Taipei Veterans General Hospital

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Sample Information

Patient Name: 吳嘉純
Gender: Female
ID No.: A221960157
History No.: 28259543
Age: 51

Ordering Doctor: DOC3016D 江起陸
Ordering REQ.: C2AAFP5
Signing in Date: 2022/01/12

Path No.: S111-98107
MP No.: F22006
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S110-40515A
Percentage of tumor cells: 50%

Reporting Doctor: DOC5466K 葉奕成 (Phone: 8#5466)

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	None detected	NTRK1	None detected
BRAF	None detected	NTRK2	None detected
EGFR	None detected	NTRK3	None detected
ERBB2	***ERBB2 amplification, ERBB2 exon 20 insertion***	RET	None detected
KRAS	None detected	ROS1	None detected
MET	None 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 **Prognostic significance:** None **Diagnostic significance:** None	None	**ado-trastuzumab emtansine** [1, 2] **irbinitinib + trastuzumab + chemotherapy** [1, 2] **lapatinib + chemotherapy** [1, 2] **lapatinib + hormone therapy** [1, 2] **lapatinib + trastuzumab** [2] **margetuximab + chemotherapy** [1] **neratinib** [1, 2] **neratinib + chemotherapy** [1] **pembrolizumab + trastuzumab + chemotherapy** [1] **pertuzumab + trastuzumab + chemotherapy** [1, 2] **pertuzumab/trastuzumab/ hyaluronidase-zzxf + chemotherapy** [1, 2] **trastuzumab and hyaluronidase-oysk** [1] **trastuzumab and hyaluronidase-oysk + chemotherapy** [1] **trastuzumab deruxtecan** [1, 2] **trastuzumab*** [1, 2] **trastuzumab* + chemotherapy** [1, 2] **trastuzumab* + hormone therapy** [2] hormone therapy lapatinib + trastuzumab + hormone therapy margetuximab pertuzumab + trastuzumab pertuzumab + trastuzumab + hormone therapy pertuzumab + trastuzumab + hormone therapy + chemotherapy trastuzumab + hormone therapy + chemotherapy trastuzumab containing regimen	0
IA	*ERBB2 exon 20 insertion* erb-b2 receptor tyrosine kinase 2 Allele Frequency: 78.93% **Prognostic significance:** None **Diagnostic significance:** None	ado-trastuzumab emtansine trastuzumab deruxtecan	None	3

Public data sources included in relevant therapies: FDA1, NCCN, **EMA**2, ESMO
Public data sources included in prognostic and diagnostic significance: NCCN, 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**

Prevalent cancer biomarkers without relevant evidence based on included data sources

FGFR4 amplification

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.(G776delinsVC)	c.2326_2327insTGT	COSM12553	chr17:37880997	78.93%	NM_004448.3	nonframeshift Insertion	1941

Copy Number Variations

Gene	Locus	Copy Number
FGFR4	chr5:176517312	7.66
ERBB2	chr17:37868126	8.08

Biomarker Descriptions

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[2]. 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[3,4,5].

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[6,7,8,9,10,11,12,13]. Recurrent somatic activating mutations in ERBB2/HER2 occur at low frequencies (<1%) in diverse cancer types[13,14,15]. 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[16,17]. Trastuzumab[18] 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[19] (2012), a humanized monoclonal antibody that inhibits HER2 dimerization, and ado-trastuzumab emtansine[20] (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[21]. In addition to monoclonal antibodies, the small molecule inhibitor lapatinib[22], 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[23], 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[23] 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[24] was FDA approved for HER2 overexpressing or amplified breast cancer in combination with trastuzumab and capecitabine. In 2021, the PD-1 blocking antibody, pembrolizumab, in combination with trastuzumab, fluoropyrimidine- and platinum-based chemotherapy, was approved for HER2 amplified gastric or gastroesophageal (GEJ) adenocarcinoma in the first line[25]. The vaccine, nelipepimut-S[26], 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[27] in patients with ERBB2 positive breast cancer previously treated with an anti-HER2 therapy. In 2019, the novel bispecific antibody, zanidatamab[28], received fast-track designation in combination with standard chemotherapy for patients with HER2-overexpressing gastroesophageal adenocarcinoma (GEA) and breakthrough therapy designation (2020) as a monotherapy for patients with HER2-amplified biliary tract cancer[29]. In 2020, BDTX-189[30] 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[31]. In 2021, the antibody-drug conjugate ARX788[32] received fast-track designation as a monotherapy for advanced or metastatic HER2-positive breast

Biomarker Descriptions (continued)

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[33,34,35,36,37]. ERBB2 kinase domain mutations R896G and V659E both showed response to afatinib in two NSCLC case studies[38,39]. Additionally, acquired HER2 mutations in estrogen receptor-positive (ER+) breast cancer have been shown to confer resistance to hormone therapy[40]. However, this was shown to be overcome by neratinib in combination with therapies targeting ER[40].

