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Sample Information

Patient Name: 歐冬青
Gender: Male
ID No.: X200230036
History No.: 38529747
Age: 65

Ordering Doctor: DOC3160J
Ordering REQ.: 0BEQYAS
Signing in Date: 2021/04/14

Path No.: S110-98593
MP No.: F21034
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S110-11678A+B
Percentage of tumor cells: 35%
Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

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Report Highlights

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56 Therapies Available
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Relevant Non-Small Cell Lung Cancer Variants

Gene	Finding	Gene	Finding
ALK	Not detected	NTRK1	Not detected
BRAF	Not detected	NTRK2	Not detected
EGFR	***EGFR p.(L858R) c.2573T>G***	NTRK3	Not detected
ERBB2	***ERBB2 amplification***	RET	Not detected
KRAS	Not detected	ROS1	Not 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.(L858R) c.2573T>G* epidermal growth factor receptor Allele Frequency: 39.28%	**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	None	191
IIC	*ERBB2 amplification* erb-b2 receptor tyrosine kinase 2	None	**ado-trastuzumab emtansine** [1, 2] **irbinitinib + trastuzumab + chemotherapy** [1] **lapatinib + chemotherapy** [1, 2] **lapatinib + hormone therapy** [1, 2] **lapatinib + trastuzumab** [2] **margetuximab + chemotherapy** [1] **neratinib** [1, 2] **neratinib + chemotherapy** [1] **pertuzumab + trastuzumab + chemotherapy** [1, 2] **pertuzumab/trastuzumab/ hyaluronidase-zzxf + chemotherapy** [1, 2] **trastuzumab deruxtecan** [1, 2] **trastuzumab*** [1, 2] **trastuzumab* + chemotherapy** [1, 2] **trastuzumab* + hormone therapy** [2] hormone therapy lapatinib + trastuzumab + hormone therapy pertuzumab + trastuzumab pertuzumab + trastuzumab + hormone therapy pertuzumab + trastuzumab + hormone therapy + chemotherapy trastuzumab + hormone therapy + chemotherapy trastuzumab containing regimen	39
IA	*MET amplification* MET proto-oncogene, receptor tyrosine kinase	capmatinib crizotinib	None	27

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

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

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
EGFR	p.(L858R)	c.2573T>G	COSM6224	chr7:55259515	39.28%	NM_005228.4	missense	1991

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

Copy Number Variations

Gene	Locus	Copy Number
MET	chr7:116313480	13.49
ERBB2	chr17:37868126	6.54

Biomarker Descriptions

EGFR (epidermal growth factor receptor)

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

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

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

Biomarker Descriptions (continued)

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. The vaccine, nelipepimut-S[54], was granted fast-track designation by the FDA (2016) in patients with low to intermediate HER2 expressing (IHC score 1+ or 2+) breast cancer. In 2018 fast-track designation was granted to the monoclonal antibody margetuximab[55] in patients with ERBB2 positive breast cancer previously treated with an anti-HER2 therapy. In 2019, the novel bispecific antibody ZW25[56] received fast-track designation for patients with HER2-amplified biliary tract cancer or in combination with standard chemotherapy for patients with HER2-overexpressing gastroesophageal adenocarcinoma (GEA). In 2020, BDTX-189[34] received fast-track designation for adult patients with solid tumors harboring an allosteric human ERBB2 mutation or exon 20 insertion, and the humanized anti-HER2 antibody drug conjugate disitamab vedotin received breakthrough designation for adult patients with HER2-positive urothelial cancer after previous platinum-chemotherapy treatment[57]. In 2021, the antibody-drug conjugate ARX788[58] received fast-track designation as a monothreapy for advanced or metastatic HER2-positive breast cancer that have progressed on one or more anti-HER2 regimens. Certain activating mutations have been observed to impart sensitivity to neratinib, afatinib, lapatinib, and trastuzumab, or dacomitinib in early and ongoing clinical studies[59,60,61,62,63]. ERBB2 kinase domain mutations R896G and V659E both showed response to afatinib in two NSCLC case studies[64,65]. Additionally, acquired HER2 mutations in estrogen receptor-positive (ER +) breast cancer have been shown to confer resistance to hormone therapy[66]. However, this was shown to be overcome by neratinib in combination with therapies targeting ER[66].

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[67,68,69]. 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[70,71].

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[72,73]. Such mutations disrupt splicing leading to the formation of an alternative transcript that joins exon 13

Biomarker Descriptions (continued)

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[74]. 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[72,75,76]. 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[77,78,79]. MET alterations are believed to be enriched in late-stage cancers where they drive tumor progression and metastasis[80,81,82].

Potential relevance: In 2020, the FDA granted accelerated approval to capmatinib[83] for NSCLC harboring MET exon 14 skipping positive as detected by an FDA-approved test[23]. The kinase inhibitor, tepotinib[84], is also approved (2021) for MET exon 14 skipping mutations in NSCLC[84]. 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[23,72,75,76]. Conversely, amplification of MET has been observed to mediate resistance to EGFR tyrosine kinase inhibitors (TKIs)[85,86,87,88,89]. 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[90].

Relevant Therapy Summary

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

EGFR p.(L858R) c.2573T>G

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
afatinib	●	●	●	●	● (IV)
dacomitinib	●	●	●	●	● (IV)
gefitinib	●	●	●	●	● (IV)
osimertinib	●	●	●	●	● (III)
erlotinib	●	●	●	●	● (II)
erlotinib + ramucirumab	●	●	●	●	✖
bevacizumab + erlotinib	✖	●	●	●	✖
afatinib + cetuximab	✖	●	✖	✖	✖
bevacizumab (Allergan) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Fujifilm Kyowa Kirin Biologics) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Pfizer) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Samsung Bioepis) + erlotinib	✖	✖	●	✖	✖
atezolizumab + bevacizumab + carboplatin + paclitaxel	✖	✖	✖	●	✖
bevacizumab + gefitinib	✖	✖	✖	●	✖
gefitinib + carboplatin + pemetrexed	✖	✖	✖	●	✖
afatinib, osimertinib	✖	✖	✖	✖	● (IV)

* 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.(L858R) c.2573T>G (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
anlotinib hydrochloride, toripalimab	✖	✖	✖	✖	● (IV)
apatinib + EGFR tyrosine kinase inhibitor	✖	✖	✖	✖	● (IV)
apatinib, gefitinib	✖	✖	✖	✖	● (IV)
bevacizumab + osimertinib, osimertinib	✖	✖	✖	✖	● (IV)
EGFR tyrosine kinase inhibitor	✖	✖	✖	✖	● (IV)
gefitinib, chemotherapy	✖	✖	✖	✖	● (IV)
gefitinib, radiation therapy	✖	✖	✖	✖	● (IV)
icotinib hydrochloride	✖	✖	✖	✖	● (IV)
icotinib hydrochloride, chemotherapy	✖	✖	✖	✖	● (IV)
icotinib hydrochloride, radiation therapy	✖	✖	✖	✖	● (IV)
natural product, gefitinib, erlotinib, icotinib hydrochloride	✖	✖	✖	✖	● (IV)
almonertinib, gefitinib	✖	✖	✖	✖	● (III)
amivantamab, lazertinib, osimertinib	✖	✖	✖	✖	● (III)
ASK120067, gefitinib	✖	✖	✖	✖	● (III)
atezolizumab, bevacizumab, chemotherapy	✖	✖	✖	✖	● (III)
atezolizumab, PF-06744547	✖	✖	✖	✖	● (III)
BPI-7711, gefitinib	✖	✖	✖	✖	● (III)
CK-101, gefitinib	✖	✖	✖	✖	● (III)
durvalumab, chemotherapy	✖	✖	✖	✖	● (III)
erlotinib, chemotherapy	✖	✖	✖	✖	● (III)
erlotinib, erlotinib + chemotherapy	✖	✖	✖	✖	● (III)
gefitinib + chemotherapy	✖	✖	✖	✖	● (III)
gefitinib, anlotinib hydrochloride	✖	✖	✖	✖	● (III)
gefitinib, icotinib hydrochloride, erlotinib, radiation therapy	✖	✖	✖	✖	● (III)
lazertinib, gefitinib	✖	✖	✖	✖	● (III)
maihuatinib, gefitinib	✖	✖	✖	✖	● (III)
osimertinib, bevacizumab	✖	✖	✖	✖	● (III)
osimertinib, chemotherapy	✖	✖	✖	✖	● (III)

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

Relevant Therapy Summary (continued)

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

EGFR p.(L858R) c.2573T>G (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
SH-1028, gefitinib	✖	✖	✖	✖	● (III)
D-0316, icotinib hydrochloride	✖	✖	✖	✖	● (II/III)
zorifertinib, erlotinib, gefitinib	✖	✖	✖	✖	● (II/III)
afatinib, chemotherapy	✖	✖	✖	✖	● (II)
afatinib, chemotherapy, radiation therapy	✖	✖	✖	✖	● (II)
almonertinib, radiation therapy	✖	✖	✖	✖	● (II)
anlotinib hydrochloride	✖	✖	✖	✖	● (II)
anlotinib hydrochloride, chemotherapy	✖	✖	✖	✖	● (II)
anlotinib hydrochloride, erlotinib, icotinib hydrochloride, gefitinib	✖	✖	✖	✖	● (II)
anlotinib hydrochloride, gefitinib	✖	✖	✖	✖	● (II)
anlotinib hydrochloride, icotinib hydrochloride	✖	✖	✖	✖	● (II)
atezolizumab, bevacizumab	✖	✖	✖	✖	● (II)
atezolizumab, chemotherapy	✖	✖	✖	✖	● (II)
avitinib, zorifertinib	✖	✖	✖	✖	● (II)
bevacizumab, atezolizumab	✖	✖	✖	✖	● (II)
bevacizumab, atezolizumab, chemotherapy	✖	✖	✖	✖	● (II)
bevacizumab, erlotinib	✖	✖	✖	✖	● (II)
bevacizumab, erlotinib, chemotherapy	✖	✖	✖	✖	● (II)
bevacizumab, gefitinib	✖	✖	✖	✖	● (II)
bevacizumab, osimertinib	✖	✖	✖	✖	● (II)
bintrafusp alfa, chemoradiation therapy, durvalumab	✖	✖	✖	✖	● (II)
camrelizumab, apatinib	✖	✖	✖	✖	● (II)
chemotherapy, atezolizumab, bevacizumab	✖	✖	✖	✖	● (II)
crizotinib	✖	✖	✖	✖	● (II)
datopotamab deruxtecan	✖	✖	✖	✖	● (II)
durvalumab, tremelimumab, chemotherapy	✖	✖	✖	✖	● (II)
EGFR tyrosine kinase inhibitor + chemotherapy, EGFR tyrosine kinase inhibitor	✖	✖	✖	✖	● (II)
EGFR tyrosine kinase inhibitor, apatinib	✖	✖	✖	✖	● (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

