



Sample Information

Patient Name: 許幸萍**Gender:** Female**ID No.:** A203503449**History No.:** 35719541**Age:** 69**Ordering Doctor:** DOC8344L 簡子軒**Ordering REQ.:** 0ASLDLJ**Signing in Date:** 2020/06/04**Path No.:** S109-99536**MP No.:** F20028**Assay:** Oncomine Focus Assay**Sample Type:** FFPE**Block No.:** S109-15576A+B**Percentage of tumor cells:** 30%**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 Findings

Gene	Finding	Gene	Finding
ALK	Not detected	NTRK1	Not detected
BRAF	Not detected	NTRK2	Not detected
EGFR	Not detected	NTRK3	Not detected
ERBB2	ERBB2 amplification	RET	Not detected
KRAS	Not detected	ROS1	Not detected
MET	Not detected		



Relevant Biomarkers

■ Indicated ■ Contraindicated

Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
ERBB2 amplification erb-b2 receptor tyrosine kinase 2 Tier: IIC	None	<div style="display: flex; flex-direction: column; gap: 5px;"> <div style="background-color: green; padding: 2px;">ado-trastuzumab emtansine^{1,2}</div> <div style="background-color: green; padding: 2px;">lapatinib + chemotherapy^{1,2}</div> <div style="background-color: green; padding: 2px;">lapatinib + letrozole^{1,2}</div> <div style="background-color: green; padding: 2px;">pertuzumab + trastuzumab + chemotherapy^{1,2}</div> <div style="background-color: green; padding: 2px;">trastuzumab* + chemotherapy^{1,2}</div> <div style="background-color: green; padding: 2px;">trastuzumab*^{1,2}</div> <div style="background-color: green; padding: 2px;">trastuzumab deruxtecan¹</div> <div style="background-color: green; padding: 2px;">neratinib^{1,2}</div> <div style="padding: 2px;">aromatase inhibitor</div> <div style="padding: 2px;">fulvestrant</div> <div style="padding: 2px;">hormone therapy</div> <div style="padding: 2px;">lapatinib + aromatase inhibitor</div> <div style="background-color: green; padding: 2px;">lapatinib + trastuzumab²</div> <div style="padding: 2px;">lapatinib + trastuzumab + aromatase inhibitor</div> <div style="padding: 2px;">pertuzumab + trastuzumab</div> <div style="padding: 2px;">pertuzumab + trastuzumab + hormone therapy + chemotherapy</div> <div style="padding: 2px;">tamoxifen</div> <div style="padding: 2px;">trastuzumab + aromatase inhibitor</div> <div style="padding: 2px;">trastuzumab + fulvestrant</div> <div style="padding: 2px;">trastuzumab + hormone therapy + chemotherapy</div> <div style="padding: 2px;">trastuzumab + tamoxifen</div> <div style="padding: 2px;">neratinib + chemotherapy</div> <div style="background-color: green; padding: 2px;">trastuzumab* + anastrozole²</div> <div style="padding: 2px;">trastuzumab containing regimen</div> <div style="padding: 2px;">pertuzumab + trastuzumab + hormone therapy</div> <div style="padding: 2px;">trastuzumab + hormone therapy</div> <div style="background-color: red; padding: 2px;">lapatinib + trastuzumab + chemotherapy</div> <div style="background-color: red; padding: 2px;">aromatase inhibitor</div> </div>	31

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



Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
JAK1	p.(=)	c.2199A>G	.	chr1:65310489	50.58%	NM_002227.3	synonymous	1997
ALK	p.(D1529E)	c.4587C>G	.	chr2:29416366	50.50%	NM_004304.4	missense	1998
ALK	p.(I1461V)	c.4381A>G	.	chr2:29416572	99.90%	NM_004304.4	missense	1998
ALK	p.(=)	c.3375C>A	.	chr2:29445458	47.67%	NM_004304.4	synonymous	1993
FGFR3	p.(=)	c.1953G>A	.	chr4:1807894	99.75%	NM_000142.4	synonymous	789
PDGFRA	p.(=)	c.1701A>G	.	chr4:55141055	100.00%	NM_006206.5	synonymous	1997
KIT	p.(M541L)	c.1621A>C	.	chr4:55593464	50.90%	NM_000222.2	missense	1996
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	99.40%	NM_213647.2	missense	2000
FGFR4	p.(=)	c.483A>G	.	chr5:176517985	4.44%	NM_213647.2	synonymous	1645
RET	p.(=)	c.2307G>T	.	chr10:43613843	99.95%	NM_020975.4	synonymous	1995
ERBB2	p.(L755del)	c.2263_2265delTTG	.	chr17:37880216	30.39%	NM_004448.3	nonframeshift Deletion	1991
ERBB2	p.(R756_E757delinsP Q)	c.2266_2269delAGG GinsCCTC	.	chr17:37880222	30.23%	NM_004448.3	missense, missense	1985

Copy Number Variations

Gene	Locus	Copy Number
ERBB2	chr17:37868126	8.1

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 family¹. 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 survival². 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



Biomarker Descriptions (continued)

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}. Trastuzumab¹⁸ 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 pertuzumab¹⁹ (2012), a humanized monoclonal antibody that inhibits HER2 dimerization, and ado-trastuzumab emtansine²⁰ (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 cancer²¹. In addition to monoclonal antibodies, the small molecule inhibitor lapatinib²², 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 neratinib²³, 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 neratinib²³ in combination with capecitabine for HER2-positive advanced or metastatic patients after two or more prior HER2-directed therapies. The FDA has granted fast-track designation to two therapies including the novel bispecific antibody ZW25²⁴ in patients with HER2-overexpressing gastroesophageal adenocarcinoma (GEA), and the vaccine nelipepimut-S²⁵ in patients with low to intermediate HER2 expressing (IHC score 1+ or 2+) breast cancer. Certain activating mutations have been observed to impart sensitivity to neratinib, afatinib, lapatinib, and trastuzumab, or dacomitinib in early and ongoing clinical studies^{26,27,28,29,30}. Additionally, acquired HER2 mutations in estrogen receptor-positive (ER+) breast cancer have been shown to confer resistance to hormone therapy³¹. However, this was shown to be overcome by neratinib in combination with therapies targeting ER³¹.

