

Medical Laboratory
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Leading a new era of precision oncology

Oncofocus®

Precision Oncology

ONC19**Surname****Forename****DOB****Gender****Histology #****Primary site****Tumour subtype****Tissue Type**

Uterus

Serous Adenocarcinoma

Uterus

Requester**Contact details****Date requested****Tumour %**

-

Tumour %

60%

(macrodissected)**Comment:**

The DNA and RNA extracted from this sample were of optimal quality. The Oncofocus assay on which the sample was run met all assay specific quality metrics.

Oncofocus currently targets 505 genes covering oncogenes, fusion genes, genes susceptible to copy number variation and tumour suppressors. Actionable genetic variants detected by Oncofocus are currently linked to 687 anti-cancer targeted therapies/therapy combinations.

Several actionable variants were detected, these are listed on the next page.

Please note;

- Two gene fusion events were also detected; **EIF3E(1) - RSPO2(2)** and **CCDC6(2) - BICC1(3)**. Unfortunately however these do not link with any therapies/clinical trials at this time.

Within the 'Current Clinical Trials Information' section of this report, starting on page 47, the NCT numbers are hyperlinks to the clinicaltrials.gov webpages which should be accessed to gain further trial specific information

Sample Cancer Type: Endometrial Cancer

Clinically Significant Biomarkers

Indicated Contraindicated

Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials	
ERBB2 (HER2) amplification	trastuzumab + chemotherapy	ado-trastuzumab emtansine ^{1,2} lapatinib + aromatase inhibitor ¹ lapatinib + chemotherapy ^{1,2} lapatinib + trastuzumab ¹ pertuzumab + trastuzumab + chemotherapy ^{1,2} trastuzumab (Celltrion) + anastrozole ¹ trastuzumab (Celltrion) ¹ trastuzumab (Celltrion) + chemotherapy ¹ trastuzumab (Samsung Bioepis) + anastrozole ¹ trastuzumab (Samsung Bioepis) ¹ trastuzumab (Samsung Bioepis) + chemotherapy ¹ trastuzumab + anastrozole ¹ trastuzumab ^{1,2} trastuzumab + chemotherapy ^{1,2} lapatinib + letrozole ²	neratinib ² trastuzumab (Biocon) ² trastuzumab (Biocon) + chemotherapy ² trastuzumab + hormone therapy + chemotherapy trastuzumab containing regimen trastuzumab + hormone therapy pertuzumab + trastuzumab hormone therapy lapatinib + trastuzumab + aromatase inhibitor pertuzumab + trastuzumab + hormone therapy + chemotherapy trastuzumab + aromatase inhibitor trastuzumab + fulvestrant trastuzumab + tamoxifen	26
KRAS amplification	Clinical trials and/or off-label	Clinical trials and/or off-label	7	
ERBB3 mutation <i>p.(G284R) c.850G>A</i>	Clinical trials and/or off-label	Clinical trials and/or off-label	4	
TP53 mutation <i>p.(C275F) c.824G>T</i>	Clinical trials and/or off-label	Clinical trials and/or off-label	2	

Sources included in relevant therapies: EMA1, FDA2, ESMO, NCCN

Hotspot variants with >10% alternate allele reads are classified as 'detected' with an assay sensitivity and positive predictive value (PPV) of 99%. Copy number variants; amplifications of CN> 6 with the 5% confidence value of ≥4 after normalization and deletions with 95% CI ≤1 are classified as present when the tumour% >50% with a sensitivity of 80% and PPV 100%. Gene Fusions are reported when occurring in >40 counts and meeting the thresholds of assay specific internal RNA quality control with a sensitivity of 92% and PPV of 99%. Supplementary technical information is available upon request. Please note this version of the Oncofocus test is an upgraded version to that accredited on our schedule

Tier Criteria Met

Genomic Alteration	Tier Classification for Endometrial Cancer
<i>ERBB2</i> amplification Tier: IA	IA: Biomarker is included in ESMO or NCCN guidelines that predict response or resistance to therapies in this cancer type IIC: Biomarker predicts response or resistance to EMA or FDA approved therapies in other cancer types IIC: Biomarker is included in ESMO or NCCN guidelines that predict response or resistance to therapies in other cancer types IIC: Biomarker is an inclusion criteria for clinical trials
<i>KRAS</i> amplification Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
<i>ERBB3</i> p.(G284R) c.850G>A Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
<i>TP53</i> p.(C275F) c.824G>T Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials

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.

Relevant Therapy Summary

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types
 ☒ Contraindicated
 ☒ Both for use and contraindicated
 ☒ No evidence

ERBB2 amplification

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
ado-trastuzumab emtansine	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/> (II)
pertuzumab + trastuzumab + docetaxel	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
trastuzumab + capecitabine + cisplatin	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
trastuzumab + cisplatin + fluorouracil	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
lapatinib + capecitabine	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
trastuzumab	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
trastuzumab + carboplatin + docetaxel	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
trastuzumab + paclitaxel	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
trastuzumab + cyclophosphamide + docetaxel + doxorubicin	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>

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

Relevant Therapy Summary (continued)

● In this cancer type
 ○ In other cancer type
 ⓘ In this cancer type and other cancer types
 ⊘ Contraindicated
 ⚠ Both for use and contraindicated
 × No evidence

ERBB2 amplification (continued)

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
trastuzumab + cyclophosphamide + doxorubicin + paclitaxel	○	○	×	×	×
lapatinib + trastuzumab	○	×	○	○	×
lapatinib + aromatase inhibitor	○	×	×	○	×
trastuzumab + docetaxel	○	×	×	○	×
trastuzumab (Celltrion)	○	×	×	×	×
trastuzumab (Celltrion) + anastrozole	○	×	×	×	×
trastuzumab (Celltrion) + capecitabine + cisplatin	○	×	×	×	×
trastuzumab (Celltrion) + carboplatin + docetaxel	○	×	×	×	×
trastuzumab (Celltrion) + cisplatin + fluorouracil	○	×	×	×	×
trastuzumab (Celltrion) + cyclophosphamide + docetaxel + doxorubicin	○	×	×	×	×
trastuzumab (Celltrion) + cyclophosphamide + doxorubicin + paclitaxel	○	×	×	×	×
trastuzumab (Celltrion) + docetaxel	○	×	×	×	×
trastuzumab (Celltrion) + paclitaxel	○	×	×	×	×
trastuzumab (Samsung Bioepis)	○	×	×	×	×
trastuzumab (Samsung Bioepis) + anastrozole	○	×	×	×	×
trastuzumab (Samsung Bioepis) + capecitabine + cisplatin	○	×	×	×	×
trastuzumab (Samsung Bioepis) + carboplatin + docetaxel	○	×	×	×	×
trastuzumab (Samsung Bioepis) + cisplatin + fluorouracil	○	×	×	×	×
trastuzumab (Samsung Bioepis) + cyclophosphamide + docetaxel + doxorubicin	○	×	×	×	×

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

Relevant Therapy Summary (continued)

● In this cancer type
 ○ In other cancer type
 ⓘ In this cancer type and other cancer types
 ⊘ Contraindicated
 ⚠ Both for use and contraindicated
 × No evidence

ERBB2 amplification (continued)

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
trastuzumab (Samsung Bioepis) + cyclophosphamide + doxorubicin + paclitaxel	○	×	×	×	×
trastuzumab (Samsung Bioepis) + docetaxel	○	×	×	×	×
trastuzumab (Samsung Bioepis) + paclitaxel	○	×	×	×	×
trastuzumab + anastrozole	○	×	×	×	×
pertuzumab + trastuzumab + chemotherapy	×	○	○	○	×
lapatinib + letrozole	×	○	×	×	×
neratinib	×	○	×	×	×
trastuzumab (Biocon)	×	○	×	×	×
trastuzumab (Biocon) + capecitabine + cisplatin	×	○	×	×	×
trastuzumab (Biocon) + carboplatin + docetaxel	×	○	×	×	×
trastuzumab (Biocon) + cisplatin + fluorouracil	×	○	×	×	×
trastuzumab (Biocon) + cyclophosphamide + docetaxel + doxorubicin	×	○	×	×	×
trastuzumab (Biocon) + cyclophosphamide + doxorubicin + paclitaxel	×	○	×	×	×
trastuzumab (Biocon) + paclitaxel	×	○	×	×	×
pertuzumab + trastuzumab + paclitaxel	×	×	○	○	×
trastuzumab + chemotherapy	×	×	○	○	×
trastuzumab + hormone therapy + chemotherapy	×	×	○	○	×
trastuzumab + vinorelbine	×	×	○	○	×
pertuzumab + trastuzumab	×	×	○	×	● (II)
pertuzumab + trastuzumab + capecitabine	×	×	○	×	×
pertuzumab + trastuzumab + nab-paclitaxel	×	×	○	×	×
pertuzumab + trastuzumab + vinorelbine	×	×	○	×	×

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

Relevant Therapy Summary (continued)

● In this cancer type
 ○ In other cancer type
 ⓘ In this cancer type and other cancer types
 ⊘ Contraindicated
 ⚠ Both for use and contraindicated
 × No evidence

ERBB2 amplification (continued)

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

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

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Other mutations, copy number variations, or fusions that were detected but not classified by the Oncofocus Test as actionable by a known therapeutic targeted agent are not listed in the results section of this report.