EGFR p.(L858R) c.2573T>G (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
EGFR tyrosine kinase inhibitor, radiation therapy	✖	✖	✖	✖	● (II)
erlotinib, bevacizumab	✖	✖	✖	✖	● (II)
famitinib, almonertinib	✖	✖	✖	✖	● (II)
gefitinib, erlotinib	✖	✖	✖	✖	● (II)
gefitinib, erlotinib, afatinib	✖	✖	✖	✖	● (II)
gefitinib, surgical intervention	✖	✖	✖	✖	● (II)
gefitinib, thalidomide	✖	✖	✖	✖	● (II)
nazartinib, gefitinib	✖	✖	✖	✖	● (II)
nivolumab, ipilimumab	✖	✖	✖	✖	● (II)
olaparib, durvalumab	✖	✖	✖	✖	● (II)
osimertinib, abemaciclib	✖	✖	✖	✖	● (II)
osimertinib, ado-trastuzumab emtansine	✖	✖	✖	✖	● (II)
osimertinib, gefitinib + osimertinib	✖	✖	✖	✖	● (II)
osimertinib, radiation therapy	✖	✖	✖	✖	● (II)
osimertinib, ramucirumab	✖	✖	✖	✖	● (II)
osimertinib, savolitinib	✖	✖	✖	✖	● (II)
osimertinib, selumetinib	✖	✖	✖	✖	● (II)
PD-1 Inhibitor, chemotherapy	✖	✖	✖	✖	● (II)
poziotinib	✖	✖	✖	✖	● (II)
ramucirumab, chemotherapy, cytokine	✖	✖	✖	✖	● (II)
ramucirumab, pembrolizumab	✖	✖	✖	✖	● (II)
savolitinib, osimertinib	✖	✖	✖	✖	● (II)
SH-1028	✖	✖	✖	✖	● (II)
tepotinib, osimertinib	✖	✖	✖	✖	● (II)
tyrosine kinase inhibitors, radiation therapy	✖	✖	✖	✖	● (II)
zoledronic acid, gefitinib	✖	✖	✖	✖	● (II)
BDTX-189	✖	✖	✖	✖	● (I/II)
CBT-502, anlotinib hydrochloride	✖	✖	✖	✖	● (I/II)
DZD-9008	✖	✖	✖	✖	● (I/II)

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

Relevant Therapy Summary (continued)

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

EGFR p.(L858R) c.2573T>G (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
EMB01	✖	✖	✖	✖	● (I/II)
erlotinib, chemotherapy, bevacizumab	✖	✖	✖	✖	● (I/II)
glumetinib, osimertinib	✖	✖	✖	✖	● (I/II)
KP-673	✖	✖	✖	✖	● (I/II)
mobocertinib	✖	✖	✖	✖	● (I/II)
ningetinib, gefitinib	✖	✖	✖	✖	● (I/II)
telaglenastat, osimertinib	✖	✖	✖	✖	● (I/II)
alisertib, osimertinib	✖	✖	✖	✖	● (I)
alisertib, sapanisertib, osimertinib	✖	✖	✖	✖	● (I)
amivantamab	✖	✖	✖	✖	● (I)
BBP-398	✖	✖	✖	✖	● (I)
BCA101	✖	✖	✖	✖	● (I)
bevacizumab + erlotinib + chemotherapy	✖	✖	✖	✖	● (I)
CK-101	✖	✖	✖	✖	● (I)
EGFR tyrosine kinase inhibitor, anlotinib hydrochloride	✖	✖	✖	✖	● (I)
etrumadenant, zimberelimab, chemotherapy	✖	✖	✖	✖	● (I)
FT500, nivolumab, pembrolizumab, atezolizumab	✖	✖	✖	✖	● (I)
genolimzumab, fruquintinib	✖	✖	✖	✖	● (I)
lazertinib, amivantamab	✖	✖	✖	✖	● (I)
nazartinib + trametinib, nazartinib + ribociclib, LXH254 + nazartinib, capmatinib + nazartinib, gefitinib + nazartinib	✖	✖	✖	✖	● (I)
neratinib, palbociclib, everolimus, trametinib	✖	✖	✖	✖	● (I)
niraparib, osimertinib	✖	✖	✖	✖	● (I)
nivolumab, ipilimumab, radiation therapy	✖	✖	✖	✖	● (I)
osimertinib, ipilimumab	✖	✖	✖	✖	● (I)
pirotinib	✖	✖	✖	✖	● (I)
ramucirumab, erlotinib, osimertinib	✖	✖	✖	✖	● (I)
telaglenastat, sapanisertib	✖	✖	✖	✖	● (I)
telisotuzumab vedotin, osimertinib	✖	✖	✖	✖	● (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.(L858R) c.2573T>G (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
TNO-155, nazartinib	✖	✖	✖	✖	● (I)
TQB 3804	✖	✖	✖	✖	● (I)
WSD-0922	✖	✖	✖	✖	● (I)

ERBB2 amplification

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

* 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 (Biocon) + paclitaxel	○	✖	○	✖	✖
trastuzumab (Celltrion)	○	✖	○	✖	✖
trastuzumab (Celltrion) + capecitabine + cisplatin	○	✖	○	✖	✖
trastuzumab (Celltrion) + carboplatin + docetaxel	○	✖	○	✖	✖
trastuzumab (Celltrion) + cisplatin + fluorouracil	○	✖	○	✖	✖
trastuzumab (Celltrion) + docetaxel	○	✖	○	✖	✖
trastuzumab (Celltrion) + paclitaxel	○	✖	○	✖	✖
trastuzumab (Pfizer)	○	✖	○	✖	✖
trastuzumab (Pfizer) + capecitabine + cisplatin	○	✖	○	✖	✖
trastuzumab (Pfizer) + carboplatin + docetaxel	○	✖	○	✖	✖
trastuzumab (Pfizer) + cisplatin + fluorouracil	○	✖	○	✖	✖
trastuzumab (Pfizer) + docetaxel	○	✖	○	✖	✖
trastuzumab (Pfizer) + paclitaxel	○	✖	○	✖	✖
trastuzumab (Samsung Bioepis)	○	✖	○	✖	✖
trastuzumab (Samsung Bioepis) + capecitabine + cisplatin	○	✖	○	✖	✖
trastuzumab (Samsung Bioepis) + carboplatin + docetaxel	○	✖	○	✖	✖
trastuzumab (Samsung Bioepis) + cisplatin + fluorouracil	○	✖	○	✖	✖
trastuzumab (Samsung Bioepis) + docetaxel	○	✖	○	✖	✖
trastuzumab (Samsung Bioepis) + paclitaxel	○	✖	○	✖	✖
margetuximab + chemotherapy	○	✖	✖	✖	✖
trastuzumab (Enhanze)	○	✖	✖	✖	✖
trastuzumab (Enhanze) + carboplatin + docetaxel	○	✖	✖	✖	✖
trastuzumab (Enhanze) + docetaxel	○	✖	✖	✖	✖
trastuzumab (Enhanze) + paclitaxel	○	✖	✖	✖	✖
lapatinib + trastuzumab	✖	○	○	○	✖
pertuzumab + trastuzumab	✖	○	✖	○	● (II)

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

Relevant Therapy Summary (continued)

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

ERBB2 amplification (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
pertuzumab + trastuzumab + hormone therapy + chemotherapy	✖	○	✖	○	✖
pertuzumab + trastuzumab + paclitaxel	✖	○	✖	○	✖
tamoxifen	✖	○	✖	○	✖
trastuzumab + chemotherapy	✖	○	✖	○	✖
trastuzumab + hormone therapy + chemotherapy	✖	○	✖	○	✖
trastuzumab + vinorelbine	✖	○	✖	○	✖
aromatase inhibitor	✖	○	✖	✖	✖
fulvestrant	✖	○	✖	✖	✖
hormone therapy	✖	○	✖	✖	✖
lapatinib + aromatase inhibitor	✖	○	✖	✖	✖
lapatinib + trastuzumab + aromatase inhibitor	✖	○	✖	✖	✖
neratinib + paclitaxel	✖	○	✖	✖	✖
pertuzumab + trastuzumab + carboplatin + docetaxel	✖	○	✖	✖	✖
trastuzumab + aromatase inhibitor	✖	○	✖	✖	✖
trastuzumab + capecitabine	✖	○	✖	✖	✖
trastuzumab + capecitabine + oxaliplatin	✖	○	✖	✖	✖
trastuzumab + carboplatin + docetaxel + fluorouracil	✖	○	✖	✖	✖
trastuzumab + carboplatin + paclitaxel	✖	○	✖	✖	✖
trastuzumab + chemotherapy (other)	✖	○	✖	✖	✖
trastuzumab + cisplatin + docetaxel	✖	○	✖	✖	✖
trastuzumab + cisplatin + docetaxel + fluorouracil	✖	○	✖	✖	✖
trastuzumab + cisplatin + paclitaxel	✖	○	✖	✖	✖
trastuzumab + cyclophosphamide + docetaxel	✖	○	✖	✖	✖
trastuzumab + docetaxel + fluorouracil + oxaliplatin	✖	○	✖	✖	✖
trastuzumab + fluorouracil	✖	○	✖	✖	✖
trastuzumab + fluorouracil + irinotecan	✖	○	✖	✖	✖
trastuzumab + fluorouracil + oxaliplatin	✖	○	✖	✖	✖
trastuzumab + fulvestrant	✖	○	✖	✖	✖

* 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 + 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	✖	✖	○	✖	✖
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	✖	✖	○	✖	✖

* 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 + CMF + doxorubicin + paclitaxel	✖	✖	○	✖	✖
aromatase inhibitor + luteinizing hormone-releasing factor	✖	✖	✖	○	✖
pertuzumab + trastuzumab + capecitabine	✖	✖	✖	○	✖
pertuzumab + trastuzumab + hormone therapy	✖	✖	✖	○	✖
pertuzumab + trastuzumab + nab-paclitaxel	✖	✖	✖	○	✖
pertuzumab + trastuzumab + vinorelbine	✖	✖	✖	○	✖
trastuzumab + hormone therapy	✖	✖	✖	○	✖
trastuzumab + taxane	✖	✖	✖	○	✖
trastuzumab containing regimen	✖	✖	✖	○	✖
ado-trastuzumab emtansine + atezolizumab	✖	✖	✖	✖	● (II)
irbinitinib, trastuzumab	✖	✖	✖	✖	● (II)
osimertinib, ado-trastuzumab emtansine	✖	✖	✖	✖	● (II)
pyrotinib, chemotherapy	✖	✖	✖	✖	● (II)
trastuzumab, pertuzumab, ado-trastuzumab emtansine, lapatinib	✖	✖	✖	✖	● (II)
A-166	✖	✖	✖	✖	● (I/II)
BAT 1306, BAT-8001	✖	✖	✖	✖	● (I/II)
BDC-1001, pembrolizumab	✖	✖	✖	✖	● (I/II)
BDTX-189	✖	✖	✖	✖	● (I/II)
zotatifin	✖	✖	✖	✖	● (I/II)
AC-101 (AbClon)	✖	✖	✖	✖	● (I)
ado-trastuzumab (Shanghai Fosun Pharma)	✖	✖	✖	✖	● (I)
AMX-3009	✖	✖	✖	✖	● (I)
ARX-788	✖	✖	✖	✖	● (I)
BAY-2701439	✖	✖	✖	✖	● (I)
CART	✖	✖	✖	✖	● (I)
CART-HER2	✖	✖	✖	✖	● (I)
disitamab vedotin	✖	✖	✖	✖	● (I)
KN026	✖	✖	✖	✖	● (I)

* 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*
M802	✖	✖	✖	✖	● (I)
MBS301	✖	✖	✖	✖	● (I)
MT-5111	✖	✖	✖	✖	● (I)
neratinib, palbociclib, everolimus, trametinib	✖	✖	✖	✖	● (I)
pirotinib	✖	✖	✖	✖	● (I)
pivotinib	✖	✖	✖	✖	● (I)
PRS-343	✖	✖	✖	✖	● (I)
SBT6050, pembrolizumab	✖	✖	✖	✖	● (I)
SHR-A1811	✖	✖	✖	✖	● (I)
tebotelimab, margetuximab	✖	✖	✖	✖	● (I)
trastuzumab deruxtecan, pembrolizumab	✖	✖	✖	✖	● (I)
zanidatamab	✖	✖	✖	✖	● (I)
ZN-A-1041	✖	✖	✖	✖	● (I)