Relevant Therapy Summary

● In this cancer type
 ○ In other cancer type
 ○ In this cancer type and other cancer types
 ⚡ Contraindicated
 ⚠ Both for use and contraindicated
 ✕ No evidence

ERBB2 amplification

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
ado-trastuzumab emtansine	○	○	○	○	● (II)
pertuzumab + trastuzumab + chemotherapy	○	○	○	○	✕
pertuzumab + trastuzumab + docetaxel	○	○	○	○	✕
trastuzumab + capecitabine + cisplatin	○	○	○	○	✕
trastuzumab + cisplatin + fluorouracil	○	○	○	○	✕
lapatinib + capecitabine	○	○	○	✕	✕
trastuzumab	○	○	○	✕	✕
trastuzumab + carboplatin + docetaxel	○	○	○	✕	✕
trastuzumab + paclitaxel	○	○	○	✕	✕
lapatinib + letrozole	○	✕	○	✕	✕
neratinib	○	✕	○	✕	✕

* 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
 Contraindicated
 Both for use and contraindicated
 No evidence

ERBB2 amplification (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
trastuzumab (Biocon)	○	×	○	×	×
trastuzumab (Biocon) + capecitabine + cisplatin	○	×	○	×	×
trastuzumab (Biocon) + carboplatin + docetaxel	○	×	○	×	×
trastuzumab (Biocon) + cisplatin + fluorouracil	○	×	○	×	×
trastuzumab (Biocon) + paclitaxel	○	×	○	×	×
trastuzumab (Celltrion)	○	×	○	×	×
trastuzumab (Celltrion) + capecitabine + cisplatin	○	×	○	×	×
trastuzumab (Celltrion) + carboplatin + docetaxel	○	×	○	×	×
trastuzumab (Celltrion) + cisplatin + fluorouracil	○	×	○	×	×
trastuzumab (Celltrion) + paclitaxel	○	×	○	×	×
trastuzumab (Pfizer)	○	×	○	×	×
trastuzumab (Pfizer) + capecitabine + cisplatin	○	×	○	×	×
trastuzumab (Pfizer) + carboplatin + docetaxel	○	×	○	×	×
trastuzumab (Pfizer) + cisplatin + fluorouracil	○	×	○	×	×
trastuzumab deruxtecan	○	×	×	×	● (II)
trastuzumab (Biocon) + cyclophosphamide + docetaxel + doxorubicin	○	×	×	×	×
trastuzumab (Biocon) + cyclophosphamide + doxorubicin + paclitaxel	○	×	×	×	×
trastuzumab (Celltrion) + cyclophosphamide + docetaxel + doxorubicin	○	×	×	×	×
trastuzumab (Celltrion) + cyclophosphamide + doxorubicin + paclitaxel	○	×	×	×	×
trastuzumab (Enhance)	○	×	×	×	×
trastuzumab (Enhance) + carboplatin + docetaxel	○	×	×	×	×
trastuzumab (Enhance) + cyclophosphamide + docetaxel + doxorubicin	○	×	×	×	×

* 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
 Contraindicated
 Both for use and contraindicated
 No evidence

ERBB2 amplification (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
trastuzumab (Enhance) + cyclophosphamide + doxorubicin + paclitaxel					
trastuzumab (Enhance) + paclitaxel					
trastuzumab (Pfizer) + cyclophosphamide + docetaxel + doxorubicin					
trastuzumab (Pfizer) + cyclophosphamide + doxorubicin + paclitaxel					
trastuzumab (Samsung Bioepis)					
trastuzumab (Samsung Bioepis) + capecitabine + cisplatin					
trastuzumab (Samsung Bioepis) + carboplatin + docetaxel					
trastuzumab (Samsung Bioepis) + cisplatin + fluorouracil					
trastuzumab (Samsung Bioepis) + cyclophosphamide + docetaxel + doxorubicin					
trastuzumab (Samsung Bioepis) + cyclophosphamide + doxorubicin + paclitaxel					
trastuzumab (Samsung Bioepis) + paclitaxel					
trastuzumab + cyclophosphamide + docetaxel + doxorubicin					
trastuzumab + cyclophosphamide + doxorubicin + paclitaxel					
lapatinib + trastuzumab					
trastuzumab + docetaxel					
pertuzumab + trastuzumab					 (II)
pertuzumab + trastuzumab + hormone therapy + chemotherapy					
pertuzumab + trastuzumab + paclitaxel					
tamoxifen					

* 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 ⛔ Contraindicated ⚠ Both for use and contraindicated ✕ No evidence

ERBB2 amplification (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
trastuzumab + chemotherapy	✕	○	✕	○	✕
trastuzumab + hormone therapy + chemotherapy	✕	○	✕	○	✕
trastuzumab + vinorelbine	✕	○	✕	○	✕
aromatase inhibitor	✕	○	✕	⛔	✕
fulvestrant	✕	○	✕	✕	✕
hormone therapy	✕	○	✕	✕	✕
lapatinib + aromatase inhibitor	✕	○	✕	✕	✕
lapatinib + trastuzumab + aromatase inhibitor	✕	○	✕	✕	✕
neratinib + capecitabine	✕	○	✕	✕	✕
neratinib + paclitaxel	✕	○	✕	✕	✕
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	✕	○	✕	✕	✕

* 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 ⛔ Contraindicated ⚠ Both for use and contraindicated ✕ No evidence

ERBB2 amplification (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
trastuzumab + fulvestrant	✕	○	✕	✕	✕
trastuzumab + tamoxifen	✕	○	✕	✕	✕
trastuzumab (Biocon) + anastrozole	✕	✕	○	✕	✕
trastuzumab (Biocon) + CMF + doxorubicin + paclitaxel	✕	✕	○	✕	✕
trastuzumab (Biocon) + docetaxel	✕	✕	○	✕	✕
trastuzumab (Celltrion) + anastrozole	✕	✕	○	✕	✕
trastuzumab (Celltrion) + CMF + doxorubicin + paclitaxel	✕	✕	○	✕	✕
trastuzumab (Celltrion) + docetaxel	✕	✕	○	✕	✕
trastuzumab (Pfizer) + anastrozole	✕	✕	○	✕	✕
trastuzumab (Pfizer) + CMF + doxorubicin + paclitaxel	✕	✕	○	✕	✕
trastuzumab (Pfizer) + docetaxel	✕	✕	○	✕	✕
trastuzumab (Pfizer) + paclitaxel	✕	✕	○	✕	✕
trastuzumab (Synthon)	✕	✕	○	✕	✕
trastuzumab (Synthon) + anastrozole	✕	✕	○	✕	✕
trastuzumab (Synthon) + capecitabine + cisplatin	✕	✕	○	✕	✕
trastuzumab (Synthon) + carboplatin + docetaxel	✕	✕	○	✕	✕
trastuzumab (Synthon) + cisplatin + fluorouracil	✕	✕	○	✕	✕
trastuzumab (Synthon) + CMF + doxorubicin + paclitaxel	✕	✕	○	✕	✕
trastuzumab (Synthon) + docetaxel	✕	✕	○	✕	✕
trastuzumab (Synthon) + paclitaxel	✕	✕	○	✕	✕
trastuzumab + anastrozole	✕	✕	○	✕	✕
trastuzumab + CMF + doxorubicin + paclitaxel	✕	✕	○	✕	✕
aromatase inhibitor + luteinizing hormone-releasing factor	✕	✕	✕	○	✕