Disclaimer: The data presented here is a result of the curation of published data sources, but may not be exhaustive. The data version is 2018.12(004).

Relevant Therapy Summary (continued)

● In this cancer type
 ○ In other cancer type
 ⓘ In this cancer type and other cancer types
 ⊘ Contraindicated
 ⚠ Both for use and contraindicated
 × No evidence

ERBB2 amplification (continued)

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
afatinib	×	×	×	×	● (II)
lapatinib	×	×	×	×	● (II)
CART-HER-2	×	×	×	×	● (I/II)
selumetinib + vistusertib	×	×	×	×	● (I/II)
TAS0728	×	×	×	×	● (I/II)
AdHER-2	×	×	×	×	● (I)
ARX-788	×	×	×	×	● (I)
atezolizumab + PRS-343	×	×	×	×	● (I)
BTRC-4017A	×	×	×	×	● (I)
everolimus + neratinib, neratinib + palbociclib, neratinib + trametinib	×	×	×	×	● (I)
everolimus + trastuzumab + letrozole	×	×	×	×	● (I)
FATE-NK100 + trastuzumab	×	×	×	×	● (I)
GBR 1302	×	×	×	×	● (I)
MP-0274	×	×	×	×	● (I)
pirotinib	×	×	×	×	● (I)
PRS-343	×	×	×	×	● (I)
pyrotonib	×	×	×	×	● (I)
RC-48	×	×	×	×	● (I)
varlitinib + chemotherapy	×	×	×	×	● (I)
ZW-25	×	×	×	×	● (I)

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

Relevant Therapy Summary (continued)

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

KRAS amplification

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
sorafenib	✕	✕	✕	✕	● (II)
ASTX029	✕	✕	✕	✕	● (I/II)
cobimetinib	✕	✕	✕	✕	● (I/II)
selumetinib + vistusertib	✕	✕	✕	✕	● (I/II)
abemaciclib + LY3214996 , LY3214996 , LY3214996 + chemotherapy, LY3214996 + midazolam	✕	✕	✕	✕	● (I)
LTT-462	✕	✕	✕	✕	● (I)
LXH254 , LXH254 + spartalizumab	✕	✕	✕	✕	● (I)

ERBB3 p.(G284R) c.850G>A

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
afatinib	✕	✕	✕	✕	● (II)
TAS0728	✕	✕	✕	✕	● (I/II)
everolimus + neratinib, neratinib + palbociclib, neratinib + trametinib	✕	✕	✕	✕	● (I)
pirotinib	✕	✕	✕	✕	● (I)

TP53 p.(C275F) c.824G>T

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
adavosertib + olaparib	✕	✕	✕	✕	● (II)
VX-970, VX-970 + chemotherapy	✕	✕	✕	✕	● (I/II)

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

Relevant Therapy Details

Current EMA Information

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

EMA information is current as of 2018-10-01. For the most up-to-date information, search www.ema.europa.eu/ema.

ERBB2 amplification

☐ ado-trastuzumab emtansine

Cancer type: Breast Cancer

Label as of: 2018-09-19

Variant class: ERBB2 overexpression or ERBB2 amplification

Reference:

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

☐ lapatinib + aromatase inhibitor

Cancer type: Breast Cancer

Label as of: 2018-09-07

Variant class: ERBB2 overexpression or ERBB2 amplification

Other criteria: ER positive, PR positive

Reference:

https://www.ema.europa.eu/documents/product-information/tyverb-epar-product-information_en-0.pdf

☐ lapatinib + capecitabine

Cancer type: Breast Cancer

Label as of: 2018-09-07

Variant class: ERBB2 overexpression or ERBB2 amplification

Reference:

https://www.ema.europa.eu/documents/product-information/tyverb-epar-product-information_en-0.pdf

☐ lapatinib + trastuzumab

Cancer type: Breast Cancer

Label as of: 2018-09-07

Variant class: ERBB2 overexpression or ERBB2 amplification

Other criteria: Hormone receptor negative

Reference:

https://www.ema.europa.eu/documents/product-information/tyverb-epar-product-information_en-0.pdf

ERBB2 amplification (continued)☐ **pertuzumab + trastuzumab + docetaxel**

Cancer type: Breast Cancer

Label as of: 2018-10-05

Variant class: ERBB2 overexpression or ERBB2 amplification

Reference:

https://www.ema.europa.eu/documents/product-information/perjeta-epar-product-information_en-0.pdf☐ **trastuzumab (Celltrion) + anastrozole**

Cancer type: Breast Cancer

Label as of: 2018-09-18

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive

Reference:

https://www.ema.europa.eu/documents/product-information/herzuma-epar-product-information_en-0.pdf☐ **trastuzumab (Celltrion), trastuzumab (Celltrion) + docetaxel, trastuzumab (Celltrion) + paclitaxel, trastuzumab (Celltrion) + capecitabine + cisplatin, trastuzumab (Celltrion) + carboplatin + docetaxel, trastuzumab (Celltrion) + cisplatin + fluorouracil, trastuzumab (Celltrion) + cyclophosphamide + docetaxel + doxorubicin, trastuzumab (Celltrion) + cyclophosphamide + doxorubicin + paclitaxel**

Cancer type: Breast Cancer, Esophageal Cancer, Gastric Cancer

Label as of: 2018-09-18

Variant class: ERBB2 amplification or ERBB2 overexpression

Reference:

https://www.ema.europa.eu/documents/product-information/herzuma-epar-product-information_en-0.pdf☐ **trastuzumab (Samsung Bioepis) + anastrozole**

Cancer type: Breast Cancer

Label as of: 2018-09-10

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive

Reference:

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

ERBB2 amplification (continued)

- ☐ **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, trastuzumab (Samsung Bioepis) + cyclophosphamide + docetaxel + doxorubicin, trastuzumab (Samsung Bioepis) + cyclophosphamide + doxorubicin + paclitaxel**

Cancer type: Breast Cancer, Esophageal Cancer, Gastric Cancer

Label as of: 2018-09-10

Variant class: ERBB2 amplification or ERBB2 overexpression

Reference:

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

- ☐ **trastuzumab + anastrozole**

Cancer type: Breast Cancer

Label as of: 2018-09-06

Variant class: ERBB2 overexpression or ERBB2 amplification

Other criteria: ER positive, PR positive

Reference:

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

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

Cancer type: Breast Cancer, Esophageal Cancer, Gastric Cancer

Label as of: 2018-09-06

Variant class: ERBB2 overexpression or ERBB2 amplification

Reference:

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

Current FDA Information

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

FDA information is current as of 2018-10-01. For the most up-to-date information, search www.fda.gov.