MET amplification

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
crizotinib	✖	●	✖	✖	● (II)
capmatinib	✖	●	✖	✖	✖
cabozantinib	✖	✖	✖	✖	● (II)
ensartinib	✖	✖	✖	✖	● (II)
osimertinib, savolitinib	✖	✖	✖	✖	● (II)
savolitinib, osimertinib	✖	✖	✖	✖	● (II)
tepotinib	✖	✖	✖	✖	● (II)
tepotinib, osimertinib	✖	✖	✖	✖	● (II)
TQ-B3139	✖	✖	✖	✖	● (II)
glumetinib	✖	✖	✖	✖	● (I/II)
glumetinib, osimertinib	✖	✖	✖	✖	● (I/II)
REGN-5093	✖	✖	✖	✖	● (I/II)
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

MET amplification (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
GST-HG161	✖	✖	✖	✖	● (I)
HLX55	✖	✖	✖	✖	● (I)
HS-10241	✖	✖	✖	✖	● (I)
metatinib	✖	✖	✖	✖	● (I)
SPH3348, osimertinib	✖	✖	✖	✖	● (I)
talazoparib, crizotinib	✖	✖	✖	✖	● (I)
TPX-0022	✖	✖	✖	✖	● (I)

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

Relevant Therapy Details

Current FDA Information

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

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

EGFR p.(L858R) c.2573T>G

● afatinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2019-10-11 **Variant class:** EGFR L858R mutation

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

EGFR p.(L858R) c.2573T>G (continued)

dacomitinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2020-12-18 **Variant class:** EGFR L858R mutation

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

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erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2016-10-18 **Variant class:** EGFR L858R mutation

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:** 2020-07-06 **Variant class:** EGFR L858R mutation

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/2020/125477s037lbl.pdf

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EGFR p.(L858R) c.2573T>G (continued)

gefitinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2018-08-22 **Variant class:** EGFR L858R mutation

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/2018/206995s003lbl.pdf

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2020-12-18 **Variant class:** EGFR L858R mutation

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/2020/208065s021lbl.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:** 2020-07-29 **Variant class:** ERBB2 overexpression

Indications and usage:

NERLYNX® is a kinase inhibitor indicated:

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

Reference:

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

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

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

Indications and usage:

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

- The treatment of HER2-overexpressing breast cancer.

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

Reference:

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

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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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ERBB2 amplification (continued)

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

Cancer type: Breast Cancer, Gastric Cancer, Gastroesophageal Junction Adenocarcinoma **Label as of:** 2018-11-29 **Variant class:** ERBB2 overexpression or ERBB2 amplification

Indications and usage:

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

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

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

Reference:

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

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Current NCCN Information

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

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

EGFR p.(L858R) c.2573T>G

● afatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

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 2.2021]

● dacomitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

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 2.2021]

● erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

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 2.2021]

● gefitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

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 2.2021]

EGFR p.(L858R) c.2573T>G (continued)

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

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 2.2021]

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afatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

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 2.2021]

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afatinib + cetuximab

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

NCCN Recommendation category: 2A

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

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

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bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

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 2.2021]

EGFR p.(L858R) c.2573T>G (continued)

dacomitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

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 2.2021]

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erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

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 2.2021]

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erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

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 2.2021]

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gefitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

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 2.2021]

EGFR p.(L858R) c.2573T>G (continued)

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

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 2.2021]

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erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

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 3.2020]

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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 3.2020]

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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 3.2020]

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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 3.2020]

ERBB2 amplification

ado-trastuzumab emtansine

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 1

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

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

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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, Invasive (Line of therapy not specified); Other recommended intervention

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

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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 (Line of therapy not specified); Preferred intervention

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

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trastuzumab + capecitabine + cisplatin

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 1

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

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

ERBB2 amplification (continued)

trastuzumab + capecitabine + cisplatin

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

NCCN Recommendation category: 1

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

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

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trastuzumab + chemotherapy

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

Other criteria: Hormone receptor negative

NCCN Recommendation category: 1

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

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

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trastuzumab + chemotherapy

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 1

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

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

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trastuzumab + cisplatin + fluorouracil

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

NCCN Recommendation category: 1

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

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

ERBB2 amplification (continued)

trastuzumab + cisplatin + fluorouracil

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

NCCN Recommendation category: 1

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

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

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aromatase inhibitor

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

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fulvestrant

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

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hormone therapy

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

ERBB2 amplification (continued)

lapatinib + aromatase inhibitor

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

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lapatinib + capecitabine

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

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

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

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

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lapatinib + trastuzumab

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

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

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

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

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lapatinib + trastuzumab

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

Other criteria: BRAF wild type, RAS wild type

NCCN Recommendation category: 2A

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

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

ERBB2 amplification (continued)

lapatinib + trastuzumab

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

Other criteria: BRAF wild type, RAS wild type

NCCN Recommendation category: 2A

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

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

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lapatinib + trastuzumab + aromatase inhibitor

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

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neratinib

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

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neratinib + capecitabine

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

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

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

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

ERBB2 amplification (continued)

pertuzumab + trastuzumab

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

Other criteria: BRAF wild type, RAS wild type

NCCN Recommendation category: 2A

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

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

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pertuzumab + trastuzumab

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

Other criteria: BRAF wild type, RAS wild type

NCCN Recommendation category: 2A

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

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

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pertuzumab + trastuzumab + carboplatin + docetaxel

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

NCCN Recommendation category: 2A

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

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

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pertuzumab + trastuzumab + chemotherapy

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

Other criteria: Hormone receptor negative

NCCN Recommendation category: 2A

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

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

ERBB2 amplification (continued)

pertuzumab + trastuzumab + hormone therapy + chemotherapy

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

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pertuzumab + trastuzumab + paclitaxel

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

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

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

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

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tamoxifen

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

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trastuzumab + aromatase inhibitor

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

ERBB2 amplification (continued)

trastuzumab + capecitabine

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

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

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

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trastuzumab + capecitabine

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

---

trastuzumab + capecitabine

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

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trastuzumab + capecitabine + oxaliplatin

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

ERBB2 amplification (continued)

trastuzumab + capecitabine + oxaliplatin

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

NCCN Recommendation category: 2A

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

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

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trastuzumab + carboplatin + docetaxel

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

NCCN Recommendation category: 2A

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

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

---

trastuzumab + carboplatin + paclitaxel

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

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

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

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

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trastuzumab + carboplatin + paclitaxel

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

NCCN Recommendation category: 2A

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

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

ERBB2 amplification (continued)

trastuzumab + carboplatin + paclitaxel

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

NCCN Recommendation category: 2A

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

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

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trastuzumab + carboplatin + paclitaxel

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

NCCN Recommendation category: 2A

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

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

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trastuzumab + chemotherapy

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

Other criteria: Hormone receptor negative

NCCN Recommendation category: 2A

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

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

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trastuzumab + chemotherapy (other)

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

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

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

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

ERBB2 amplification (continued)

trastuzumab + cisplatin + docetaxel

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

---

trastuzumab + cisplatin + docetaxel

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

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trastuzumab + cisplatin + docetaxel + fluorouracil

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

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trastuzumab + cisplatin + docetaxel + fluorouracil

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

ERBB2 amplification (continued)

trastuzumab + cisplatin + paclitaxel

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

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trastuzumab + cisplatin + paclitaxel

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

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trastuzumab + cyclophosphamide + docetaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

---

trastuzumab + docetaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

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

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

ERBB2 amplification (continued)

trastuzumab + docetaxel

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

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trastuzumab + docetaxel

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

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trastuzumab + docetaxel + fluorouracil + oxaliplatin

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

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trastuzumab + docetaxel + fluorouracil + oxaliplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

ERBB2 amplification (continued)

trastuzumab + fluorouracil

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

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trastuzumab + fluorouracil

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

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trastuzumab + fluorouracil + irinotecan

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

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trastuzumab + fluorouracil + irinotecan

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

ERBB2 amplification (continued)

trastuzumab + fluorouracil + oxaliplatin

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

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trastuzumab + fluorouracil + oxaliplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

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trastuzumab + fulvestrant

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

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trastuzumab + hormone therapy + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

ERBB2 amplification (continued)

trastuzumab + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor negative

NCCN Recommendation category: 2A

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

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

---

trastuzumab + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

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trastuzumab + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

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

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

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trastuzumab + paclitaxel

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

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

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

ERBB2 amplification (continued)

trastuzumab + paclitaxel

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

NCCN Recommendation category: 2A

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

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

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trastuzumab + tamoxifen

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2A

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

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

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trastuzumab + vinorelbine

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

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

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

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

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trastuzumab deruxtecan

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

Other criteria: Hormone receptor status

NCCN Recommendation category: 2A

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

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

ERBB2 amplification (continued)

trastuzumab deruxtecan

Cancer type: Colon Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: BRAF wild type, RAS wild type

NCCN Recommendation category: 2A

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

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

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trastuzumab deruxtecan

Cancer type: Rectal Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: BRAF wild type, RAS wild type

NCCN Recommendation category: 2A

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

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

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hormone therapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2B

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

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

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trastuzumab + carboplatin + docetaxel + fluorouracil

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

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

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

ERBB2 amplification (continued)

trastuzumab + carboplatin + docetaxel + fluorouracil

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

NCCN Recommendation category: 2B

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

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

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trastuzumab + chemotherapy

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

Other criteria: Hormone receptor negative

NCCN Recommendation category: 2B

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

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

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trastuzumab + hormone therapy + chemotherapy

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

Other criteria: Hormone receptor positive

NCCN Recommendation category: 2B

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

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

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trastuzumab + paclitaxel

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

Other criteria: Hormone receptor negative

NCCN Recommendation category: 2B

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

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

ERBB2 amplification (continued)

ado-trastuzumab emtansine

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

NCCN Recommendation category: 2A

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

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

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irbinitinib + trastuzumab + capecitabine

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

NCCN Recommendation category: 2A

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

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

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lapatinib + capecitabine

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

NCCN Recommendation category: 2A

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

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

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neratinib + capecitabine

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

NCCN Recommendation category: 2A

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

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

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pertuzumab + trastuzumab

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

NCCN Recommendation category: 2A

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

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

ERBB2 amplification (continued)

trastuzumab

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

NCCN Recommendation category: 2A

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

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

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trastuzumab + chemotherapy

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

NCCN Recommendation category: 2A

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

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

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trastuzumab + docetaxel

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

NCCN Recommendation category: 2A

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

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

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neratinib + paclitaxel

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

NCCN Recommendation category: 2B

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

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

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 2.2021]

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 2.2021]

Current EMA Information

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

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

EGFR p.(L858R) c.2573T>G

● afatinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2020-11-04 **Variant class:** EGFR L858R mutation

Reference:

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

● bevacizumab (Allergan) + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2020-11-03 **Variant class:** EGFR L858R mutation

Reference:

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

● bevacizumab (Fujifilm Kyowa Kirin Biologics) + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2020-11-16 **Variant class:** EGFR L858R mutation

Reference:

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

● bevacizumab (Pfizer) + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-01-07 **Variant class:** EGFR L858R mutation

Reference:

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

● bevacizumab (Samsung Bioepis) + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2020-12-09 **Variant class:** EGFR L858R mutation

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 L858R mutation

Reference:

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

EGFR p.(L858R) c.2573T>G (continued)

dacomitinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2019-06-05 **Variant class:** EGFR L858R mutation

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 L858R mutation

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 L858R mutation

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:** 2019-05-28 **Variant class:** EGFR L858R mutation

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:** 2020-10-16 **Variant class:** EGFR L858R mutation

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

ERBB2 amplification (continued)

