Biocon) + cisplatin + fluorouracil, trastuzumab (Biocon) + CMF + doxorubicin + paclitaxel

Cancer type: Breast Cancer, Gastric Cancer, Gastroesophageal Junction Adenocarcinoma **Label as of:** 2021-01-29 **Variant class:** ERBB2 overexpression

Other criteria: ER positive, PR positive

Reference:

https://www.ema.europa.eu/en/documents/product-information/ogivri-epar-product-information_en.pdf

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trastuzumab (Biocon), trastuzumab (Biocon) + anastrozole, trastuzumab (Biocon) + docetaxel, trastuzumab (Biocon) + paclitaxel, trastuzumab (Biocon) + carboplatin + docetaxel, trastuzumab (Biocon) + CMF + doxorubicin + paclitaxel

Cancer type: Breast Cancer **Label as of:** 2021-01-29 **Variant class:** ERBB2 amplification

Other criteria: ER positive, PR positive

Reference:

https://www.ema.europa.eu/en/documents/product-information/ogivri-epar-product-information_en.pdf

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trastuzumab (Celltrion), trastuzumab (Celltrion) + anastrozole, trastuzumab (Celltrion) + docetaxel, trastuzumab (Celltrion) + paclitaxel, trastuzumab (Celltrion) + capecitabine + cisplatin, trastuzumab (Celltrion) + carboplatin + docetaxel, trastuzumab (Celltrion) + cisplatin + fluorouracil, trastuzumab (Celltrion) + CMF + doxorubicin + paclitaxel

Cancer type: Breast Cancer, Gastric Cancer, Gastroesophageal Junction Adenocarcinoma **Label as of:** 2021-02-10 **Variant class:** ERBB2 overexpression

Other criteria: ER positive, PR positive

Reference:

https://www.ema.europa.eu/en/documents/product-information/herzuma-epar-product-information_en.pdf

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ERBB2 amplification (continued)

trastuzumab (Celltrion), trastuzumab (Celltrion) + anastrozole, trastuzumab (Celltrion) + docetaxel, trastuzumab (Celltrion) + paclitaxel, trastuzumab (Celltrion) + carboplatin + docetaxel, trastuzumab (Celltrion) + CMF + doxorubicin + paclitaxel

Cancer type: Breast Cancer **Label as of:** 2021-02-10 **Variant class:** ERBB2 amplification

Other criteria: ER positive, PR positive

Reference:

https://www.ema.europa.eu/en/documents/product-information/herzuma-epar-product-information_en.pdf

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trastuzumab (Henlius), trastuzumab (Henlius) + anastrozole, trastuzumab (Henlius) + docetaxel, trastuzumab (Henlius) + paclitaxel, trastuzumab (Henlius) + capecitabine + cisplatin, trastuzumab (Henlius) + carboplatin + docetaxel, trastuzumab (Henlius) + cisplatin + fluorouracil, trastuzumab (Henlius) + CMF + doxorubicin + paclitaxel

Cancer type: Breast Cancer, Gastric Cancer, Gastroesophageal Junction Adenocarcinoma **Label as of:** 2021-02-09 **Variant class:** ERBB2 overexpression

Other criteria: ER positive, PR positive

Reference:

https://www.ema.europa.eu/en/documents/product-information/zercepac-epar-product-information_en.pdf

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trastuzumab (Henlius), trastuzumab (Henlius) + anastrozole, trastuzumab (Henlius) + docetaxel, trastuzumab (Henlius) + paclitaxel, trastuzumab (Henlius) + carboplatin + docetaxel, trastuzumab (Henlius) + CMF + doxorubicin + paclitaxel

Cancer type: Breast Cancer **Label as of:** 2021-02-09 **Variant class:** ERBB2 amplification

Other criteria: ER positive, PR positive

Reference:

https://www.ema.europa.eu/en/documents/product-information/zercepac-epar-product-information_en.pdf

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trastuzumab (Pfizer), trastuzumab (Pfizer) + anastrozole, trastuzumab (Pfizer) + docetaxel, trastuzumab (Pfizer) + paclitaxel, trastuzumab (Pfizer) + capecitabine + cisplatin, trastuzumab (Pfizer) + carboplatin + docetaxel, trastuzumab (Pfizer) + cisplatin + fluorouracil, trastuzumab (Pfizer) + CMF + doxorubicin + paclitaxel

Cancer type: Breast Cancer, Gastric Cancer, Gastroesophageal Junction Adenocarcinoma **Label as of:** 2020-07-09 **Variant class:** ERBB2 overexpression

Other criteria: ER positive, PR positive

Reference:

https://www.ema.europa.eu/en/documents/product-information/trazimera-epar-product-information_en.pdf

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ERBB2 amplification (continued)

trastuzumab (Pfizer), trastuzumab (Pfizer) + anastrozole, trastuzumab (Pfizer) + docetaxel, trastuzumab (Pfizer) + paclitaxel, trastuzumab (Pfizer) + carboplatin + docetaxel, trastuzumab (Pfizer) + CMF + doxorubicin + paclitaxel

Cancer type: Breast Cancer **Label as of:** 2020-07-09 **Variant class:** ERBB2 amplification

Other criteria: ER positive, PR positive

Reference:

https://www.ema.europa.eu/en/documents/product-information/trazimera-epar-product-information_en.pdf

