Taipei Veterans General Hospital

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Sample Information

Patient Name: 黃媛禎
Gender: Female
ID No.: G200065626
History No.: 41161915
Age: 76

Ordering Doctor: DOC3078B 談啟蘋
Ordering REQ.: 0BMQPZC
Signing in Date: 2021/10/28

Path No.: S110-99863
MP No.: F21087
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: C110-32599
Percentage of tumor cells: 70%

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

Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

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Report Highlights

3 Relevant Biomarkers
59 Therapies Available
18 Clinical Trials

Relevant Non-Small Cell Lung Cancer Variants

Gene	Finding	Gene	Finding
ALK	None detected	NTRK1	None detected
BRAF	None detected	NTRK2	None detected
EGFR	***EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAAC AinsAACT (EGFR exon 19 deletion)***	NTRK3	None detected
ERBB2	***ERBB2 amplification***	RET	None detected
KRAS	None detected	ROS1	None detected
MET	***MET amplification***		

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	*EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT* EGFR exon 19 deletion epidermal growth factor receptor Allele Frequency: 53.57% **Prognostic significance:** None **Diagnostic significance:** None	**afatinib** [1, 2] **bevacizumab* + erlotinib** [2] **dacomitinib** [1, 2] **erlotinib** [1, 2] **erlotinib + ramucirumab** [1, 2] **gefitinib** [1, 2] **osimertinib** [1, 2] afatinib + cetuximab atezolizumab + bevacizumab + chemotherapy bevacizumab + gefitinib gefitinib + chemotherapy osimertinib + chemotherapy	None	17
IIC	*ERBB2 amplification* erb-b2 receptor tyrosine kinase 2 **Prognostic significance:** None **Diagnostic significance:** None	None	**ado-trastuzumab emtansine** [1, 2] **irbinitinib + trastuzumab + chemotherapy** [1, 2] **lapatinib + chemotherapy** [1, 2] **lapatinib + hormone therapy** [1, 2] **lapatinib + trastuzumab** [2] **margetuximab + chemotherapy** [1] **neratinib** [1, 2] **neratinib + chemotherapy** [1] **pembrolizumab + trastuzumab + chemotherapy** [1] **pertuzumab + trastuzumab + chemotherapy** [1, 2] **pertuzumab/trastuzumab/ hyaluronidase-zzxf + chemotherapy** [1, 2] **trastuzumab and hyaluronidase-oysk** [1] **trastuzumab and hyaluronidase-oysk + chemotherapy** [1] **trastuzumab deruxtecan** [1, 2] **trastuzumab*** [1, 2] **trastuzumab* + chemotherapy** [1, 2] **trastuzumab* + hormone therapy** [2] hormone therapy lapatinib + trastuzumab + hormone therapy pertuzumab + trastuzumab pertuzumab + trastuzumab + hormone therapy pertuzumab + trastuzumab + hormone therapy + chemotherapy trastuzumab + hormone therapy + chemotherapy trastuzumab containing regimen	0

Public data sources included in relevant therapies: FDA[1], NCCN, **EMA**[2], ESMO
Public data sources included in prognostic and diagnostic significance: NCCN, ESMO
Tier Reference: Li et al. *Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists.* J Mol Diagn. 2017 Jan;19(1):4-23.
*** Includes biosimilars**

Relevant Biomarkers (continued)

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	*MET amplification* MET proto-oncogene, receptor tyrosine kinase **Prognostic significance:** None **Diagnostic significance:** None	capmatinib crizotinib	None	5

Public data sources included in relevant therapies: FDA[1], NCCN, **EMA**[2], ESMO
Public data sources included in prognostic and diagnostic significance: NCCN, ESMO
Tier Reference: Li et al. *Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists.* J Mol Diagn. 2017 Jan;19(1):4-23.
*** Includes biosimilars**

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

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
EGFR	p.(E746_A750del)	c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT	.	chr7:55242465	53.57%	NM_005228.5	nonframeshift Block Substitution	1973

Copy Number Variations

Gene	Locus	Copy Number
MET	chr7:116313480	10.77
ERBB2	chr17:37868126	10.61

Biomarker Descriptions

EGFR (epidermal growth factor receptor)

Background: The EGFR gene encodes the epidermal growth factor receptor (EGFR) tyrosine kinase, a member of the ERBB/human epidermal growth factor receptor (HER) family. In addition to EGFR/ERBB1/HER1, other members of the ERBB/HER family include ERBB2/HER2, ERBB3/HER3, and ERBB4/HER4[1]. EGFR ligand induced dimerization results in kinase activation and leads to stimulation of oncogenic signaling pathways including the PI3K/AKT/MTOR and RAS/RAF/MEK/ERK pathways. Activation of these pathways promote cell proliferation, differentiation, and survival[2,3].

Alterations and prevalence: Recurrent somatic mutations in the tyrosine kinase domain (TKD) of EGFR are observed in approximately 10-20% of lung adenocarcinoma, and at higher frequencies in never-smoker, female, and Asian populations[4,5,6,7]. The most common mutations occur near the ATP-binding pocket of the TKD and include short in-frame deletions in exon 19 (EGFR exon 19 deletion) and the L858R amino acid substitution in exon 21[8]. These mutations constitutively activate EGFR resulting in downstream signaling, and represent 80% of the EGFR mutations observed in lung cancer. A second group of less prevalent activating mutations include E709K, G719X, S768I, L861Q, and short in-frame insertion mutations in exon 20[9,10,11,12]. EGFR activating mutations in lung cancer tend to be mutually exclusive to KRAS activating mutations[13]. In contrast, a different set of recurrent activating EGFR mutations in the extracellular domain include R108K, A289V and G598V and are primarily observed in glioblastoma[8,14]. Amplification of EGFR is observed in several cancer types including 30% of glioblastoma, 12% of esophageal cancer, 10% of head and neck cancer, 5% of bladder cancer, and 5% of lung squamous cell carcinoma[5,6,7,14,15]. Deletion of exons 2-7, encoding the extracellular domain of EGFR (EGFRvIII), results in overexpression of a ligand-independent constitutively active protein and is observed in approximately 30% of glioblastoma[16,17,18].

Potential relevance: Approved first-generation EGFR tyrosine kinase inhibitors (TKIs) include erlotinib[19] (2004) and gefitinib[20] (2015), which block the activation of downstream signaling by reversible interaction with the ATP-binding site. Although initially approved for advanced lung cancer, the discovery that drug sensitivity was associated with exon 19 and exon 21 activating mutations allowed first-generation TKIs to become subsequently approved for front-line therapy in lung cancer tumors containing exon 19 or exon 21

Biomarker Descriptions (continued)

activating mutations. Second-generation TKIs afatinib[21] (2013) and dacomitinib[22] (2018) bind EGFR and other ERBB/HER gene family members irreversibly and were subsequently approved. First- and second-generation TKIs afatinib, dacomitinib, erlotinib, and gefitinib are recommended for the treatment NSCLC harboring EGFR exon 19 insertions, exon 19 deletions, point mutations L861Q, L858R, S768I, and codon 719 mutations, whereas most EGFR exon 20 insertions, except p.A763_Y764insFQEA, confer resistance to the same therapies[23,24,25,26]. In lung cancer containing EGFR exon 19 or 21 activating mutations, treatment with TKIs is eventually associated with the emergence of drug resistance[27]. The primary resistance mutation that emerges following treatment with first-generation TKI is T790M, accounting for 50-60% of resistant cases[8]. Third generation TKIs were developed to maintain sensitivity in the presence of T790M. Osimertinib[28] (2015) is an irreversible inhibitor indicated for metastatic EGFR T790M positive lung cancer and for the first-line treatment of metastatic NSCLC containing EGFR exon 19 deletions or exon 21 L858R mutations. Like first-generation TKIs, treatment with osimertinib is associated with acquired resistance. In this case, resistance is associated with the C797S mutation, and occurs in 22-44% of cases[27]. The T790M and C797S mutations may be each selected following sequential treatment with a first-generation TKI followed by a third-generation TKI or vice versa[29]. T790M and C797S can occur in either cis or trans allelic orientation[29]. If C797S is observed following progression after treatment with a third-generation TKI in the first-line setting, sensitivity may be retained to first-generation TKIs[29]. If C797S co-occurs in trans with T790M following sequential treatment with first- and third-generation TKIs, patients may exhibit sensitivity to combination first- and third-generation TKIs, but resistance to third-generation TKIs alone[29,30]. However, C797S occurring in cis conformation with T790M, confers resistance to first- and third-generation TKIs[29]. Fourth-generation TKIs are in development to overcome acquired C797S and T790M resistance mutations after osimertinib treatment. EGFR targeting antibodies including cetuximab (2004), panitumumab (2006), and necitumumab (2016) are under investigation in combination with EGFR-targeting TKIs for efficacy against EGFR mutations. The bispecific antibody, JNJ-61186372[31], targeting EGFR and MET, and the TKI mobocertinib[32], each received a breakthrough designation from the FDA (2020) for NSCLC tumors harboring EGFR exon 20 insertion mutations. The Oncoprex immunogene therapy CNVN-202[33] in combination with osimertinib received a fast track designation from the FDA (2020) for NSCLC tumors harboring EGFR mutations that progressed on osimertinib alone. BDTX-189[34] was granted a fast track designation (2020) for the treatment of solid tumors harboring an EGFR exon 20 insertion mutation.