ERBB2 amplification

☐ ado-trastuzumab emtansine

Cancer type: Breast Cancer

Label as of: 2018-09-20

Variant class: ERBB2 overexpression or ERBB2 amplification

Indications and usage:

KADCYLA® is a HER2-targeted antibody and microtubule inhibitor conjugate indicated, as a single agent, for the treatment of patients with HER2-positive, metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:

- Received prior therapy for metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/125427s102lbl.pdf

☐ lapatinib + capecitabine

Cancer type: Breast Cancer

Label as of: 2017-04-06

Variant class: ERBB2 overexpression

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 HER2 and who have received prior therapy including an anthracycline, a taxane, and trastuzumab.
- Limitation 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/2017/022059s022lbl.pdf

ERBB2 amplification (continued)**○ lapatinib + letrozole****Cancer type:** Breast Cancer**Label as of:** 2017-04-06**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 HER2 and who have received prior therapy including an anthracycline, a taxane, and trastuzumab.
- Limitation 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/2017/022059s022lbl.pdf**○ neratinib****Cancer type:** Breast Cancer**Label as of:** 2018-06-28**Variant class:** ERBB2 overexpression or ERBB2 amplification**Indications and usage:**

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

Reference:https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/208051s002lbl.pdf

ERBB2 amplification (continued)**○ pertuzumab + trastuzumab + chemotherapy, pertuzumab + trastuzumab + docetaxel**

Cancer type: Breast Cancer

Label as of: 2018-09-20

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/2018/125409s121lbl.pdf**○ trastuzumab (Biocon)**

Cancer type: Breast Cancer

Label as of: 2017-12-01

Variant class: ERBB2 overexpression or
ERBB2 amplification**Other criteria:** ER negative, PR negative**Indications and usage:**

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

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

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

Reference:https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/761074s000lbl.pdf

ERBB2 amplification (continued)

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

Cancer type: Breast Cancer

Label as of: 2017-12-01

Variant class: ERBB2 overexpression or ERBB2 amplification

Other criteria: ERBB2 negative, PR negative

Indications and usage:

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

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

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

Reference:https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/761074s000lbl.pdf

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

Cancer type: Breast Cancer, Esophageal Cancer, Gastric Cancer

Label as of: 2017-12-01

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/2017/761074s000lbl.pdf

ERBB2 amplification (continued)**○ trastuzumab, trastuzumab + carboplatin + docetaxel, trastuzumab + cyclophosphamide + docetaxel + doxorubicin, trastuzumab + cyclophosphamide + doxorubicin + paclitaxel**

Cancer type: Breast Cancer

Label as of: 2018-10-17

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, PR negative

Indications and usage:

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

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

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

Reference:https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/103792s5347lbl.pdf**○ trastuzumab, trastuzumab + paclitaxel, trastuzumab + capecitabine + cisplatin, trastuzumab + carboplatin + docetaxel, trastuzumab + cisplatin + fluorouracil, trastuzumab + cyclophosphamide + docetaxel + doxorubicin, trastuzumab + cyclophosphamide + doxorubicin + paclitaxel**

Cancer type: Breast Cancer, Esophageal Cancer, Gastric Cancer

Label as of: 2018-10-17

Variant class: ERBB2 amplification or ERBB2 overexpression

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/2018/103792s5347lbl.pdf

Current ESMO Information

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

ESMO information is current as of 2018-08-16. For the most up-to-date information, search www.esmo.org.

ERBB2 amplification☐ **trastuzumab + capecitabine + cisplatin**

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

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

Population segment (Line of therapy):

- Not specified

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

☐ **trastuzumab + chemotherapy**

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, PR negative

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

Population segment (Line of therapy):

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

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

☐ **trastuzumab + chemotherapy**

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

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

Population segment (Line of therapy):

- Primary Breast Cancer (Neoadjuvant therapy)

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

ERBB2 amplification (continued)

○ trastuzumab + cisplatin + fluorouracil

Cancer type: Gastric Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

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

Population segment (Line of therapy):

- Not specified

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

○ trastuzumab + hormone therapy + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive

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

Population segment (Line of therapy):

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

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

○ 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):

- Not Specified

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

○ trastuzumab + hormone therapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive

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

Population segment (Line of therapy):

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

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018) 00: 1–24.]

○ pertuzumab + trastuzumab + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 positive

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

Population segment (Line of therapy):

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

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018) 00: 1–24.]

○ pertuzumab + trastuzumab + docetaxel

Cancer type: Breast Cancer

Variant class: ERBB2 positive

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

Population segment (Line of therapy):

- Advanced Breast Cancer (Not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018) 00: 1–24.]

○ trastuzumab + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 positive

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

Population segment (Line of therapy):

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

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018) 00: 1–24.]

ERBB2 amplification (continued)**○ trastuzumab + taxane**

Cancer type: Breast Cancer

Variant class: ERBB2 positive

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

Population segment (Line of therapy):

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

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018) 00: 1–24.]

○ trastuzumab + vinorelbine

Cancer type: Breast Cancer

Variant class: ERBB2 positive

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

Population segment (Line of therapy):

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

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018) 00: 1–24.]

○ lapatinib + trastuzumab

Cancer type: Breast Cancer

Variant class: ERBB2 positive

Other criteria: ER positive

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

Population segment (Line of therapy):

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

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018) 00: 1–24.]

○ lapatinib + trastuzumab

Cancer type: Breast Cancer

Variant class: ERBB2 positive

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

Population segment (Line of therapy):

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

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018) 00: 1–24.]

ERBB2 amplification (continued)**○ pertuzumab + trastuzumab**

Cancer type: Breast Cancer

Variant class: ERBB2 positive

Other criteria: ER positive

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

Population segment (Line of therapy):

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

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018) 00: 1–24.]

○ pertuzumab + trastuzumab + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 positive

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

Population segment (Line of therapy):

- Advanced Breast Cancer (Not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018) 00: 1–24.]

○ pertuzumab + trastuzumab + capecitabine

Cancer type: Breast Cancer

Variant class: ERBB2 positive

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

Population segment (Line of therapy):

- Advanced Breast Cancer (Not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018) 00: 1–24.]

○ pertuzumab + trastuzumab + vinorelbine

Cancer type: Breast Cancer

Variant class: ERBB2 positive

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

Population segment (Line of therapy):

- Advanced Breast Cancer (Not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018) 00: 1–24.]

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

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018) 00: 1–24.]

○ pertuzumab + trastuzumab + nab-paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 positive

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

Population segment (Line of therapy):

- Advanced Breast Cancer (Not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Ann Oncol (2018) 00: 1–24.]

🗨️ pertuzumab + trastuzumab

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Summary:

ESMO Clinical Practice Guidelines include the following supporting statement:

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

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

Current NCCN Information

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

NCCN information is current as of 2018-08-16. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

ERBB2 amplification☒ **trastuzumab + carboplatin + paclitaxel**

Cancer type: Endometrial Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Advanced or Recurrent Uterine Serous Carcinoma; Stage IA-Stage IV (Adjuvant therapy) (Preferred if tolerated)

Reference: NCCN Guidelines® - NCCN-Uterine Neoplasms [Version 2.2018]

☐ **pertuzumab + trastuzumab + docetaxel**

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

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

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer (First-line therapy) Preferred

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

☐ **trastuzumab + capecitabine + cisplatin**

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2018]

ERBB2 amplification (continued)**○ trastuzumab + capecitabine + cisplatin**

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 2.2018]

○ trastuzumab + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification

Other criteria: ER negative, PR negative

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Ductal, Lobular, Mixed, Metaplastic Histology; Node metastasis ≤2 mm axillary; pT1, pT2, or pT3 and pN0 or pN1m; Tumor >1 cm (Not specified)
- Ductal, Lobular, Mixed, Metaplastic Histology; Node positive (one or more metastases >2 mm to one or more ipsilateral axillary lymph nodes) (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

○ trastuzumab + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Ductal, Lobular, Mixed, Metaplastic Histology; pN0 or pN1mi (≤2 mm axillary node metastasis), pT1, pT2, or pT3; Tumor >1 cm (Not Specified)
- Ductal, Lobular, Mixed, Metaplastic Histology; Node positive (one or more metastases >2 mm to one or more ipsilateral axillary lymph nodes) (Not Specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

ERBB2 amplification (continued)**○ trastuzumab + chemotherapy**

Cancer type: Breast Cancer

Variant class: ERBB2 overexpression

Other criteria: ER negative, PR negative

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Ductal, Lobular, Mixed, Metaplastic Histology; Node metastasis ≤ 2 mm axillary; pT1, pT2, or pT3 and pN0 or pN1m; Tumor >1 cm (Not specified)
- Ductal, Lobular, Mixed, Metaplastic Histology; Node positive (one or more metastases >2 mm to one or more ipsilateral axillary lymph nodes) (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

