Medical Laboratory
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UKAS MEDICAL 9376

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Leading a new era of precision oncology

Oncofocus®

Precision Oncology

ONCOFOCUS® TEST REPORT

Oncologica UK Ltd
Suite 2, The Newnham Building,
Chesterford Research Park
Little Chesterford, Cambridge, CB10 1XL

Tel: +44(0)1223 785327
Email: info@oncologica.com

Surname	**Requester**
Forename	**Contact details**
DOB	**Date requested**
Gender	
Histology #	**Tumour %**
Primary site	**Tumour %**
Tumour subtype	**(macrodissected)**
Tissue Type	

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.

The following actionable variants were detected:
Please note; There is limited evidence available in the literature to determine the pathogenicity of the TP53 variant detected. However, this variant is a disruptive frameshift, and studies have suggested that ovarian cancers with TP53 disruptive variants are responsive to Olaparib, independent of BRCA status.

Within the 'Current Clinical Trials Information' section of this report, starting on page 46, the NCT numbers are hyperlinks to the clinicaltrials.gov webpages which should be accessed to gain further trial specific information

Sample Cancer Type: Ovarian 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*	Clinical trials and/or off-label	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
AKT2 amplification	Clinical trials and/or off-label	Clinical trials and/or off-label	8
CCNE1 amplification	Clinical trials and/or off-label	Clinical trials and/or off-label	5
TP53 p.(S314fs) c.940delT	Clinical trials and/or off-label	Clinical trials and/or off-label	4

Sources included in relevant therapies: EMA[1], FDA[2], 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*

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.

Tier Criteria Met

Genomic Alteration	Tier Classification for Ovarian Cancer
ERBB2 amplification Tier: IIC	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
AKT2 amplification Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
CCNE1 amplification Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
TP53 p.(S314fs) c.940delT 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	○	○	○	○	● (II)
pertuzumab + trastuzumab + docetaxel	○	○	○	○	✖
trastuzumab + capecitabine + cisplatin	○	○	○	○	✖
trastuzumab + cisplatin + fluorouracil	○	○	○	○	✖
lapatinib + capecitabine	○	○	✖	○	✖
trastuzumab	○	○	✖	○	✖
trastuzumab + carboplatin + docetaxel	○	○	✖	○	✖
trastuzumab + paclitaxel	○	○	✖	○	✖
trastuzumab + cyclophosphamide + docetaxel + doxorubicin	○	○	✖	✖	✖
trastuzumab + cyclophosphamide + doxorubicin + paclitaxel	○	○	✖	✖	✖

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

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.

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*
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	○	✖	✖	✖	✖
trastuzumab (Samsung Bioepis) + cyclophosphamide + doxorubicin + paclitaxel	○	✖	✖	✖	✖

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

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.

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) + 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	✖	✖	○	✖	✖
trastuzumab + hormone therapy	✖	✖	○	✖	✖

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

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.

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 + taxane	✖	✖	○	✖	✖
trastuzumab containing regimen	✖	✖	○	✖	✖
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 + carboplatin + paclitaxel	✖	✖	✖	○	✖
trastuzumab + chemotherapy (other)	✖	✖	✖	○	✖
trastuzumab + cisplatin + docetaxel	✖	✖	✖	○	✖
trastuzumab + cisplatin + docetaxel + fluorouracil	✖	✖	✖	○	✖
trastuzumab + cisplatin + paclitaxel	✖	✖	✖	○	✖
trastuzumab + cyclophosphamide + docetaxel	✖	✖	✖	○	✖
trastuzumab + docetaxel + fluorouracil + oxaliplatin	✖	✖	✖	○	✖
trastuzumab + fluorouracil	✖	✖	✖	○	✖
trastuzumab + fluorouracil + irinotecan	✖	✖	✖	○	✖
trastuzumab + fluorouracil + oxaliplatin	✖	✖	✖	○	✖
trastuzumab + fulvestrant	✖	✖	✖	○	✖
trastuzumab + tamoxifen	✖	✖	✖	○	✖
lapatinib	✖	✖	✖	✖	● (II)

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

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.

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*
A-166	✖	✖	✖	✖	● (I/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)
pyrotinib	✖	✖	✖	✖	● (I)
RC-48	✖	✖	✖	✖	● (I)
varlitinib + chemotherapy	✖	✖	✖	✖	● (I)
ZW-25	✖	✖	✖	✖	● (I)

AKT2 amplification

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
capivasertib + olaparib	✖	✖	✖	✖	● (II)

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

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.