ERBB2 (erb-b2 receptor tyrosine kinase 2)

Background: The ERBB2 gene encodes the erb-b2 receptor tyrosine kinase 2, a member of the human epidermal growth factor receptor (HER) family. Along with ERBB2/HER2, EGFR/ERBB1/HER1, ERBB3/HER3, and ERBB4/HER4 make up the HER protein family[1]. All ERBB/HER proteins encode transmembrane receptor tyrosine kinases. However, ERBB2/HER2 is an orphan receptor with no known ligand. ERBB2 preferentially binds other ligand bound ERBB/HER family members to form hetero-dimers resulting in the activation of ERBB2 tyrosine kinase activity and subsequent activation of the PI3K/AKT/MTOR and RAS/RAF/MAPK/ERK signaling pathways which promote cell proliferation, differentiation, and survival[3]. Recurrent focal amplification of the ERBB2 gene leads to increased expression in several cancer types. ERBB2 overexpression in immortalized cell lines is oncogenic and leads to ERBB2 homo-dimerization and activation without ligand binding[35,36,37].

Alterations and prevalence: ERBB2 gene amplification occurs in 10-20% of breast, esophageal, and gastric cancers, 5-10% of bladder, cervical, pancreas, and uterine cancers, and 1-5% of colorectal, lung, and ovarian cancers[5,6,7,38,39,40,41,42]. Recurrent somatic activating mutations in ERBB2/HER2 occur at low frequencies (<1%) in diverse cancer types[7,43,44]. In breast, bladder, and colorectal cancers, the most common recurrent ERBB2 activating mutations include kinase domain mutations L755S and V777L and the extracellular domain mutation S310F. In lung cancer, the most common recurrent ERBB2 activating mutations include in-frame exon 20 insertions, particularly Y772_A775dup.

Potential relevance: The discovery of ERBB2/HER2 as an important driver of breast cancer in 1987 led to the development of trastuzumab, a humanized monoclonal antibody with specificity to the extracellular domain of HER2[45,46]. Trastuzumab[47] was FDA approved for the treatment of HER2 positive breast cancer in 1998, and subsequently in HER2 positive metastatic gastric and gastroesophageal junction adenocarcinoma in 2010. Additional monoclonal antibody therapies have been approved by the FDA for HER2-positive breast cancer including pertuzumab[48] (2012), a humanized monoclonal antibody that inhibits HER2 dimerization, and ado-trastuzumab emtansine[49] (2013), a conjugate of trastuzumab and a potent antimicrotubule agent. The combination of pertuzumab, trastuzumab, and a taxane is the preferred front-line regimen for HER2-positive metastatic breast cancer[50]. In addition to monoclonal antibodies, the small molecule inhibitor lapatinib[51], with specificity for both EGFR and ERBB2, was FDA approved (2007) for the treatment of patients with advanced HER2-positive breast cancer who have received prior therapy including trastuzumab. In 2017, the FDA approved the use of neratinib[52], an irreversible kinase inhibitor of EGFR, ERBB2/HER2, and ERBB4, for the extended adjuvant treatment of adult patients with early stage HER2-positive breast cancer. In 2020, the FDA approved neratinib[52] in combination with capecitabine for HER2-positive advanced or metastatic patients after two or more prior HER2-directed therapies. Also in 2020, the TKI irbinitinib[53] was FDA approved for HER2 overexpressing or amplified breast cancer in combination with trastuzumab and capecitabine. In 2021, the PD-1 blocking antibody, pembrolizumab, in combination with trastuzumab, fluoropyrimidine- and platinum-based chemotherapy, was approved for HER2 amplified gastric or gastroesophageal (GEJ) adenocarcinoma in the first line[54]. The vaccine, nelipepimut-S[55], was granted fast-track designation by the FDA (2016) in patients with low to intermediate HER2 expressing (IHC score 1+ or 2+) breast cancer. In 2018 fast-track designation was granted to the monoclonal antibody margetuximab[56] in patients with ERBB2 positive breast cancer previously treated with an anti-HER2 therapy. In 2019, the novel bispecific antibody ZW25[57] received fast-track designation for patients with HER2-amplified biliary tract cancer or in combination with standard chemotherapy for patients

Biomarker Descriptions (continued)

with HER2-overexpressing gastroesophageal adenocarcinoma (GEA). In 2020, BDTX-189[34] received fast-track designation for adult patients with solid tumors harboring an allosteric human ERBB2 mutation or exon 20 insertion, and the humanized anti-HER2 antibody drug conjugate disitamab vedotin received breakthrough designation for adult patients with HER2-positive urothelial cancer after previous platinum-chemotherapy treatment[58]. In 2021, the antibody-drug conjugate ARX788[59] received fast-track designation as a monotherapy for advanced or metastatic HER2-positive breast cancer that have progressed on one or more anti-HER2 regimens. Certain activating mutations have been observed to impart sensitivity to neratinib, afatinib, lapatinib, and trastuzumab, or dacomitinib in early and ongoing clinical studies[60,61,62,63,64]. ERBB2 kinase domain mutations R896G and V659E both showed response to afatinib in two NSCLC case studies[65,66]. Additionally, acquired HER2 mutations in estrogen receptor-positive (ER+) breast cancer have been shown to confer resistance to hormone therapy[67]. However, this was shown to be overcome by neratinib in combination with therapies targeting ER[67].

MET (MET proto-oncogene, receptor tyrosine kinase)

Background: The MET proto-oncogene encodes a receptor tyrosine kinase for the hepatocyte growth factor (HGF) protein, which is expressed by mesenchymal cells. Ubiquitin-dependent proteolysis regulates the steady state level of the MET protein via recognition of the tyrosine phosphorylation site Y1003 in the MET Cbl-binding domain within the juxtamembrane region[68,69,70]. Growth factor signaling leads to MET dimerization and subsequent initiation of downstream effectors including those involved in the RAS/RAF/MEK/ERK and PI3K/AKT signaling pathways, which regulate cell migration, proliferation, and survival[71,72].

Alterations and prevalence: Recurrent somatic MET alterations include activating mutations, gene amplification, and translocations generating MET gene fusions. Recurrent somatic mutations fall into two classes, mutations in the MET kinase domain, which are uncommon, and splice-site mutations affecting exon 14. Recurrent kinase domain mutations are observed in papillary renal cell carcinoma (PRCC) (1-2%) and include M1250T, H1094Y, and V1070E. Mutation of the Y1003 phosphorylation site is reported in lung cancer but is uncommon (<1%)[7,14]. In contrast, splice-site mutations flanking exon 14 are observed in 4% of non-small cell lung cancer (NSCLC). These mutations include canonical splice site mutations affecting exon 14 and deletions that extend into the splicing motifs within intron 13[73,74]. Such mutations disrupt splicing leading to the formation of an alternative transcript that joins exon 13 directly to exon 15 and skips exon 14 entirely. The MET exon 14 skipping transcript lacks the juxtamembrane domain that contains the recognition motif for ubiquitin-dependent proteolysis and thus leads to a marked increase in steady-state level of the MET protein[75]. MET exon 14 skipping mutations act as oncogenic drivers in lung cancer mutually exclusive to activating mutations in EGFR and KRAS and other oncogenic fusions such as ALK and ROS1[73,76,77]. MET is amplified in 2-5% of ovarian cancer, esophageal adenocarcinoma, stomach adenocarcinoma, glioblastoma, and lung adenocarcinoma[7,14,39]. Recurrent MET fusions, although infrequent, are observed in adult and pediatric glioblastoma, papillary renal cell carcinoma, lung cancer, liver cancer, thyroid cancer, and melanoma[78,79,80]. MET alterations are believed to be enriched in late-stage cancers where they drive tumor progression and metastasis[81,82,83].