○ trastuzumab + cisplatin + fluorouracil

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2018]

○ trastuzumab + cisplatin + fluorouracil

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 2.2018]

ERBB2 amplification (continued)**○ trastuzumab + hormone therapy + chemotherapy**

Cancer type: Breast Cancer

Variant class: ERBB2 amplification

Other criteria: ER positive, PR positive

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Ductal, Lobular, Mixed, Metaplastic Histology; Node metastasis ≤ 2 mm axillary; Tumor >1 cm (Not specified)
- Ductal, Lobular, Mixed, Metaplastic Histology; Node positive (one or more metastases >2 mm to one or more ipsilateral axillary lymph nodes)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

○ trastuzumab + hormone therapy + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Ductal, Lobular, Mixed, Metaplastic Histology; Node metastasis ≤ 2 mm axillary; Tumor >1 cm (Not specified)
- Ductal, Lobular, Mixed, Metaplastic Histology; Node positive (one or more metastases >2 mm to one or more ipsilateral axillary lymph nodes)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

○ ado-trastuzumab emtansine

Cancer type: Breast Cancer

Variant class: ERBB2 amplification

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or stage IV Invasive Breast Cancer; With or without prior endocrine therapy within 1 yr; Premenopausal or Postmenopausal (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

ERBB2 amplification (continued)☐ **ado-trastuzumab emtansine**

Cancer type: Breast Cancer

Variant class: ERBB2 overexpression

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or stage IV Invasive Breast Cancer; With or without prior endocrine therapy within 1 year; Premenopausal or Postmenopausal (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

☐ **hormone therapy**

Cancer type: Breast Cancer

Variant class: ERBB2 amplification

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Ductal, Lobular, Mixed, Metaplastic Histology; Node metastasis ≤2 mm axillary; pT1, pT2, or pT3; Tumor ≤0.5 cm including microinvasive; pN1mi or Tumor 0.6-1.0 cm (Not specified)
- Recurrent or stage IV Invasive Breast Cancer; No prior endocrine therapy within 1 year; Postmenopausal (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

☐ **hormone therapy**

Cancer type: Breast Cancer

Variant class: ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Ductal, Lobular, Mixed, Metaplastic Histology; Node metastasis ≤2 mm axillary; pT1, pT2, or pT3; Tumor ≤0.5 cm including microinvasive; pN1mi or Tumor 0.6-1.0 cm (Not specified)
- Recurrent or stage IV Invasive Breast Cancer; No prior endocrine therapy within 1 year; Postmenopausal (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

ERBB2 amplification (continued)☐ **lapatinib + aromatase inhibitor**

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or stage IV Invasive Breast Cancer; No prior endocrine therapy within 1 year; Postmenopausal (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

☐ **lapatinib + capecitabine**

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

☐ **lapatinib + trastuzumab**

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer; Without cytotoxic therapy (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

ERBB2 amplification (continued)**○ lapatinib + trastuzumab + aromatase inhibitor**

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or stage IV Invasive Breast Cancer; No prior endocrine therapy within 1 year; Postmenopausal (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

○ pertuzumab + trastuzumab + carboplatin + docetaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

○ pertuzumab + trastuzumab + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, PR negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Ductal, Lobular, Mixed, Metaplastic Histology; Node positive (one or more metastases >2 mm to one or more ipsilateral axillary lymph nodes) (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

ERBB2 amplification (continued)**○ pertuzumab + trastuzumab + hormone therapy + chemotherapy**

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Ductal, Lobular, Mixed, Metaplastic Histology; Node positive (one or more metastases >2 mm to one or more ipsilateral axillary lymph nodes) (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

○ pertuzumab + trastuzumab + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer (First-line therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

○ pertuzumab + trastuzumab + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 overexpression

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or Stage IV Invasive Breast Cancer (First-line therapy) Preferred

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

ERBB2 amplification (continued)☐ **trastuzumab + aromatase inhibitor**

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or stage IV Invasive Breast Cancer; No prior endocrine therapy within 1 year; Postmenopausal (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

☐ **trastuzumab + capecitabine**

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

☐ **trastuzumab + carboplatin + docetaxel**

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

ERBB2 amplification (continued)☐ **trastuzumab + carboplatin + paclitaxel**

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

☐ **trastuzumab + chemotherapy**

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, PR negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Ductal, Lobular, Mixed, Metaplastic Histology; pT1, pT2, or pT3, and pN0 or pN1mi (node metastasis ≤2 mm axillary); Tumor ≤0.5 cm including microinvasive pN1mi or Tumor 0.6-1.0 cm (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

☐ **trastuzumab + chemotherapy (other)**

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or stage IV Invasive Breast Cancer (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

ERBB2 amplification (continued)**○ trastuzumab + cyclophosphamide + docetaxel**

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

○ trastuzumab + docetaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

○ trastuzumab + fulvestrant

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or stage IV Invasive Breast Cancer; No prior endocrine therapy within 1 year; Postmenopausal (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

ERBB2 amplification (continued)**○ trastuzumab + hormone therapy + chemotherapy**

Cancer type: Breast Cancer

Variant class: ERBB2 amplification

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Ductal, Lobular, Mixed, Metaplastic Histology; Node metastasis ≤ 2 mm axillary; pT1, pT2, or pT3; Tumor ≤ 0.5 cm including microinvasive; pN1mi or Tumor 0.6-1.0 cm (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

○ trastuzumab + hormone therapy + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Ductal, Lobular, Mixed, Metaplastic Histology; Node metastasis ≤ 2 mm axillary; pT1, pT2, or pT3; Tumor ≤ 0.5 cm including microinvasive; pN1mi or Tumor 0.6-1.0 cm (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

○ trastuzumab + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Low-risk stage I Breast Cancer; Particularly those not eligible for other standard adjuvant regimens due to comorbidities (Not specified)
- Recurrent or Stage IV Invasive Breast Cancer (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

ERBB2 amplification (continued)☐ **trastuzumab + tamoxifen**

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent or stage IV Invasive Breast Cancer; No prior endocrine therapy within 1 year; Postmenopausal (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

☐ **trastuzumab + vinorelbine**

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

☐ **trastuzumab + capecitabine**

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2018]

☐ **trastuzumab + capecitabine**

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 2.2018]

ERBB2 amplification (continued)**○ trastuzumab + capecitabine + oxaliplatin**

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2018]

○ trastuzumab + capecitabine + oxaliplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 2.2018]

○ trastuzumab + carboplatin + docetaxel + fluorouracil

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2018]

○ trastuzumab + carboplatin + docetaxel + fluorouracil

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 2.2018]

ERBB2 amplification (continued)**○ trastuzumab + carboplatin + paclitaxel**

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2018]

○ trastuzumab + carboplatin + paclitaxel

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 2.2018]

○ trastuzumab + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER negative, PR negative

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Ductal, Lobular, Mixed, Metaplastic Histology; Node metastasis ≤2 mm axillary; pT1, pT2, or pT3 and pN0 or pN1m; Tumor ≤0.5 cm including microinvasive; pN0 (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

○ trastuzumab + cisplatin + docetaxel

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2018]

ERBB2 amplification (continued)**○ trastuzumab + cisplatin + docetaxel**

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 2.2018]

○ trastuzumab + cisplatin + docetaxel + fluorouracil

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2018]

○ trastuzumab + cisplatin + docetaxel + fluorouracil

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 2.2018]

○ trastuzumab + cisplatin + paclitaxel

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2018]

ERBB2 amplification (continued)**○ trastuzumab + cisplatin + paclitaxel**

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 2.2018]

○ trastuzumab + docetaxel

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2018]

○ trastuzumab + docetaxel

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 2.2018]

○ trastuzumab + docetaxel + fluorouracil + oxaliplatin

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2018]

ERBB2 amplification (continued)☐ **trastuzumab + docetaxel + fluorouracil + oxaliplatin**

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 2.2018]

☐ **trastuzumab + fluorouracil**

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2018]