* 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 ⛔ Contraindicated ⚠ Both for use and contraindicated ✕ No evidence

ERBB2 amplification (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
pertuzumab + trastuzumab + capecitabine	✕	✕	✕	○	✕
pertuzumab + trastuzumab + hormone therapy	✕	✕	✕	○	✕
pertuzumab + trastuzumab + nab-paclitaxel	✕	✕	✕	○	✕
pertuzumab + trastuzumab + vinorelbine	✕	✕	✕	○	✕
trastuzumab + hormone therapy	✕	✕	✕	○	✕
trastuzumab + taxane	✕	✕	✕	○	✕
trastuzumab containing regimen	✕	✕	✕	○	✕
lapatinib + trastuzumab + chemotherapy	✕	✕	✕	⛔	✕
pertuzumab, trastuzumab	✕	✕	✕	✕	● (II)
RC-48	✕	✕	✕	✕	● (II)
targeted therapy, chemotherapy	✕	✕	✕	✕	● (II)
trastuzumab, pertuzumab	✕	✕	✕	✕	● (II)
BAT 1306, BAT-8001	✕	✕	✕	✕	● (I/II)
CART-PD1	✕	✕	✕	✕	● (I/II)
chemotherapy	✕	✕	✕	✕	● (I/II)
AC-101 (AbClon)	✕	✕	✕	✕	● (I)
ACTR707 + trastuzumab, ACTR087 + trastuzumab	✕	✕	✕	✕	● (I)
ARX-788	✕	✕	✕	✕	● (I)
BTRC-4017A	✕	✕	✕	✕	● (I)
CART-HER2	✕	✕	✕	✕	● (I)
everolimus + neratinib, neratinib + palbociclib, neratinib + trametinib	✕	✕	✕	✕	● (I)
KN026, KN046	✕	✕	✕	✕	● (I)
M802	✕	✕	✕	✕	● (I)
MBS301	✕	✕	✕	✕	● (I)
MGD-013, margetuximab	✕	✕	✕	✕	● (I)

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



Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ● In this cancer type and other cancer types ⛔ Contraindicated ⚠ Both for use and contraindicated ✕ No evidence

ERBB2 amplification (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
MP-0274	✕	✕	✕	✕	● (I)
MT-5111	✕	✕	✕	✕	● (I)
NJH-395	✕	✕	✕	✕	● (I)
pirotinib	✕	✕	✕	✕	● (I)
PRS-343	✕	✕	✕	✕	● (I)
PRS-343, atezolizumab	✕	✕	✕	✕	● (I)
ZW-25	✕	✕	✕	✕	● (I)

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



Relevant Therapy Details

Current FDA Information

☒ In this cancer type
 ☐ In other cancer type
 ☐ In this cancer type and other cancer types
 ☒ Contraindicated
 ☒ Not recommended
 ☒ Resistance

FDA information is current as of 2020-02-28. For the most up-to-date information, search www.fda.gov.

ERBB2 amplification

☐ ado-trastuzumab emtansine

Cancer type: Breast Cancer

Label as of: 2019-05-03

Variant class: ERBB2 overexpression or ERBB2 amplification

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/2019/125427s105lbl.pdf



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

○ 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



ERBB2 amplification (continued)

- **trastuzumab (Biocon), trastuzumab (Biocon) + paclitaxel, trastuzumab (Biocon) + capecitabine + cisplatin, trastuzumab (Biocon) + carboplatin + docetaxel, trastuzumab (Biocon) + cisplatin + fluorouracil, trastuzumab (Biocon) + cyclophosphamide + docetaxel + doxorubicin, trastuzumab (Biocon) + cyclophosphamide + doxorubicin + paclitaxel**

Cancer type: Breast Cancer, Gastric Cancer, **Label as of:** 2019-04-17
Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression or ERBB2 amplification

Other criteria: ER negative, PR negative

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

- **trastuzumab (Celltrion), trastuzumab (Celltrion) + paclitaxel, trastuzumab (Celltrion) + capecitabine + cisplatin, trastuzumab (Celltrion) + carboplatin + docetaxel, trastuzumab (Celltrion) + cisplatin + fluorouracil, trastuzumab (Celltrion) + cyclophosphamide + docetaxel + doxorubicin, trastuzumab (Celltrion) + cyclophosphamide + doxorubicin + paclitaxel**

Cancer type: Breast Cancer, Gastric Cancer, **Label as of:** 2019-05-16
Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression or ERBB2 amplification

Other criteria: ER negative, PR negative

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



ERBB2 amplification (continued)

- **trastuzumab (Enhance), trastuzumab (Enhance) + paclitaxel, trastuzumab (Enhance) + carboplatin + docetaxel, trastuzumab (Enhance) + cyclophosphamide + docetaxel + doxorubicin, trastuzumab (Enhance) + cyclophosphamide + doxorubicin + paclitaxel**

Cancer type: Breast Cancer

Label as of: 2019-02-28

Variant class: ERBB2 amplification or 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

- **trastuzumab (Pfizer), trastuzumab (Pfizer) + capecitabine + cisplatin, trastuzumab (Pfizer) + carboplatin + docetaxel, trastuzumab (Pfizer) + cisplatin + fluorouracil, trastuzumab (Pfizer) + cyclophosphamide + docetaxel + doxorubicin, trastuzumab (Pfizer) + cyclophosphamide + doxorubicin + paclitaxel**