Potential relevance: In 2020, the FDA granted accelerated approval to capmatinib[84] for NSCLC harboring MET exon 14 skipping positive as detected by an FDA-approved test[23]. The kinase inhibitor, tepotinib[85], is also approved (2021) for MET exon 14 skipping mutations in NSCLC[85]. MET exon 14 skipping mutations confer sensitivity to approved kinase inhibitors including crizotinib (2011), which is recommended for MET amplifications and exon 14 skipping mutations[23,73,76,77]. The FDA also granted breakthrough therapy designation (2018) to crizotinib for metastatic non-small cell lung cancer (NSCLC) with MET exon 14 alterations with disease progression on or after platinum-based chemotherapy[86]. Conversely, amplification of MET has been observed to mediate resistance to EGFR tyrosine kinase inhibitors (TKIs)[87,88,89,90,91]. In a phase II trial testing the MET inhibitor savolitinib, patients with advanced PRCC exhibited median progression free survival (PFS) of 6.2 and 1.4 months for MET-driven and MET-independent PRCC, respectively[92].

Relevant Therapy Summary

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

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
osimertinib	●	●	●	●	● (III)
afatinib	●	●	●	●	✖
dacomitinib	●	●	●	●	✖

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

Relevant Therapy Summary (continued)

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

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
erlotinib	●	●	●	●	✖
erlotinib + ramucirumab	●	●	●	●	✖
gefitinib	●	●	●	●	✖
bevacizumab + erlotinib	✖	●	●	●	✖
afatinib + cetuximab	✖	●	✖	✖	✖
osimertinib + chemotherapy	✖	●	✖	✖	✖
osimertinib + chemotherapy + surgical intervention	✖	●	✖	✖	✖
bevacizumab (Allergan) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Fujifilm Kyowa Kirin Biologics) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Mabxience) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Pfizer) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Samsung Bioepis) + erlotinib	✖	✖	●	✖	✖
atezolizumab + bevacizumab + carboplatin + paclitaxel	✖	✖	✖	●	✖
bevacizumab + gefitinib	✖	✖	✖	●	✖
gefitinib + carboplatin + pemetrexed	✖	✖	✖	●	✖
amivantamab, lazertinib, osimertinib	✖	✖	✖	✖	● (III)
osimertinib, chemotherapy	✖	✖	✖	✖	● (III)
atezolizumab, bevacizumab, chemotherapy	✖	✖	✖	✖	● (II)
bevacizumab, erlotinib	✖	✖	✖	✖	● (II)
datopotamab deruxtecan	✖	✖	✖	✖	● (II)
durvalumab, tremelimumab, chemotherapy	✖	✖	✖	✖	● (II)
osimertinib, savolitinib	✖	✖	✖	✖	● (II)
patritumab deruxtecan	✖	✖	✖	✖	● (II)
savolitinib, osimertinib	✖	✖	✖	✖	● (II)
tepotinib, osimertinib	✖	✖	✖	✖	● (II)
DZD-9008	✖	✖	✖	✖	● (I/II)
amivantamab	✖	✖	✖	✖	● (I)
lazertinib, amivantamab	✖	✖	✖	✖	● (I)

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

Relevant Therapy Summary (continued)

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

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
telisotuzumab vedotin, osimertinib	✖	✖	✖	✖	● (I)
TNO-155, nazartinib	✖	✖	✖	✖	● (I)

ERBB2 amplification

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
ado-trastuzumab emtansine	○	○	○	○	✖
pertuzumab + trastuzumab + chemotherapy	○	○	○	○	✖
pertuzumab + trastuzumab + docetaxel	○	○	○	○	✖
trastuzumab + capecitabine + cisplatin	○	○	○	○	✖
trastuzumab + cisplatin + fluorouracil	○	○	○	○	✖
trastuzumab deruxtecan	○	○	○	○	✖
irbinitinib + trastuzumab + capecitabine	○	○	○	✖	✖
lapatinib + capecitabine	○	○	○	✖	✖
neratinib	○	○	○	✖	✖
trastuzumab	○	○	○	✖	✖
trastuzumab + carboplatin + docetaxel	○	○	○	✖	✖
trastuzumab + docetaxel	○	○	○	✖	✖
trastuzumab + paclitaxel	○	○	○	✖	✖
neratinib + capecitabine	○	○	✖	✖	✖
lapatinib + letrozole	○	✖	○	✖	✖
pertuzumab/trastuzumab/hyaluronidase-zzxf + cyclophosphamide + doxorubicin	○	✖	○	✖	✖
pertuzumab/trastuzumab/hyaluronidase-zzxf + docetaxel	○	✖	○	✖	✖
trastuzumab (Biocon)	○	✖	○	✖	✖
trastuzumab (Biocon) + capecitabine + cisplatin	○	✖	○	✖	✖
trastuzumab (Biocon) + carboplatin + docetaxel	○	✖	○	✖	✖
trastuzumab (Biocon) + cisplatin + fluorouracil	○	✖	○	✖	✖
trastuzumab (Biocon) + docetaxel	○	✖	○	✖	✖
trastuzumab (Biocon) + paclitaxel	○	✖	○	✖	✖

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

Relevant Therapy Summary (continued)

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

ERBB2 amplification (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
trastuzumab (Celltrion)	○	✖	○	✖	✖
trastuzumab (Celltrion) + capecitabine + cisplatin	○	✖	○	✖	✖
trastuzumab (Celltrion) + carboplatin + docetaxel	○	✖	○	✖	✖
trastuzumab (Celltrion) + cisplatin + fluorouracil	○	✖	○	✖	✖
trastuzumab (Celltrion) + docetaxel	○	✖	○	✖	✖
trastuzumab (Celltrion) + paclitaxel	○	✖	○	✖	✖
trastuzumab (Pfizer)	○	✖	○	✖	✖
trastuzumab (Pfizer) + capecitabine + cisplatin	○	✖	○	✖	✖
trastuzumab (Pfizer) + carboplatin + docetaxel	○	✖	○	✖	✖
trastuzumab (Pfizer) + cisplatin + fluorouracil	○	✖	○	✖	✖
trastuzumab (Pfizer) + docetaxel	○	✖	○	✖	✖
trastuzumab (Pfizer) + paclitaxel	○	✖	○	✖	✖
trastuzumab (Samsung Bioepis)	○	✖	○	✖	✖
trastuzumab (Samsung Bioepis) + capecitabine + cisplatin	○	✖	○	✖	✖
trastuzumab (Samsung Bioepis) + carboplatin + docetaxel	○	✖	○	✖	✖
trastuzumab (Samsung Bioepis) + cisplatin + fluorouracil	○	✖	○	✖	✖
trastuzumab (Samsung Bioepis) + docetaxel	○	✖	○	✖	✖
trastuzumab (Samsung Bioepis) + paclitaxel	○	✖	○	✖	✖
margetuximab + chemotherapy	○	✖	✖	✖	✖
pembrolizumab + trastuzumab + chemotherapy + fluoropyrimidine	○	✖	✖	✖	✖
trastuzumab and hyaluronidase-oysk	○	✖	✖	✖	✖
trastuzumab and hyaluronidase-oysk + carboplatin + docetaxel	○	✖	✖	✖	✖
trastuzumab and hyaluronidase-oysk + cyclophosphamide + doxorubicin + paclitaxel	○	✖	✖	✖	✖
trastuzumab and hyaluronidase-oysk + docetaxel	○	✖	✖	✖	✖
trastuzumab and hyaluronidase-oysk + paclitaxel	○	✖	✖	✖	✖

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

Relevant Therapy Summary (continued)