☐ **trastuzumab + fluorouracil**

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 2.2018]

☐ **trastuzumab + fluorouracil + irinotecan**

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2018]

ERBB2 amplification (continued)**○ trastuzumab + fluorouracil + irinotecan**

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 2.2018]

○ trastuzumab + fluorouracil + oxaliplatin

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2018]

○ trastuzumab + fluorouracil + oxaliplatin

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 2.2018]

○ trastuzumab + hormone therapy + chemotherapy

Cancer type: Breast Cancer

Variant class: ERBB2 amplification or ERBB2 overexpression

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Ductal, Lobular, Mixed, Metaplastic Histology; Node metastasis ≤2 mm axillary; pT1, pT2, or pT3; Tumor ≤0.5 cm including microinvasive; pN0 (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

ERBB2 amplification (continued)**○ trastuzumab + paclitaxel**

Cancer type: Breast Cancer

Variant class: ERBB2 amplification

Other criteria: ER negative, PR negative

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Ductal, Lobular, Mixed, Metaplastic Histology; Node metastasis ≤ 2 mm axillary; pT1, pT2, or pT3 and pN0 or pN1m; Tumor ≤ 0.5 cm including microinvasive; pN0 (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

○ trastuzumab + paclitaxel

Cancer type: Breast Cancer

Variant class: ERBB2 overexpression

Other criteria: ER negative, PR negative

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Ductal, Lobular, Mixed, Metaplastic Histology; Node metastasis ≤ 2 mm axillary; pT1, pT2, or pT3 and pN0 or pN1m; Tumor ≤ 0.5 cm including microinvasive; pN0 (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 1.2018]

○ trastuzumab + paclitaxel

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2018]

ERBB2 amplification (continued)**○ trastuzumab + paclitaxel**

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Metastatic Adenocarcinoma; Local therapy is not indicated (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 2.2018]

○ trastuzumab

Cancer type: Head and Neck Cancer

Variant class: ERBB2 positive

NCCN Recommendation category: 2B

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 2.2018]

🗨️ 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 1.2018]

🗨️ 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 1.2018]

ERBB2 amplification (continued) **trastuzumab + capecitabine + cisplatin + epirubicin**

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

Summary:

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

- "Trastuzumab is not recommended for use with anthracyclines"

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2018]

 **trastuzumab + capecitabine + cisplatin + epirubicin**

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

Summary:

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

- "Trastuzumab is not recommended for use with anthracyclines"

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 2.2018]

 **trastuzumab + capecitabine + epirubicin + oxaliplatin**

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

Summary:

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

- "Trastuzumab is not recommended for use with anthracyclines"

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2018]

 **trastuzumab + capecitabine + epirubicin + oxaliplatin**

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

Summary:

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

- "Trastuzumab is not recommended for use with anthracyclines"

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 2.2018]

ERBB2 amplification (continued) **trastuzumab + cisplatin + epirubicin + fluorouracil**

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

Summary:

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

- "Trastuzumab is not recommended for use with anthracyclines"

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2018]

 **trastuzumab + cisplatin + epirubicin + fluorouracil**

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

Summary:

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

- "Trastuzumab is not recommended for use with anthracyclines"

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 2.2018]

 **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 1.2018]

 **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 1.2018]

ERBB2 amplification (continued) **trastuzumab + epirubicin + fluorouracil + oxaliplatin**

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

Summary:

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

- "Trastuzumab is not recommended for use with anthracyclines"

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2018]

 **trastuzumab + epirubicin + fluorouracil + oxaliplatin**

Cancer type: Gastric Cancer

Variant class: ERBB2 overexpression

Summary:

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

- "Trastuzumab is not recommended for use with anthracyclines"

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 2.2018]

Current Clinical Trials Information

Clinical Trials information is current as of 2018-09-04. For the most up-to-date information regarding a particular trial, search www.clinicaltrials.gov by NCT ID or search local clinical trials authority website by local identifier listed in 'Other identifiers'.

ERBB2 amplification

NCT02491099

A Phase II Evaluation of Afatinib, an Irreversible Human Epidermal Growth Factor Receptor 2 (Her2/Neu) Tyrosine Kinase Inhibitor, in Patients With Persistent or Recurrent HER2-positive Uterine Serous Carcinoma

Cancer type: Endometrial Cancer

Variant class: ERBB2 overexpression

Other identifiers: 1503015437, UC1402

Population segments: (N/A), Second line

Phase: II

Therapy: afatinib

Location: United States

US States: AZ, CT, MA

US Contact: Dr. Alessandro D. Santin [203-737-4450; alessandro.santin@yale.edu]

NCT01935843

Clinical Study of Chimeric HER-2 Antigen Receptor-modified T Cells in Chemotherapy Refractory HER-2 Advanced Solid Tumors.

Cancer type: Endometrial Cancer

Variant class: ERBB2 positive

Other identifier: CHN-PLAGH-BT-009

Population segments: HER2 positive, Second line, Stage III, Stage IV

Phase: I/II

Therapy: CART-HER-2

Location: China

NCT02583542

A Phase Ib/IIa Study of AZD2014 in Combination With Selumetinib in Patients With Advanced Cancers

Cancer type: Endometrial Cancer

Variant class: ERBB2 aberration

Other identifiers: 009896QM, EudraCT Number: 2014-002613-31, IRAS ID 172356, Torcmek, UKCRN ID:18725

Population segments: Adenocarcinoma, EGFR, FGFR, HER2 negative, KRAS, Large Cell, Second line, Squamous Cell, Stage III, Stage IV, Triple receptor negative

Phase: I/II

Therapy: selumetinib + vistusertib

Location: United Kingdom

ERBB2 amplification (continued)**NCT02675829**

A Phase II Trial of Ado-Trastuzumab Emtansine for Patients With HER2 Amplified or Mutant Cancers

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 amplification

Other identifiers: 15-335, NCI-2016-00262

Population segments: First line, Fourth line or greater, Second line, Stage III, Stage IV, Third line

Phase: II

Therapy: ado-trastuzumab emtansine

Location: United States

US State: NY

US Contact: Dr. Bob Li [646-888-4201]

NCT02029001

A Two-period, Multicenter, Randomized, Open-label, Phase II Study Evaluating the Clinical Benefit of a Maintenance Treatment Targeting Tumor Molecular Alterations in Patients With Progressive Locally-advanced or Metastatic Solid Tumors MOST: My own specific treatment

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 amplification

Other identifiers: ET12-081, EudraCT number: 2012-004510-34, MOST, ProfiLER

Population segments: Maintenance/Consolidation, Second line, Stage III, Stage IV

Phase: II

Therapy: lapatinib

Location: France

ERBB2 amplification (continued)

NCT02465060

Molecular Analysis for Therapy Choice (MATCH)

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 amplification

Other identifiers: 15-7002, CTSU/EAY131, EAY131, EAY131-A, EAY131-B, EAY131-C1, EAY131-C2, EAY131-E, EAY131-F, EAY131-G, EAY131-H, EAY131-I, EAY131-J, EAY131-L, EAY131-M, EAY131-MATCH, EAY131-N, EAY131-P, EAY131-Q, EAY131-R, EAY131-S1, EAY131-S2, EAY131-T, EAY131-U, EAY131-V, EAY131-W, EAY131-X, EAY131-Y, EAY131-Z1A, EAY131-Z1B, EAY131-Z1C, EAY131-Z1D, EAY131-Z1E, EAY131-Z1F, EAY131-Z1G, EAY131-Z1H, EAY131-Z1I, EAY131-Z1J, ECOGEAY131-M, MATCH, NCI-2015-00054, NCI-MATCH

Population segments: (N/A), Aggressive, Classical, Fourth line or greater, HER2 positive, Indolent, Nodular lymphocyte-predominant, Second line, Stage III, Stage IV, Third line

Phase: II

Therapy: pertuzumab + trastuzumab

Locations: Puerto Rico, United States

US States: AK, AL, AR, AZ, CA, CO, CT, DC, DE, FL, GA, HI, IA, ID, IL, IN, KS, KY, LA, MA, MD, ME, MI, MN, MO, MS, MT, NC, ND, NE, NH, NJ, NM, NV, NY, OH, OK, OR, PA, RI, SC, SD, TN, TX, UT, VA, VT, WA, WI, WV, WY