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

Label as of: 2019-03-11

Variant class: ERBB2 overexpression or ERBB2 amplification

Other criteria: ER negative, PR negative

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



ERBB2 amplification (continued)

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

Cancer type: Breast Cancer, Gastric Cancer, Label as of: 2019-01-18
Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression or ERBB2 amplification

Other criteria: ER negative, PR negative

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

○ trastuzumab deruxtecan

Cancer type: Breast Cancer

Label as of: 2019-12-20

Variant class: ERBB2 amplification or 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.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761139s000lbl.pdf



ERBB2 amplification (continued)

- **trastuzumab, trastuzumab + paclitaxel, trastuzumab + capecitabine + cisplatin, trastuzumab + carboplatin + docetaxel, trastuzumab + cisplatin + fluorouracil, trastuzumab + cyclophosphamide + docetaxel + doxorubicin, trastuzumab + cyclophosphamide + doxorubicin + paclitaxel**

Cancer type: Breast Cancer, Gastric Cancer, Gastroesophageal Junction Adenocarcinoma
Label as of: 2018-11-29

Variant class: ERBB2 overexpression or ERBB2 amplification

Other criteria: ER negative, PR negative

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

○ neratinib

Cancer type: Breast Cancer

Label as of: 2019-10-01

Variant class: ERBB2 positive

Indications and usage:

NERLYNX® is a kinase inhibitor indicated for the extended adjuvant treatment of adult patients with early stage HER2-positive breast cancer, to follow adjuvant trastuzumab-based therapy.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/208051s004lbl.pdf



Current NCCN Information

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types
 ☒ Contraindicated
 ☒ Not recommended
 ☒ Resistance

NCCN information is current as of 2019-11-01. 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

☐ pertuzumab + trastuzumab + docetaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, ER positive, PR negative, PR positive

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer (Not specified) (Preferred)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

☐ trastuzumab + capecitabine + cisplatin

Cancer type: Esophageal Cancer,
Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 4.2019]

☐ trastuzumab + capecitabine + cisplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2019]



ERBB2 amplification (continued)

○ trastuzumab + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, PR negative

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; pT1, pT2, or pT3; pN0 or pN1mi (≤ 2 mm axillary node metastasis); Tumor >1 cm (Adjuvant therapy)
- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; Node positive (1 or more ipsilateral metastases >2 mm) (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

○ trastuzumab + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; pT1, pT2, or pT3; pN0 or pN1mi (≤ 2 mm axillary node metastasis); Tumor >1 cm (Adjuvant therapy)
- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; Node positive (1 or more ipsilateral metastases >2 mm) (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

○ trastuzumab + cisplatin + fluorouracil

Cancer type: Esophageal Cancer,
Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 4.2019]



ERBB2 amplification (continued)

○ trastuzumab + cisplatin + fluorouracil

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2019]

○ ado-trastuzumab emtansine

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, ER positive, PR negative, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer (Not specified) (Other recommended regimens)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

○ aromatase inhibitor

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer; Postmenopausal or Premenopausal receiving ovarian ablation or suppression (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

○ fulvestrant

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer; Postmenopausal or Premenopausal receiving ovarian ablation or suppression (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]



ERBB2 amplification (continued)

○ hormone therapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; pT1, pT2, or pT3; pN0 or pN1mi (≤ 2 mm axillary node metastasis); Tumor ≤ 0.5 cm and pN1mi or Tumor 0.6-1.0 cm or Tumor >1 cm (Adjuvant therapy)
- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; Node Positive (1 or more ipsilateral metastases >2 mm) (Adjuvant Therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

○ hormone therapy

Cancer type: Breast Cancer

Variant class: ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; pT1, pT2, or pT3; pN0 or pN1mi (≤ 2 mm axillary node metastasis); Tumor ≤ 0.5 cm and pN1mi or Tumor 0.6-1.0 cm or Tumor >1 cm (Adjuvant therapy)
- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; Node Positive (1 or more ipsilateral metastases >2 mm) (Adjuvant Therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

○ lapatinib + aromatase inhibitor

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer; Postmenopausal or Premenopausal receiving ovarian ablation or suppression (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]



ERBB2 amplification (continued)

○ lapatinib + capecitabine

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, ER positive, PR negative, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer (Not specified) (Other recommended regimens)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

○ lapatinib + trastuzumab

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, ER positive, PR negative, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer (Not specified) (Other recommended regimens)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

○ lapatinib + trastuzumab

Cancer type: Colon Cancer

Variant class: ERBB2 amplification

Other criteria: BRAF wild type, RAS wild type

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Advanced or Metastatic Colon Cancer; Not appropriate for intensive therapy (Initial Therapy)
- Advanced or Metastatic Colon Cancer; Progression after initial therapy; Previous oxaliplatin based therapy without irinotecan; If no previous treatment with HER2 inhibitor (Subsequent therapy)
- Advanced or Metastatic Colon Cancer; Progression after initial therapy; Previous irinotecan based therapy without oxaliplatin; If no previous treatment with HER2 inhibitor (Subsequent therapy)
- Advanced or Metastatic Colon Cancer; Progression after initial therapy; Previous treatment with oxaliplatin and irinotecan; If no previous treatment with HER2 inhibitor (Subsequent therapy)
- Advanced or Metastatic Colon Cancer; Progression after initial therapy; Previous fluoropyrimidine without irinotecan or oxaliplatin; If no previous treatment with HER2 inhibitor (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 1.2020]



ERBB2 amplification (continued)

○ lapatinib + trastuzumab

Cancer type: Rectal Cancer

Variant class: ERBB2 amplification

Other criteria: BRAF wild type, RAS wild type

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Advanced or Metastatic Rectal Cancer; Not appropriate for intensive therapy (Initial therapy)
- Advanced or Metastatic Rectal Cancer; Progression after initial therapy; Previous oxaliplatin based therapy without irinotecan; If no previous treatment with HER2 inhibitor (Subsequent therapy)
- Advanced or Metastatic Rectal Cancer; Progression after initial therapy; Previous irinotecan based therapy without oxaliplatin; If no previous treatment with HER2 inhibitor (Subsequent therapy)
- Advanced or Metastatic Rectal Cancer; Progression after initial therapy; Previous treatment with oxaliplatin and irinotecan; If no previous treatment with HER2 inhibitor (Subsequent therapy)
- Advanced or Metastatic Rectal Cancer; Progression after initial therapy; Previous fluoropyrimidine without irinotecan or oxaliplatin; If no previous treatment with HER2 inhibitor (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 1.2020]