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

ERBB2 amplification (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
lapatinib + trastuzumab	✖	○	○	○	✖
pertuzumab + trastuzumab	✖	○	✖	○	✖
pertuzumab + trastuzumab + hormone therapy + chemotherapy	✖	○	✖	○	✖
pertuzumab + trastuzumab + paclitaxel	✖	○	✖	○	✖
tamoxifen	✖	○	✖	○	✖
trastuzumab + chemotherapy	✖	○	✖	○	✖
trastuzumab + hormone therapy + chemotherapy	✖	○	✖	○	✖
trastuzumab + vinorelbine	✖	○	✖	○	✖
aromatase inhibitor	✖	○	✖	✖	✖
fulvestrant	✖	○	✖	✖	✖
hormone therapy	✖	○	✖	✖	✖
lapatinib + aromatase inhibitor	✖	○	✖	✖	✖
lapatinib + trastuzumab + aromatase inhibitor	✖	○	✖	✖	✖
margetuximab + capecitabine	✖	○	✖	✖	✖
margetuximab + eribulin	✖	○	✖	✖	✖
margetuximab + gemcitabine	✖	○	✖	✖	✖
margetuximab + vinorelbine	✖	○	✖	✖	✖
neratinib + paclitaxel	✖	○	✖	✖	✖
pembrolizumab + trastuzumab + capecitabine + cisplatin	✖	○	✖	✖	✖
pembrolizumab + trastuzumab + capecitabine + oxaliplatin	✖	○	✖	✖	✖
pembrolizumab + trastuzumab + cisplatin + fluorouracil	✖	○	✖	✖	✖
pembrolizumab + trastuzumab + fluorouracil + oxaliplatin	✖	○	✖	✖	✖
pertuzumab + trastuzumab + carboplatin + docetaxel	✖	○	✖	✖	✖
trastuzumab + aromatase inhibitor	✖	○	✖	✖	✖
trastuzumab + capecitabine	✖	○	✖	✖	✖
trastuzumab + capecitabine + 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 ✖ No evidence

ERBB2 amplification (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
trastuzumab + carboplatin + docetaxel + fluorouracil	✖	○	✖	✖	✖
trastuzumab + carboplatin + paclitaxel	✖	○	✖	✖	✖
trastuzumab + chemotherapy (other)	✖	○	✖	✖	✖
trastuzumab + cisplatin + docetaxel	✖	○	✖	✖	✖
trastuzumab + cisplatin + docetaxel + fluorouracil	✖	○	✖	✖	✖
trastuzumab + cisplatin + paclitaxel	✖	○	✖	✖	✖
trastuzumab + cyclophosphamide + docetaxel	✖	○	✖	✖	✖
trastuzumab + docetaxel + fluorouracil + oxaliplatin	✖	○	✖	✖	✖
trastuzumab + fluorouracil	✖	○	✖	✖	✖
trastuzumab + fluorouracil + irinotecan	✖	○	✖	✖	✖
trastuzumab + fluorouracil + oxaliplatin	✖	○	✖	✖	✖
trastuzumab + fulvestrant	✖	○	✖	✖	✖
trastuzumab + tamoxifen	✖	○	✖	✖	✖
trastuzumab (Biocon) + anastrozole	✖	✖	○	✖	✖
trastuzumab (Biocon) + CMF + doxorubicin + paclitaxel	✖	✖	○	✖	✖
trastuzumab (Celltrion) + anastrozole	✖	✖	○	✖	✖
trastuzumab (Celltrion) + CMF + doxorubicin + paclitaxel	✖	✖	○	✖	✖
trastuzumab (Henlius)	✖	✖	○	✖	✖
trastuzumab (Henlius) + anastrozole	✖	✖	○	✖	✖
trastuzumab (Henlius) + capecitabine + cisplatin	✖	✖	○	✖	✖
trastuzumab (Henlius) + carboplatin + docetaxel	✖	✖	○	✖	✖
trastuzumab (Henlius) + cisplatin + fluorouracil	✖	✖	○	✖	✖
trastuzumab (Henlius) + CMF + doxorubicin + paclitaxel	✖	✖	○	✖	✖
trastuzumab (Henlius) + docetaxel	✖	✖	○	✖	✖
trastuzumab (Henlius) + paclitaxel	✖	✖	○	✖	✖
trastuzumab (Pfizer) + anastrozole	✖	✖	○	✖	✖
trastuzumab (Pfizer) + CMF + doxorubicin + paclitaxel	✖	✖	○	✖	✖

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

Relevant Therapy Summary (continued)

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

ERBB2 amplification (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
trastuzumab (Samsung Bioepis) + anastrozole	✖	✖	○	✖	✖
trastuzumab (Samsung Bioepis) + CMF + doxorubicin + paclitaxel	✖	✖	○	✖	✖
trastuzumab (Synthon)	✖	✖	○	✖	✖
trastuzumab (Synthon) + anastrozole	✖	✖	○	✖	✖
trastuzumab (Synthon) + capecitabine + cisplatin	✖	✖	○	✖	✖
trastuzumab (Synthon) + carboplatin + docetaxel	✖	✖	○	✖	✖
trastuzumab (Synthon) + cisplatin + fluorouracil	✖	✖	○	✖	✖
trastuzumab (Synthon) + CMF + doxorubicin + paclitaxel	✖	✖	○	✖	✖
trastuzumab (Synthon) + docetaxel	✖	✖	○	✖	✖
trastuzumab (Synthon) + paclitaxel	✖	✖	○	✖	✖
trastuzumab + anastrozole	✖	✖	○	✖	✖
trastuzumab + CMF + doxorubicin + paclitaxel	✖	✖	○	✖	✖
aromatase inhibitor + luteinizing hormone-releasing factor	✖	✖	✖	○	✖
pertuzumab + trastuzumab + capecitabine	✖	✖	✖	○	✖
pertuzumab + trastuzumab + hormone therapy	✖	✖	✖	○	✖
pertuzumab + trastuzumab + nab-paclitaxel	✖	✖	✖	○	✖
pertuzumab + trastuzumab + vinorelbine	✖	✖	✖	○	✖
trastuzumab + hormone therapy	✖	✖	✖	○	✖
trastuzumab + taxane	✖	✖	✖	○	✖
trastuzumab containing regimen	✖	✖	✖	○	✖

MET amplification

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
capmatinib	✖	●	✖	✖	✖
crizotinib	✖	●	✖	✖	✖
osimertinib, savolitinib	✖	✖	✖	✖	● (II)
savolitinib, osimertinib	✖	✖	✖	✖	● (II)

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

Relevant Therapy Summary (continued)

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

MET amplification (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
tepotinib, osimertinib	✖	✖	✖	✖	● (II)
amivantamab	✖	✖	✖	✖	● (I)
HLX55	✖	✖	✖	✖	● (I)

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

Relevant Therapy Details

Current FDA Information

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

FDA information is current as of 2021-08-18. For the most up-to-date information, search www.fda.gov.

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT

● afatinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2019-10-11 **Variant class:** EGFR exon 19 deletion

Indications and usage:

GILOTRIF® is a kinase inhibitor indicated for:

- First-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have non-resistant epidermal growth factor receptor (EGFR) mutations as detected by an FDA-approved test.

Limitation of Use: Safety and efficacy of GILOTRIF® were not established in patients whose tumors have resistant EGFR mutations

- Treatment of patients with metastatic, squamous NSCLC progressing after platinum-based chemotherapy

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/201292s015lbl.pdf

● dacomitinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2020-12-18 **Variant class:** EGFR exon 19 deletion

Indications and usage:
VIZIMPRO® is a kinase inhibitor indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R substitution mutations as detected by an FDA-approved test.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/211288s003lbl.pdf

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT (continued)

erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2016-10-18 **Variant class:** EGFR exon 19 deletion

Indications and usage:

TARCEVA® is a kinase inhibitor indicated for:

- The treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test receiving first-line, maintenance, or second or greater line treatment after progression following at least one prior chemotherapy regimen.
- First-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer, in combination with gemcitabine.

Limitations of Use:

- Safety and efficacy of TARCEVA® have not been established in patients with NSCLC whose tumors have other EGFR mutations.
- TARCEVA® is not recommended for use in combination with platinum-based chemotherapy.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/021743s025lbl.pdf

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erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-06-15 **Variant class:** EGFR exon 19 deletion

Indications and usage:

CYRAMZA® is a human vascular endothelial growth factor receptor 2 (VEGFR2) antagonist indicated:

- as a single agent or in combination with paclitaxel, for treatment of advanced or metastatic gastric or gastro-esophageal junction adenocarcinoma with disease progression on or after prior fluoropyrimidine- or platinum-containing chemotherapy.
- in combination with erlotinib, for first-line treatment of metastatic non-small cell lung cancer with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) mutations.
- in combination with docetaxel, for treatment of metastatic non-small cell lung cancer with disease progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving CYRAMZA®.
- in combination with FOLFIRI, for the treatment of metastatic colorectal cancer with disease progression on or after prior therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine.
- as a single agent, for the treatment of hepatocellular carcinoma in patients who have an alpha fetoprotein of ≥400 ng/mL and have been treated with sorafenib.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125477s039lbl.pdf

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EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT (continued)

gefitinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-05-05 **Variant class:** EGFR exon 19 deletion

Indications and usage:

IRESSA® is a tyrosine kinase inhibitor indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test.