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trastuzumab (Samsung Bioepis), trastuzumab (Samsung Bioepis) + anastrozole, trastuzumab (Samsung Bioepis) + docetaxel, trastuzumab (Samsung Bioepis) + paclitaxel, trastuzumab (Samsung Bioepis) + capecitabine + cisplatin, trastuzumab (Samsung Bioepis) + carboplatin + docetaxel, trastuzumab (Samsung Bioepis) + cisplatin + fluorouracil, trastuzumab (Samsung Bioepis) + CMF + doxorubicin + paclitaxel

Cancer type: Breast Cancer, Gastric Cancer, Gastroesophageal Junction Adenocarcinoma **Label as of:** 2021-02-10 **Variant class:** ERBB2 overexpression

Other criteria: ER positive, PR positive

Reference:

https://www.ema.europa.eu/en/documents/product-information/ontruzant-epar-product-information_en.pdf

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trastuzumab (Samsung Bioepis), trastuzumab (Samsung Bioepis) + anastrozole, trastuzumab (Samsung Bioepis) + docetaxel, trastuzumab (Samsung Bioepis) + paclitaxel, trastuzumab (Samsung Bioepis) + carboplatin + docetaxel, trastuzumab (Samsung Bioepis) + CMF + doxorubicin + paclitaxel

Cancer type: Breast Cancer **Label as of:** 2021-02-10 **Variant class:** ERBB2 amplification

Other criteria: ER positive, PR positive

Reference:

https://www.ema.europa.eu/en/documents/product-information/ontruzant-epar-product-information_en.pdf

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trastuzumab (Synthon), trastuzumab (Synthon) + anastrozole, trastuzumab (Synthon) + docetaxel, trastuzumab (Synthon) + paclitaxel, trastuzumab (Synthon) + capecitabine + cisplatin, trastuzumab (Synthon) + carboplatin + docetaxel, trastuzumab (Synthon) + cisplatin + fluorouracil, trastuzumab (Synthon) + CMF + doxorubicin + paclitaxel

Cancer type: Breast Cancer, Gastric Cancer, Gastroesophageal Junction Adenocarcinoma **Label as of:** 2019-11-29 **Variant class:** ERBB2 overexpression or ERBB2 overexpression

Other criteria: ER positive, PR positive

Reference:

https://www.ema.europa.eu/en/documents/product-information/kanjinti-epar-product-information_en.pdf

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ERBB2 amplification (continued)

trastuzumab (Synthon), trastuzumab (Synthon) + anastrozole, trastuzumab (Synthon) + docetaxel, trastuzumab (Synthon) + paclitaxel, trastuzumab (Synthon) + carboplatin + docetaxel, trastuzumab (Synthon) + CMF + doxorubicin + paclitaxel

Cancer type: Breast Cancer
Label as of: 2019-11-29
Variant class: ERBB2 amplification or ERBB2 amplification

Other criteria: ER positive, PR positive

Reference:

https://www.ema.europa.eu/en/documents/product-information/kanjinti-epar-product-information_en.pdf

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trastuzumab deruxtecan

Cancer type: Breast Cancer
Label as of: 2021-02-08
Variant class: ERBB2 amplification or ERBB2 overexpression

Reference:

https://www.ema.europa.eu/en/documents/product-information/enhertu-epar-product-information_en.pdf

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trastuzumab, trastuzumab + anastrozole, trastuzumab + docetaxel, trastuzumab + paclitaxel, trastuzumab + capecitabine + cisplatin, trastuzumab + carboplatin + docetaxel, trastuzumab + cisplatin + fluorouracil, trastuzumab + CMF + doxorubicin + paclitaxel

Cancer type: Breast Cancer, Gastric Cancer, Gastroesophageal Junction Adenocarcinoma
Label as of: 2020-08-27
Variant class: ERBB2 overexpression

Other criteria: ER positive, PR positive

Reference:

https://www.ema.europa.eu/en/documents/product-information/herceptin-epar-product-information_en.pdf

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trastuzumab, trastuzumab + anastrozole, trastuzumab + docetaxel, trastuzumab + paclitaxel, trastuzumab + carboplatin + docetaxel, trastuzumab + CMF + doxorubicin + paclitaxel

Cancer type: Breast Cancer
Label as of: 2020-08-27
Variant class: ERBB2 amplification

Other criteria: ER positive, PR positive

Reference:

https://www.ema.europa.eu/en/documents/product-information/herceptin-epar-product-information_en.pdf

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Current ESMO Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

ESMO information is current as of 2021-02-01. For the most up-to-date information, search www.esmo.org.

ERBB2 amplification

○ ado-trastuzumab emtansine

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Residual, Invasive, Local (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Ann Oncol (2019); 30: 1194-1220.]

○ pertuzumab + trastuzumab + chemotherapy

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, PR negative

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Local (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Ann Oncol (2019); 30: 1194-1220.]

○ pertuzumab + trastuzumab + hormone therapy + chemotherapy

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR status

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Luminal B; Local (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Ann Oncol (2019); 30: 1194-1220.]