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:** 2020-11-13 **Variant class:** ERBB2 amplification or ERBB2 overexpression

Other criteria: Hormone receptor positive

Reference:

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

pertuzumab + trastuzumab + chemotherapy, pertuzumab + trastuzumab + docetaxel

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

Reference:

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

pertuzumab/trastuzumab/hyaluronidase-zzxf + cyclophosphamide + doxorubicin

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

Reference:

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

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

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

Reference:

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

ERBB2 amplification (continued)

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

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

Other criteria: ER positive, PR positive

Reference:

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

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

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

Other criteria: ER positive, PR positive

Reference:

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

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

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

Other criteria: ER positive, PR positive

Reference:

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

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

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

Other criteria: ER positive, PR positive

Reference:

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

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ERBB2 amplification (continued)

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

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

Other criteria: ER positive, PR positive

Reference:

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

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

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

Other criteria: ER positive, PR positive

Reference:

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

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

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

Other criteria: ER positive, PR positive

Reference:

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

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

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

Other criteria: ER positive, PR positive

Reference:

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

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ERBB2 amplification (continued)

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

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

Label as of: 2021-02-10

Variant class: ERBB2 overexpression

Other criteria: ER positive, PR positive

Reference:

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

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

Cancer type: Breast Cancer

Label as of: 2021-02-10

Variant class: ERBB2 amplification

Other criteria: ER positive, PR positive

Reference:

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

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

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

Label as of: 2019-11-29

Variant class: ERBB2 overexpression or ERBB2 overexpression

Other criteria: ER positive, PR positive

Reference:

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

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

Cancer type: Breast Cancer

Label as of: 2019-11-29

Variant class: ERBB2 amplification or ERBB2 amplification

Other criteria: ER positive, PR positive

Reference:

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

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ERBB2 amplification (continued)

trastuzumab deruxtecan

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

Reference:

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

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

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

Other criteria: ER positive, PR positive

Reference:

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

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

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

Other criteria: ER positive, PR positive

Reference:

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

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Current ESMO Information

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

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

EGFR p.(L858R) c.2573T>G

● atezolizumab + bevacizumab + carboplatin + paclitaxel

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR L858R mutation

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.(L858R) c.2573T>G (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.(L858R) c.2573T>G (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.]

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.]

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.]

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.(L858R) c.2573T>G (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.(L858R) c.2573T>G (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.(L858R) c.2573T>G (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.(L858R) c.2573T>G (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 Summary

EGFR p.(L858R) c.2573T>G + 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
NCT04338243	Open Label, Multicenter Phase Ib / II Study of Glumetinib Combined With Osimertinib in the Treatment of Relapsed and Metastatic Non-small Cell Lung Cancer Patients Who Failed to Receive EGFR Inhibitors	I/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
NCT03944772	A Biomarker-directed Phase II Platform Study in Patients With Advanced Non-Small Lung Cancer Whose Disease Has Progressed on First-Line Osimertinib Therapy	II
NCT03940703	A Phase II, Two-arm Study to Investigate Tepotinib Combined With Osimertinib in MET Amplified, Advanced or Metastatic Non-small Cell Lung Cancer (NSCLC) Harboring Activating EGFR Mutations and Having Acquired Resistance to Prior Osimertinib Therapy (INSIGHT 2 Study)	II

EGFR p.(L858R) c.2573T>G + ERBB2 amplification

NCT ID	Title	Phase
NCT03784599	Trastuzumab-emtansine and Osimertinib Combination Treatment to Target HER2 Bypass Track Resistance in EGFR Mutation Positive NSCLC	II

EGFR p.(L858R) c.2573T>G

NCT ID	Title	Phase
No NCT ID	The Efficacy and Safety of Osimertinib Combined with Bevacizumab in the Treatment of SD Patients with Non-Squamous Cell Lung Cancer	IV
NCT03264794	Evaluation of the Efficacy of Domestic Gefitinib Tablets in the Treatment of Locally Advanced or Metastatic Non-small Cell Lung Cancer Patients Using a Multicenter, Randomized, Positive Drug Gefitinib Pharmacodynamics and Pharmacodynamics	IV
NCT01665417	Randomized, Open Label, Positive Controlled, Multicenter Trial to Evaluate Icotinib as First-line and Maintenance Treatment in EGFR Mutated Patients With Lung Adenocarcinoma	IV
NCT02103257	Sequential Icotinib Plus Chemotherapy Versus Icotinib Alone as First-line Treatment in Stage IIIB/IV Lung Adenocarcinoma: a Randomized, Open-label, Multicenter Study	IV
NCT04401059	Synergistic Real-World Study and Evidence-based Medicine Evaluation of Elemene Combined With Tyrosine Kinase Inhibitors(TKIs)in the Treatment of Advanced Non-small Cell Lung Cancer (NSCLC): Prospective Study	IV
NCT03849768	A Randomized, Open-Label, Multi Center, Phase III Study to Assess the Efficacy and Safety of HS-10296 Versus Gefitinib as First-Line Treatment in Patients With EGFR Mutation Positive, Locally Advanced or Metastatic NSCLC	III
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

Clinical Trials Summary (continued)

EGFR p.(L858R) c.2573T>G (continued)

NCT ID	Title	Phase
NCT04143607	A Phase III,Double-Blind, Randomised Study to Assess the Efficacy and Safety of ASK120067 Versus Gefitinib as First-Line Treatment in Patients With Epidermal Growth Factor Receptor Mutation Positive, Locally Advanced or Metastatic Non-Small Cell Lung Cancer	III
NCT02886195	EGFR-TKIs Combine Chemotherapy as First-line Therapy for Patients With Advanced EGFR Mutation-positive NSCLC	III
NCT02518802	Pemetrexed Disodium and Cisplatin Chemotherapy Combined With Synchronous Gefitinib vs Chemotherapy Alone as Adjuvant Therapy in Patient With Stage II-IIIA, Epidermal Growth Factor Receptor Mutant Expressing Lung Adenocarcinoma	III
NCT04028778	A Multicenter, Randomized, Double-Blind Study of Gefitinib in Combination With Anlotinib or Placebo in Previously Untreated Patients With EGFR Mutation-Positive Advanced Non-Small-Cell Lung Cancer	III
No NCT ID	A Phase III Study Comparing Gefitinib And Inserted Cisplatin And Pemetrexed With Gefitinib As A First-Line Treatment For Patients With Advanced Non-Squamous Non-Small-Cell Lung Cancer Harboring EGFR Activating Mutation (JCOG1404/WJOG8214L, AGAIN study)	III
NCT03381066	A Phase III, Randomized, Multi-center Study to Determine the Efficacy of the Intercalating Combination Treatment of Chemotherapy and Gefitinib or Chemotherapy as Adjuvant Treatment in NSCLC With Common EGFR Mutations.	III
NCT04058704	A Multi-center, Prospective Study to Determine the Efficiency of Icotinib Combined With Radiation Therapy Early Intervention or Late Intervention For NSCLC Patients With Brain Metastases and EGFR(Epidermal Growth Factor Receptor) Mutation	III
NCT04248829	A Phase III, Randomized, Double-blind Study to Assess the Efficacy and Safety of Lazertinib Versus Gefitinib as the First-line Treatment in Patients With Epidermal Growth Factor Receptor Sensitizing Mutation Positive, Locally Advanced or Metastatic Non-Small Cell Lung Cancer	III
No NCT ID	A Phase III Trial for Mefatinib (MET-306) Versus Gefitinib in the Treatment of 1st Line EGFR Mutation of Patients with Advanced 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
NCT04181060	Randomized Phase III Study of Combination AZD9291 (Osimertinib) and Bevacizumab Versus AZD9291 (Osimertinib) Alone as First-Line Treatment for Patients With Metastatic EGFR-Mutant Non-Small Cell Lung Cancer (NSCLC)	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
NCT04239833	A Phase III, Double-blind, Randomised Study of SH-1028 Tablets Versus Gefiitinib as First Line Treatment in Patients With Epidermal Growth Factor Receptor Mutation Positive, Locally Advanced or Metastatic Non Small Cell Lung Cancer	III
NCT04206072	A Phase II/III, Open-Label, Randomised Study to Assess the Safety and Efficacy of D-0316 Versus Icotinib as First Line Treatment in Patients With EGFR Sensitising Mutation, Locally Advanced or Metastatic NSCLC	II/III

Clinical Trials Summary (continued)

EGFR p.(L858R) c.2573T>G (continued)

NCT ID	Title	Phase
NCT02338011	Gefitinib Alone or With Concomitant Whole Brain Radiotherapy for Patients Harboring an EGFR Mutation With Multiple Brain Metastases From Non-Small-cell Lung Cancer: a Phase II/III Randomized Controlled Trial	II/III
NCT03653546	A Randomized, Open-label, Controlled, Multi-Center Phase II/III Study to Assess the Efficacy and Safety of AZD3759 vs. a Standard of Care EGFR TKI, as First Line Treatment to EGFR Mutation Positive Advanced NSCLC With CNS Metastases	II/III
No NCT ID	Phase II Study Of Low-Dose Afatinib For Elderly Patients With Non-Small Cell Lung Cancer Harboring EGFR Mutation	II
No NCT ID	Multicenter, Prospective Interventional Study To Evaluate Therapeutic Effect of Afatinib in Patients With Advanced Non-Small Cell Lung Cancer, EGFR Mutation Positive And Brain Metastasis.	II
No NCT ID	The feasibility study and biomarker research of afatinib in patients with previously treated advanced NSCLC harboring EGFR mutation.	II
No NCT ID	A phase II study of afatinib in combination with pemetrexed and carboplatin in Japanese patients with EGFR mutation positive (mEGFR +) non-squamous (SQ), advanced non-small cell lung cancer (NSCLC) refractory to first-line osimertinib treatment (NEJ025B)	II
NCT04636593	Almonertinib With Concurrent Radiotherapy in The Treatment of Unresectable, Stage III Non-small-cell Lung Cancer Harboring EGFR Mutations: A Phase II Cohort Study	II
NCT03720873	An Multicenter,Phase II Trial of EGFR-TKIs Combine With Anlotinib as First-line Treatment for Patients With Advanced EGFR Mutation-positive NSCLC	II
NCT03736837	A Multi-center, One-arm Clinical Study of Anlotinib Combined With Icotinib as the First-line Treatment in Patients With EGFR Mutation-positive Advanced NSCLC. The Trial Aims to Evaluate the Efficacy and Safety of This Treatment.	II
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
NCT04245085	A Randomised Non-comparative Open Label Phase II Trial of Atezolizumab Plus Bevacizumab, With Carboplatin-paclitaxel or Pemetrexed, in EGFR-mutant Non-small Cell Lung Carcinoma With Acquired Resistance	II
No NCT ID	Phase II Study of Platinum-Based Doublet Chemotherapy Plus Atezolizumab, In Completely Resected, P-Stage II-IIIA NSCLC Patients Harboring EGFR Mutation. (WJOG11719L Investigator-Initiated Clinical Trial)	II
NCT04099836	Single Arm Phase II Trial of Atezolizumab and Bevacizumab in Epidermal Growth Factor Receptor (EGFR) Mutant Non-Small Cell Lung Cancer in Patients With Progressive Disease After Receiving Osimertinib (TOP 1901).	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
No NCT ID	Phase II Study Of Combination Chemotherapy Of Carboplatin, Pemetrexed, Bevacizumab And Erlotinib In Patients With Advanced Non-Squamous Non-Small Cell Lung Cancer Harboring EGFR Active Mutation.	II
NCT04425187	Bevacizumab Combined With Gefitinib in the Treatment of Advanced NSCLC Clinical Study of L858R Positive Mutation Patients	II
No NCT ID	Clinical Study of Camrelizumab Combined With Apatinib in the Treatment of EGFR-TKI Resistance in NSCLC	II