Limitation of Use: Safety and efficacy of IRESSA® have not been established in patients whose tumors have EGFR mutations other than exon 19 deletions or exon 21 (L858R) substitution mutations.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/206995s004lbl.pdf

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-07-26 **Variant class:** EGFR exon 19 deletion

Indications and usage:

TAGRISSO® is a kinase inhibitor indicated for:

- as adjuvant therapy after tumor resection in adult patients with non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
- the first-line treatment of adult patients with metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
- the treatment of adult patients with metastatic EGFR T790M mutation positive NSCLC, as detected by an FDA-approved test, whose disease has progressed on or after EGFR TKI therapy.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/208065s022lbl.pdf

ERBB2 amplification

ado-trastuzumab emtansine

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

Indications and usage:

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

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

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

Reference:

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

ERBB2 amplification (continued)

irbinitinib + trastuzumab + capecitabine

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

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

Reference:

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

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lapatinib + capecitabine, lapatinib + letrozole

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

Other criteria: ER positive, PR positive

Indications and usage:

TYKERB® is a kinase inhibitor indicated in combination with:

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

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

Reference:

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

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margetuximab + chemotherapy

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

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

Reference:

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

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ERBB2 amplification (continued)

neratinib, neratinib + capecitabine

Cancer type: Breast Cancer **Label as of:** 2021-06-28 **Variant class:** ERBB2 overexpression

Indications and usage:

NERLYNX® is a kinase inhibitor indicated:

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

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/208051s009lbl.pdf

ERBB2 amplification (continued)

○ pembrolizumab + trastuzumab + chemotherapy + fluoropyrimidine

Cancer type: Gastric Cancer, Gastroesophageal Junction Adenocarcinoma

Label as of: 2021-08-10

Variant class: ERBB2 amplification or ERBB2 overexpression

Indications and usage:

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

Melanoma

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

Non-Small Cell Lung Cancer (NSCLC)

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

Head and Neck Squamous Cell Cancer (HNSCC)

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

Classical Hodgkin Lymphoma (cHL)

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

Primary Mediastinal Large B-Cell Lymphoma (PMBCL)

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

Urothelial Carcinoma

- for the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy and whose tumors express PD-L1 [Combined Positive Score (CPS) ≥ 10] as determined by an FDA-approved test, or in patients who are not eligible for any platinum-containing chemotherapy regardless of PD-L1 status.[1]
- for the treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
- for the treatment of patients with Bacillus Calmette-Guerin (BCG)-unresponsive, high-risk, non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy.

Microsatellite Instability-High or Mismatch Repair Deficient Cancer

ERBB2 amplification (continued)

- for the treatment of adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options.[1]
- Limitations of Use: The safety and effectiveness of KEYTRUDA® in pediatric patients with MSI-H central nervous system cancers have not been established.

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

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

Gastric Cancer

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

Esophageal Cancer

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

Cervical Cancer

- for the treatment of patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumors express PD-L1 [Combined Positive Score (CPS) ≥ 1] as determined by an FDA-approved test.[1]

Hepatocellular Carcinoma (HCC)

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

Merkel Cell Carcinoma (MCC)

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

Renal Cell Carcinoma (RCC)

- in combination with axitinib, for the first-line treatment of adult patients with advanced RCC.
- in combination with lenvatinib, for the first-line treatment of adult patients with advanced RCC.

Endometrial Carcinoma

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

Tumor Mutational Burden-High (TMB-H) Cancer

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

Cutaneous Squamous Cell Carcinoma (cSCC)

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

Triple-Negative Breast Cancer (TNBC)

- for the treatment of patients with high-risk early-stage TNBC in combination with chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery.
- in combination with chemotherapy, for the treatment of patients with locally recurrent unresectable or metastatic TNBC whose tumors express PD-L1 [Combined Positive Score (CPS) ≥10] as determined by an FDA approved test.

ERBB2 amplification (continued)

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

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

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

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

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125514s102lbl.pdf

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

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

Indications and usage:

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

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

Reference:

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

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

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

Indications and usage:

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

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

Reference:

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

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ERBB2 amplification (continued)

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

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

Indications and usage:

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

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

Reference:

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

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

Cancer type: Breast Cancer, Gastric Cancer, Gastroesophageal Junction Adenocarcinoma **Label as of:** 2019-04-17 **Variant class:** ERBB2 overexpression or ERBB2 amplification

Indications and usage:

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

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

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

Reference:

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

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

Cancer type: Breast Cancer, Gastric Cancer, Gastroesophageal Junction Adenocarcinoma **Label as of:** 2019-05-16 **Variant class:** ERBB2 overexpression or ERBB2 amplification

Indications and usage:

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

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

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

Reference:

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

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ERBB2 amplification (continued)

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

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

Label as of: 2019-03-11

Variant class: ERBB2 amplification or ERBB2 overexpression

Indications and usage:

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

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

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

Reference:

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

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

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

Label as of: 2019-01-18

Variant class: ERBB2 amplification or ERBB2 overexpression

Indications and usage:

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

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

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

Reference:

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

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

Cancer type: Breast Cancer

Label as of: 2019-02-28

Variant class: ERBB2 amplification

Indications and usage:

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

- The treatment of HER2-overexpressing breast cancer.

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

Reference:

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

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ERBB2 amplification (continued)

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

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

Other criteria: ER negative, PR negative

Indications and usage:

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

- The treatment of HER2-overexpressing breast cancer.

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

Reference:

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

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trastuzumab deruxtecan

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

Indications and usage:

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

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

Reference:

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

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trastuzumab deruxtecan

Cancer type: Breast Cancer, Gastric Cancer, Gastroesophageal Junction Adenocarcinoma **Label as of:** 2021-01-15 **Variant class:** ERBB2 overexpression

Indications and usage:

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

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

Reference:

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

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ERBB2 amplification (continued)

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

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

Label as of: 2018-11-29

Variant class: ERBB2 overexpression or ERBB2 amplification

Indications and usage:

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

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

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

Reference:

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

Current NCCN Information

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

NCCN information is current as of 2021-08-02. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT

● afatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

● dacomitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

● erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

● gefitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT (continued)

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

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afatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

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afatinib + cetuximab

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

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bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Other recommended intervention
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT (continued)

dacomitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

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erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

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erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Other recommended intervention
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

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gefitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT (continued)

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2021]

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osimertinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

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osimertinib + chemotherapy

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IIB, Stage IIIA, Stage IIIB (Adjuvant therapy)
- Stage IIIA; Resectable (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

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osimertinib + chemotherapy + surgical intervention

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IIB (Adjuvant therapy)
- Stage IIIA; Resectable (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT (continued)

erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

NCCN Recommendation category: 2B

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

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2021]

---

erlotinib

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2021]

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afatinib

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

NCCN Recommendation category: 2B

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

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2021]

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gefitinib

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

NCCN Recommendation category: 2B

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

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2021]

ERBB2 amplification

ado-trastuzumab emtansine

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive, Unresectable, Local (Second-line therapy); Preferred intervention

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

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irbinitinib + trastuzumab + capecitabine

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Stage IV; Recurrent, Unresectable, Invasive, Local (Third-line therapy, Subsequent therapy); Other recommended intervention

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

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pertuzumab + trastuzumab + docetaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive, Unresectable, Local (First-line therapy); Preferred intervention

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

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trastuzumab + capecitabine + cisplatin

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 3.2021]

ERBB2 amplification (continued)

trastuzumab + capecitabine + cisplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2021]

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trastuzumab + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor negative

NCCN Recommendation category: 1

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

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

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trastuzumab + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

NCCN Recommendation category: 1

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

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

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trastuzumab + cisplatin + fluorouracil

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 3.2021]

ERBB2 amplification (continued)

trastuzumab + cisplatin + fluorouracil

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

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2021]

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ado-trastuzumab emtansine

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 3.2021]

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aromatase inhibitor

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

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fulvestrant

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

ERBB2 amplification (continued)

hormone therapy

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

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lapatinib + aromatase inhibitor

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

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lapatinib + capecitabine

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

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive, Unresectable, Local (Third-line therapy, Subsequent therapy); Other recommended intervention

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

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lapatinib + trastuzumab

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

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive, Unresectable, Local (Third-line therapy, Subsequent therapy); Other recommended intervention