○ lapatinib + trastuzumab + aromatase inhibitor

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer; Postmenopausal or Premenopausal receiving ovarian ablation or suppression (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]



ERBB2 amplification (continued)

○ pertuzumab + trastuzumab

Cancer type: Colon Cancer

Variant class: ERBB2 amplification

Other criteria: BRAF wild type, RAS wild type

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Advanced or Metastatic Colon Cancer; Not appropriate for intensive therapy (Initial Therapy)
- Advanced or Metastatic Colon Cancer; Progression after initial therapy; Previous oxaliplatin based therapy without irinotecan; If no previous treatment with HER2 inhibitor (Subsequent therapy)
- Advanced or Metastatic Colon Cancer; Progression after initial therapy; Previous irinotecan based therapy without oxaliplatin; If no previous treatment with HER2 inhibitor (Subsequent therapy)
- Advanced or Metastatic Colon Cancer; Progression after initial therapy; Previous treatment with oxaliplatin and irinotecan; If no previous treatment with HER2 inhibitor (Subsequent therapy)
- Advanced or Metastatic Colon Cancer; Progression after initial therapy; Previous fluoropyrimidine without irinotecan or oxaliplatin; If no previous treatment with HER2 inhibitor (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 1.2020]

○ pertuzumab + trastuzumab

Cancer type: Rectal Cancer

Variant class: ERBB2 amplification

Other criteria: BRAF wild type, RAS wild type

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Advanced or Metastatic Rectal Cancer; Not appropriate for intensive therapy (Initial therapy)
- Advanced or Metastatic Rectal Cancer; Progression after initial therapy; Previous oxaliplatin based therapy without irinotecan; If no previous treatment with HER2 inhibitor (Subsequent therapy)
- Advanced or Metastatic Rectal Cancer; Progression after initial therapy; Previous irinotecan based therapy without oxaliplatin; If no previous treatment with HER2 inhibitor (Subsequent therapy)
- Advanced or Metastatic Rectal Cancer; Progression after initial therapy; Previous treatment with oxaliplatin and irinotecan; If no previous treatment with HER2 inhibitor (Subsequent therapy)
- Advanced or Metastatic Rectal Cancer; Progression after initial therapy; Previous fluoropyrimidine without irinotecan or oxaliplatin; If no previous treatment with HER2 inhibitor (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 1.2020]



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):

- Recurrent or Stage IV Invasive Breast Cancer; Preoperative (Adjuvant therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

☐ pertuzumab + trastuzumab + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, PR negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; Node positive (1 or more ipsilateral metastases >2 mm) (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

☐ pertuzumab + trastuzumab + docetaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer; Preoperative (Adjuvant therapy) given after doxorubicin/cyclophosphamide (Other Recommended)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

☐ pertuzumab + trastuzumab + hormone therapy + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; Node positive (1 or more ipsilateral metastases >2 mm) (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]



ERBB2 amplification (continued)

☐ pertuzumab + trastuzumab + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, ER positive, PR negative, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer (Not specified) (Preferred)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

☐ pertuzumab + trastuzumab + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer; Preoperative (Adjuvant therapy) given after doxorubicin/cyclophosphamide (Preferred)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

☐ tamoxifen

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer; Postmenopausal or Premenopausal receiving ovarian ablation or suppression (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

☐ trastuzumab + aromatase inhibitor

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer; Postmenopausal or Premenopausal receiving ovarian ablation or suppression (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]



ERBB2 amplification (continued)

○ trastuzumab + capecitabine

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, ER positive, PR negative, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer (Not specified) (Other recommended regimens)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

○ trastuzumab + capecitabine + oxaliplatin

Cancer type: Esophageal Cancer,
Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 4.2019]

○ trastuzumab + capecitabine + oxaliplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2019]

○ trastuzumab + carboplatin + docetaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer; Preoperative (Adjuvant therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]



ERBB2 amplification (continued)

○ trastuzumab + carboplatin + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, ER positive, PR negative, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer (Not specified) (Other recommended regimens)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

○ trastuzumab + carboplatin + paclitaxel

Cancer type: Endometrial Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Stage III/IV Recurrent Uterine Serous Carcinoma (Adjuvant therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Uterine Neoplasms [Version 5.2019]

○ trastuzumab + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification

Other criteria: ER negative, PR negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; pT1, pT2, or pT3; pN0 or pN1mi (≤ 2 mm axillary node metastasis); Tumor ≤ 0.5 cm and pN1mi or Tumor 0.6-1.0 cm (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

○ trastuzumab + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 overexpression

Other criteria: ER negative, PR negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; pT1, pT2, or pT3; pN0 or pN1mi (≤ 2 mm axillary node metastasis); Tumor ≤ 0.5 cm and pN1mi or Tumor 0.6-1.0 cm (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]



ERBB2 amplification (continued)

☐ trastuzumab + chemotherapy (other)

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, ER positive, PR negative, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer (Not specified) (Other recommended regimens)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

☐ trastuzumab + cyclophosphamide + docetaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer; Preoperative (Adjuvant therapy) (Useful in Certain Circumstances)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

☐ trastuzumab + docetaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, ER positive, PR negative, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer (Not specified) (Other recommended regimens)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

☐ trastuzumab + docetaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer; Preoperative (Adjuvant therapy) given after doxorubicin/cyclophosphamide (Other Recommended)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]



ERBB2 amplification (continued)

☐ trastuzumab + fluorouracil + oxaliplatin

Cancer type: Esophageal Cancer,
Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 4.2019]

☐ trastuzumab + fluorouracil + oxaliplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2019]

☐ trastuzumab + fulvestrant

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer; Postmenopausal or Premenopausal receiving ovarian ablation or suppression (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]



ERBB2 amplification (continued)

○ trastuzumab + hormone therapy + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; pT1, pT2, or pT3; pN0 or pN1mi (≤ 2 mm axillary node metastasis); Tumor ≤ 0.5 cm and pN1mi or Tumor 0.6-1.0 cm or Tumor > 1 cm (Adjuvant therapy)
- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; Node positive (1 or more ipsilateral metastases > 2 mm) (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