○ trastuzumab + capecitabine + cisplatin

Cancer type: Gastric Cancer **Variant class:** ERBB2 overexpression

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Advanced (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Gastric Cancer [Ann Oncol (2016) 27 (suppl 5): v38-v49. (eUpdate: 6 May 2019, 4 November 2019)]

ERBB2 amplification (continued)

trastuzumab + chemotherapy

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, PR negative

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Local (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Ann Oncol (2019); 30: 1194-1220.]

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trastuzumab + cisplatin + fluorouracil

Cancer type: Gastric Cancer **Variant class:** ERBB2 overexpression

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Advanced (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Gastric Cancer [Ann Oncol (2016) 27 (suppl 5): v38-v49. (eUpdate: 6 May 2019, 4 November 2019)]

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trastuzumab + hormone therapy + chemotherapy

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR status

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Luminal B; Local (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Ann Oncol (2019); 30: 1194-1220.]

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pertuzumab + trastuzumab + chemotherapy

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

ESMO Level of Evidence/Grade of Recommendation: II / B

Population segment (Line of therapy):
- Local (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Ann Oncol (2019); 30: 1194-1220.]

ERBB2 amplification (continued)

trastuzumab containing regimen

Cancer type: Esophageal Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

ESMO Level of Evidence/Grade of Recommendation: II / B

Population segment (Line of therapy):
- Adenocarcinoma; Metastatic (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Oesophageal Cancer [Ann Oncol (2016) 27 (suppl 5): v50-v57.]

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pertuzumab + trastuzumab + hormone therapy

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR status

ESMO Level of Evidence/Grade of Recommendation: III / B

Population segment (Line of therapy):
- Luminal B; Local (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Ann Oncol (2019); 30: 1194-1220.]

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trastuzumab + hormone therapy

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR status

ESMO Level of Evidence/Grade of Recommendation: III / B

Population segment (Line of therapy):
- Luminal B; Local (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Ann Oncol (2019); 30: 1194-1220.]

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tamoxifen

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

Other criteria: ER positive, PR status

ESMO Level of Evidence/Grade of Recommendation: IV / A

Population segment (Line of therapy):
- Luminal-like, Ductal, Male Breast Cancer; Invasive (Adjuvant therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Ann Oncol (2019); 30: 1194-1220.]

ERBB2 amplification (continued)

tamoxifen

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

Other criteria: ER positive, PR status

ESMO Level of Evidence/Grade of Recommendation: IV / A

Population segment (Line of therapy):
- Luminal A, Luminal B, Ductal; Invasive, Local (Adjuvant therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Ann Oncol (2019); 30: 1194-1220.]

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aromatase inhibitor + luteinizing hormone-releasing factor

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

Other criteria: ER positive, PR status

ESMO Level of Evidence/Grade of Recommendation: IV / B

Population segment (Line of therapy):
- Luminal A, Luminal B, Ductal, Male Breast Cancer; Local, Invasive (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Ann Oncol (2019); 30: 1194-1220.]

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aromatase inhibitor + luteinizing hormone-releasing factor

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

Other criteria: ER positive, PR status

ESMO Level of Evidence/Grade of Recommendation: IV / B

Population segment (Line of therapy):
- Luminal A, Luminal B, Ductal; Invasive, Local (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Ann Oncol (2019); 30: 1194-1220.]

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trastuzumab + hormone therapy

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive

ESMO Level of Evidence/Grade of Recommendation: V / A

Population segment (Line of therapy):
- Luminal B; Local (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Ann Oncol (2019); 30: 1194-1220.]

ERBB2 amplification (continued)

ado-trastuzumab emtansine

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

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Advanced, Progression (Second-line therapy); ESMO-MCBS v1.1 score: 4

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Annals of Oncology (2020), doi: https://doi.org/10.1016/j.annonc.2020.09.010 (ABC 5)]

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pertuzumab + trastuzumab + capecitabine

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

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Advanced (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Annals of Oncology (2020), doi: https://doi.org/10.1016/j.annonc.2020.09.010 (ABC 5)]

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pertuzumab + trastuzumab + chemotherapy

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

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Advanced (First-line therapy); ESMO-MCBS v1.1 score: 4
- Advanced (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Annals of Oncology (2020), doi: https://doi.org/10.1016/j.annonc.2020.09.010 (ABC 5)]

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pertuzumab + trastuzumab + docetaxel

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

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Advanced (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Annals of Oncology (2020), doi: https://doi.org/10.1016/j.annonc.2020.09.010 (ABC 5)]

ERBB2 amplification (continued)

trastuzumab + chemotherapy

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

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Advanced (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Annals of Oncology (2020), doi: https://doi.org/10.1016/j.annonc.2020.09.010 (ABC 5)]

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trastuzumab + taxane

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

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Advanced (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Annals of Oncology (2020), doi: https://doi.org/10.1016/j.annonc.2020.09.010 (ABC 5)]

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trastuzumab + vinorelbine

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

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Advanced (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Annals of Oncology (2020), doi: https://doi.org/10.1016/j.annonc.2020.09.010 (ABC 5)]

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lapatinib + trastuzumab

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

Other criteria: ER positive

ESMO Level of Evidence/Grade of Recommendation: I / B

Population segment (Line of therapy):
- Advanced (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Annals of Oncology (2020), doi: https://doi.org/10.1016/j.annonc.2020.09.010 (ABC 5)]