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

ERBB2 amplification (continued)

lapatinib + trastuzumab

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

Other criteria: BRAF wild type, RAS wild type

NCCN Recommendation category: 2A

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

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

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lapatinib + trastuzumab

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

Other criteria: BRAF wild type, RAS wild type

NCCN Recommendation category: 2A

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

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

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lapatinib + trastuzumab + aromatase inhibitor

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

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margetuximab + capecitabine

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

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive, Unresectable, Local (Third-line therapy, Subsequent therapy); Other recommended intervention

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

ERBB2 amplification (continued)

margetuximab + eribulin

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

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive, Unresectable, Local (Third-line therapy, Subsequent therapy); Other recommended intervention

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

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margetuximab + gemcitabine

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

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive, Unresectable, Local (Third-line therapy, Subsequent therapy); Other recommended intervention

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

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margetuximab + vinorelbine

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

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive, Unresectable, Local (Third-line therapy, Subsequent therapy); Other recommended intervention

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

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neratinib

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

ERBB2 amplification (continued)

neratinib + capecitabine

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive, Unresectable, Local (Third-line therapy, Subsequent therapy); Other recommended intervention

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

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pembrolizumab + trastuzumab + capecitabine + cisplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2021]

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pembrolizumab + trastuzumab + capecitabine + oxaliplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2021]

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pembrolizumab + trastuzumab + cisplatin + fluorouracil

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2021]

ERBB2 amplification (continued)

pembrolizumab + trastuzumab + fluorouracil + oxaliplatin

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2021]

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pertuzumab + trastuzumab

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

Other criteria: BRAF wild type, RAS wild type

NCCN Recommendation category: 2A

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

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

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pertuzumab + trastuzumab

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 3.2021]

---

pertuzumab + trastuzumab

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

Other criteria: BRAF wild type, RAS wild type

NCCN Recommendation category: 2A

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

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

ERBB2 amplification (continued)

pertuzumab + trastuzumab + carboplatin + docetaxel

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

NCCN Recommendation category: 2A

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

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

---

pertuzumab + trastuzumab + chemotherapy

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

Other criteria: Hormone receptor negative

NCCN Recommendation category: 2A

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

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

---

pertuzumab + trastuzumab + hormone therapy + chemotherapy

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

---

pertuzumab + trastuzumab + paclitaxel

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

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive, Unresectable, Local (First-line therapy); Preferred intervention

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

ERBB2 amplification (continued)

tamoxifen

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

---

trastuzumab

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 3.2021]

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trastuzumab + aromatase inhibitor

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

---

trastuzumab + capecitabine

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

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive, Unresectable, Local (Third-line therapy, Subsequent therapy); Other recommended intervention

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

ERBB2 amplification (continued)

trastuzumab + capecitabine

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 3.2021]

---

trastuzumab + capecitabine

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2021]

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trastuzumab + capecitabine + oxaliplatin

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 3.2021]

---

trastuzumab + capecitabine + oxaliplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2021]

ERBB2 amplification (continued)

trastuzumab + carboplatin + docetaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

---

trastuzumab + carboplatin + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive, Unresectable, Local (Third-line therapy, Subsequent therapy); Other recommended intervention

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

---

trastuzumab + carboplatin + paclitaxel

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 3.2021]

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trastuzumab + carboplatin + paclitaxel

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2021]

ERBB2 amplification (continued)

trastuzumab + carboplatin + paclitaxel

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Uterine Neoplasms [Version 3.2021]

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trastuzumab + chemotherapy

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

Other criteria: Hormone receptor negative

NCCN Recommendation category: 2A

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

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

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trastuzumab + chemotherapy (other)

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

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive, Unresectable, Local (Third-line therapy, Subsequent therapy); Other recommended intervention

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

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trastuzumab + cisplatin + docetaxel

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 3.2021]

ERBB2 amplification (continued)

trastuzumab + cisplatin + docetaxel

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2021]

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trastuzumab + cisplatin + docetaxel + fluorouracil

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 3.2021]

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trastuzumab + cisplatin + docetaxel + fluorouracil

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2021]

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trastuzumab + cisplatin + paclitaxel

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 3.2021]

ERBB2 amplification (continued)

trastuzumab + cisplatin + paclitaxel

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2021]

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trastuzumab + cyclophosphamide + docetaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

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trastuzumab + docetaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive, Unresectable, Local (Third-line therapy, Subsequent therapy); Other recommended intervention

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

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trastuzumab + docetaxel

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 3.2021]

ERBB2 amplification (continued)

trastuzumab + docetaxel

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2021]

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trastuzumab + docetaxel

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 3.2021]

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trastuzumab + docetaxel + fluorouracil + oxaliplatin

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 3.2021]

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trastuzumab + docetaxel + fluorouracil + oxaliplatin

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2021]

ERBB2 amplification (continued)

trastuzumab + fluorouracil

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 3.2021]

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trastuzumab + fluorouracil

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2021]

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trastuzumab + fluorouracil + irinotecan

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 3.2021]

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trastuzumab + fluorouracil + irinotecan

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2021]

ERBB2 amplification (continued)

trastuzumab + fluorouracil + oxaliplatin

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 3.2021]

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trastuzumab + fluorouracil + oxaliplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2021]

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trastuzumab + fulvestrant

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

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trastuzumab + hormone therapy + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

ERBB2 amplification (continued)

trastuzumab + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor negative

NCCN Recommendation category: 2A

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

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

---

trastuzumab + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

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trastuzumab + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive, Unresectable, Local (Third-line therapy, Subsequent therapy); Other recommended intervention

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

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trastuzumab + paclitaxel

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 3.2021]

ERBB2 amplification (continued)

trastuzumab + paclitaxel

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2021]

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trastuzumab + tamoxifen

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

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trastuzumab + vinorelbine

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

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive, Unresectable, Local (Third-line therapy, Subsequent therapy); Other recommended intervention

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

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trastuzumab deruxtecan

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

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IV; Recurrent, Invasive, Unresectable, Local (Third-line therapy, Subsequent therapy); Other recommended intervention

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

ERBB2 amplification (continued)

trastuzumab deruxtecan

Cancer type: Colon Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: BRAF wild type, RAS wild type

NCCN Recommendation category: 2A

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

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

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trastuzumab deruxtecan

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 3.2021]

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trastuzumab deruxtecan

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2021]

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trastuzumab deruxtecan

Cancer type: Rectal Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: BRAF wild type, RAS wild type

NCCN Recommendation category: 2A

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

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

ERBB2 amplification (continued)

hormone therapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2B

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

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

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trastuzumab + carboplatin + docetaxel + fluorouracil

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2B

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

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 3.2021]

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trastuzumab + carboplatin + docetaxel + fluorouracil

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2B

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

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2021]

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trastuzumab + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor negative

NCCN Recommendation category: 2B

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

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

ERBB2 amplification (continued)

trastuzumab + hormone therapy + chemotherapy

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2B

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

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

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trastuzumab + paclitaxel

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

Other criteria: Hormone receptor negative

NCCN Recommendation category: 2B

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

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

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irbinitinib + trastuzumab + capecitabine

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

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2021]

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ado-trastuzumab emtansine

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2021]

ERBB2 amplification (continued)

lapatinib + capecitabine

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2021]

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neratinib + capecitabine

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2021]

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trastuzumab + chemotherapy

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2021]

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neratinib + paclitaxel

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

NCCN Recommendation category: 2B

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

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2021]

MET amplification

capmatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** MET amplification

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

crizotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** MET amplification

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

Current EMA Information

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

EMA information is current as of 2021-08-18. For the most up-to-date information, search www.ema.europa.eu/ema.