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

AKT2 amplification (continued)

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
everolimus	✖	✖	✖	✖	● (II)
temsirolimus	✖	✖	✖	✖	● (II)
selumetinib + vistusertib	✖	✖	✖	✖	● (I/II)
ARQ-751	✖	✖	✖	✖	● (I)
capivasertib	✖	✖	✖	✖	● (I)
gedatolisib + palbociclib	✖	✖	✖	✖	● (I)
palbociclib + pictilisib, palbociclib + taselisib	✖	✖	✖	✖	● (I)

CCNE1 amplification

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
palbociclib	✖	✖	✖	✖	● (II)
prexasertib	✖	✖	✖	✖	● (II)
PNT-737	✖	✖	✖	✖	● (I/II)
CYC065	✖	✖	✖	✖	● (I)

TP53 p.(S314fs) c.940delT

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
adavosertib + olaparib	✖	✖	✖	✖	● (II)
PNT-737	✖	✖	✖	✖	● (I/II)
VX-970, VX-970 + chemotherapy	✖	✖	✖	✖	● (I/II)
LY3143921	✖	✖	✖	✖	● (I)

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

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.

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

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.

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

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.

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

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.

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

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.

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

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.

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

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.

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

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.

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

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.

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.]

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.

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.]

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.

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.]

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pertuzumab + trastuzumab + chemotherapy

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

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

Population segment (Line of therapy):
- Advanced 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.]

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pertuzumab + trastuzumab + docetaxel

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

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

Population segment (Line of therapy):
- Advanced Breast Cancer (Not specified)

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

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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.]

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.

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.]

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.

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.]

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.

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.]

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.

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

○ 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]

○ 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]

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.

ERBB2 amplification (continued)

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]

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]

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.

ERBB2 amplification (continued)

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]

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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]

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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]

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.

ERBB2 amplification (continued)

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]

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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]

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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]

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.

ERBB2 amplification (continued)

hormone therapy

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

Other criteria: ER positive, PR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Ductal, 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]

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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]

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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]

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.

ERBB2 amplification (continued)

○ lapatinib + capecitabine

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

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Recurrent or Stage IV Invasive Breast Cancer (Not specified)

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]

○ 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]

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.

ERBB2 amplification (continued)

○ pertuzumab + trastuzumab + carboplatin + docetaxel

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Recurrent or Stage IV Invasive Breast Cancer (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]

○ 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]

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.

ERBB2 amplification (continued)

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]

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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]

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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]

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.

ERBB2 amplification (continued)

trastuzumab + capecitabine

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

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Recurrent or Stage IV Invasive Breast Cancer (Not specified)

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

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trastuzumab + carboplatin + docetaxel

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Recurrent or Stage IV Invasive Breast Cancer (Not specified)

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

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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]

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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]

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.

ERBB2 amplification (continued)

trastuzumab + chemotherapy

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

Other criteria: ER negative, PR negative

NCCN Recommendation category: 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]

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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]

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trastuzumab + cyclophosphamide + docetaxel

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Recurrent or Stage IV Invasive Breast Cancer (Not specified)

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

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.

ERBB2 amplification (continued)

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]

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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]

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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]

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.

ERBB2 amplification (continued)

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]

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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]

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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]

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.

ERBB2 amplification (continued)

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]

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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]

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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]

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.

ERBB2 amplification (continued)

○ 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]

○ 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]

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.

ERBB2 amplification (continued)

○ 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]

○ 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]

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.

ERBB2 amplification (continued)

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]

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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]

---

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]

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.

ERBB2 amplification (continued)

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]

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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]

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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]

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.

ERBB2 amplification (continued)

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]

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]

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.

ERBB2 amplification (continued)

○ 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]

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.

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]

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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]

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.

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]

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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]

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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]

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pertuzumab + trastuzumab + cyclophosphamide + doxorubicin + paclitaxel

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

Summary:

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

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

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.

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]

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.

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]

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.

Oncologica UK Ltd
Suite 2, The Newnham Building,
Chesterford Research Park
Little Chesterford, Cambridge, CB10 1XL

Tel: +44(0)1223 785327
Email: info@oncologica.com

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]

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.

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

NCT03602079
A Phase I-II, FIH Study of A166 in Locally Advanced/Metastatic Solid Tumors Expressing Human Epidermal Growth Factor Receptor 2 (HER2) or Are HER2 Amplified That Did Not Respond or Stopped Responding to Approved Therapies

Cancer type: Ovarian Cancer

Variant class: ERBB2 overexpression

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

Phase: I/II

Therapy: A-166

Location: United States

US State: TX

US Contact: Clinical Trials Info at Kluspharma [609-662-1913; Clinicaltrialinfo@kluspharma.com]

NCT01935843
Clinical Study of Chimeric HER-2 Antigen Receptor-modified T Cells in Chemotherapy Refractory HER-2 Advanced Solid Tumors.