FGFR4 (fibroblast growth factor receptor 4)

Background: The FGFR4 gene encodes fibroblast growth receptor 4, a member of the fibroblast growth-factor receptor (FGFR) family that also includes FGFR1, 2, and 3. These proteins are single-transmembrane receptors composed of three extracellular immunoglobulin (Ig)-type domains and an intracellular kinase domain. Upon FGF-mediated stimulation, FGFRs activate several oncogenic signaling pathways, including the RAS/RAF/MEK/ERK, PI3K/AKT/MTOR, PLC/PKC, and JAK/STAT pathways influencing cell proliferation, migration, and survival[41,42,43]. FGFR4 selectively binds the ligand FGF19, wherein FGF19-mediated aberrant signaling has been identified as an oncogenic driver in hepatocellular carcinoma[44,45].

Alterations and prevalence: Aberrations most common to the FGFR family are amplifications, followed by mutations and fusions. The majority of these aberrations result in gain of function[46]. FGFR4 exhibits amplification in up to 15% of clear-cell renal cell carcinomas, with somatic mutations observed in up to 6% of melanomas and uterine cancer[12,13].

Potential relevance: Currently, no targeted therapies are approved for FGFR4 aberrations. However, FDA-approved multi-kinase inhibitors known to inhibit FGFR family members, including regorafenib (2013), ponatinib (2012), lenvatinib (2015), nintedanib (2014), and pazopanib (2009), have demonstrated anti-tumor activity in select cancer types harboring FGFR alterations[47,48,49,50,51,52,53]. Selective, irreversible FGFR4 inhibitors, including BLU-554, are under current clinical- trial evaluation. In a phase-I clinical study of BLU-554 in patients with FGF19-positive advanced hepatocellular carcinoma, the overall response rate was 16%[54].

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	○	○	○	○	✖
irbinitinib + trastuzumab + capecitabine	○	○	○	○	✖
lapatinib + capecitabine	○	○	○	○	✖
neratinib	○	○	○	○	✖
pertuzumab + trastuzumab + chemotherapy	○	○	○	○	✖
pertuzumab + trastuzumab + docetaxel	○	○	○	○	✖
trastuzumab + capecitabine + cisplatin	○	○	○	○	✖
trastuzumab + cisplatin + fluorouracil	○	○	○	○	✖
trastuzumab deruxtecan	○	○	○	○	✖
trastuzumab	○	○	○	✖	✖
trastuzumab + carboplatin + docetaxel	○	○	○	✖	✖
trastuzumab + docetaxel	○	○	○	✖	✖
trastuzumab + 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*
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	○	✖	○	✖	✖
trastuzumab (Samsung Bioepis)	○	✖	○	✖	✖
trastuzumab (Samsung Bioepis) + capecitabine + cisplatin	○	✖	○	✖	✖
trastuzumab (Samsung Bioepis) + carboplatin + docetaxel	○	✖	○	✖	✖
trastuzumab (Samsung Bioepis) + cisplatin + fluorouracil	○	✖	○	✖	✖