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT

● **afatinib**

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-04-21 **Variant class:** EGFR exon 19 deletion

Reference:

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

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● **bevacizumab (Allergan) + erlotinib**

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-05-21 **Variant class:** EGFR exon 19 deletion

Reference:

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

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● **bevacizumab (Fujifilm Kyowa Kirin Biologics) + erlotinib**

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-06-23 **Variant class:** EGFR exon 19 deletion

Reference:

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

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● **bevacizumab (Mabxience) + erlotinib**

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-08-11 **Variant class:** EGFR exon 19 deletion

Reference:

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

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● **bevacizumab (Pfizer) + erlotinib**

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-07-07 **Variant class:** EGFR exon 19 deletion

Reference:

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

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● **bevacizumab (Samsung Bioepis) + erlotinib**

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-05-18 **Variant class:** EGFR exon 19 deletion

Reference:

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

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EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT (continued)

bevacizumab (Samsung Bioepis) + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-06-21 **Variant class:** EGFR exon 19 deletion

Reference:

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

bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-01-28 **Variant class:** EGFR exon 19 deletion

Reference:

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

dacomitinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-07-21 **Variant class:** EGFR exon 19 deletion

Reference:

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

erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2019-04-24 **Variant class:** EGFR exon 19 deletion

Reference:

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

erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2020-07-02 **Variant class:** EGFR exon 19 deletion

Reference:

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

gefitinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-03-05 **Variant class:** EGFR exon 19 deletion

Reference:

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

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-07-01 **Variant class:** EGFR exon 19 deletion

Reference:

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

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

irbinitinib + trastuzumab + capecitabine

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

Reference:

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

lapatinib + capecitabine, lapatinib + letrozole, lapatinib + trastuzumab

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

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

Reference:

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

neratinib

Cancer type: Breast Cancer **Label as of:** 2021-07-29 **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

Reference:

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

pertuzumab + trastuzumab + chemotherapy, pertuzumab + trastuzumab + docetaxel

Cancer type: Breast Cancer **Label as of:** 2021-05-07 **Variant class:** ERBB2 amplification or ERBB2 overexpression

Reference:

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

ERBB2 amplification (continued)

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

Cancer type: Breast Cancer **Label as of:** 2021-08-03 **Variant class:** ERBB2 amplification or ERBB2 overexpression

Reference:

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

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

Cancer type: Breast Cancer, Gastric Cancer, Gastroesophageal Junction Adenocarcinoma **Label as of:** 2021-04-09 **Variant class:** ERBB2 overexpression

Other criteria: ER positive, PR positive

Reference:

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

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

Cancer type: Breast Cancer **Label as of:** 2021-04-09 **Variant class:** ERBB2 amplification

Other criteria: ER positive, PR positive

Reference:

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

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

Cancer type: Breast Cancer, Gastric Cancer, Gastroesophageal Junction Adenocarcinoma **Label as of:** 2021-03-01 **Variant class:** ERBB2 overexpression

Other criteria: ER positive, PR positive

Reference:

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

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ERBB2 amplification (continued)

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

Cancer type: Breast Cancer **Label as of:** 2021-03-01 **Variant class:** ERBB2 amplification

Other criteria: ER positive, PR positive

Reference:

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

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

Cancer type: Breast Cancer, Gastric Cancer, Gastroesophageal Junction Adenocarcinoma **Label as of:** 2021-06-17 **Variant class:** ERBB2 overexpression

Other criteria: ER positive, PR positive

Reference:

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

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

Cancer type: Breast Cancer **Label as of:** 2021-06-17 **Variant class:** ERBB2 amplification

Other criteria: ER positive, PR positive

Reference:

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

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

Cancer type: Breast Cancer, Gastric Cancer, Gastroesophageal Junction Adenocarcinoma **Label as of:** 2021-05-21 **Variant class:** ERBB2 overexpression

Other criteria: ER positive, PR positive

Reference:

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

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ERBB2 amplification (continued)

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

Cancer type: Breast Cancer **Label as of:** 2021-05-21 **Variant class:** ERBB2 amplification

Other criteria: ER positive, PR positive

Reference:

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

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

Cancer type: Breast Cancer, Gastric Cancer, Gastroesophageal Junction Adenocarcinoma **Label as of:** 2021-04-22 **Variant class:** ERBB2 overexpression

Other criteria: ER positive, PR positive

Reference:

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

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

Cancer type: Breast Cancer **Label as of:** 2021-04-22 **Variant class:** ERBB2 amplification

Other criteria: ER positive, PR positive

Reference:

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

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

Cancer type: Breast Cancer, Gastric Cancer, Gastroesophageal Junction Adenocarcinoma **Label as of:** 2021-02-22 **Variant class:** ERBB2 overexpression

Other criteria: ER positive, PR positive

Reference:

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

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ERBB2 amplification (continued)

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

Cancer type: Breast Cancer **Label as of:** 2021-02-22 **Variant class:** ERBB2 amplification

Other criteria: ER positive, PR positive

Reference:

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

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trastuzumab deruxtecan

Cancer type: Breast Cancer **Label as of:** 2021-05-25 **Variant class:** ERBB2 amplification or ERBB2 overexpression

Reference:

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

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

Cancer type: Breast Cancer, Gastric Cancer, Gastroesophageal Junction Adenocarcinoma **Label as of:** 2021-07-28 **Variant class:** ERBB2 overexpression

Other criteria: ER positive, PR positive

Reference:

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

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

Cancer type: Breast Cancer **Label as of:** 2021-07-28 **Variant class:** ERBB2 amplification

Other criteria: ER positive, PR positive

Reference:

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

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Current ESMO Information

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

ESMO information is current as of 2021-08-02. For the most up-to-date information, search www.esmo.org.

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT

● atezolizumab + bevacizumab + carboplatin + paclitaxel

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

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

Population segment (Line of therapy):
- Non-squamous Cell; Metastatic (First-line therapy); ESMO-MCBS v1.1 score: 3
- Metastatic (Second-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

● afatinib

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

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

● erlotinib

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

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT (continued)

gefitinib

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

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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osimertinib

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

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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dacomitinib

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

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

Population segment (Line of therapy):
- Advanced (First-line therapy); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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erlotinib

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

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

Population segment (Line of therapy):
- Non-squamous Cell (Maintenance therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT (continued)

afatinib

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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bevacizumab + erlotinib

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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bevacizumab + gefitinib

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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dacomitinib

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT (continued)

erlotinib

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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erlotinib + ramucirumab

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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gefitinib

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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gefitinib + carboplatin + pemetrexed

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT (continued)

bevacizumab + erlotinib

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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bevacizumab + gefitinib

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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erlotinib + ramucirumab

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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gefitinib + carboplatin + pemetrexed

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

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT (continued)

afatinib

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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bevacizumab + erlotinib

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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bevacizumab + gefitinib

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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dacomitinib

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT (continued)

erlotinib

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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erlotinib + ramucirumab

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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gefitinib

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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gefitinib + carboplatin + pemetrexed

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

ERBB2 amplification

ado-trastuzumab emtansine

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

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

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

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

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pertuzumab + trastuzumab + chemotherapy

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

Other criteria: ER negative, PR negative

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

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

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

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pertuzumab + trastuzumab + hormone therapy + chemotherapy

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

Other criteria: ER positive, PR status

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

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

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

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trastuzumab + capecitabine + cisplatin

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

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

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

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

ERBB2 amplification (continued)

trastuzumab + chemotherapy

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

Other criteria: ER negative, PR negative

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

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

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

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trastuzumab + cisplatin + fluorouracil

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

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

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

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

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trastuzumab + hormone therapy + chemotherapy

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

Other criteria: ER positive, PR status

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

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

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

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pertuzumab + trastuzumab + chemotherapy

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

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

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

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

ERBB2 amplification (continued)

trastuzumab containing regimen

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

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

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

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

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pertuzumab + trastuzumab + hormone therapy

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

Other criteria: ER positive, PR status

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

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

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

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trastuzumab + hormone therapy

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

Other criteria: ER positive, PR status

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

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

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

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tamoxifen

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

Other criteria: ER positive, PR status

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

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

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

ERBB2 amplification (continued)

tamoxifen

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

Other criteria: ER positive, PR status

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

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

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

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aromatase inhibitor + luteinizing hormone-releasing factor

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

Other criteria: ER positive, PR status

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

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

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

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aromatase inhibitor + luteinizing hormone-releasing factor

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

Other criteria: ER positive, PR status

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

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

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

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trastuzumab + hormone therapy

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

Other criteria: ER positive

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

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

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

ERBB2 amplification (continued)

ado-trastuzumab emtansine

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

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

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

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

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pertuzumab + trastuzumab + capecitabine

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

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

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

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

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pertuzumab + trastuzumab + chemotherapy

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

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

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

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

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pertuzumab + trastuzumab + docetaxel

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

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

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

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

ERBB2 amplification (continued)

trastuzumab + chemotherapy

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

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

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

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

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trastuzumab + taxane

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

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

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

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

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trastuzumab + vinorelbine

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

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

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

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

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lapatinib + trastuzumab

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

Other criteria: ER positive

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

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

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

ERBB2 amplification (continued)

lapatinib + trastuzumab

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

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

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

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

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pertuzumab + trastuzumab

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

Other criteria: ER positive

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

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

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

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pertuzumab + trastuzumab + paclitaxel