Cancer type: Ovarian 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: Ovarian 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

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.

ERBB2 amplification (continued)

NCT01730118
A Phase I Study of an Adenoviral Transduced Autologous Dendritic Cell Vaccine Expressing Human HER2/Neu ECTM in Adults withTumors With 1-3+ HER2/Neu Expression

Cancer type: Ovarian Cancer

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.england@nih.gov]

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

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.

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]

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.

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]

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.

ERBB2 amplification (continued)

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]

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]

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.

ERBB2 amplification (continued)

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; clinicaltrialsdisclosuredesk@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

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]

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.

ERBB2 amplification (continued)

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

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]

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.

ERBB2 amplification (continued)

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: GO40311

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: GO40311 [888-662-6728; global-roche-genentech-trials@gene.com]

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]

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.

ERBB2 amplification (continued)

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]

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

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.

AKT2 amplification

NCT02583542
A Phase Ib/IIa Study of AZD2014 in Combination With Selumetinib in Patients With Advanced Cancers

Cancer type: Ovarian Cancer

Variant class: AKT 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: AKT2 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: everolimus

Location: France

NCT03297606
Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial

Cancer type: Unspecified Solid Tumor

Variant class: AKT2 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: temsirolimus

Location: Canada

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.

AKT2 amplification (continued)

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: PI3K/AKT/MTOR pathway

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

Population segments: First line, Second line, Stage IV

Phase: II

Therapy: capivasertib + olaparib

Location: United States

US States: CT, MA, OH, TN

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

NCT02761694
A Phase I Dose Escalation Study of ARQ 751 in Adult Subjects With Advanced Solid Tumors With AKT1, 2, 3 Genetic Alterations, Activating PI3K Mutations, PTEN-null, or Other Known Actionable PTEN Mutations

Cancer type: Unspecified Solid Tumor

Variant class: AKT2 aberration

Other identifiers: 2016-0212, ARQ 751-101, PTEN-null

Population segments: Second line, Stage III, Stage IV

Phase: I

Therapy: ARQ-751

Location: United States

US State: TX

US Contact: ArQule [781-994-0300; ClinicalTrials@arqule.com]

NCT01226316
A Phase I, Open-Label, Multicentre Study to Assess the Safety, Tolerability, Pharmacokinetics and Preliminary Anti-tumour Activity of Ascending Doses of AZD5363 Under Adaptable Dosing Schedules in Patients With Advanced Solid Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: PI3K/AKT/MTOR pathway

Other identifiers: 0C-14-10, 102084, 14-214, 14-430, 2014-0160, CR1322AZ, CSET 2365, D3610C00001, EudraCT Number: 2010-022167-35, IRAS ID: 62131, JapicCTI-152844, M10AZD, NCI-2014-01803, NL33755.031.10, P1TGIVEN, PRO 09

Population segments: (N/A), Adenocarcinoma, Estrogen receptor positive, Fourth line or greater, HER2 positive, Hormone refractory, Second line, Stage III, Stage IV, Third line

Phase: I

Therapy: capivasertib

Locations: Canada, Denmark, France, Italy, Japan, Singapore, Spain, United States

US States: CA, CO, NY, OK, PA, TN, TX

US Contact: AstraZeneca Clinical Study Information Center [877-240-9479; information.center@astrazeneca.com]

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.

AKT2 amplification (continued)

NCT03065062
Phase I Study of the CDK4/6 Inhibitor Palbociclib (PD-0332991) in Combination With the PI3K/mTOR Inhibitor Gedatolisib (PF-05212384) for Patients With Advanced Squamous Cell Lung, Pancreatic, Head & Neck and Other Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: PI3K/AKT/MTOR pathway

Other identifiers: 16-499, NCI-2017-00434

Population segments: Second line, Squamous Cell, Stage III, Stage IV

Phase: I

Therapy: gedatolisib + palbociclib

Location: United States

US State: MA

US Contact: Dr. Nicole Chau [617-632-3090]

NCT02389842
PIPA: A Phase Ib Study to Assess the Safety, Tolerability and Efficacy of the PI3K Inhibitors, Taselisib (GDC-0032) or Pictilisib (GDC-0941), in Combination With PAlbociclib, With the Subsequent Addition of Fulvestrant in PIK3CA-mutant Breast Cancers