* 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) + docetaxel	○	✖	○	✖	✖
trastuzumab (Samsung Bioepis) + paclitaxel	○	✖	○	✖	✖
margetuximab + chemotherapy	○	✖	✖	○	✖
pembrolizumab + trastuzumab + chemotherapy + fluoropyrimidine	○	✖	✖	✖	✖
trastuzumab and hyaluronidase-oysk	○	✖	✖	✖	✖
trastuzumab and hyaluronidase-oysk + carboplatin + docetaxel	○	✖	✖	✖	✖
trastuzumab and hyaluronidase-oysk + cyclophosphamide + doxorubicin + paclitaxel	○	✖	✖	✖	✖
trastuzumab and hyaluronidase-oysk + docetaxel	○	✖	✖	✖	✖
trastuzumab and hyaluronidase-oysk + paclitaxel	○	✖	✖	✖	✖
lapatinib + trastuzumab	✖	○	○	○	✖
pertuzumab + trastuzumab	✖	○	✖	○	✖
pertuzumab + trastuzumab + hormone therapy + chemotherapy	✖	○	✖	○	✖
pertuzumab + trastuzumab + paclitaxel	✖	○	✖	○	✖
tamoxifen	✖	○	✖	○	✖
trastuzumab + chemotherapy	✖	○	✖	○	✖
trastuzumab + hormone therapy + chemotherapy	✖	○	✖	○	✖
aromatase inhibitor	✖	○	✖	✖	✖
fulvestrant	✖	○	✖	✖	✖
hormone therapy	✖	○	✖	✖	✖
lapatinib + aromatase inhibitor	✖	○	✖	✖	✖
lapatinib + trastuzumab + aromatase inhibitor	✖	○	✖	✖	✖
margetuximab + capecitabine	✖	○	✖	✖	✖
margetuximab + eribulin	✖	○	✖	✖	✖
margetuximab + gemcitabine	✖	○	✖	✖	✖
margetuximab + vinorelbine	✖	○	✖	✖	✖
neratinib + 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*
pembrolizumab + trastuzumab + capecitabine + cisplatin	✖	○	✖	✖	✖
pembrolizumab + trastuzumab + capecitabine + oxaliplatin	✖	○	✖	✖	✖
pembrolizumab + trastuzumab + cisplatin + fluorouracil	✖	○	✖	✖	✖
pembrolizumab + trastuzumab + fluorouracil + oxaliplatin	✖	○	✖	✖	✖
pertuzumab + trastuzumab + carboplatin + docetaxel	✖	○	✖	✖	✖
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 + vinorelbine	✖	○	✖	✖	✖
pertuzumab/trastuzumab/hyaluronidase-zzxf + carboplatin + docetaxel	✖	✖	○	✖	✖
pertuzumab/trastuzumab/hyaluronidase-zzxf + cyclophosphamide + doxorubicin + fluorouracil	✖	✖	○	✖	✖
pertuzumab/trastuzumab/hyaluronidase-zzxf + cyclophosphamide + epirubicin	✖	✖	○	✖	✖

* 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*
pertuzumab/trastuzumab/hyaluronidase-zzxf + paclitaxel	✖	✖	○	✖	✖
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	✖	✖	○	✖	✖
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	✖	✖	○	✖	✖

* 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 + anastrozole	✖	✖	○	✖	✖
trastuzumab + CMF + doxorubicin + paclitaxel	✖	✖	○	✖	✖
aromatase inhibitor + luteinizing hormone-releasing factor	✖	✖	✖	○	✖
lapatinib + hormone therapy	✖	✖	✖	○	✖
lapatinib + trastuzumab + hormone therapy	✖	✖	✖	○	✖
margetuximab	✖	✖	✖	○	✖
neratinib + chemotherapy	✖	✖	✖	○	✖
pertuzumab + trastuzumab + hormone therapy	✖	✖	✖	○	✖
pertuzumab + trastuzumab + nab-paclitaxel	✖	✖	✖	○	✖
trastuzumab + hormone therapy	✖	✖	✖	○	✖
trastuzumab containing regimen	✖	✖	✖	○	✖

ERBB2 exon 20 insertion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
ado-trastuzumab emtansine	✖	●	✖	✖	● (II)
trastuzumab deruxtecan	✖	●	✖	✖	✖
pyrotinib	✖	✖	✖	✖	● (III)
DZD-9008	✖	✖	✖	✖	● (I/II)

* 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 2021-11-17. 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 overexpression or ERBB2 amplification

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:** 2021-06-28 **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/2021/208051s009lbl.pdf

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ERBB2 amplification (continued)

pembrolizumab + trastuzumab + chemotherapy + fluoropyrimidine

Cancer type: Gastric Cancer, Gastroesophageal Junction Adenocarcinoma **Label as of:** 2021-11-17 **Variant class:** ERBB2 overexpression

Indications and usage:

KEYTRUDA® is a programmed death receptor-1 (PD-1)-blocking antibody indicated:

Melanoma

- for the treatment of patients with unresectable or metastatic melanoma.
- for the adjuvant treatment of patients with melanoma with involvement of lymph node(s) following complete resection.

Non-Small Cell Lung Cancer (NSCLC)

- in combination with pemetrexed and platinum chemotherapy, as first-line treatment of patients with metastatic nonsquamous NSCLC, with no EGFR or ALK genomic tumor aberrations.
- in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, as first-line treatment of patients with metastatic squamous NSCLC.
- as a single agent for the first-line treatment of patients with NSCLC expressing PD-L1 [Tumor Proportion Score (TPS) ≥ 1%] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is:
  - stage III where patients are not candidates for surgical resection or definitive chemoradiation, or
  - metastatic.
- as a single agent for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥1%) as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving KEYTRUDA®.