US Contact: Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

NCT02693535

Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 amplification

Other identifiers: NCI-2017-00510, Pro00014171, TAPUR

Population segments: (N/A), Aggressive, Diffuse large B-cell lymphoma (DLBCL), Extranodal marginal zone B-cell lymphoma (MALT), Follicular lymphoma (FL), Indolent, Lymphoblastic lymphoma (LBL), Mantle cell lymphoma (MCL), Other subtype, Second line, Small lymphocytic lymphoma (SLL), Stage III, Stage IV, Waldenstrom's macroglobulinemia (WM)

Phase: II

Therapy: pertuzumab + trastuzumab

Location: United States

US States: AL, AZ, CA, FL, GA, IL, MI, NC, ND, NE, OK, OR, PA, SD, TX, UT, VA, WA

US Contact: Pam Mangat [pam.mangat@asco.org]

ERBB2 amplification (continued)

NCT02925234

A Dutch National Study on behalf of the Center for Personalized Cancer Treatment (CPCT) to Facilitate Patient Access to Commercially Available, Targeted Anti-cancer Drugs to determine the Potential Efficacy in Treatment of Advanced Cancers with a Known Molecular Profile

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 amplification or ERBB2 overexpression

Other identifiers: DRUP, EudraCT Number: 2015-004398-33, M15DRU, NL54757.031.16

Population segments: Aggressive, Diffuse large B-cell lymphoma (DLBCL), First line, Follicular lymphoma (FL), Indolent, Mantle cell lymphoma (MCL), Other subtype, Second line, Small lymphocytic lymphoma (SLL), Stage III, Stage IV, Waldenstrom's macroglobulinemia (WM)

Phase: II

Therapy: pertuzumab + trastuzumab

Location: Netherlands

NCT03297606

Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 aberration

Other identifiers: CA209-9DL, CAPTUR, ESR-17-12831, ML39800, PM1, WI233446

Population segments: Aggressive, Diffuse large B-cell lymphoma (DLBCL), Extranodal marginal zone B-cell lymphoma (MALT), First line, Follicular lymphoma (FL), Indolent, Lymphoblastic lymphoma (LBL), Mantle cell lymphoma (MCL), Other subtype, Second line, Stage III, Stage IV, Waldenstrom's macroglobulinemia (WM)

Phase: II

Therapy: pertuzumab + trastuzumab

Location: Canada

NCT03410927

A Phase I/II, Open Label, Multicenter Study to Investigate the Safety, Pharmacokinetics, and Efficacy of TAS0728, an Oral Covalent Binding Inhibitor of HER2, in Subjects With Advanced Solid Tumors With HER2 or HER3 Abnormalities

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 aberration

Other identifiers: 18116, 2017-0994, EudraCT Number: 2017-004415-39, NCI-2018-00211, REFMAL 555, TO-TAS0728-101

Population segments: Adenocarcinoma, Fourth line or greater, HER2 positive, Large Cell, Second line, Stage III, Stage IV, Third line

Phase: I/II

Therapy: TAS0728

Locations: United Kingdom, United States

US States: NY, TN, TX

US Contact: Dr. Mark Kirshbaum [609-750-5300; MKirschbaum@taihooncology.com]

ERBB2 amplification (continued)

NCT01730118

A Phase I Study of an Adenoviral Transduced Autologous Dendritic Cell Vaccine Expressing Human HER2/Neu ECTM in Adults with Tumors With 1-3+ HER2/Neu Expression

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 amplification or ERBB2 overexpression

Other identifiers: 1207-1179, 13-C-0016, 130016, NCI-13-C-0016, US-1179

Population segments: Estrogen receptor positive, First line, Fourth line or greater, HER2 positive, Second line, Stage III, Stage IV, Third line

Phase: I

Therapy: AdHER-2

Location: United States

US State: MD

US Contact: Lee C. England [301-451-0492; lee.english@nih.gov]

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

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 overexpression or ERBB2 amplification

Other identifiers: ARX788-1711, NCI-2018-00274

Population segments: HER2 positive, Second line, Stage IV

Phase: I

Therapy: ARX-788

Locations: Australia, United States

US State: MO

US Contact: Dr. Yong Jiang Hei [858-875-2400; yong.hei@ambrx.com]

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

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 amplification

Other identifiers: 2016-0430, NCI-2018-01218

Population segments: HER2 negative, HER2 positive, Second line, Stage III, Stage IV

Phase: I

Therapies: everolimus + neratinib, neratinib + palbociclib, neratinib + trametinib

Location: United States

US State: TX

US Contact: Dr. Sarina Piha-Paul [713-563-1930; spihapau@mdanderson.org]

ERBB2 amplification (continued)

NCT02152943

Combination Treatment With Everolimus, Letrozole and Trastuzumab in Hormone Receptor and HER2/Neu-positive Patients With Advanced Metastatic Breast Cancer and Other Solid Tumors: Evaluating Synergy and Overcoming Resistance

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 overexpression

Other identifiers: 2014-0119, NCI-2014-01615

Population segments: Estrogen receptor positive, Fourth line or greater, HER2 positive, Maintenance/Consolidation, Progesterone receptor positive, Second line, Stage III, Stage IV, Third line

Other inclusion criteria: ER positive, PR positive

Phase: I

Therapy: everolimus + trastuzumab + letrozole

Location: United States

US State: TX

US Contact: Dr. Filip Janku [713-563-1930]

NCT02829372

A Phase 1, First-in-man, Multicenter, Open-label, Dose-escalation Study of Single-agent GBR 1302 in Subjects With HER2 Positive Cancers

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 overexpression

Other identifiers: EudraCT Number: 2015-002926-38, GBR 1302-101, NCI-2017-02411

Population segments: (N/A), HER2 positive, Line of therapy N/A

Phase: I

Therapy: GBR 1302

Locations: Germany, United States

US States: KS, MI, TX, UT

US Contact: Phumla Adesanya [201-684-8000; clinicaltrialsdisclosuresdesk@glenmarkpharma.com]

No NCT ID - see other identifier(s)

Phase I Clinical Study With Advanced Solid Tumors KBP-5209 Treatment

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 overexpression or ERBB2 amplification

Other identifiers: 5209-CPK-1002, CTR20150792

Population segments: EGFR, HER2 positive, Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: I

Therapy: pirotinib

Location: China

ERBB2 amplification (continued)

NCT02500199

A Two-part Phase I, Open Label, Dose Escalation Study to Evaluate the Safety, Tolerability and Pharmacokinetics of Pyrotinib in Patients With HER2-positive Solid Tumors Whose Disease Progressed on Prior HER2 Targeted Therapy

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 overexpression or ERBB2 amplification

Other identifiers: NCI-2017-00491, SHRUS 1001

Population segments: HER2 positive, Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: I

Therapy: pyrotinib

Location: United States

US States: FL, MA, MI, MO, NY, TN

US Contact: Dr. Ewa Matczak [609-423-2155 ext 215; ewa.matczak@hengruitherapeutics.com]

NCT02881138

Safety, Tolerability, Open Label, Pharmacokinetics Ascending Dose Clinical Study Of RC48 In Patients With HER2-Positive Malignant in Advanced Malignant Solid Tumors.