ERBB2 amplification (continued)

lapatinib + trastuzumab

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

ESMO Level of Evidence/Grade of Recommendation: I / B

Population segment (Line of therapy):
- Advanced, Progression (Line of therapy not specified); ESMO-MCBS v1.1 score: 4

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Annals of Oncology (2020), doi: https://doi.org/10.1016/j.annonc.2020.09.010 (ABC 5)]

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pertuzumab + trastuzumab

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

Other criteria: ER positive

ESMO Level of Evidence/Grade of Recommendation: I / B

Population segment (Line of therapy):
- Advanced (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Annals of Oncology (2020), doi: https://doi.org/10.1016/j.annonc.2020.09.010 (ABC 5)]

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pertuzumab + trastuzumab + paclitaxel

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

ESMO Level of Evidence/Grade of Recommendation: I / B

Population segment (Line of therapy):
- Advanced (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Annals of Oncology (2020), doi: https://doi.org/10.1016/j.annonc.2020.09.010 (ABC 5)]

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pertuzumab + trastuzumab + vinorelbine

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

ESMO Level of Evidence/Grade of Recommendation: II / A

Population segment (Line of therapy):
- Advanced (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Annals of Oncology (2020), doi: https://doi.org/10.1016/j.annonc.2020.09.010 (ABC 5)]

ERBB2 amplification (continued)

pertuzumab + trastuzumab + chemotherapy

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

ESMO Level of Evidence/Grade of Recommendation: II / B

Population segment (Line of therapy):
- Advanced (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Annals of Oncology (2020), doi: https://doi.org/10.1016/j.annonc.2020.09.010 (ABC 5)]

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pertuzumab + trastuzumab + chemotherapy

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

ESMO Level of Evidence/Grade of Recommendation: II / B

Population segment (Line of therapy):
- Advanced (Subsequent therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Annals of Oncology (2020), doi: https://doi.org/10.1016/j.annonc.2020.09.010 (ABC 5)]

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pertuzumab + trastuzumab + nab-paclitaxel

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

ESMO Level of Evidence/Grade of Recommendation: II / B

Population segment (Line of therapy):
- Advanced (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Annals of Oncology (2020), doi: https://doi.org/10.1016/j.annonc.2020.09.010 (ABC 5)]

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trastuzumab deruxtecan

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

ESMO Level of Evidence/Grade of Recommendation: II / B

Population segment (Line of therapy):
- Advanced (Line of therapy not specified); ESMO-MCBS v1.1 score: 2

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Annals of Oncology (2020), doi: https://doi.org/10.1016/j.annonc.2020.09.010 (ABC 5)]

Clinical Trials Summary

ERBB2 amplification

NCT ID	Title	Phase
NCT02314481	Deciphering Antitumour Response and Resistance With INtratumour Heterogeneity - DARWINII	II
NCT04579380	A Phase II Basket Study of Tucatinib in Combination With Trastuzumab in Subjects With Previously Treated, Locally Advanced Unresectable or Metastatic Solid Tumors Driven by HER2 Alterations	II
NCT04706949	A Prospective, Single Center, Single Arm, Phase II Clinical Trial of Pyrotinib Combined With Pemetrexed Plus Carboplatin in the First-line Treatment of Patients With HER2 Mutant or Amplified Recurrent / Metastatic Non-small Cell Lung Cancer	II
No NCT ID	A Single-center, Open-label , Non-randomized Control Clinical Trial On Clinical Features and Medical Treatment of Advanced NSCLC With Rare Gene Mutations	II
NCT04591431	The Rome Trial From Histology to Target: the Road to Personalize Target Therapy and Immunotherapy	II
NCT03602079	A Phase I-II, FIH Study of A166 in Locally Advanced/Metastatic Solid Tumors Expressing Human Epidermal Growth Factor Receptor 2 (HER2) or Are HER2 Amplified That Did Not Respond or Stopped Responding to Approved Therapies	I/II
NCT04311034	A Phase Ib Study to Evaluate the Efficacy and Safety of RC48-ADC for Injection in Subjects With Advanced Non-small Cell Lung Cancer With HER2 Overexpression or HER2 Mutation	I
NCT04460456	A Phase 1/1B, Open-Label, Dose Escalation and Expansion Study of SBT6050 Alone and in Combination With Pembrolizumab in Subjects With Advanced Solid Tumors Expressing HER2	I
NCT04686305	A Phase Ib Multicenter, Open-label Dose-escalation Study to Evaluate the Safety and Tolerability of Trastuzumab Deruxtecan (T-DXd) and Durvalumab in Combination With Cisplatin, Carboplatin or Pemetrexed in First-line Treatment of Patients With Advanced or Metastatic Non-squamous Non-small Cell Lung Cancer (NSCLC) and Human Epidermal Growth Factor Receptor 2 Overexpression (HER2+) (DESTINY-Lung03)	I
NCT04042701	A Phase Ib, Multicenter, Two-Part, Open-Label Study of Trastuzumab Deruxtecan (DS-8201a), An Anti-Human Epidermal Growth Factor Receptor-2 (HER2)-Antibody Drug Conjugate (ADC), In Combination With Pembrolizumab, An Anti-PD-1 Antibody, In Subjects With Locally Advanced/Metastatic Breast Or Non-Small Cell Lung Cancer (NSCLC).	I
NCT02892123	Phase I Trial of ZW25 in Patients With Locally Advanced (Unresectable) and/or Metastatic HER2-expressing Cancers.	I
NCT02675829	A Phase II Trial of Ado-Trastuzumab Emtansine for Patients With HER2 Amplified or Mutant Cancers	II
NCT04632992	MyTACTIC: An Open-Label Phase II Study Evaluating Targeted Therapies in Patients Who Have Advanced Solid Tumors With Genomic Alterations or Protein Expression Patterns Predictive of Response	II
NCT02693535	Targeted Agent and Profiling Utilization Registry (TAPUR) Study	II
NCT03239015	Efficacy and Safety of Targeted Precision Therapy in Refractory Tumor With Druggable Molecular Event	II
NCT04151329	Evaluation for the Safety of BAT1306 and BAT8001 Injection for the Treatment of Patients With HER2-positive Advanced Solid Tumors Phase I/IIa Clinical Trials of Safety, Tolerability and Pharmacokinetic Characteristics	I/II
NCT04278144	Phase I/II Study of BDC-1001 as a Single Agent and in Combination With Pembrolizumab in Patients With Advanced HER2-Expressing Solid Tumors	I/II
NCT04209465	MasterKey-01: A Phase I/II, Open-label, Two-part, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics & Antitumor Activity of BDTX-189, an Inhibitor of Allosteric ErbB Mutations, in Patients w/ Advanced Solid Malignancies	I/II