Head and Neck Squamous Cell Cancer (HNSCC)

- in combination with platinum and FU for the first-line treatment of patients with metastatic or with unresectable, recurrent HNSCC.
- as a single agent for the first-line treatment of patients with metastatic or with unresectable, recurrent HNSCC whose tumors express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by an FDA-approved test.
- as a single agent for the treatment of patients with recurrent or metastatic HNSCC with disease progression on or after platinum-containing chemotherapy.

Classical Hodgkin Lymphoma (cHL)

- for the treatment of adult patients with relapsed or refractory cHL.
- for the treatment of pediatric patients with refractory cHL, or cHL that has relapsed after 2 or more lines of therapy.

Primary Mediastinal Large B-Cell Lymphoma (PMBCL)

- for the treatment of adult and pediatric patients with refractory PMBCL, or who have relapsed after 2 or more prior lines of therapy.
- Limitations of Use: KEYTRUDA® is not recommended for treatment of patients with PMBCL who require urgent cytoreductive therapy.

Urothelial Carcinoma

- for the treatment of patients with locally advanced or metastatic urothelial carcinoma who:
  - are not eligible for any platinum-containing chemotherapy, or
  - who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy
- for the treatment of patients with Bacillus Calmette-Guerin (BCG)-unresponsive, high-risk, non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy.

Microsatellite Instability-High or Mismatch Repair Deficient Cancer

- for the treatment of adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options.[1]

ERBB2 amplification (continued)

- Limitations of Use: The safety and effectiveness of KEYTRUDA® in pediatric patients with MSI-H central nervous system cancers have not been established.

Microsatellite Instability-High or Mismatch Repair Deficient Colorectal Cancer (CRC)

- for the treatment of patients with unresectable or metastatic MSI-H or dMMR colorectal cancer (CRC).

Gastric Cancer

- in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy, for the first-line treatment of patients with locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma.[1]
- as a single agent for the treatment of patients with recurrent locally advanced or metastatic gastric or GEJ adenocarcinoma whose tumors express PD-L1 (CPS ≥1) as determined by an FDA-approved test, with disease progression on or after 2 or more prior lines of therapy including fluoropyrimidine- and platinum-containing chemotherapy and if appropriate, HER2/neu-targeted therapy.[1]

Esophageal Cancer

- for the treatment of patients with locally advanced or metastatic esophageal or gastroesophageal junction (GEJ) (tumors with epicenter 1 to 5 centimeters above the GEJ) carcinoma that is not amenable to surgical resection or definitive chemoradiation either:
  - in combination with platinum- and fluoropyrimidine-based chemotherapy, or
  - as a single agent after one or more prior lines of systemic therapy for patients with tumors of squamous cell histology that express PD-L1 (CPS ≥10) as determined by an FDA-approved test.

Cervical Cancer

- in combination with chemotherapy, with or without bevacizumab, for the treatment of patients with persistent, recurrent, or metastatic cervical cancer whose tumors express PD-L1 (CPS ≥1) as determined by an FDA-approved test.
- as a single agent for the treatment of patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumors express PD-L1 (CPS ≥1) as determined by an FDA-approved test.

Hepatocellular Carcinoma (HCC)

- for the treatment of patients with HCC who have been previously treated with sorafenib.[1]

Merkel Cell Carcinoma (MCC)

- for the treatment of adult and pediatric patients with recurrent locally advanced or metastatic Merkel cell carcinoma.[1]

Renal Cell Carcinoma (RCC)

- in combination with axitinib, for the first-line treatment of adult patients with advanced RCC.
- in combination with lenvatinib, for the first-line treatment of adult patients with advanced RCC.
- for the adjuvant treatment of patients with RCC at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions.

Endometrial Carcinoma

- in combination with lenvatinib, for the treatment of patients with advanced endometrial carcinoma that is not MSI-H or dMMR, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.

Tumor Mutational Burden-High (TMB-H) Cancer

- for the treatment of adult and pediatric patients with unresectable or metastatic tumor mutational burden-high (TMB-H) [≥10 mutations/megabase (mut/Mb)] solid tumors, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options.[1]
- Limitations of Use: The safety and effectiveness of KEYTRUDA® in pediatric patients with TMB-H central nervous system cancers have not been established.

Cutaneous Squamous Cell Carcinoma (cSCC)and description of clinical benefit in the confirmatory trial

- for the treatment of patients with recurrent or metastatic cSCC or locally advanced cSCC that is not curable by surgery or radiation.

Triple-Negative Breast Cancer (TNBC)

- for the treatment of patients with high-risk early-stage TNBC in combination with chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery.

ERBB2 amplification (continued)

- in combination with chemotherapy, for the treatment of patients with locally recurrent unresectable or metastatic TNBC whose tumors express PD-L1 (CPS ≥10) as determined by an FDA approved test.