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 overexpression

Other identifiers: C001 CANCER, CTR20150876

Population segments: Estrogen receptor positive, First line, Fourth line or greater, HER2 positive, Progesterone receptor positive, Second line, Stage III, Stage IV, Third line

Phase: I

Therapy: RC-48

Location: China

NCT02881190

A Tolerance, Safety and Pharmacokinetic Ascending Dose Phase I Study of RC48-ADC Administered Intravenously to Subjects With HER2-Positive Malignant in Advanced Malignant Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 overexpression

Other identifiers: C002 CANCER, CTR20150822

Population segments: First line, HER2 positive, Second line, Stage III, Stage IV

Phase: I

Therapy: RC-48

Location: China

ERBB2 amplification (continued)

NCT02892123

Phase I Trial of ZW25 in Patients With Locally Advanced (Unresectable) and/or Metastatic HER2-expressing Cancers

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 overexpression or ERBB2 amplification

Other identifiers: 2016-0532, NCI-2017-01210, ZWI-ZW25-101

Population segments: Fourth line or greater, HER2 positive, Stage III, Stage IV

Phase: I

Therapy: ZW-25

Locations: Canada, United States

US States: CA, CO, IL, TN, TX, WA

US Contact: Dr. Linda Lai [206-260-2078; linda.lai@zymeworks.com]

NCT03650348

A Phase Ib, Open-Label, Dose Escalation Study of PRS-343 in Combination With Atezolizumab in Patients With HER2-Positive Advanced or Metastatic Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 positive

Other identifier: PRS-343-PCS_08_18

Population segments: HER2 positive, Second line, Stage III, Stage IV

Phase: I

Therapy: atezolizumab + PRS-343

Location: United States

US State: TX

US Contact: Dr. Ingmar Bruns [857-246-8998; bruns@pieris.com]

NCT03448042

A Phase I, Open-Label, Dose-Escalation Study of the Safety and Pharmacokinetics of BTRC4017A Administered Intravenously in Patients With Locally Advanced or Metastatic HER2-Expressing Cancers

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 positive

Other identifier: G040311

Population segments: HER2 negative, HER2 positive, Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: I

Therapy: BTRC-4017A

Location: United States

US State: TN

US Contact: Reference Study ID Number: G040311 [888-662-6728; global-roche-genentech-trials@gene.com]

ERBB2 amplification (continued)

NCT03319459

FATE-NK100 as Monotherapy and in Combination With Monoclonal Antibody in Subjects With Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 positive

Other identifiers: DIMENSION, NK-101

Population segments: HER2 positive, Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: I

Therapy: FATE-NK100 + trastuzumab

Location: United States

US State: MN

US Contact: Sara Weymer [858-875-1800; clinical@fatetherapeutics.com]

NCT03084926

A Phase I, First-in-human, Single-arm, Multi-center, Open-label, Repeated-Dose, Dose Escalation Study to Assess Safety, Tolerability and Pharmacokinetics of MP0274 in Patients With Advanced HER2-positive Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 positive

Other identifiers: 2017-00921, EudraCT Number: 2016-004712-36, IRAS ID: 222863, MP0274-CP101, SNCTP000002338

Population segments: HER2 positive, Second line, Stage III, Stage IV

Phase: I

Therapy: MP-0274

Locations: Germany, Switzerland, United Kingdom

NCT03330561

A Phase I, Open-Label, Dose Escalation Study of PRS-343 in Patients With HER2-Positive Advanced or Metastatic Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 positive

Other identifier: PRS-343-PCS_04_16

Population segments: HER2 positive, Second line or greater/Refractory/Relapsed, Stage II, Stage III, Stage IV

Phase: I

Therapy: PRS-343

Location: United States

US States: NY, TN, TX

US Contact: Dr. Ingmar Bruns [857-246-8998; bruns@pieris.com]

ERBB2 amplification (continued)**NCT02435927**

Phase I Study to Evaluate the Safety and Tolerability of ASLAN001 in Combination with Oxaliplatin and Capecitabine or Oxaliplatin and 5-FU with Leucovorin

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 aberration

Other identifier: ASLAN001-002SG

Population segments: Second line, Stage IV

Exclusion criteria variant class: EGFR T790M mutation

Phase: I

Therapy: varlitinib + chemotherapy

Location: Singapore

KRAS amplification**NCT02583542**

A Phase Ib/IIa Study of AZD2014 in Combination With Selumetinib in Patients With Advanced Cancers

Cancer type: Endometrial Cancer

Variant class: KRAS aberration

Other identifiers: 009896QM, EudraCT Number: 2014-002613-31, IRAS ID 172356, Torcmek, UKCRN ID:18725

Population segments: Adenocarcinoma, EGFR, FGFR, HER2 negative, KRAS, Large Cell, Second line, Squamous Cell, Stage III, Stage IV, Triple receptor negative

Phase: I/II

Therapy: selumetinib + vistusertib

Location: United Kingdom

NCT02029001

A Two-period, Multicenter, Randomized, Open-label, Phase II Study Evaluating the Clinical Benefit of a Maintenance Treatment Targeting Tumor Molecular Alterations in Patients With Progressive Locally-advanced or Metastatic Solid Tumors MOST: My own specific treatment

Cancer type: Unspecified Solid Tumor

Variant class: KRAS amplification

Other identifiers: ET12-081, EudraCT number: 2012-004510-34, MOST, ProfiLER

Population segments: Maintenance/Consolidation, Second line, Stage III, Stage IV

Exclusion criteria variant class: BRAF V600 mutation

Phase: II

Therapy: sorafenib

Location: France

KRAS amplification (continued)

NCT03520075

A Phase I/II Study of the Safety, Pharmacokinetics, and Activity of ASTX029 in Subjects With Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: RAS/RAF/MEK/ERK pathway

Other identifier: ASTX029-01

Population segments: Second line, Stage III, Stage IV

Phase: I/II

Therapy: ASTX029

Location: United States

US States: CT, TX, VA

US Contact: Richard J. Morishige [925-560-2882; Richard.Morishige@astx.com]

NCT02639546

A Phase I/II, Multicenter, Open-Label, Dose-Escalation Study of The Safety And Pharmacokinetics of Cobimetinib In Pediatric And Young Adult Patients With Previously Treated Solid Tumors - iMATRIX Cobi

Cancer type: Unspecified Solid Tumor

Variant class: RAS/RAF/MEK/ERK pathway

Other identifiers: 15-524, 16-041, 2015-0929, CTSC#15-0005, DRKS00010690, EudraCT Number: 2014-004685-25, GO29665, iMATRIX Cobi, iMATRIXcobi, IRAS ID: 174562, NCI-2016-00541, NL52503.078.16

Population segments: (N/A), Pediatric or Adolescent, Second line or greater/Refractory/Relapsed

Phase: I/II

Therapy: cobimetinib

Locations: Canada, France, Germany, Israel, Italy, Spain, United Kingdom, United States

US States: AR, AZ, CA, FL, MA, NY, PA, TX

US Contact: Reference Study ID Number: GO29665 [888-662-6728; global-roche-genentech-trials@gene.com]

NCT02857270

A Phase I Study of an ERK1/2 Inhibitor (LY3214996) Administered Alone or in Combination With Other Agents in Advanced Cancer

Cancer type: Unspecified Solid Tumor

Variant class: RAS/RAF/MEK/ERK pathway

Other identifiers: 16419, EudraCT Number: 2016-001907-21, I8S-MC-JUAB, JUAB, NCI-2017-00039

Population segments: Second line, Stage III, Stage IV

Phase: I

Therapies: abemaciclib + LY3214996, LY3214996, LY3214996 + chemotherapy, LY3214996 + midazolam

Locations: Australia, France, United States

US States: FL, MA, TN, TX

US Contact: Eli Lilly and Company [877-285-4559]

KRAS amplification (continued)**NCT02711345**

A Phase I Dose Finding Study of Oral LTT462 in Adult Patients With Advanced Solid Tumors Harboring MAPK Pathway Alterations

Cancer type: Unspecified Solid Tumor

Variant class: RAS/RAF/MEK/ERK pathway

Other identifiers: CLTT462X2101, EudraCT number: 2015-003614-24, JapicCTI-163207, NCI-2016-00539, NL57739.031.16

Population segments: First line, KRAS, Second line, Stage III, Stage IV

Phase: I

Therapy: LTT-462

Locations: Germany, Italy, Japan, Netherlands, Singapore, Spain, Switzerland, United States

US States: NY, TX

US Contact: Novartis Pharmaceuticals [888-669-6682; Novartis.email@novartis.com]

NCT02607813

A Phase I Dose Finding Study of Oral LXH254 in Adult Patients With Advanced Solid Tumors Harboring MAPK Pathway Alterations

Cancer type: Unspecified Solid Tumor

Variant class: RAS/RAF/MEK/ERK pathway

Other identifiers: 16-225, 2015-0913, CLXH254X2101, EudraCT Number: 2015-003421-33, NCI-2015-02280, NL55506.078.15, Nov RAFi (CLXH254X2101), REec-2016-2132, SNCTP000002708