Clinical Trials Summary (continued)

ERBB2 amplification (continued)

NCT ID	Title	Phase
NCT04092673	A Phase 1-2 Dose-Escalation and Cohort-Expansion Study of Intravenous Zotatifin (eFT226) in Subjects With Selected Advanced Solid Tumor Malignancies	I/II
No NCT ID	Phase I Clinical Study of Safety, Tolerability, Pharmacokinetics and Initial Efficacy of A166 in the Treatment of Patients with Locally Advanced or Metastatic Solid Tumors with HER2.	I
NCT03916094	A Phase I Clinical Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Preliminary Pharmacodynamics of HLX22 Monoclonal Antibody Injection (HER2 Monoclonal Antibody) in Patients With Advanced Solid Tumours Overexpressing HER2	I
NCT03944499	A Phase I, Multicenter, Open-label, Single-arm Study: A Dose-escalation Phase (Phase 1a) Evaluating FS-1502 in Patients With HER2 Expressed Advanced Solid Tumors; and a Dose-expanded Cohort (Phase 1b) Evaluating FS-1502 in Patients With Local Advanced or Metastatic, HER2 Positive Breast Cancer.	I
No NCT ID	Single-Arm, Open-Label, Single-Dose And Multiple-Dose Phase Ia Clinical Study Of Tolerability And Pharmacokinetics Of AMX3009 In Patients With HER2-Positive Advanced Solid Tumors	I
NCT03255070	A Phase I, Multicenter, Open-label, Multiple Dose-escalation Study of ARX788, Intravenously Administered as a Single Agent in Subjects With Advanced Cancers With HER2 Expression	I
NCT04147819	A Phase I Open-label, First-in-human, Multi-center Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Anti-tumor Activity of Thorium-227 Labeled Antibody-chelator Conjugate BAY2701439, in Participants With Advanced HER2-expressing Tumors	I
NCT04511871	A Phase I Trial to Assess Safety, Tolerability and Anti-tumor Activity of Autologous T Cell Modified Chimeric Antigen Receptor (CAR) (CCT303-406) in Patients With Relapsed or Refractory HER2 Positive Solid Tumors	I
NCT03696030	A Phase I Cellular Immunotherapy Study of Intraventricularly Administered Autologous HER2-Targeted Chimeric Antigen Receptor (HER2-CAR) T Cells in Patients With Brain and/or Leptomeningeal Metastases From HER2 Positive Cancers	I
NCT03847168	Phase I Study of KN026 in HER2 Expressing Breast Cancer, Astric/Gastroesophageal Junction Cancer and Other Locally Advanced/Metastatic Solid Tumors	I
NCT04501770	A Phase I Study to Evaluate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics and Immunogenicity Profiles of the Recombinant Anti-HER2 and Anti-CD3 Humanized Bispecific Antibody (M802) in HER2-Positive Advanced Solid Tumors	I
NCT03842085	Evaluation on the Safety and Pharmacokinetics of Recombinant Humanized Bispecific Monoclonal Antibody MBS301 for Injection in Treatment of HER2 Positive Recurrent or Metastatic Malignant Solid Tumor	I
NCT04029922	A Phase I Open-label, Multicenter Dose Escalation Study of MT-5111 in Subjects With Previously Treated Advanced HER2-positive Solid Tumors	I
NCT03065387	Phase I Study of the Pan-ERBB Inhibitor Neratinib Given in Combination With Everolimus, Palbociclib, or Trametinib in Advanced Cancer Subjects With EGFR Mutation/Amplification, HER2 Mutation/ Amplification, or HER3/4 Mutation or KRAS Mutation	I
No NCT ID	Phase I Clinical Study With Advanced Solid Tumors KBP-5209 Treatment	I
No NCT ID	Tolerance And Pharmacokinetics Of Pivotinib In Patients With Advanced Solid Tumors With HER2 Expression	I
NCT03219268	A Phase I, First-in-Human, Open-Label, Dose Escalation Study of MGD013, A Bispecific DART Protein Binding PD-1 and LAG-3 in Patients With Unresectable or Metastatic Neoplasms	I