Adult Indications: Additional Dosing Regimen of 400 mg Every 6 Weeks

- for use at an additional recommended dosage of 400 mg every 6 weeks for all approved adult indications.[2]

[1] This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

[2] This indication is approved under accelerated approval based on pharmacokinetic data, the relationship of exposure to efficacy, and the relationship of exposure to safety. Continued approval for this dosing may be contingent upon verification and description of clinical benefit in the confirmatory trials.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125514s113lbl.pdf

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○ 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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ERBB2 amplification (continued)

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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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 amplification or ERBB2 overexpression

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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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 overexpression or ERBB2 amplification

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 overexpression or ERBB2 amplification

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 and hyaluronidase-oysk, trastuzumab and hyaluronidase-oysk + docetaxel, trastuzumab and hyaluronidase-oysk + paclitaxel, trastuzumab and hyaluronidase-oysk + carboplatin + docetaxel

Cancer type: Breast Cancer

Label as of: 2019-02-28

Variant class: 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 and hyaluronidase-oysk, trastuzumab and hyaluronidase-oysk + docetaxel, trastuzumab and hyaluronidase-oysk + paclitaxel, trastuzumab and hyaluronidase-oysk + carboplatin + docetaxel, trastuzumab and hyaluronidase-oysk + cyclophosphamide + doxorubicin + paclitaxel

Cancer type: Breast Cancer **Label as of:** 2019-02-28 **Variant class:** ERBB2 overexpression

Other criteria: ER negative, PR negative

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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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 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, 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

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 2021-11-01. 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; Invasive, Recurrent, Unresectable, Local, Regional (Second-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

○ 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; Invasive, Recurrent, Unresectable, Local, Regional (Third-line therapy, Subsequent therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

○ 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; Invasive, Recurrent, Unresectable, Local, Regional (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

ERBB2 amplification (continued)

trastuzumab + capecitabine + cisplatin

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or 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 4.2021]

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trastuzumab + capecitabine + cisplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or 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 5.2021]

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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: 1

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

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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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 8.2021]

ERBB2 amplification (continued)

trastuzumab + cisplatin + fluorouracil

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or 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 4.2021]

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trastuzumab + cisplatin + fluorouracil

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or 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 5.2021]

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ado-trastuzumab emtansine

Cancer type: Head and Neck Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

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 3.2021]

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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; Invasive, Recurrent, Unresectable, Local, Regional (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

ERBB2 amplification (continued)

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; Invasive, Recurrent, Unresectable, Local, Regional (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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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 8.2021]

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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; Invasive, Recurrent, Unresectable, Local, Regional (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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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; Invasive, Recurrent, Unresectable, Local, Regional (Third-line therapy, Subsequent therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

ERBB2 amplification (continued)

lapatinib + capecitabine

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

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 2.2021]

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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; Invasive, Recurrent, Unresectable, Local, Regional (Third-line therapy, Subsequent therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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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 3.2021]

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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 2.2021]

ERBB2 amplification (continued)

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; Invasive, Recurrent, Unresectable, Local, Regional (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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margetuximab + 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; Invasive, Recurrent, Unresectable, Local, Regional (Third-line therapy, Subsequent therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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margetuximab + eribulin

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; Invasive, Recurrent, Unresectable, Local, Regional (Third-line therapy, Subsequent therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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margetuximab + gemcitabine

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; Invasive, Recurrent, Unresectable, Local, Regional (Third-line therapy, Subsequent therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

ERBB2 amplification (continued)

margetuximab + 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; Invasive, Recurrent, Unresectable, Local, Regional (Third-line therapy, Subsequent therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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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); Consider

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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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; Invasive, Recurrent, Unresectable, Local, Regional (Third-line therapy, Subsequent therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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neratinib + capecitabine

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

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 2.2021]

ERBB2 amplification (continued)

pembrolizumab + trastuzumab + capecitabine + cisplatin

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or 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 4.2021]

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pembrolizumab + trastuzumab + capecitabine + cisplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or 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 5.2021]

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pembrolizumab + trastuzumab + capecitabine + oxaliplatin

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or 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 4.2021]

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pembrolizumab + trastuzumab + capecitabine + oxaliplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or 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 5.2021]

ERBB2 amplification (continued)

pembrolizumab + trastuzumab + cisplatin + fluorouracil

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or 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 4.2021]

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pembrolizumab + trastuzumab + cisplatin + fluorouracil

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or 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 5.2021]

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pembrolizumab + trastuzumab + fluorouracil + oxaliplatin

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or 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 4.2021]