○ trastuzumab + hormone therapy + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; pT1, pT2, or pT3; pN0 or pN1mi (≤ 2 mm axillary node metastasis); Tumor ≤ 0.5 cm and pN1mi or Tumor 0.6-1.0 cm or Tumor > 1 cm (Adjuvant therapy)
- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; Node positive (1 or more ipsilateral metastases > 2 mm) (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

○ trastuzumab + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, PR negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; pT1 and pN0; Tumor ≤ 0.5 cm or Tumor 0.6-1.0 cm (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]



ERBB2 amplification (continued)

☐ trastuzumab + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, ER positive, PR negative, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer (Not specified) (Other recommended regimens)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

☐ trastuzumab + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer; Preoperative (Adjuvant therapy) given after doxorubicin/cyclophosphamide (Preferred)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

☐ trastuzumab + tamoxifen

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer; Postmenopausal or Premenopausal receiving ovarian ablation or suppression (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

☐ trastuzumab + vinorelbine

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, ER positive, PR negative, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer (Not specified) (Other recommended regimens)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]



ERBB2 amplification (continued)

○ hormone therapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; pT1, pT2, or pT3; Tumor ≤0.5 cm and pN0 (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

○ neratinib + capecitabine

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, ER positive, PR negative, PR positive

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer (Not specified) (Other recommended regimens)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

○ trastuzumab + capecitabine

Cancer type: Esophageal Cancer,
Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 4.2019]

○ trastuzumab + capecitabine

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2019]



ERBB2 amplification (continued)

○ trastuzumab + carboplatin + docetaxel + fluorouracil

Cancer type: Esophageal Cancer,
Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)
(Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 4.2019]

○ trastuzumab + carboplatin + docetaxel + fluorouracil

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)
(Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2019]

○ trastuzumab + carboplatin + paclitaxel

Cancer type: Esophageal Cancer,
Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)
(Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 4.2019]

○ trastuzumab + carboplatin + paclitaxel

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)
(Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2019]



ERBB2 amplification (continued)

○ trastuzumab + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, PR negative

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; pT1, pT2, or pT3; Tumor ≤0.5 cm and pN0 (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

○ trastuzumab + cisplatin + docetaxel

Cancer type: Esophageal Cancer,
Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 4.2019]

○ trastuzumab + cisplatin + docetaxel

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2019]

○ trastuzumab + cisplatin + docetaxel + fluorouracil

Cancer type: Esophageal Cancer,
Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 4.2019]



ERBB2 amplification (continued)

○ trastuzumab + cisplatin + docetaxel + fluorouracil

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2019]

○ trastuzumab + cisplatin + paclitaxel

Cancer type: Esophageal Cancer,
Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 4.2019]

○ trastuzumab + cisplatin + paclitaxel

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2019]

○ trastuzumab + docetaxel

Cancer type: Esophageal Cancer,
Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 4.2019]



ERBB2 amplification (continued)

☐ trastuzumab + docetaxel

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2019]

☐ trastuzumab + docetaxel + fluorouracil + oxaliplatin

Cancer type: Esophageal Cancer,
Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 4.2019]

☐ trastuzumab + docetaxel + fluorouracil + oxaliplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2019]

☐ trastuzumab + fluorouracil

Cancer type: Esophageal Cancer,
Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 4.2019]



ERBB2 amplification (continued)

○ trastuzumab + fluorouracil

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2019]

○ trastuzumab + fluorouracil + irinotecan

Cancer type: Esophageal Cancer,
Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 4.2019]

○ trastuzumab + fluorouracil + irinotecan

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2019]

○ trastuzumab + hormone therapy + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; pT1, pT2, or pT3; Tumor ≤0.5 cm and pN0 (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]



ERBB2 amplification (continued)

☐ trastuzumab + hormone therapy + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; pT1, pT2, or pT3; Tumor ≤0.5 cm and pN0 (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

☐ trastuzumab + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification

Other criteria: ER negative, PR negative

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; pT1 and pN0; Tumor ≤0.5 cm (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

☐ trastuzumab + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 overexpression

Other criteria: ER negative, PR negative

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Ductal/No Special Type, Lobular, Mixed, Micropapillary Invasive Breast Cancer; pT1 and pN0; Tumor ≤0.5 cm (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]



ERBB2 amplification (continued)

☐ trastuzumab + paclitaxel

Cancer type: Esophageal Cancer,
Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 4.2019]

☐ trastuzumab + paclitaxel

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Unresectable Locally Advanced, Recurrent or Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy) (Other recommended regimen)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2019]

☐ lapatinib + capecitabine

Cancer type: Breast Cancer

Variant class: ERBB2 positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Breast Cancer; Brain metastases; Recurrent disease; Use agents active against primary tumor (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2019]

☐ neratinib + capecitabine

Cancer type: Breast Cancer

Variant class: ERBB2 positive

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Breast Cancer; Brain metastases; Recurrent disease; Use agents active against primary tumor (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2019]



ERBB2 amplification (continued)

☐ neratinib + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 positive

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Breast Cancer; Brain metastases; Recurrent disease; Use agents active against primary tumor (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2019]

☐ trastuzumab

Cancer type: Head and Neck Cancer

Variant class: ERBB2 positive

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Recurrent Metastatic Salivary Gland Tumors; Distant metastases; PS 0-3 (Therapy for recurrence)

Reference: NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 3.2019]

☒ pertuzumab + trastuzumab + cyclophosphamide + docetaxel + doxorubicin

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Summary:

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

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

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

☒ pertuzumab + trastuzumab + cyclophosphamide + doxorubicin + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Summary:

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

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

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]



ERBB2 amplification (continued)

trastuzumab + capecitabine + cisplatin + epirubicin

Cancer type: Esophageal Cancer,
Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

Summary:

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

- "Trastuzumab is not recommended for use with anthracyclines"
- "The use of trastuzumab in combination with anthracyclines is not recommended"

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 4.2019]

trastuzumab + capecitabine + cisplatin + epirubicin

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

Summary:

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

- "Trastuzumab is not recommended for use with anthracyclines"

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2019]

trastuzumab + capecitabine + epirubicin + oxaliplatin

Cancer type: Esophageal Cancer,
Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

Summary:

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

- "Trastuzumab is not recommended for use with anthracyclines"
- "The use of trastuzumab in combination with anthracyclines is not recommended"

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 4.2019]

trastuzumab + capecitabine + epirubicin + oxaliplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

Summary:

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

- "Trastuzumab is not recommended for use with anthracyclines"