Clinical Trials Summary (continued)

EGFR p.(L858R) c.2573T>G (continued)

NCT ID	Title	Phase
No NCT ID	A Phase IIa Clinical Study of crizotinib in the Treatment of Advanced Non-small Cell Lung Cancer	II
NCT04027647	A Single-arm, Open-label, Phase II Study of Dacomitinib With or Without Dose Titration for the First-line Treatment of Locally Advanced or Metastatic Non-small Cell Lung Cancer in Subjects With Epidermal Growth Factor Receptor (EGFR) Activation Mutation	II
NCT04675008	A Phase II Study of Dacomitinib in Advanced Epidermal Growth Factor Receptor (EGFR)-Mutant Non-small Cell Lung Cancer (NSCLC) Patients Who Have Non-irradiated Brain Metastasis	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
No NCT ID	A Phase II Trial of Induction Erlotinib Followed by Surgical Resection in Patients with Pathologically Confirmed Stage IIIA-N2 EGFR Mutated Non-small cell lung cancer	II
NCT03126799	A Randomized Phase II Study of Erlotinib Alone Versus Erlotinib Plus Bevacizumab for Advanced Non-small Cell Lung Cancer With Epidermal Growth Factor Receptor Activating Mutations	II
NCT02098954	Second Line Erlitinib Combination With Gemcitabine Cisplatinum in Non-small Cell Lung Cancer Patients Who Harbored EGFR Sensitive Mutation Developed Resistance After First Line TKI Treatment	II
NCT03267654	Gefitinib Versus Combination of Gefitinib With Chemotherapy or Anti-angiogenesis as 1st Line Treatment in Advanced NSCLC Patients Detected With Bim Deletion or Low EGFR Activating Mutation Abundance:A Randomized, Multicentre, Phase II Study	II
No NCT ID	A randomized phase II trial of docetaxel or pemetrexed with or without gefitinib in elderly advanced non-small cell lung cancer patients harboring activating EGFR mutation after failure of the therapy as first-line treatment.	II
NCT03457337	A Randomized, Controlled, Open-label, Prospective Trial of S-1 Plus Gefitinib Versus Gefitinib Monotherapy for First-line Treatment of Advanced Non-squamous Non-small Cell Lung Cancer With EGFR-sensitive Mutation	II
NCT03382795	Retreatment With 1st Generation EGFR TKIs in Sensitizing EGFR Mutation Positive Non-Squamous Cell Carcinoma Patients Who Previously Treated With EGFR TKI and Cytotoxic Chemotherapy	II
NCT03341494	A Randomized Phase II Study of Gefitinib Alone Versus Gefitinib Plus Thalidomide for Advanced Non-small Cell Lung Cancer With Epidermal Growth Factor Receptor Activating Mutations	II
NCT03349203	Icotinib as Neoadjuvant and Adjuvant Therapy in EGFR-mutant Stage IIIB or Oligometastasis Non-small Cell Lung Cancer: a Single Arm, Phase II Clinical Study	II
NCT03396185	Icotinib as Consolidation Therapy After Synchronous or Sequential Chemoradiotherapy in Stage IIIA-IIIB Non-small Cell Lung Cancer With EGFR Sensitive Mutation: A Single Center, Single Arm, Open Label and Prospective Clinical Study	II
NCT03749213	Icotinib as Neoadjuvant Therapy in EGFR-mutant Stage IIIA-N2 Non-small Cell Lung Cancer: a Single Arm, Phase II Clinical Study	II
NCT02726568	A Phase II Study to Determine the Efficacy and Safety of High Dose Icotinib Combined With Stereotatic Radiosurgery for NSCLC Patients Harboring EGFR Mutation With Brain Metastases	II
NCT03292133	A Phase II Study of EGF816 and Gefitinib in TKI-naive EGFR-mutant Non-Small Cell Lung Cancer	II
No NCT ID	A Phase II, Noncomparative, Open Label, Multicentre, Study Of AZD9291 In Patients With Locally Advanced Or Metastatic EGFR Mutated “T790M Undetectable Or Unknown” Non-Small Cell Lung Cancer (Stage IIIb-IV) After No Immediate Prior EGFR TKI (OSIRIS Study)	II

Clinical Trials Summary (continued)

EGFR p.(L858R) c.2573T>G (continued)

NCT ID	Title	Phase
NCT02736513	Pilot, Phase II Study Assessing Intracranial Activity of AZD9291 (TAGRISSO) in Advanced EGFRm(EGFR Mutation) NSCLC Patients With Asymptomatic Brain Metastases	II
NCT03433469	A Phase II Study to Evaluate Neoadjuvant Osimertinib Therapy in Patients with Surgically Resectable, EGFR-Mutant Non-Small Cell Lung Cancer	II
NCT03586453	A Phase II Study of Osimertinib With On-study and Post-progression Biopsy in the First Line Treatment of EGFR Inhibitor naive Advanced EGFR Mutant Lung Cancer	II
NCT03969823	Whole Genomic Landscape of EGFR Mutation-Positive Advanced Non-Small Cell Lung Cancer Treated With First-Line Osimertinib (WARRIOR)	II
NCT04233021	A Phase II, Multi-centre Study, to Evaluate the Efficacy and Safety of Osimertinib Treatment for Patients With EGFR-mutated Non-small Cell Lung Cancer (NSCLC) With Brain or Leptomeningeal Metastases	II
NCT04545710	A Phase II Trial of Osimertinib and Abemaciclib With a Focus on Non-Small Cell Lung Cancer Patients With EGFR Activating Mutations With Osimertinib Resistance	II
NCT02856893	APPLE Trial: Feasibility and Activity of AZD9291 (Osimertinib) Treatment on Positive PLasma T790M in EGFR Mutant NSCLC Patients	II
NCT03497767	A Randomised Phase II Trial of Osimertinib With or Without Stereotactic Radiosurgery for EGFR Mutated Non-Small Cell Lung Cancer (NSCLC) With Brain Metastases	II
NCT03769103	Open Label, Multicenter, Phase II Study of Patients With Treatment Naive Metastatic Epidermal Growth Factor Receptor (EGFR) Mutation-Positive Non-Small Cell Lung Cancer (NSCLC) With Brain Metastases Randomized to Stereotactic Radiosurgery (SRS) and Osimertinib or Osimertinib Alone	II
NCT03909334	An Open-Label Randomized Phase II Study of Combining Osimertinib With and Without Ramucirumab in Tyrosine Kinase Inhibitor (TKI)-naïve Epidermal Growth Factor Receptor (EGFR)-Mutant Locally Advanced or Metastatic NSCLC	II
NCT03392246	A Phase II Study of Osimertinib in Combination With Selumetinib in EGFR Inhibitor naive Advanced EGFR Mutant Lung Cancer	II
NCT03823807	A Multicenter, Open-label, Phase II Study to Evaluate the Safety and Efficacy of SH-1028 in Locally Advanced or Metastatic NSCLC	II
No NCT ID	Afatinib Translational Study in Patients with EGFR Mutation-Positive Non-Squamous Non-small Cell Lung Cancer Acquired Resistance to Osimertinib (ASPEC)	I/II
NCT03706287	Efficacy and Safety of Anlotinib Combined With Platinum Plus Pemetrexed in T790M Mutation Negative Metastastic Non-squamous Non-small-cell Lung Cancer After Progression on First-line EGFR TKI: a Phase II, Muti-center, Single Arm Study	I/II
NCT03446417	A Phase 1/2 Open Label, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics, and Anti-tumor Activity of ZN-e4 (KP-673) in Patients With Advanced Non-Small Cell Lung Cancer with Activating Epidermal Growth Factor Receptor (EGFR) Mutations	I/II
NCT02716116	A Phase I/II Study of the Safety, Pharmacokinetics, and Anti-Tumor Activity of the Oral EGFR/HER2 Inhibitor TAK-788 (AP32788) in Non-Small Cell Lung Cancer	I/II
NCT03831932	A Phase I/II Study of AZD9291 (Osimertinib) and CB-839 HCl in Patients With EGFR Mutant Non-Small Cell Lung Cancer	I/II
No NCT ID	A Non-interventional, Single-arm, Prospective Clinical Study for the Efficacy and Safety of Low-dose Alfaatinib Combined with Pemetrexed and Carboplatin in First-line Treatment of Advanced EGFR Mutant Non-squamous Non-small Cell Lung Cancer	I

Clinical Trials Summary (continued)

EGFR p.(L858R) c.2573T>G (continued)

NCT ID	Title	Phase
NCT04085315	A Phase I/Ib Study of Alisertib in Combination With Osimertinib in Metastatic EGFR-mutant Lung Cancer	I
NCT04479306	A Ph Ib Study of Osimertinib + Alisertib or Sapanisertib for Osimertinib-Resistant EGFR Mutant Non-Small Cell Lung Cancer (NSCLC) (Crossover Study)	I
No NCT ID	Phase I Clinical Study of Safety, Tolerability, Pharmacokinetics and Initial Efficacy of RX518 in Patients with Advanced Non-small Cell Lung Cancer	I
No NCT ID	Study for Efficacy and Safety of Continuing to Treat with TKI Combined with Anlotinib Monotherapy in Advanced NSCLC Patients with T790M Mutation-negative after Tki Treatment Failure	I
NCT03976856	A Phase Ib Clinical Study With Extension Phase to Evaluate Safety and Efficacy of Genolimzumab (GB226) in Combination With Fruquintinib in the Treatment of Relapsed or Metastatic NSCLC Patients	I
NCT03333343	A Phase Ib, Open Label, Multi-center Study to Characterize the Safety, Tolerability and Preliminary Efficacy of EGF816 in Combination With Selected Targeted Agents in EGFR Mutant NSCLC	I
No NCT ID	Study Of Immunologic Factor In Re-Biopsy Specimen, Peritumoral BALF, And The Peripheral Blood For Predicting Response To Osimertinib In NSCLC Patients	I
No NCT ID	Single-arm Phase I Study of Erlotinib or Osmeltinib plus Ramcilmab in Patients with Untreated EGFR Gene Mutation-Positive Non-Small Cell Lung Cancer with Brain Metastases	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
NCT04197934	Phase I Study to Evaluate Safety, Tolerability, Pharmacokinetics and Anti-Tumor Activity of WSD0922-FUFU	I
NCT04132102	An Open-label, Single-arm Clinical Study to Evaluate the Efficacy of Afatinib in Advanced Lung Squamous Cell Carcinoma With EGFR Sensitive Mutation	IV
NCT04116918	Efficacy and Safety of the Combination of Anlotinib and JS001 in EGFR-TKI Resistant T790M-Negative NSCLC	IV
No NCT ID	Gefitinib Combined with Vinorelbine Soft Capsules vs Gefitinib Monotherapy in the Treatment of Stage IIIB-IV NSCLC Patients with EGFR-sensitive Mutation	IV
No NCT ID	Phase III Study of Afatinib or Chemotherapy in Patients with Non-small Cell Lung Cancer Harboring Sensitizing Uncommon Epidermal Growth Factor Receptor Mutations (ACHILLES study/TORG1834)	III
NCT03735121	A Randomized, Multicenter, Phase Ib/II Study to Investigate the Pharmacokinetics, Efficacy, and Safety of Atezolizumab Subcutaneous Compared With Atezolizumab Intravenous in Patients With Previously Treated Locally Advanced or Metastatic Non-Small Cell Lung Cancer	III
NCT03866499	A Randomized, Double-blind, Positive Controlled Phase III Study to Evaluate the Efficacy and Safety of BPI-7711 Capsule in Locally Advanced or Recurrent/Metastatic Treatment-naive Non-small Cell Lung Cancer Patients With EGFR Mutation	III
No NCT ID	Phase III Clinical Study Of The Effectiveness And Safety Of RX518 As The First-line Treatment For Patients With Locally Advanced Or Metastatic Non-small Cell Lung Cancer With EGFR Mutations	III
No NCT ID	A Randomized Phase III Study Of Erlotinib Compared To Intercalated Erlotinib With Cisplatinum Pemetrexed As First-Line Therapy For Advanced EGFR Mutated Non-Small-Cell Lung Cancer. The NVALT-17 Study	III
NCT01996098	A Multicenter, Randomized, Phase III Trial of Chemotherapy Followed by 6-month or 12-month Icotinib Versus Chemotherapy as Adjuvant Therapy in Stage IIA-IIIA Non-small Cell Lung Cancer Harboring Epidermal Growth Factor Receptor Mutation	III