Population segments: Second line, Stage III, Stage IV

Phase: I

Therapies: LXH254, LXH254 + spartalizumab

Locations: Canada, France, Germany, Japan, Netherlands, Republic of Korea, Spain, Switzerland, United States

US States: NY, TX

US Contact: Novartis Pharmaceuticals [888-669-6682; Novartis.email@novartis.com]

ERBB3 p.(G284R) c.850G>A

NCT03410927

A Phase I/II, Open Label, Multicenter Study to Investigate the Safety, Pharmacokinetics, and Efficacy of TAS0728, an Oral Covalent Binding Inhibitor of HER2, in Subjects With Advanced Solid Tumors With HER2 or HER3 Abnormalities

Cancer type: Endometrial Cancer

Variant class: ERBB3 mutation

Other identifiers: 18116, 2017-0994, EudraCT Number: 2017-004415-39, NCI-2018-00211, REFMAL 555, TO-TAS0728-101

Population segments: Adenocarcinoma, Fourth line or greater, HER2 positive, Large Cell, Second line, Stage III, Stage IV, Third line

Phase: I/II

Therapy: TAS0728

Locations: United Kingdom, United States

US States: NY, TN, TX

US Contact: Dr. Mark Kirshbaum [609-750-5300; MKirschbaum@taihooncology.com]

No NCT ID - see other identifier(s)

Precision 2: 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.

Cancer type: Unspecified Cancer

Variant class: ERBB3 mutation

Other identifiers: 1200.264, EudraCT Number: 2016-003411-34, Precision 2

Population segments: HER2 positive, Line of therapy N/A, Stage III, Stage IV

Phase: II

Therapy: afatinib

Location: Belgium

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

Cancer type: Unspecified Solid Tumor

Variant class: ERBB3 mutation

Other identifiers: 2016-0430, NCI-2018-01218

Population segments: HER2 negative, HER2 positive, Second line, Stage III, Stage IV

Phase: I

Therapies: everolimus + neratinib, neratinib + palbociclib, neratinib + trametinib

Location: United States

US State: TX

US Contact: Dr. Sarina Piha-Paul [713-563-1930; spihapau@mdanderson.org]

ERBB3 p.(G284R) c.850G>A (continued)

No NCT ID - see other identifier(s)
Phase I Clinical Study With Advanced
Solid Tumors KBP-5209 Treatment

Cancer type: Unspecified Solid Tumor

Variant class: ERBB3 mutation

Other identifiers: 5209-CPK-1002, CTR20150792

Population segments: EGFR, HER2 positive, Second line or greater/Refractory/
Relapsed, Stage III, Stage IV

Phase: I

Therapy: pirotinib

Location: China

TP53 p.(C275F) c.824G>T

NCT02576444

A Phase II Study of the PARP Inhibitor
Olaparib (AZD2281) Alone and in
Combination With AZD1775, AZD5363, or
AZD6738 in Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: TP53 mutation

Other identifiers: 1508016363, 16-314, NCI-2016-00922, OLAPCO, VICCMD1672

Population segments: First line, Second line, Stage IV

Phase: II

Therapy: adavosertib + olaparib

Location: United States

US States: CT, MA, OH, TN

US Contact: Manuel Avedissian [203-737-3669; manuel.avedissian@yale.edu]

No NCT ID - see other identifier(s)
An Open-Label Study of the Safety,
Tolerability, and Pharmacokinetic/
Pharmacodynamic Profile of VX-970
as a Single Agent in Combination with
Carboplatin in Subjects with Advanced
Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: TP53 mutation

Other identifiers: EudraCT Number: 2013-005100-34, VX13-970-002

Population segments: (N/A), Adenocarcinoma, HER2 negative, Second line or greater/
Refractory/Relapsed, Stage III, Stage IV, Triple receptor negative

Phase: I/II

Therapies: VX-970, VX-970 + chemotherapy

Location: United Kingdom

Evidence Summary by Variant Class

A variant class hierarchy was created to summarize gene variants with associated clinical evidence. Evidence items refers to citations across the different global data sources.

ERBB2 amplification

Variant Class	Evidence Items
ERBB aberration	0
↳ ERBB2 status	0
↳ ERBB2 aberration	4
↳ ERBB2 positive	21
↳ ERBB2 amplification	72
ERBB aberration	0
↳ ERBB2 status	0
↳ ERBB2 aberration	4
↳ ERBB2 positive	21
↳ ERBB2 overexpression	113

KRAS amplification

Variant Class	Evidence Items
RAS/RAF/MEK/ERK pathway	5
↳ RAS amplification	0
↳ KRAS amplification	1
↳ KRAS aberration	1
↳ KRAS positive	0
↳ KRAS amplification	1

Evidence Summary by Variant Class (continued)

A variant class hierarchy was created to summarize gene variants with associated clinical evidence. Evidence items refers to citations across the different global data sources.

ERBB3 p.(G284R) c.850G>A

Variant Class	Evidence Items
ERBB aberration	0
↳ ERBB3 aberration	0
↳ ERBB3 mutation	4

TP53 p.(C275F) c.824G>T

Variant Class	Evidence Items
TP53 aberration	0
↳ TP53 mutation	2
↳ TP53 exon 8 mutation	0

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Allele Frequency	Transcript	Variant Effect	Gene Class	Variant Class
ERBB3	p.(G284R)	c.850G>A	COSM941488	65.54%	NM_001982.3	missense	Gain of Function	Hotspot
TP53	p.(C275F)	c.824G>T	COSM10701	50.61%	NM_000546.5	missense	Loss of Function	Hotspot

Copy Number Variations

Gene	Locus	Copy Number
KRAS	chr12:25362715	7.17
ERBB2	chr17:37868168	20.45



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PD-1/PD-L1 TESTING

ONC19

Surname

Forename

DOB

Gender

Histology #

Primary site

Tumour subtype

Tissue Type

Uterus

Serous Adenocarcinoma

Uterus

Requester

Contact details

Date requested

Tumour %

-

Tumour %

60%

(macrodissected)

PD-L1 test

PD-L1 IHC assays are used to help identify those patients most likely to benefit from anti-PD-1/PD-L1 directed immunotherapies. Assessment involves the determination of a range of cut-off/threshold values for PD-L1 positive tumour cells and PD-L1 positive immune cells. These cut off values are identified as predictors of response to anti-PD-L1 directed therapies used in the treatment of a range of different cancer types and include pembrolizumab, atezolizumab, avelumab, nivolumab, and durvalumab. The established cut off values for tumour proportion scores (>1%, >25%, >50%) and PD-L1 positive immune cells (10%), which vary according to immunotherapy, tumour type and whether first or second line therapy is to be used.

The Oncologica® Immunofocus PD-L1 immunocytochemistry assay quantifies the proportion of tumour cells that express PD-L1 (Tumour Proportion Score) and the area occupied by tumour infiltrating PD-L1 positive immune cells.

The Oncologica® Immunofocus PD-L1 immunocytochemistry assay is a Laboratory Developed Test utilising the RUO rabbit monoclonal antibody clone E1L3N (Cell Signalling Technologies) and Leica Bond III instrumentation. The performance of the Immunofocus assay is continually assessed by involvement in recognised External Quality Assessment schemes and returns performance levels commensurate with approved the PD-L1 diagnostic assays. All Immunofocus assay testing is performed within the scope of UKAS/ISO 15189:2012 accreditation. Clone E1L3N is not licensed and approved for use in clinical testing to direct the use of PD-1/PD-L1 therapies. The PD-L1 protein expression levels in tumour cells generated by the Immunofocus PD-L1 assay should therefore be interpreted within the context of these facts.

PD-L1 Result

Occasional tumour cells show weak intensity immunostaining for PD-L1 with partial and complete patterns of surface membrane expression. The proportion of PD-L1 expressing tumour cells amounts to <1% of the total tumour cell population. The tumour is associated with a focal patchy PD-L1 expressing immune cell (IC) infiltrate. PD-L1 expressing tumour infiltrating immune cells (ICs) cover 2-3% of the tumour area occupied by tumour cells, intratumoural and contiguous peritumoural stroma.

Summary; PD-L1 Tumour Proportion Score <1%; PD-L1 positive ICs 2-3% of tumour area



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