Clinical Trials Summary (continued)

ERBB2 amplification (continued)

NCT ID	Title	Phase
NCT04487236	A Phase I Clinical Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Efficacy of ZN-A-1041 Enteric Capsules as a Single Agent or in Combination With Capecitabine Tablets in Patients With HER2-Positive Advanced Solid Tumors	I
NCT02442297	Phase I Study of Intracranial Injection of T Cells Expressing HER2-specific Chimeric Antigen Receptors (CAR) in Subjects With HER2-Positive Tumors of the Central Nervous System (iCAR)	I
NCT03330561	A Phase I, Open-Label, Dose Escalation Study of PRS-343 in Patients With HER2-Positive Advanced or Metastatic Solid Tumors	I
NCT04446260	A Phase I Multi-Country, Multi-Center, Open-Label Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Efficacy of SHR-A1811 in HER2 Expressing or Mutated Advanced Malignant Solid Tumor Subjects	I
NCT03297606	Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial	II

ERBB2 exon 20 insertion

NCT ID	Title	Phase
NCT03066206	A Phase II Study of Poziotinib in EGFR in Exon 20 Mutant Advanced Non Small Cell Lung Cancer (NSCLC)	II
NCT03318939	A Phase II Study of Poziotinib in Patients With Non-Small Cell Lung Cancer (NSCLC), Locally Advanced or Metastatic, With EGFR or HER2 Exon 20 Insertion Mutation (ZENITH20).	II
NCT04382300	Safety and Efficacy of Pyrotinib Combined With Thalidomide in Advanced Non-Small-Cell Lung Cancer With HER2 Exon 20 Insertions: A Prospective, Single-arm, Open-label Phase II Study	II
No NCT ID	A Prospective, Single-center, Single-arm Phase II Clinical Study for Advanced Non-small Cell Lung Cancer with EGFR/HER2 gene exon 20 insertion Mutations Treated with Sintilimab	II
NCT03974022	A Phase I/II, Open-Label, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics and Anti-tumor Efficacy of DZD9008 in Patients With Advanced Non-Small Cell Lung Cancer (NSCLC) With EGFR or HER2 Mutation	I/II
NCT02716116	A Phase I/II Study of the Safety, Pharmacokinetics, and Anti-Tumor Activity of the Oral EGFR/HER2 Inhibitor TAK-788 (AP32788) in Non-Small Cell Lung Cancer	I/II
NCT04402008	A Phase I/II Dose Finding Study of Poziotinib in Japanese Patients With Locally Advanced or Metastatic Non-Small Cell Lung Cancer (NSCLC)	I/II
NCT04447118	A Phase III, Randomized, Open-label, Multicenter Study of the Efficacy and Safety of Pyrotinib Versus Docetaxel in Patients With Advanced Non-squamous Non-small Cell Lung Cancer (NSCLC) Harboring a HER2 Exon 20 Mutation Who Progressed on or After Treatment With Platinum Based Chemotherapy	III
NCT04144569	The Effectiveness and Safety Study on PD-1 Combined With Pyrotinib for First-line Chemotherapy Failed HER2 Insertion Mutation Advanced Non-small Cell Lung Cancer	II
NCT04579380	A Phase II Basket Study of Tucatinib in Combination With Trastuzumab in Subjects With Previously Treated, Locally Advanced Unresectable or Metastatic Solid Tumors Driven by HER2 Alterations	II
No NCT ID	A Single-center, Open-label , Non-randomized Control Clinical Trial On Clinical Features and Medical Treatment of Advanced NSCLC With Rare Gene Mutations	II
NCT03805841	Phase II Study - Evaluate the Clinical Activity of Tarloxotinib in Patients With Non-Small Cell Lung Cancer That Harbors an EGFR Exon 20 Insertion or HER2-Activating Mutation and Other Advanced Solid Tumors With NRG1/ERBB Family Gene Fusions.	II

Clinical Trials Summary (continued)

ERBB2 exon 20 insertion (continued)