Clinical Trials Summary (continued)

EGFR p.(L858R) c.2573T>G (continued)

NCT ID	Title	Phase
NCT02183883	Deciphering Afatinib Response and Resistance With INtratumour Heterogeneity	II
NCT04201756	Neoadjuvant Afatinib Therapy for Resectable Stage III EGFR Mutation-Positive Lung Adenocarcinoma: A Single-Arm, Open-Label, Phase II Clinical Trial	II
No NCT ID	Hypothesis generative H2H study comparing the efficacy between afatinib and osimertinib based on the immunological biomarker in the NSCLC patients with EGFR mutations (HeaT ON BeaT)	II
NCT04426825	A Single Arm, Phase II Study of Atezolizumab (MPDL3280A, Anti-PD-L1 Antibody) in Combination With Bevacizumab in Patients With EGFR Mutation Positive Stage IIIB/IV Non-Squamous Non-Small Cell Lung Cancer Pretreated With Epidermal Growth Factor Receptor Tyrosine-Kinase Inhibitors	II
NCT03574402	An Open-label, Multi-center, Phase II Umbrella Study to Assess Efficacy of Targeted Therapy or Immunotherapy Directed by Next Generation Sequencing (NGS) in Chinese Patients With Advanced NSCLC (TRUMP)	II
NCT04042558	A Multicentre Phase II, Open-label, Non-randomized Study Evaluating Platinum-Pemetrexed-Atezolizumab (+/- Bevacizumab) for Patients With Stage IIIB/IV Non-squamous Non-small Cell Lung Cancer With EGFR Mutations, ALK Rearrangement or ROS1 Fusion Progressing After Targeted Therapies	II
NCT03840902	A Multicenter, Double Blind, Randomized, Controlled Study of M7824 With Concurrent Chemoradiation Followed by M7824 Versus Concurrent Chemoradiation Plus Placebo Followed by Durvalumab in Participants With Unresectable Stage III Non-small Cell Lung Cancer	II
NCT02347839	A Multicenter Phase II Trial of Neoadjuvant Gefitinib Followed by Surgery, Followed by Adjuvant Gefitinib in Patients With Unresectable Stage III Non-Small Cell Lung Cancer Harboring Activating Epidermal Growth Factor Receptor Mutations NEoadjuvant Gefitinib fOllowed by Surgery and gefiTinib In unresectAble sTage III NSCLC With EGFR Mutations (NEGOTIATE)	II
NCT02264210	A Randomized, Phase II Trial of Icotinib Versus Observation as Adjuvant Treatment in Stage IB Non-Small Cell Lung Cancer Harboring Activating Epidermal Growth Factor Receptor Mutation	II
NCT02820116	An Open-label, Multicenter,Single-arm, Phase II Clinical Study of Icotinib for IIIA - IIIB NSCLC Patients with Epidermal Growth Factor Receptor Mutation	II
NCT02824952	Neo-adjuvant Trial With AZD9291 in EGFRm+ Stage IIIA/B NSCLC - a Phase II Open-label Study	II
NCT04120454	An Investigator-Sponsored Phase II Single Arm Trial of Ramucirumab and Pembrolizumab in Patients With EGFR Mutant Non-Small Cell Lung Cancer	II
NCT03983928	A Phase Ib, Open-label, Single Center, Non-randomized Study for Safety and Efficacy of TQB2450 Combined With Anlotinib in Subjects With Advanced Mutation Positive Non-Small Cell Lung Cancer	I/II
NCT03846310	A Phase I/Ib Study to Evaluate the Safety and Tolerability of Immunotherapy Combinations in Participants With Lung Cancer	I
NCT04141644	A Phase Ib Study to Evaluate the Safety and Efficacy of Osimertinib in Combination With Ipilimumab in Patients With EGFR Mutated Non-Small-Cell Lung Cancer Tumors	I
NCT04511533	Single Arm Study to Evaluate the Safety of Dacomitinib for the First-Line Treatment of Participants in India With Metastatic Non-Small Cell Lung Cancer With Epidermal Growth Factor Receptor (EGFR)-Activating Mutations	IV
No NCT ID	The Continuous Evaluation of EGFR Mutation in EGFR-mutation Positive Lung Cancer Patients During EGFR TKI Treatment.	IV
NCT02404675	High Dose Icotinib in Advanced Non-small Cell Lung Cancer With EGFR 21 Exon Mutation (INCREASE): a Randomized, Open-label Study	IV

Clinical Trials Summary (continued)

EGFR p.(L858R) c.2573T>G (continued)

NCT ID	Title	Phase
NCT03991403	Study of Atezolizumab in Combination With Carboplatin + Paclitaxel +Bevacizumab vs With Pemetrexed + Cisplatin or Carboplatin With Stage IV NON-SQUAMOUS NON-SMALL CELL LUNG CANCER With EGFR(+) or ALK(+)	III
NCT02714010	Whole Brain Radiotherapy Concurrent With EGFR-TKI Versus EGFR-TKI Alone in the Treatment of Non-small Cell Lung Cancer Patients With Brain Metastasis	III
NCT02448797	Icotinib as Adjuvant Therapy Compared With Standard Chemotherapy in Stage II-IIIA Non-small Cell Lung Cancer With EGFR-mutation: a Randomized, Positive-controlled, Phase 3 Study (EVIDENCE, CCTC-1501)	III
NCT03786692	TH-138: Phase II Randomized Trial of Carboplatin + Pemetrexed + Bevacizumab, With or Without Atezolizumab in Stage IV Non-squamous NSCLC Patients Who Harbor a Sensitizing EGFR Mutation or Have Never Smoked	II
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
NCT01470716	A Phase II Study of Neo-adjuvant Erlotinib for Operable Stage IIB or IIIA Non-small Cell Lunc Cancer With Epidermal Growth Factor Receptor Activation Mutations	II
No NCT ID	ITAC 2 TRIAL: Intermittent TKI and Chemotherapy for Patients with Advanced Non-Small Cell Lung Cancer	II
NCT01951469	Multicenter Phase II Study of Gefitinib Mono-therapy or Gefitinib Combined With Pemetrexed/Cisplatin in Patients With Brain Metastases From Non-small Cell Lung Cancer Harboring EGFR Mutation	II
NCT02044328	Icotinib as an Adjuvant Therapy for Patients With Stage IIA-IIIA Adenocarcinoma With EGFR Mutation: a Prospective, Exploratory Study	II
NCT03804580	First-Line Treatment With Osimertinib In EGFR-Mutated Non-Small Cell Lung Cancer, Coupled To Extensive Translational Studies	II
NCT04335292	Osimertinib Then Chemotherapy in EGFR-mutated Lung Cancer With Osimertinib Third-line Rechallenge	II
NCT04410796	A Phase 2 Randomized Study of Osimertinib Versus Osimertinib Plus Chemotherapy for Patients With Metastatic EGFR-Mutant Lung Cancers That Have Detectable EGFR-Mutant cfDNA in Plasma After Initiation of Osimertinib	II
NCT03667820	Phase II Trial of Osimertinib in Combination With Stereotactic Ablative Radiation (SABR) in EGFR Mutant Advanced Non-Small Cell Lung Cancer (NSCLC)	II
NCT03318939	A Phase II Study of Poziotinib in Patients With Non-Small Cell Lung Cancer (NSCLC), Locally Advanced or Metastatic, With EGFR or HER2 Exon 20 Insertion Mutation (ZENITH20).	II
No NCT ID	Zoledronate combinate with gefitinib in advanced non-small cell lung cancer with EGFR activation mutation: a multicenter, randomised controlled, phase II trial	II
No NCT ID	A Phase I Study Afatinib In Combination Of Osimertinib In Patients With Relapsed Non-Small Cell Lung Cancer After Failure of Prior Osimertinib	I
NCT03891615	Phase I Study of Niraparib in Combination With Osimertinib in EGFR-Mutated Advanced Lung Cancer	I
NCT04250545	A Phase I Trial of MLN0128 (Sapanisertib) and CB-839 HCl (Telaglenastat) in Advanced NSCLC Patients	I
NCT03114319	An Open-label, Multi-center, Phase I, Dose Finding Study of Oral TNO155 in Adult Patients With Advanced Solid Tumors	I

Clinical Trials Summary (continued)

EGFR p.(L858R) c.2573T>G (continued)

NCT ID	Title	Phase
NCT04413201	AFAMOSI: Prospective, Randomized, Multicenter Phase IV Study to Evaluate the Efficacy and Safety of Afatinib Followed by Osimertinib Compared to Osimertinib in Patients With EGFRmutated/T790M Mutation Negative Non-squamous NSCLC in the First-line Setting	IV
No NCT ID	Apatinib Combined With EGFR-TKI For Patients With EGFR Mutation Who Failed EGFR-TKI: A Prospective Study	IV
No NCT ID	A Real World Study Of Apatinib Combined With Gefitinib In The Treatment Of EGFRm+ Advanced Non-Squamous Non-Small Cell Lung Cancer	IV
No NCT ID	Clinical Study Of Combined Action Of Gefitinib And Brain Radiotherapy On EGFR-Mutated Non-Small-Cell Lung Cancer Patients With Brain Metastasis	IV
No NCT ID	Clinical Study Of Combined Action Of Icotinib And Brain Radiotherapy On EGFR-Mutated Non-Small-Cell Lung Cancer Patients With Brain Metastasis	IV
NCT03800134	A Phase III, Double-blind, Placebo-controlled, Multi-center International Study of Neoadjuvant/Adjuvant Durvalumab for the Treatment of Patients With Resectable Stages II and III Non-small Cell Lung Cancer (AEGEAN)	III
NCT03656393	Observational Clinical Trial of Adjuvant Chemotherapy for Non-squamous Cell Carcinoma of Non-small Cell Lung Cancer	III
NCT03992885	Combination Therapy With Icotinib, Pemetrexed and Platinum in Patients With Metastatic Non-squamous Non-small Cell Lung Cancer With EGFR Mutations Who Did Not Progress After Pemetrexed in Combination With Platinum-based Chemotherapy:a Single-arm, Open, Multicenter Clinical Study.	III
No NCT ID	A Phase II Study Of Afatinib For Advanced Non-Small Cell Lung Cancer With Uncommon Epidermal Growth Factor Receptor (EGFR) Mutation Including Compound Mutation Detected By Next Generation Sequencing	II
NCT01553942	Afatinib Sequenced With Concurrent Chemotherapy and Radiation in EGFR-Mutant Non-Small Cell Lung Tumors: The ASCENT Trial	II
No NCT ID	A Single-center, Open Label, Phase II Study of Anlotinib as Second/Third-line Treatment for Advanced Non-small Cell Lung Cancer	II
NCT04619563	A Single-arm Exploratory Clinical Study of Anlotinib Hydrochloride Combined With Docetaxel in EGFR Mutations Advanced Non Small Cell Lung Cancer Patients Who Have Progressed After Targeted Therapy and Chemotherapy	II
No NCT ID	Clinical Study And Safety Analysis On The Treatment Of Advanced Non-Small Cell Lung Cancer With Anlotinib And Gefitinib	II
No NCT ID	Osimertinib Combined Bevacizumab in Untreated Epidermal Growth Factor Receptor Mutated Non-small-cell Lung Cancer Patients with Malignant Pleural And/Or Pericardial Effusion -phase II Trial	II
No NCT ID	Randomized Controlled Trial for EGFR-TKIs Plus S-1 or EGFR-TKIs as the First-Line Therapy for Patients with Advanced Non-small Cell Lung Cancer Harboring EGFR Mutations	II
No NCT ID	Single arm, Exploratory Study for Apatinib mesylate Combined with EGFR-TKI in Patients with EGFR Mutation-positive Advanced Non-squamous Non–small-cell Lung Cancer	II
No NCT ID	EGFR-TKI Combined With Stereotactic Body Radiation Therapy Versus TKI alone for Stage IV Oncogene-Driven Non-Small Cell Lung Cancer.	II
No NCT ID	Efficacy and Safety of Erlotinib in Elderly Patients With Non-small-cell Lung Cancer Harboring Epidermal Growth Factor Receptor Mutations	II
NCT04591431	The Rome Trial From Histology to Target: the Road to Personalize Target Therapy and Immunotherapy	II