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pembrolizumab + trastuzumab + fluorouracil + oxaliplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or 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 5.2021]

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 3.2021]

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pertuzumab + trastuzumab

Cancer type: Head and Neck Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

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 3.2021]

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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 2.2021]

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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):
- Invasive (Adjuvant therapy); Consider

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

ERBB2 amplification (continued)

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 8.2021]

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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 8.2021]

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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 8.2021]

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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; Invasive, Recurrent, Unresectable, Local, Regional (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

ERBB2 amplification (continued)

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; Invasive, Recurrent, Unresectable, Local, Regional (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

---

trastuzumab

Cancer type: Head and Neck Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

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 3.2021]

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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; Invasive, Recurrent, Unresectable, Local, Regional (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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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; Invasive, Recurrent, Unresectable, Local, Regional (Third-line therapy, Subsequent therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

ERBB2 amplification (continued)

trastuzumab + capecitabine

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or 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 4.2021]

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trastuzumab + capecitabine

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or 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 5.2021]

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trastuzumab + capecitabine + oxaliplatin

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or 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 4.2021]

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trastuzumab + capecitabine + oxaliplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or 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 5.2021]

ERBB2 amplification (continued)

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 8.2021]

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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; Invasive, Recurrent, Unresectable, Local, Regional (Third-line therapy, Subsequent therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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trastuzumab + carboplatin + paclitaxel

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma **Variant class:** ERBB2 amplification or 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 4.2021]

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trastuzumab + carboplatin + paclitaxel

Cancer type: Gastric Cancer **Variant class:** ERBB2 amplification or 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 5.2021]

ERBB2 amplification (continued)

trastuzumab + carboplatin + paclitaxel

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Uterine Neoplasms [Version 4.2021]

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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); Consider

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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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; Invasive, Recurrent, Unresectable, Local, Regional (Third-line therapy, Subsequent therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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trastuzumab + cisplatin + docetaxel

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma **Variant class:** ERBB2 amplification or 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 4.2021]

ERBB2 amplification (continued)

trastuzumab + cisplatin + docetaxel

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or 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 5.2021]

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trastuzumab + cisplatin + docetaxel + fluorouracil

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or 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 4.2021]

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trastuzumab + cisplatin + docetaxel + fluorouracil

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or 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 5.2021]

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trastuzumab + cisplatin + paclitaxel

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or 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 4.2021]

ERBB2 amplification (continued)

trastuzumab + cisplatin + paclitaxel

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or 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 5.2021]

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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 8.2021]

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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; Invasive, Recurrent, Unresectable, Local, Regional (Third-line therapy, Subsequent therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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trastuzumab + docetaxel

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or 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 4.2021]

ERBB2 amplification (continued)

trastuzumab + docetaxel

Cancer type: Gastric Cancer **Variant class:** ERBB2 amplification or 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 5.2021]

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trastuzumab + docetaxel

Cancer type: Head and Neck Cancer **Variant class:** ERBB2 amplification or ERBB2 overexpression

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 3.2021]

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trastuzumab + docetaxel + fluorouracil + oxaliplatin

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma **Variant class:** ERBB2 amplification or 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 4.2021]

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trastuzumab + docetaxel + fluorouracil + oxaliplatin

Cancer type: Gastric Cancer **Variant class:** ERBB2 amplification or 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 5.2021]

ERBB2 amplification (continued)

trastuzumab + fluorouracil

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or 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 4.2021]

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trastuzumab + fluorouracil

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or 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 5.2021]

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trastuzumab + fluorouracil + irinotecan

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or 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 4.2021]

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trastuzumab + fluorouracil + irinotecan

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or 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 5.2021]

ERBB2 amplification (continued)

trastuzumab + fluorouracil + oxaliplatin

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or 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 4.2021]

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trastuzumab + fluorouracil + oxaliplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or 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 5.2021]

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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; Invasive, Recurrent, Unresectable, Local, Regional (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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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 8.2021]

ERBB2 amplification (continued)

trastuzumab + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Invasive (Adjuvant therapy); Consider

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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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; Invasive, Recurrent, Unresectable, Local, Regional (Third-line therapy, Subsequent therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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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 8.2021]

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trastuzumab + paclitaxel

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or 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 4.2021]

ERBB2 amplification (continued)

trastuzumab + paclitaxel

Cancer type: Gastric Cancer **Variant class:** ERBB2 amplification or 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 5.2021]

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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; Invasive, Recurrent, Unresectable, Local, Regional (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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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; Invasive, Recurrent, Unresectable, Local, Regional (Third-line therapy, Subsequent therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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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; Invasive, Recurrent, Unresectable, Local, Regional (Third-line therapy, Subsequent therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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 3.2021]