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2019]



ERBB2 amplification (continued)

trastuzumab + cisplatin + epirubicin + fluorouracil

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

Summary:

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

- "Trastuzumab is not recommended for use with anthracyclines"
- "The use of trastuzumab in combination with anthracyclines is not recommended"

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 4.2019]

trastuzumab + cisplatin + epirubicin + fluorouracil

Cancer type: Gastric Cancer
Variant class: ERBB2 overexpression

Summary:

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

- "Trastuzumab is not recommended for use with anthracyclines"

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2019]

trastuzumab + cyclophosphamide + docetaxel + doxorubicin

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

Summary:

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

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

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]

trastuzumab + cyclophosphamide + doxorubicin + paclitaxel

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

Summary:

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

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

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2020]



ERBB2 amplification (continued)

trastuzumab + epirubicin + fluorouracil + oxaliplatin

Cancer type: Esophageal Cancer,
Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

Summary:

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

- "Trastuzumab is not recommended for use with anthracyclines"
- "The use of trastuzumab in combination with anthracyclines is not recommended"

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 4.2019]

trastuzumab + epirubicin + fluorouracil + oxaliplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

Summary:

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

- "Trastuzumab is not recommended for use with anthracyclines"

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 4.2019]



Current EMA Information

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types
 ☒ Contraindicated
 ☒ Not recommended
 ☒ Resistance

EMA information is current as of 2020-02-28. For the most up-to-date information, search www.ema.europa.eu/ema.

ERBB2 amplification

☐ ado-trastuzumab emtansine

Cancer type: Breast Cancer

Label as of: 2020-01-20

Variant class: ERBB2 overexpression or ERBB2 amplification

Reference:

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

☐ lapatinib + capecitabine, lapatinib + letrozole, lapatinib + trastuzumab

Cancer type: Breast Cancer

Label as of: 2019-10-15

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

☐ neratinib

Cancer type: Breast Cancer

Label as of: 2020-02-11

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive

Reference:

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

☐ pertuzumab + trastuzumab + chemotherapy, pertuzumab + trastuzumab + docetaxel

Cancer type: Breast Cancer

Label as of: 2019-04-15

Variant class: ERBB2 amplification or ERBB2 overexpression

Reference:

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



ERBB2 amplification (continued)

- **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, **Label as of:** 2019-08-05
Gastroesophageal Junction Adenocarcinoma

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

- **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: 2019-08-05

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

- **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, **Label as of:** 2020-02-14
Gastroesophageal Junction Adenocarcinoma

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

- **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: 2020-02-14

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



ERBB2 amplification (continued)

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

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

Label as of: 2020-01-14

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

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

Cancer type: Breast Cancer

Label as of: 2020-01-14

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

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

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

Label as of: 2019-11-29

Variant class: ERBB2 overexpression

Other criteria: ER positive, PR positive

Reference:

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

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

Cancer type: Breast Cancer

Label as of: 2019-11-29

Variant class: ERBB2 amplification

Other criteria: ER positive, PR positive

Reference:

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



ERBB2 amplification (continued)

- **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: 2019-10-14

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

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

Cancer type: Breast Cancer

Label as of: 2019-10-14

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



Current ESMO Information

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types
 ☒ Contraindicated
 ☒ Not recommended
 ☒ Resistance

ESMO information is current as of 2019-11-01. 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 Early Breast Cancer; No pathological complete response after completion of neoadjuvant chemotherapy combined with anti-HER2 therapy; substitute for adjuvant trastuzumab (Not Specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Annals of Oncology, Volume 30, Issue 8, August 2019, Pages 1194–1220.]

☐ pertuzumab + trastuzumab + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification

Other criteria: ER negative

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

Population segment (Line of therapy):

- Non-luminal Early Breast Cancer

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Annals of Oncology, Volume 30, Issue 8, August 2019, Pages 1194–1220.]

☐ pertuzumab + trastuzumab + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 overexpression

Other criteria: ER negative

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

Population segment (Line of therapy):

- Non-luminal Early Breast Cancer (Not Specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Annals of Oncology, Volume 30, Issue 8, August 2019, Pages 1194–1220.]



ERBB2 amplification (continued)

○ pertuzumab + trastuzumab + hormone therapy + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR negative, PR positive

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

Population segment (Line of therapy):

- Luminal B-like Early Breast Cancer (Not Specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Annals of Oncology, Volume 30, Issue 8, August 2019, Pages 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):

- Inoperable or Metastatic Gastric Adenocarcinoma (Not specified)

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

○ trastuzumab + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative

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

Population segment (Line of therapy):

- Non-luminal Early Breast Cancer (Not Specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Annals of Oncology, Volume 30, Issue 8, August 2019, Pages 1194–1220.]

○ 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):

- ERBB2(+) Non-Luminal Cancer; Except very low risk, such as T1aN0 (Neoadjuvant therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Primary Breast Cancer [Ann Oncol (2015) 26 (suppl 5): v8-v30.]



ERBB2 amplification (continued)

○ trastuzumab + chemotherapy

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):

- Primary Breast Cancer (Neoadjuvant therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Primary Breast Cancer [Ann Oncol (2015) 26 (suppl 5): v8-v30.]

○ 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):

- Inoperable or Metastatic Gastric Adenocarcinoma (Not specified)

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

○ trastuzumab + hormone therapy + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR negative, PR positive

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

Population segment (Line of therapy):

- Luminal B-like Early Breast Cancer (Not Specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Annals of Oncology, Volume 30, Issue 8, August 2019, Pages 1194–1220.]

○ trastuzumab + hormone therapy + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive

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

Population segment (Line of therapy):

- Luminal B ERBB2-positive Breast Cancer; Except low-risk T1a (Neoadjuvant therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Primary Breast Cancer [Ann Oncol (2015) 26 (suppl 5): v8-v30.]



ERBB2 amplification (continued)

○ 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):

- Early Breast Cancer; Higher-risk cases (Primary systemic therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Annals of Oncology, Volume 30, Issue 8, August 2019, Pages 1194–1220.]

○ 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):

- Metastatic Esophageal Adenocarcinoma (Not specified)

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

○ pertuzumab + trastuzumab + hormone therapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR negative, PR positive

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

Population segment (Line of therapy):

- Luminal B-like Early Breast Cancer; Low-risk; T1abN0 (Not Specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Annals of Oncology, Volume 30, Issue 8, August 2019, Pages 1194–1220.]