Clinical Trials Summary (continued)

EGFR p.(L858R) c.2573T>G (continued)

NCT ID	Title	Phase
NCT03904823	An Open, Single-arm, Multi-center, Phase II Clinical Trial of Famitinib Combined With Epidermal Growth Factor Receptor (EGFR) Inhibitor HS-10296 in Patients With Advanced EGFR-mutant Non-Small Cell Lung Cancer (NSCLC)	II
NCT01784549	A Multi-center Phase II Randomized Study of Customized Neoadjuvant Therapy Versus Standard Chemotherapy in Non-small Cell Lung Cancer (NSLC) Patients With Resectable Stage IIIA (N2) Disease	II
NCT02960607	A Phase II Study of High-dose Icotinib in Previously Treated Non-small Cell Lung Cancer Patients With Epidermal Growth Factor Receptor Mutation	II
NCT03091491	Randomised Phase II Study of Nivolumab Versus Nivolumab and Ipilimumab Combination in EGFR Mutant Non-small Cell Lung Cancer	II
NCT04538378	Phase II Trial of Olaparib (LYNPARZA) Plus Durvalumab (IMFINZI) in EGFR-Mutated Adenocarcinomas That Transform to Small Cell Lung Cancer (SCLC) and Other Neuroendocrine Tumors.	II
NCT03460275	Osimertinib as First-line Therapy for Patients With EGFR Mutation-positive Locally Advanced or Metastatic Non-squamous Non-Small Cell Lung Cancer(NSCLC), a Single-Arm, Open-Label, Prospective, Multicenter, Phase II Clinical Trial	II
No NCT ID	Efficacy Of Osimertinib With Platinum And Pemetrexed In EGFR Mutant Non-Small Cell Lung Cancer Patients Bearing CNS Metastasis, And Have Systemic Progression But Stable Intracranial Disease On Osimertinib Resistance. (EPONA)	II
No NCT ID	An Exploratory Clinical Study Of PD-1 Inhibitor Combined With Chemotherapy In The Treatment Of Advanced Non-small Cell Lung Cancer With EGFR Mutation Positive And T790M Negative After Failure Of TKI Combined With Antiangiogenic Drugs	II
No NCT ID	Phase II Trial Of Docetaxel Plus Ramucirumab Combination Therapy In Patients With Advanced EGFR Gene Mutation Positive Advanced Stage Non-Squamous Cell Non small Cell Lung Cancer	II
No NCT ID	Clinical Study of Combined Action of the First Generation of TKIs and Brain Radiotherapy on EGFR-Mutated Non-Small-Cell Lung Cancer Patients with Brain Metastasis	II
NCT03974022	A Phase I/II, Open-Label, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics and Anti-tumor Efficacy of DZD9008 in Patients With Advanced Non-Small Cell Lung Cancer (NSCLC) With EGFR or HER2 Mutation	I/II
NCT03797391	First-in-human, Phase I/II, Multicenter, Open-Label Study of EMB-01 in Patients With Advanced/ Metastatic Solid Tumors	I/II
No NCT ID	A phase I/II study of erlotinib/carboplatin/pemetrexed/bevacizumab in chemotherapy-naive patients with EGFR mutation positive advanced non-squamous non-small-cell lung cancer	I/II
NCT03758287	A Phase Ib, Multi-center, Open Label Study of Ningetinib (CT053PTSA) in Combination With Gefitinib in Stage IIIB or IV NSCLC Patients With EGFR Mutation and T790M Negative Who Have Progressed After EGFR TKI Therapy	I/II
NCT03711422	A Dose Finding Study of Continuous and Intermittent High-dose (HDI) Afatinib (EGFR TKI) on CNS Metastases and Leptomeningeal Disease (LMD) in Patients With Advanced Refractory EGFR Mutation Positive Non-small Cell Lung Cancer	I
NCT04528836	A Phase I/IB First-in-Human Study of the SHP2 Inhibitor BBP-398 (Formerly Known as IACS-15509) in Patients With Advanced Solid Tumors	I
No NCT ID	Feasibility Study of Pemetrexed / Bevacizumab / Erlotinib in Chemotherapy Naive Patients With Non-Small Cell Lung Cancer Harboring EGFR Mutation	I
No NCT ID	Phase I Study of DZD9008 in EGFR or HER2 Mutant NSCLC Chinese Patients	I

Clinical Trials Summary (continued)

EGFR p.(L858R) c.2573T>G (continued)

NCT ID	Title	Phase
NCT04077463	An Open-label Phase 1/1b 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
NCT04013542	A Pilot Trial of Ipilimumab-Nivolumab in Local-Regionally Advanced Non Small Cell Lung Cancer (NSCLC)	I
No NCT ID	Pharmacokinetic and dose finding study of osimertinib in patients with impaired renal function and low body weight	I
NCT03535363	Phase I Trial of Osimertinib With Stereotactic Radiosurgery (SRS) in Patients With Brain Metastases From EGFR Positive Non-Small-Cell Lung Cancer (NSCLC)	I
No NCT ID	A Pilot Study for Apatinib Mesylate Combined with Gefitinib in First-line Treatment of Lung Adenocarcinoma with Malignant Pleural Effusion or Pericardial Effusion	IV
NCT03346811	Efficiency of Icotinib in Plasma ctDNA EGFR Mutation-positive Patients Diagnosed With Lung Cancer:a Single Arm,Multi-center,Open-label Study	II
NCT04209465	MasterKey-01: A Phase I/II, Open-label, Two-part, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics & Antitumor Activity of BDTX-189, an Inhibitor of Allosteric ErbB Mutations, in Patients w/ Advanced Solid Malignancies	I/II
NCT03618043	A Phase I, Open-label Study to Assess the Safety and Tolerability of Ascending Doses of SH-1028 Tablets in Patients With Advanced Solid Cancer.	I
NCT03810872	An Open Explorative Phase II, Open Label Study of Afatinib in the Treatment of Advanced Cancer Carrying an EGFR, a HER2 or a HER3 Mutation	II
NCT03239015	Efficacy and Safety of Targeted Precision Therapy in Refractory Tumor With Druggable Molecular Event	II
NCT03065387	Phase I Study of the Pan-ERBB Inhibitor Neratinib Given in Combination With Everolimus, Palbociclib, or Trametinib in Advanced Cancer Subjects With EGFR Mutation/Amplification, HER2 Mutation/ Amplification, or HER3/4 Mutation or KRAS Mutation	I
No NCT ID	Phase I Clinical Study With Advanced Solid Tumors KBP-5209 Treatment	I
NCT04128085	A Phase I, Open-label, Multicenter, Dose Escalation and Expansion Study to Evaluate the Tolerance and Pharmacokinetics of TQB3804 in Subjects With Advanced Malignant Tumors	I
NCT03841110	FT500 as Monotherapy and in Combination With Immune Checkpoint Inhibitors in Subjects With Advanced Solid Tumors (Phase I)	I
NCT03297606	Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial	II
NCT04429542	First-in-Human, Phase I/Ib, Open-label, Multicenter Study of Bifunctional EGFR/TGFß Fusion Protein BCA101 Alone and in Combination With Pembrolizumab in Patients With EGFR-Driven Advanced Solid Tumors	I

ERBB2 amplification

NCT ID	Title	Phase
NCT02314481	Deciphering Antitumour Response and Resistance With INtratumour Heterogeneity - DARWINII	II
NCT04579380	A Phase II Basket Study of Tucatinib in Combination With Trastuzumab in Subjects With Previously Treated, Locally Advanced Unresectable or Metastatic Solid Tumors Driven by HER2 Alterations	II

Clinical Trials Summary (continued)

ERBB2 amplification (continued)

NCT ID	Title	Phase
NCT04706949	A Prospective, Single Center, Single Arm, Phase II Clinical Trial of Pyrotinib Combined With Pemetrexed Plus Carboplatin in the First-line Treatment of Patients With HER2 Mutant or Amplified Recurrent / Metastatic Non-small Cell Lung Cancer	II
NCT04591431	The Rome Trial From Histology to Target: the Road to Personalize Target Therapy and Immunotherapy	II
NCT03602079	A Phase I-II, FIH Study of A166 in Locally Advanced/Metastatic Solid Tumors Expressing Human Epidermal Growth Factor Receptor 2 (HER2) or Are HER2 Amplified That Did Not Respond or Stopped Responding to Approved Therapies	I/II
NCT04311034	A Phase Ib Study to Evaluate the Efficacy and Safety of RC48-ADC for Injection in Subjects With Advanced Non-small Cell Lung Cancer With HER2 Overexpression or HER2 Mutation	I
NCT04460456	A Phase 1/1B, Open-Label, Dose Escalation and Expansion Study of SBT6050 Alone and in Combination With Pembrolizumab in Subjects With Advanced Solid Tumors Expressing HER2	I
NCT04042701	A Phase Ib, Multicenter, Two-Part, Open-Label Study of Trastuzumab Deruxtecan (DS-8201a), An Anti-Human Epidermal Growth Factor Receptor-2 (HER2)-Antibody Drug Conjugate (ADC), In Combination With Pembrolizumab, An Anti-PD-1 Antibody, In Subjects With Locally Advanced/Metastatic Breast Or Non-Small Cell Lung Cancer (NSCLC).	I
NCT02892123	Phase I Trial of ZW25 in Patients With Locally Advanced (Unresectable) and/or Metastatic HER2-expressing Cancers.	I
NCT02675829	A Phase II Trial of Ado-Trastuzumab Emtansine for Patients With HER2 Amplified or Mutant Cancers	II
NCT04632992	MyTACTIC: An Open-Label Phase II Study Evaluating Targeted Therapies in Patients Who Have Advanced Solid Tumors With Genomic Alterations or Protein Expression Patterns Predictive of Response	II
NCT02693535	Targeted Agent and Profiling Utilization Registry (TAPUR) Study	II
NCT03239015	Efficacy and Safety of Targeted Precision Therapy in Refractory Tumor With Druggable Molecular Event	II
NCT04151329	Evaluation for the Safety of BAT1306 and BAT8001 Injection for the Treatment of Patients With HER2-positive Advanced Solid Tumors Phase I/IIa Clinical Trials of Safety, Tolerability and Pharmacokinetic Characteristics	I/II
NCT04278144	Phase I/II Study of BDC-1001 as a Single Agent and in Combination With Pembrolizumab in Patients With Advanced HER2-Expressing Solid Tumors	I/II
NCT04209465	MasterKey-01: A Phase I/II, Open-label, Two-part, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics & Antitumor Activity of BDTX-189, an Inhibitor of Allosteric ErbB Mutations, in Patients w/ Advanced Solid Malignancies	I/II
NCT04092673	A Phase 1-2 Dose-Escalation and Cohort-Expansion Study of Intravenous Zotatifin (eFT226) in Subjects With Selected Advanced Solid Tumor Malignancies	I/II
No NCT ID	Phase I Clinical Study of Safety, Tolerability, Pharmacokinetics and Initial Efficacy of A166 in the Treatment of Patients with Locally Advanced or Metastatic Solid Tumors with HER2.	I
NCT03916094	A Phase I Clinical Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Preliminary Pharmacodynamics of HLX22 Monoclonal Antibody Injection (HER2 Monoclonal Antibody) in Patients With Advanced Solid Tumours Overexpressing HER2	I
NCT03944499	A Phase I, Multicenter, Open-label, Single-arm Study: A Dose-escalation Phase (Phase 1a) Evaluating FS-1502 in Patients With HER2 Expressed Advanced Solid Tumors; and a Dose-expanded Cohort (Phase 1b) Evaluating FS-1502 in Patients With Local Advanced or Metastatic, HER2 Positive Breast Cancer.	I