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trastuzumab deruxtecan

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 4.2021]

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trastuzumab deruxtecan

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 5.2021]

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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 2.2021]

ERBB2 amplification (continued)

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); Consider

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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trastuzumab + carboplatin + docetaxel + fluorouracil

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or 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 4.2021]

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trastuzumab + carboplatin + docetaxel + fluorouracil

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or 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 5.2021]

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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: 2B

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

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

ERBB2 amplification (continued)

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); Consider

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 8.2021]

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irbinitinib + trastuzumab + capecitabine

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

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 2.2021]

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ado-trastuzumab emtansine

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 2.2021]

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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 2.2021]

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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 2.2021]

ERBB2 exon 20 insertion

ado-trastuzumab emtansine

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ERBB2 G776delinsVC 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 7.2021]

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 7.2021]

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 2021-11-17. 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:** 2021-08-27 **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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○ irbinitinib + trastuzumab + capecitabine

Cancer type: Breast Cancer **Label as of:** 2021-05-26 **Variant class:** ERBB2 overexpression or ERBB2 amplification

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

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

Cancer type: Breast Cancer **Label as of:** 2021-10-06 **Variant class:** ERBB2 overexpression or ERBB2 amplification

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:** 2021-10-11 **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:** 2021-09-06 **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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ERBB2 amplification (continued)

pertuzumab/trastuzumab/hyaluronidase-zzxf + docetaxel, pertuzumab/trastuzumab/hyaluronidase-zzxf + paclitaxel, pertuzumab/trastuzumab/hyaluronidase-zzxf + carboplatin + docetaxel, pertuzumab/trastuzumab/hyaluronidase-zzxf + cyclophosphamide + doxorubicin, pertuzumab/trastuzumab/hyaluronidase-zzxf + cyclophosphamide + epirubicin, pertuzumab/trastuzumab/hyaluronidase-zzxf + cyclophosphamide + doxorubicin + fluorouracil

Cancer type: Breast Cancer **Label as of:** 2021-11-09 **Variant class:** ERBB2 overexpression or ERBB2 amplification

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:** 2021-04-09 **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:** 2021-04-09 **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:** 2021-10-18 **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:** 2021-10-18 **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:** 2021-08-19 **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:** 2021-08-19 **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:** 2021-10-26 **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:** 2021-10-26 **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:** 2021-11-16 **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:** 2021-11-16 **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:** 2021-09-13 **Variant class:** 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:** 2021-09-13 **Variant class:** 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:** 2021-05-25 **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:** 2021-09-10 **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:** 2021-09-10 **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 2021-11-01. 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, Metastatic, Progression (Second-line therapy); ESMO-MCBS v1.1 score: 4
- Advanced, Metastatic (Third-line therapy); ESMO-MCBS v1.1 score: 4

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

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irbinitinib + 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, Metastatic (Third-line therapy); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

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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, Metastatic (First-line therapy); ESMO-MCBS v1.1 score: 4

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

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trastuzumab deruxtecan

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

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

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, Metastatic (Subsequent therapy); ESMO-MCBS v1.1 score: 4

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

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margetuximab

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

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

Population segment (Line of therapy):
- Advanced, Metastatic (Subsequent therapy); ESMO-MCBS v1.1 score: 2

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

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margetuximab + chemotherapy

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

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

Population segment (Line of therapy):
- Advanced, Metastatic (Subsequent therapy); ESMO-MCBS v1.1 score: 2

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

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lapatinib + capecitabine

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

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

ERBB2 amplification (continued)

lapatinib + hormone therapy

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

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

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lapatinib + trastuzumab

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

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

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neratinib

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

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

Population segment (Line of therapy):
- Advanced, Metastatic (Subsequent therapy); ESMO-MCBS v1.1 score: 1

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

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neratinib + chemotherapy

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

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

Population segment (Line of therapy):
- Advanced, Metastatic (Subsequent therapy); ESMO-MCBS v1.1 score: 1

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

ERBB2 amplification (continued)

irbinitinib + trastuzumab + capecitabine

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

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

Population segment (Line of therapy):
- Advanced, Brain Metastases (Second-line therapy, Third-line therapy); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

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pertuzumab + trastuzumab + hormone therapy

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

Other criteria: Hormone receptor positive

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

Population segment (Line of therapy):
- Advanced, Metastatic (Maintenance therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

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pertuzumab + trastuzumab + nab-paclitaxel

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

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

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pertuzumab + trastuzumab + paclitaxel