○ trastuzumab + hormone therapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR negative, PR positive

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

Population segment (Line of therapy):

- Luminal B-like Early Breast Cancer; Low-risk; T1abN0 (Not Specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Annals of Oncology, Volume 30, Issue 8, August 2019, Pages 1194–1220.]



ERBB2 amplification (continued)

☐ tamoxifen

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR negative, PR positive

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

Population segment (Line of therapy):

- Luminal-like Ductal Invasive Early Male Breast Cancer (Adjuvant therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Annals of Oncology, Volume 30, Issue 8, August 2019, Pages 1194–1220.]

☐ aromatase inhibitor + luteinizing hormone-releasing factor

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR negative, PR positive

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

Population segment (Line of therapy):

- Luminal-like Ductal Invasive Early Male Breast Cancer; If a strong contraindication exists for the use of tamoxifen (Not Specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Annals of Oncology, Volume 30, Issue 8, August 2019, Pages 1194–1220.]

☐ trastuzumab + hormone therapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification

Other criteria: ER positive

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

Population segment (Line of therapy):

- Luminal B-like Early Breast Cancer; Small, node-negative tumours; If contraindication for chemotherapy (Not Specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Annals of Oncology, Volume 30, Issue 8, August 2019, Pages 1194–1220.]



ERBB2 amplification (continued)

○ trastuzumab + hormone therapy

Cancer type: Breast Cancer

Variant class: ERBB2 overexpression

Other criteria: ER positive

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

Population segment (Line of therapy):

- Luminal B-like Early Breast Cancer; Small, node-negative tumours; If contraindication to chemotherapy (Not Specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Annals of Oncology, Volume 30, Issue 8, August 2019, Pages 1194–1220.]

○ 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 ERBB2-positive; If contraindication or refusal of chemotherapy (Neoadjuvant therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Primary Breast Cancer [Ann Oncol (2015) 26 (suppl 5): v8-v30.]

○ 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 Breast Cancer; Progression after one line of trastuzumab-based therapy (Second-line therapy) (Preferred)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018); 29: 1634–1657.]

○ pertuzumab + trastuzumab + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 positive

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

Population segment (Line of therapy):

- Advanced Breast Cancer; Previously untreated with anti-HER2 therapy (First-line therapy)
- Advanced Breast Cancer; Previously treated (in the (neo)adjuvant setting) with anti-HER2 therapy (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018); 29: 1634–1657.]



ERBB2 amplification (continued)

☐ 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 Breast Cancer (Not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018); 29: 1634–1657.]

☐ trastuzumab + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 positive

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

Population segment (Line of therapy):

- Advanced Breast Cancer; Previously treated in the adjuvant setting (First-line therapy)
- Advanced Breast Cancer; Untreated with trastuzumab (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018); 29: 1634–1657.]

☐ trastuzumab + taxane

Cancer type: Breast Cancer

Variant class: ERBB2 positive

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

Population segment (Line of therapy):

- Advanced Breast Cancer; Pertuzumab is not given (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018); 29: 1634–1657.]

☐ trastuzumab + vinorelbine

Cancer type: Breast Cancer

Variant class: ERBB2 positive

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

Population segment (Line of therapy):

- Advanced Breast Cancer; Pertuzumab is not given (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018); 29: 1634–1657.]



ERBB2 amplification (continued)

○ lapatinib + trastuzumab

Cancer type: Breast Cancer

Variant class: ERBB2 positive

Other criteria: ER positive

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

Population segment (Line of therapy):

- Advanced Breast Cancer; First-line therapy was endocrine therapy and anti-HER2 therapy (Not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018); 29: 1634–1657.]

○ 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 Breast Cancer; Progression on trastuzumab-based therapy (Not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018); 29: 1634–1657.]

○ pertuzumab + trastuzumab

Cancer type: Breast Cancer

Variant class: ERBB2 positive

Other criteria: ER positive

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

Population segment (Line of therapy):

- Advanced Breast Cancer; First-line therapy was endocrine therapy and anti-HER2 therapy (Not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018); 29: 1634–1657.]

○ pertuzumab + trastuzumab + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 positive

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

Population segment (Line of therapy):

- Advanced Breast Cancer (Not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018); 29: 1634–1657.]



ERBB2 amplification (continued)

☐ pertuzumab + 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 Breast Cancer (Not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018); 29: 1634–1657.]

☐ pertuzumab + trastuzumab + vinorelbine

Cancer type: Breast Cancer

Variant class: ERBB2 positive

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

Population segment (Line of therapy):

- Advanced Breast Cancer (Not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018); 29: 1634–1657.]

☐ pertuzumab + trastuzumab + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 positive

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

Population segment (Line of therapy):

- Advanced Breast Cancer; Previously untreated with the combination of chemotherapy + trastuzumab + pertuzumab (After first-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018); 29: 1634–1657.]

☐ pertuzumab + trastuzumab + nab-paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 positive

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

Population segment (Line of therapy):

- Advanced Breast Cancer (Not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018); 29: 1634–1657.]



ERBB2 amplification (continued)

❌ lapatinib + trastuzumab + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

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

Population segment (Line of therapy):

- Male Breast Cancer

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Annals of Oncology, Volume 30, Issue 8, August 2019, Pages 1194–1220.]

❌ aromatase inhibitor

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR negative, PR positive

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

Population segment (Line of therapy):

- Male Breast Cancer

Reference: ESMO Clinical Practice Guidelines - ESMO-Early Breast Cancer [Annals of Oncology, Volume 30, Issue 8, August 2019, Pages 1194–1220.]

🗨️ 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 [Annals of Oncology, Volume 30, Issue 8, August 2019, Pages 1194–1220.]

🗨️ pertuzumab + trastuzumab

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Summary:

ESMO Clinical Practice Guidelines include the following supporting statement:

- "The role of dual HER2 blockade (including a combination of trastuzumab and pertuzumab) is not well proven and such treatment is not recommended for routine use, although it may be discussed on a case-by-case basis."

Reference: ESMO Clinical Practice Guidelines - ESMO-Primary Breast Cancer [Ann Oncol (2015) 26 (suppl 5): v8-v30.]



Signatures

Testing Personnel:

Laboratory Supervisor:

Pathologist:



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