NCT ID	Title	Phase
NCT04311034	A Phase Ib Study to Evaluate the Efficacy and Safety of RC48-ADC for Injection in Subjects With Advanced Non-small Cell Lung Cancer With HER2 Overexpression or HER2 Mutation	I
NCT02183883	Deciphering Afatinib Response and Resistance With INtratumour Heterogeneity	II
NCT02535507	Single Arm Phase II Clinical Trial to Investigate the Efficacy and Safety of Pyrotinib as a Single Agent in HER2 Mutation Advanced Non-small Cell Lung Cancer Patients Who Failed to Previous at Least 2nd Line Treatments	II
NCT03574402	An Open-label, Multi-center, Phase II Umbrella Study to Assess Efficacy of Targeted Therapy or Immunotherapy Directed by Next Generation Sequencing (NGS) in Chinese Patients With Advanced NSCLC (TRUMP)	II
NCT04706949	A Prospective, Single Center, Single Arm, Phase II Clinical Trial of Pyrotinib Combined With Pemetrexed Plus Carboplatin in the First-line Treatment of Patients With HER2 Mutant or Amplified Recurrent / Metastatic Non-small Cell Lung Cancer	II
NCT04591431	The Rome Trial From Histology to Target: the Road to Personalize Target Therapy and Immunotherapy	II
NCT03983928	A Phase Ib, Open-label, Single Center, Non-randomized Study for Safety and Efficacy of TQB2450 Combined With Anlotinib in Subjects With Advanced Mutation Positive Non-Small Cell Lung Cancer	I/II
No NCT ID	Phase I Study of DZD9008 in EGFR or HER2 Mutant NSCLC Chinese Patients	I
NCT04042701	A Phase Ib, Multicenter, Two-Part, Open-Label Study of Trastuzumab Deruxtecan (DS-8201a), An Anti-Human Epidermal Growth Factor Receptor-2 (HER2)-Antibody Drug Conjugate (ADC), In Combination With Pembrolizumab, An Anti-PD-1 Antibody, In Subjects With Locally Advanced/Metastatic Breast Or Non-Small Cell Lung Cancer (NSCLC).	I
NCT04209465	MasterKey-01: A Phase I/II, Open-label, Two-part, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics & Antitumor Activity of BDTX-189, an Inhibitor of Allosteric ErbB Mutations, in Patients w/ Advanced Solid Malignancies	I/II
NCT02675829	A Phase II Trial of Ado-Trastuzumab Emtansine for Patients With HER2 Amplified or Mutant Cancers	II
NCT01953926	An Open-Label, Phase II Basket Study of Neratinib in Patients With Solid Tumors With Somatic Activating HER Mutations	II
NCT04092673	A Phase 1-2 Dose-Escalation and Cohort-Expansion Study of Intravenous Zotatifin (eFT226) in Subjects With Selected Advanced Solid Tumor Malignancies	I/II
NCT04589845	Tumor-Agnostic Precision Immunooncology and Somatic Targeting Rational for You (TAPISTRY) Phase II Platform Trial	II
NCT04632992	MyTACTIC: An Open-Label Phase II Study Evaluating Targeted Therapies in Patients Who Have Advanced Solid Tumors With Genomic Alterations or Protein Expression Patterns Predictive of Response	II
NCT03810872	An Open Explorative Phase II, Open Label Study of Afatinib in the Treatment of Advanced Cancer Carrying an EGFR, a HER2 or a HER3 Mutation	II
NCT02693535	Targeted Agent and Profiling Utilization Registry (TAPUR) Study	II
NCT03065387	Phase I Study of the Pan-ERBB Inhibitor Neratinib Given in Combination With Everolimus, Palbociclib, or Trametinib in Advanced Cancer Subjects With EGFR Mutation/Amplification, HER2 Mutation/ Amplification, or HER3/4 Mutation or KRAS Mutation	I
No NCT ID	Phase I Clinical Study With Advanced Solid Tumors KBP-5209 Treatment	I

Clinical Trials Summary (continued)

ERBB2 exon 20 insertion (continued)

NCT ID	Title	Phase
NCT04446260	A Phase I Multi-Country, Multi-Center, Open-Label Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Efficacy of SHR-A1811 in HER2 Expressing or Mutated Advanced Malignant Solid Tumor Subjects	I
NCT03297606	Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial	II

EGFR amplification

NCT ID	Title	Phase
NCT03574402	An Open-label, Multi-center, Phase II Umbrella Study to Assess Efficacy of Targeted Therapy or Immunotherapy Directed by Next Generation Sequencing (NGS) in Chinese Patients With Advanced NSCLC (TRUMP)	II
NCT04429542	First-in-Human, Phase I/Ib, Open-label, Multicenter Study of Bifunctional EGFR/TGFß Fusion Protein BCA101 Alone and in Combination With Pembrolizumab in Patients With EGFR-Driven Advanced Solid Tumors	I
No NCT ID	A Pilot Study for Apatinib Mesylate Combined with Gefitinib in First-line Treatment of Lung Adenocarcinoma with Malignant Pleural Effusion or Pericardial Effusion	IV
No NCT ID	A Phase IIa Clinical Study of crizotinib in the Treatment of Advanced Non-small Cell Lung Cancer	II
NCT02447419	Study to Evaluate the Safety and Efficacy of Gefitinib, in Subjects With EFGR Amplification Refractory Solid Tumors	II
NCT03065387	Phase I Study of the Pan-ERBB Inhibitor Neratinib Given in Combination With Everolimus, Palbociclib, or Trametinib in Advanced Cancer Subjects With EGFR Mutation/Amplification, HER2 Mutation/ Amplification, or HER3/4 Mutation or KRAS Mutation	I
NCT03841110	FT500 as Monotherapy and in Combination With Immune Checkpoint Inhibitors in Subjects With Advanced Solid Tumors (Phase I)	I
NCT03297606	Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial	II

Alerts Informed By Public Data Sources

Current FDA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

FDA information is current as of 2021-02-17. For the most up-to-date information, search www.fda.gov.

ERBB2 amplification

zanidatamab

Cancer type: Cholangiocarcinoma

Variant class: ERBB2 amplification

Supporting Statement:

The FDA has granted Breakthrough Therapy Designation to the HER2 targeted bispecific antibody, zanidatamab, for:

- Previously-treated HER2 gene-amplified biliary tract cancer (BTC).