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

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

ERBB2 amplification (continued)

trastuzumab deruxtecan

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

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

Population segment (Line of therapy):
- Advanced, Brain Metastases (Second-line therapy)
- Advanced, Brain Metastases (Subsequent therapy); ESMO-MCBS v1.1 score: 2

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

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lapatinib + hormone therapy

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

Other criteria: Hormone receptor positive

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

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lapatinib + trastuzumab + hormone therapy

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

Other criteria: Hormone receptor positive

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

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pertuzumab + trastuzumab

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

Other criteria: Hormone receptor negative

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

ERBB2 amplification (continued)

pertuzumab + trastuzumab + hormone therapy

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

Other criteria: Hormone receptor positive

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

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trastuzumab + hormone therapy

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

Other criteria: Hormone receptor positive

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

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trastuzumab + chemotherapy

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

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

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trastuzumab deruxtecan

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

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

Population segment (Line of therapy):
- Advanced, Metastatic (Third-line therapy); ESMO-MCBS v1.1 score: 2

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

Clinical Trials in Taiwan region:

Clinical Trials Summary

ERBB2 exon 20 insertion

NCT ID	Title	Phase
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
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
NCT04589845	Tumor-Agnostic Precision Immunooncology and Somatic Targeting Rational for You (TAPISTRY) Phase II Platform Trial	II

Alerts Informed By Public Data Sources

Current FDA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

FDA information is current as of 2021-11-17. For the most up-to-date information, search www.fda.gov.

ERBB2 amplification

zanidatamab

Cancer type: Biliary Tract Carcinoma

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).

Reference:

https://www.targetedonc.com/view/fda-grants-breakthrough-designation-to-zanidatamab-for-her2-amplified-biliary-tract-cancer

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

ERBB2 amplification (continued)

CT-0508

Cancer type: Solid Tumor

Variant class: ERBB2 overexpression

Supporting Statement:

The FDA has granted Fast Track Designation to the HER2 targeted chimeric antigen receptor macrophage (CAR-M), CT-0508, for HER2-overexpressing solid tumors.

Reference:

https://www.prnewswire.com/news-releases/carisma-therapeutics-announces-us-food-and-drug-administration-grants-fast-track-designation-to-ct-0508-for-the-treatment-of-patients-with-solid-tumors-301381843.html

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zanidatamab + chemotherapy

Cancer type: Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

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

Reference:

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

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amcenestrant

Cancer type: Breast Cancer

Variant class: ERBB2 positive

Supporting Statement:
The FDA has granted Fast Track Designation to the HER2-targeting antibody drug conjugate, amcenestrant, for HER2-positive advanced or metastatic breast cancer after one or more prior anti-HER2 based regimens.

Reference:

https://www.prnewswire.com/news-releases/fda-grants-arx788-fast-track-designation-for-her2-positive-metastatic-breast-cancer-301199951.html

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evorpacept

Cancer type: Gastric Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 positive

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

Reference:

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

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ERBB2 exon 20 insertion

trastuzumab deruxtecan

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

Supporting Statement:
The FDA has granted Breakthrough Designation for the HER2-directed antibody drug conjugate, Enhertu (trastuzumab deruxtecan), for the treatment of HER2 mutated metastatic non-small cell lung cancer (NSCLC) with disease progression on or after platinum-based therapy.

Reference:

https://www.astrazeneca.com/media-centre/press-releases/2020/enhertu-granted-breakthrough-therapy-designation-in-the-us-for-her2-mutant-metastatic-non-small-cell-lung-cancer.html

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 2021-11-01. 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

trastuzumab + anthracycline

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma **Variant class:** ERBB2 amplification or 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. Trastuzumab should not be continued in second-line therapy."

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 4.2021]

ERBB2 amplification (continued)

trastuzumab + anthracycline

Cancer type: Gastric Cancer **Variant class:** ERBB2 amplification or 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. Trastuzumab should not be continued in second-line therapy"

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 5.2021]

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 7.2021]

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 7.2021]

Current ESMO Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

ESMO information is current as of 2021-11-01. 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.]

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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.]

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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.]

ERBB2 amplification (continued)

hormone therapy

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

Other criteria: Hormone receptor positive

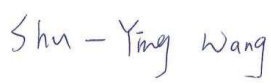
ESMO Level of Evidence/Grade of Recommendation: III / C

Population segment (Line of therapy):
- Advanced, Metastatic

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Breast Cancer [Ann Oncol (2021); DOI:https://doi.org/10.1016/j.annonc.2021.09.019]

Signatures

Testing Personnel:



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Laboratory Supervisor:

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16:35:57 +08'00'

Pathologist:

2022.01.13
16:36:11 +08'00'

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