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

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

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

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

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pertuzumab + trastuzumab + vinorelbine

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

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

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

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

ERBB2 amplification (continued)

pertuzumab + trastuzumab + chemotherapy

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

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

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

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

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pertuzumab + trastuzumab + chemotherapy

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

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

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

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

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pertuzumab + trastuzumab + nab-paclitaxel

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

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

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

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

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trastuzumab deruxtecan

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

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

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

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

Clinical Trials in Taiwan region:

Clinical Trials Summary

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT + MET amplification

NCT ID	Title	Phase
NCT03778229	A Phase II, Single Arm Study Assessing Efficacy of Osimertinib With Savolitinib in Patients With EGFRm + MET+, Locally Advanced or Metastatic Non Small Cell Lung Cancer Who Have Progressed Following Osimertinib Treatment (SAVANNAH Study)	II
NCT04606771	A Multi-centre Phase II, Double-Blind, Randomised Study of Savolitinib in Combination With Osimertinib vs Savolitinib in Combination With Placebo in Patients With EGFRm+ and MET Amplified Locally Advanced or Metastatic Non-Small Cell Lung Cancer Who Have Progressed Following Treatment With Osimertinib	II
NCT02609776	A Phase I, First-in-Human, Open-Label, Dose Escalation Study of JNJ-61186372, a Human Bispecific EGFR and cMet Antibody, in Subjects With Advanced Non-Small Cell Lung Cancer.	I
NCT03940703	A Phase II, Two-arm Study to Investigate Tepotinib Combined With Osimertinib in MET Amplified, Advanced or Metastatic NSCLC Harboring Activating EGFR Mutations and Having Acquired Resistance to Prior Osimertinib Therapy (INSIGHT 2)	II

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT

NCT ID	Title	Phase
NCT04487080	A Phase III, Randomized Study of Amivantamab and Lazertinib Combination Therapy Versus Osimertinib Versus Lazertinib as First-Line Treatment in Patients With EGFR-Mutated Locally Advanced or Metastatic Non-Small Cell Lung Cancer.	III
NCT03521154	A Phase III, Randomized, Double-blind, Placebo-controlled, Multicenter, International Study of Osimertinib as Maintenance Therapy in Patients With Locally Advanced, Unresectable EGFR Mutation-positive Non-Small Cell Lung Cancer (Stage III) Whose Disease Has Not Progressed Following Definitive Platinum-based Chemoradiation Therapy (LAURA)	III
NCT04035486	A Phase III, Open-label, Randomized Study of Osimertinib With or Without Platinum Plus Pemetrexed Chemo, as First-line Treatment in Patients With Epidermal Growth Factor Receptor (EGFR) Mutation Positive, Locally Advanced or Metastatic Non-small Cell Lung Cancer (FLAURA2)	III
NCT04351555	A Phase III, Randomised, Controlled, Multi-center, 3-Arm Study of Neoadjuvant Osimertinib as Monotherapy or in Combination With Chemotherapy Versus Standard of Care Chemotherapy Alone for the Treatment of Patients With Epidermal Growth Factor Receptor Mutation Positive, Resectable Non-small Cell Lung Cancer	III
NCT04147351	A Phase II Study of Atezolizumab in Combination With Bevacizumab, Carboplatin or Cisplatin, and Pemetrexed for EGFR-mutant Metastatic Non-small Cell Lung Cancer Patients After Failure of EGFR Tyrosine Kinase Inhibitors.	II
NCT02655536	A Phase II, Open Label, Multicenter Study of Bevacizumab in Combination With Erlotinib Versus Erlotinib Alone in Patients With EGFR Mutant Non-small Cell Lung Cancer Who Have Brain Metastases	II
NCT03994393	A Phase II Trial of Durvalumab (MEDI4736) and Tremelimumab With Chemotherapy in Metastatic EGFR Mutant Non-squamous Non-small Cell Lung Cancer (NSCLC) Following Progression on EGFR Tyrosine Kinase Inhibitors (TKIs)	II
NCT04619004	HERTHENA-Lung01: A Phase II Randomized Open-Label Study of Patritumab Deruxtecan (U3-1402) in Subjects With Previously Treated Metastatic or Locally Advanced EGFR-mutated Non-Small Cell Lung Cancer (NSCLC)	II

Clinical Trials Summary (continued)

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT (continued)

NCT ID	Title	Phase
NCT04077463	An Open-label Phase I/Ib Study to Evaluate the Safety and Pharmacokinetics of JNJ-73841937 (Lazertinib), a Third Generation EGFR-TKI, as Monotherapy or in Combinations With JNJ-61186372, a Human Bispecific EGFR and cMet Antibody in Participants With Advanced Non-Small Cell Lung Cancer	I
NCT02099058	A Multicenter, Phase I/Ib, Open-Label, Dose-Escalation Study of ABBV-399, an Antibody Drug Conjugate, in Subjects With Advanced Solid Tumors	I
NCT04484142	Phase II, Single-arm, Open-label Study of DS-1062a in Advanced or Metastatic Non-small Cell Lung Cancer With Actionable Genomic Alterations and Progressed on or After Kinase Inhibitor Therapy and Platinum Based Chemotherapy (TROPION-Lung05)	II
NCT03114319	An Open-label, Multi-center, Phase I, Dose Finding Study of Oral TNO155 in Adult Patients With Advanced Solid Tumors.	I
NCT03974022	A Phase I/II, Open-Label, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics and Anti-tumor Efficacy of DZD9008 in Patients With Advanced Non-Small Cell Lung Cancer (NSCLC) With EGFR or HER2 Mutation	I/II

MET amplification

NCT ID	Title	Phase
NCT04169178	A Phase I Dose Finding/Expansion Study of HLX55, A Monoclonal Antibody Targeting Tyrosine-Protein Kinase MET (C-MET) in Patients With Advanced Solide Tumors Refactory to Standard Therapy	I

Alerts Informed By Public Data Sources

Current FDA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

FDA information is current as of 2021-08-18. For the most up-to-date information, search www.fda.gov.

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT

osimertinib + quaratusugene ozeplasmid

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR mutation

Supporting Statement:
The FDA has granted Fast Track Designation to the immunogene therapy, quaratusugene ozeplasmid, in combination with EGFR inhibitor osimertinib for the treatment of non-small cell lung cancer (NSCLC) with EFGR mutations that progressed after treatment with osimertinib alone.

Reference:

https://www.genprex.com/news/genprex-receives-u-s-fda-fast-track-designation-for-gene-therapy-that-targets-lung-cancer/

ERBB2 amplification

zanidatamab

Cancer type: Biliary Tract Carcinoma

Variant class: ERBB2 amplification

Supporting Statement:
The FDA has granted Breakthrough Therapy Designation to the HER2 targeted bispecific antibody, zanidatamab, for previously-treated HER2 gene-amplified biliary tract cancer (BTC).

Reference:

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

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disitamab vedotin

Cancer type: Bladder Urothelial Carcinoma

Variant class: ERBB2 positive

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

Reference:

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

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zanidatamab

Cancer type: Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

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

Reference:

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

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evorpacept

Cancer type: Gastric Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 positive

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

Reference:

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

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ERBB2 amplification (continued)

SAR439859

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

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

Reference:

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

Current NCCN Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

NCCN information is current as of 2021-08-02. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT

alectinib

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

brigatinib

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

ceritinib

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

EGFR p.(E746_A750del) c.2235_2253delGGAATTAAGAGAAGCAACAinsAACT (continued)

crizotinib

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

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lorlatinib

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

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atezolizumab

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK fusions."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

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nivolumab

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK fusions."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

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pembrolizumab

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK fusions."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

ERBB2 amplification

pertuzumab + trastuzumab + cyclophosphamide + docetaxel + doxorubicin

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

Summary:

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

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

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

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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 5.2021]

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trastuzumab + anthracycline

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

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

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

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 3.2021]

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trastuzumab + anthracycline

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

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

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

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2021]

ERBB2 amplification (continued)

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 5.2021]

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 5.2021]

Current ESMO Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

ESMO information is current as of 2021-08-02. For the most up-to-date information, search www.esmo.org.

ERBB2 amplification

lapatinib + trastuzumab + chemotherapy

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

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

Summary:

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

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

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

ERBB2 amplification (continued)

aromatase inhibitor

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

Other criteria: ER positive, PR status

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

Summary:

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

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

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

trastuzumab + anthracycline

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

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

Summary:

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

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

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

Signatures

Testing Personnel:

Laboratory Supervisor:

Pathologist:

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