Clinical Trials Summary (continued)

ERBB2 amplification (continued)

NCT ID	Title	Phase
No NCT ID	Single-Arm, Open-Label, Single-Dose And Multiple-Dose Phase Ia Clinical Study Of Tolerability And Pharmacokinetics Of AMX3009 In Patients With HER2-Positive Advanced Solid Tumors	I
NCT03255070	A Phase I, Multicenter, Open-label, Multiple Dose-escalation Study of ARX788, Intravenously Administered as a Single Agent in Subjects With Advanced Cancers With HER2 Expression	I
NCT04147819	A Phase I Open-label, First-in-human, Multi-center Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Anti-tumor Activity of Thorium-227 Labeled Antibody-chelator Conjugate BAY2701439, in Participants With Advanced HER2-expressing Tumors	I
NCT04511871	A Phase I Trial to Assess Safety, Tolerability and Anti-tumor Activity of Autologous T Cell Modified Chimeric Antigen Receptor (CAR) (CCT303-406) in Patients With Relapsed or Refractory HER2 Positive Solid Tumors	I
NCT03696030	A Phase I Cellular Immunotherapy Study of Intraventricularly Administered Autologous HER2-Targeted Chimeric Antigen Receptor (HER2-CAR) T Cells in Patients With Brain and/or Leptomeningeal Metastases From HER2 Positive Cancers	I
NCT03847168	Phase I Study of KN026 in HER2 Expressing Breast Cancer, Astric/Gastroesophageal Junction Cancer and Other Locally Advanced/Metastatic Solid Tumors	I
NCT04501770	A Phase I Study to Evaluate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics and Immunogenicity Profiles of the Recombinant Anti-HER2 and Anti-CD3 Humanized Bispecific Antibody (M802) in HER2-Positive Advanced Solid Tumors	I
NCT03842085	Evaluation on the Safety and Pharmacokinetics of Recombinant Humanized Bispecific Monoclonal Antibody MBS301 for Injection in Treatment of HER2 Positive Recurrent or Metastatic Malignant Solid Tumor	I
NCT04029922	A Phase I Open-label, Multicenter Dose Escalation Study of MT-5111 in Subjects With Previously Treated Advanced HER2-positive Solid Tumors	I
NCT03065387	Phase I Study of the Pan-ERBB Inhibitor Neratinib Given in Combination With Everolimus, Palbociclib, or Trametinib in Advanced Cancer Subjects With EGFR Mutation/Amplification, HER2 Mutation/ Amplification, or HER3/4 Mutation or KRAS Mutation	I
No NCT ID	Phase I Clinical Study With Advanced Solid Tumors KBP-5209 Treatment	I
No NCT ID	Tolerance And Pharmacokinetics Of Pivotinib In Patients With Advanced Solid Tumors With HER2 Expression	I
NCT03219268	A Phase I, First-in-Human, Open-Label, Dose Escalation Study of MGD013, A Bispecific DART Protein Binding PD-1 and LAG-3 in Patients With Unresectable or Metastatic Neoplasms	I
NCT04487236	A Phase I Clinical Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Efficacy of ZN-A-1041 Enteric Capsules as a Single Agent or in Combination With Capecitabine Tablets in Patients With HER2-Positive Advanced Solid Tumors	I
NCT02442297	Phase I Study of Intracranial Injection of T Cells Expressing HER2-specific Chimeric Antigen Receptors (CAR) in Subjects With HER2-Positive Tumors of the Central Nervous System (iCAR)	I
NCT03330561	A Phase I, Open-Label, Dose Escalation Study of PRS-343 in Patients With HER2-Positive Advanced or Metastatic Solid Tumors	I
NCT04446260	A Phase I Multi-Country, Multi-Center, Open-Label Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Efficacy of SHR-A1811 in HER2 Expressing or Mutated Advanced Malignant Solid Tumor Subjects	I
NCT03297606	Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial	II

Clinical Trials Summary (continued)

MET amplification

NCT ID	Title	Phase
NCT01639508	A Phase II Study of Cabozantinib in Patients With RET Fusion-Positive Advanced Non-Small Cell Lung Cancer and Those With Other Genotypes: ROS1 or NTRK Fusions or Increased MET or AXL Activity	II
NCT02664935	National Lung Matrix Trial: Multi-drug, Genetic Marker-directed, Non-comparative, Multi-centre, Multi-arm Phase II Trial in Non-small Cell Lung Cancer	II
NCT04084717	Phase II Study of Crizotinib for ROS1 and MET Activated Lung Cancer (CROME)	II
NCT03574402	An Open-label, Multi-center, Phase II Umbrella Study to Assess Efficacy of Targeted Therapy or Immunotherapy Directed by Next Generation Sequencing (NGS) in Chinese Patients With Advanced NSCLC (TRUMP)	II
NCT04647838	A Phase II Study of Tepotinib in Patients With Solid Cancers Harboring c-MET Amplification or Exon 14 Mutation Who Progressed After Standard Treatment for Advanced/Metastatic Disease	II
NCT04270591	A Phase Ib/II, Open-Label, Multicenter Study to Evaluate the Efficacy and Safety of Glumetinib (SCC244), a Selective MET Inhibitor in Patients With Advanced Non-Small Cell Lung Cancer Harboring MET-alterations	I/II
NCT04077099	A Phase I/II Study of REGN5093 in Patients With MET-Altered Advanced Non-Small Cell Lung Cancer	I/II
NCT03466268	A Phase I Clinical Study to Assess the Safety, Pharmacokinetics and Antitumor Activity of SCC244 in Patients with Advanced Solid Tumors	I
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
NCT02650375	A Phase Ib Clinical Study of the Tolerance, Safety and Preliminary Efficacy Observation of Single-/ Multiple- Doses of Metatinib Tromethamine Tablets in Patients With Advanced or Metastatic Solid Tumor	I
NCT03993873	A Phase I, Open-Label, Multi-Center, First-in-Human Study of the Safety, Tolerability, Pharmacokinetics, and Anti-Tumor Activity of TPX-0022, a Novel MET/CSF1R/SRC Inhibitor, in Patients With Advanced Solid Tumors Harboring Genetic Alterations in MET	I
NCT04398940	A Single-arm, Multicenter Study to Evaluate the Efficacy and Safety of TQ-B3139 in Subjects With MET-Altered Advanced Non-small Cell Lung Cancer	II
NCT04116541	MegaMOST - A Multicenter, Open-label, Biology Driven, Phase II Study Evaluating the Activity of Anti-cancer Treatments Targeting Tumor Molecular Alterations /Characteristics in Advanced / Metastatic Tumors.	II
NCT02465060	Molecular Analysis for Therapy Choice (MATCH).	II
NCT02693535	Targeted Agent and Profiling Utilization Registry (TAPUR) Study	II
No NCT ID	A Phase IB study of Crizotinib Either in Combination or as Single Agent in Pediatric Patients with ALK, ROS1 or MET Positive Malignancies	I
NCT04228406	Safety, Tolerability, Pharmacokinetic Characteristics, and Preliminary Efficacy Evaluation of the Selective c-MET Inhibitor GST-HG161 in Patients With Advanced or Metastatic Solid Tumors	I
NCT02977364	Phase I Trial to Investigate Safety and Tolerability Profile and Pharmacokinetics of C-met Kinase Inhibitor HS-10241 in Subjects With Advanced Solid Tumours	I
No NCT ID	Phase I Clinical Trial of SPH3348 Single-agent Combined with Oxitinib in Patients with Advanced Solid Tumors with Abnormal c-Met in China.	I
NCT04693468	Modular Phase IB Hypothesis-Testing, Biomarker-Driven, Talazoparib Combination Trial (TalaCom)	I
NCT03297606	Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial	II

Alerts Informed By Public Data Sources

Current FDA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

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

EGFR p.(L858R) c.2573T>G

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 the EGFR inhibitor osimertinib, for EGFR mutated non-small cell lung cancer after progression on 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: Cholangiocarcinoma **Variant class:** ERBB2 amplification

Supporting Statement:

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

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

The FDA has granted Fast Track Designation to the HER2 targeted bispecific antibody, zanidatamab, for:

- HER2-overexpressing gastroesophageal adenocarcinoma (GEA) to be used in combination with standard-of-care chemotherapy.

Reference:

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

ERBB2 amplification (continued)

zanidatamab + chemotherapy

Cancer type: Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

Supporting Statement:

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

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

The FDA has granted Fast Track Designation to the HER2 targeted bispecific antibody, zanidatamab, for:

- HER2-overexpressing gastroesophageal adenocarcinoma (GEA) to be used in combination with standard-of-care chemotherapy.

Reference:

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

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

Current NCCN Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

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

EGFR p.(L858R) c.2573T>G

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 2.2021]

EGFR p.(L858R) c.2573T>G (continued)

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 2.2021]

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 2.2021]

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 2.2021]

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 2.2021]

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 2.2021]

EGFR p.(L858R) c.2573T>G (continued)

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 2.2021]

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 2.2021]

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 1.2021]

pertuzumab + trastuzumab + cyclophosphamide + doxorubicin + paclitaxel

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

Summary:

NCCN Guidelines® include the following supporting statement(s):
- "Trastuzumab given in combination with an anthracycline is associated with significant cardiac toxicity. Concurrent use of trastuzumab and pertuzumab with an anthracycline should be avoided."

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

ERBB2 amplification (continued)

trastuzumab + anthracycline

Cancer type: Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

Variant class: ERBB2 overexpression

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

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

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

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trastuzumab + cyclophosphamide + docetaxel + doxorubicin

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Summary:

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

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

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

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trastuzumab + cyclophosphamide + doxorubicin + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Summary:

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

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

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

Current ESMO Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

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

ERBB2 amplification

lapatinib + trastuzumab + chemotherapy

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

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

Summary:

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

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

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

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aromatase inhibitor

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

Other criteria: ER positive, PR status

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

Summary:

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

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

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

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trastuzumab + anthracycline

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

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

Summary:

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

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

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

Signatures

Testing Personnel:

2021.04.15
17:15:44 +08'00'

Laboratory Supervisor:

2021.04.15
17:15:59 +08'00'

Pathologist:

2021.04.15
17:16:16 +08'00'

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