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://ir.zymeworks.com/News-Releases/news-details/2020/Zymeworks-Receives-FDA-Breakthrough-Therapy-Designation-for-HER2-Targeted-Bispecific-Antibody-Zanidatamab-in-Patients-with-Biliary-Tract-Cancer/default.aspx

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zanidatamab + chemotherapy

Cancer type: Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

Supporting Statement:

The FDA has granted Breakthrough Therapy Designation to the HER2 targeted bispecific antibody, zanidatamab, for:

- Previously-treated HER2 gene-amplified biliary tract cancer (BTC).

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://ir.zymeworks.com/News-Releases/news-details/2020/Zymeworks-Receives-FDA-Breakthrough-Therapy-Designation-for-HER2-Targeted-Bispecific-Antibody-Zanidatamab-in-Patients-with-Biliary-Tract-Cancer/default.aspx

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disitamab vedotin

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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ERBB2 exon 20 insertion

BDTX-189

Cancer type: Solid Tumor **Variant class:** ERBB2 exon 20 insertion

Supporting Statement:
The FDA has granted Fast Track Designation to BDTX-189 for solid tumors harboring a HER2 mutation or an EGFR or HER2 exon 20 insertion after progression on prior therapy.

Reference:

https://investors.blackdiamondtherapeutics.com/news-releases/news-release-details/black-diamond-therapeutics-granted-fast-track-designation-fda

Current NCCN Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

NCCN information is current as of 2021-02-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

ERBB2 amplification

pertuzumab + trastuzumab + cyclophosphamide + docetaxel + doxorubicin

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Summary:

NCCN Guidelines® include the following supporting statement(s):

- "Trastuzumab given in combination with an anthracycline is associated with significant cardiac toxicity. Concurrent use of trastuzumab and pertuzumab with an anthracycline should be avoided."

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

pertuzumab + trastuzumab + cyclophosphamide + doxorubicin + paclitaxel

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Summary:

NCCN Guidelines® include the following supporting statement(s):

- "Trastuzumab given in combination with an anthracycline is associated with significant cardiac toxicity. Concurrent use of trastuzumab and pertuzumab with an anthracycline should be avoided."

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

ERBB2 amplification (continued)

trastuzumab + anthracycline

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

Summary:
NCCN Guidelines® include the following supporting statement(s):

- "The use of trastuzumab in combination with anthracyclines is not recommended"
- "Trastuzumab may be combined with other chemotherapy agents for first-line therapy, but is not recommended for use with anthracyclines."

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 5.2020]

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trastuzumab + cyclophosphamide + docetaxel + doxorubicin

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Summary:

NCCN Guidelines® include the following supporting statement(s):

- "Trastuzumab given in combination with an anthracycline is associated with significant cardiac toxicity. Concurrent use of trastuzumab and pertuzumab with an anthracycline should be avoided."

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

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trastuzumab + cyclophosphamide + doxorubicin + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Summary:

NCCN Guidelines® include the following supporting statement(s):

- "Trastuzumab given in combination with an anthracycline is associated with significant cardiac toxicity. Concurrent use of trastuzumab and pertuzumab with an anthracycline should be avoided."

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2021]

ERBB2 exon 20 insertion

afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ERBB2 mutation

Summary:

NCCN Guidelines® include the following supporting statement(s):

- "The NCCN NSCLC Panel does not recommend single-agent therapy with trastuzumab or afatinib (both for ERBB2 mutations), because response rates are lower and treatment is less effective when these agents are used for patients with ERBB2 mutations."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2021]

ERBB2 exon 20 insertion (continued)

trastuzumab

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ERBB2 mutation

Summary:

NCCN Guidelines® include the following supporting statement(s):

- "The NCCN NSCLC Panel does not recommend single-agent therapy with trastuzumab or afatinib (both for ERBB2 mutations), because response rates are lower and treatment is less effective when these agents are used for patients with ERBB2 mutations."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2021]

Current ESMO Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

ESMO information is current as of 2021-02-01. For the most up-to-date information, search www.esmo.org.

ERBB2 amplification

lapatinib + trastuzumab + chemotherapy

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

ESMO Level of Evidence/Grade of Recommendation: I / E

Summary:

ESMO Clinical Practice Guidelines include the following supporting statement(s):

- "Dual blockade with trastuzumab/lapatinib has not led to improved long-term outcomes and cannot therefore be recommended [I, E]."

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Ann Oncol (2019); 30: 1194-1220.]

aromatase inhibitor

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR status

ESMO Level of Evidence/Grade of Recommendation: IV / E

Summary:

ESMO Clinical Practice Guidelines include the following supporting statement(s):

- "An AI alone should not be used as adjuvant ET in male breast cancer patients [IV, E]."

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Ann Oncol (2019); 30: 1194-1220.]

ERBB2 amplification (continued)

trastuzumab + anthracycline

Cancer type: Breast Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

ESMO Level of Evidence/Grade of Recommendation: I / D

Summary:

ESMO Clinical Practice Guidelines include the following supporting statement(s):

- "Trastuzumab should usually not be given concomitantly with anthracycline-based ChT [I, D]".

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Ann Oncol (2019); 30: 1194-1220.]

Signatures

Testing Personnel:

2021.04.09
09:41:18 +08'00'

Laboratory Supervisor:

2021.04.09
09:41:32 +08'00'

Pathologist:

2021.04.09
09:41:44 +08'00'

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