Cancer type: Unspecified Solid Tumor

Variant class: PI3K/AKT/MTOR pathway

Other identifiers: CCR4191, EudraCT Number: 2014-002658-37, IRAS ID:159997, PIPA

Population segments: Estrogen receptor positive, Fourth line or greater, HER2 negative, HER2 positive, KRAS, Stage III, Stage IV, Triple receptor negative

Phase: I

Therapies: palbociclib + pictilisib, palbociclib + taselisib

Location: United Kingdom

CCNE1 amplification

NCT02797964
A Phase I/II Trial of SRA737 (a Chk1 Inhibitor) Administered Orally in Subjects With Advanced Cancer

Cancer type: Ovarian Cancer

Variant class: CCNE1 aberration

Other identifiers: 198451, 30500, CRUKD/16/002, EudraCT Number: 2015-004486-86, IRAS ID: 198451, PNT737-01, SRA737-01

Population segments: Aggressive, BRCA, First line, Hormone refractory, Indolent, KRAS, N/A, Second line, Stage III, Stage IV

Phase: I/II

Therapy: PNT-737

Location: United Kingdom

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.

CCNE1 amplification (continued)

NCT02552953
A Phase I Pharmacologic Study of CYC065, a Cyclin Dependent Kinase Inhibitor, in Patients With Advanced Cancers

Cancer type: Ovarian Cancer

Variant class: CCNE1 amplification

Other identifiers: 15-281, CYC065-01, NCI-2015-01709

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

Phase: I

Therapy: CYC065

Location: United States

US State: MA

US Contact: Dr. Judy Chiao [908-517-7330]

NCT02896335
A Phase II Study of Palbociclib in Progressive Brain Metastases Harboring Alterations in the CDK Pathway

Cancer type: Unspecified Solid Tumor

Variant class: CCNE1 amplification

Other identifiers: 16-254, NCI-2016-02025

Population segments: CNS mets, Second line, Stage IV

Phase: II

Therapy: palbociclib

Location: United States

US State: MA

US Contact: Dr. Priscilla Brastianos [617-724-8770; PBRASTIANOS@mgh.harvard.edu]

NCT02873975
A Phase II Study of the CHK1 Inhibitor LY2606368 in Patients With Advanced Solid Tumors Exhibiting Replicative Stress or Homologous Recombination Repair Deficiency

Cancer type: Unspecified Solid Tumor

Variant class: CCNE1 amplification

Other identifiers: 16-281, I4D-MC-E006, NCI-2016-01564

Population segments: Second line, Stage III, Stage IV

Phase: II

Therapy: prexasertib

Location: United States

US State: MA

US Contact: Dr. Geoffrey Shapiro [617-632-4942; Geoffrey_Shapiro@dfci.harvard.edu]

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.

CCNE1 amplification (continued)

NCT01037790
Phase II Trial of the Cyclin-Dependent Kinase Inhibitor PD 0332991 in Patients With Cancer

Cancer type: Unspecified Solid Tumor

Variant class: G1/S cell cycle pathway

Other identifiers: NCI-2009-01467, Study 1006, UPCC 03909, UPCC03909

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

Phase: II

Therapy: palbociclib

Location: United States

US State: PA

US Contact: Dr. Peter O. Dwyer [855-216-0098; PennCancerTrials@emergingmed.com]

TP53 p.(S314fs) c.940delT

NCT02797964
A Phase I/II Trial of SRA737 (a Chk1 Inhibitor) Administered Orally in Subjects With Advanced Cancer

Cancer type: Ovarian Cancer

Variant class: TP53 aberration

Other identifiers: 198451, 30500, CRUKD/16/002, EudraCT Number: 2015-004486-86, IRAS ID: 198451, PNT737-01, SRA737-01

Population segments: Aggressive, BRCA, First line, Hormone refractory, Indolent, KRAS, N/A, Second line, Stage III, Stage IV

Phase: I/II

Therapy: PNT-737

Location: United Kingdom

NCT03096054
A Cancer Research UK (CR-UK) Phase I Trial of LY3143921 a Cdc7 Inhibitor in Adult Patients With Advanced Solid Tumours

Cancer type: Ovarian Cancer

Variant class: TP53 mutation

Other identifiers: CPMS ID 35213, CRUKD/17/004, EudraCT Number: 2016-001245-80, IRAS ID 216105, MREC No. 17/NI/0005

Population segments: HER2 negative, Line of therapy N/A, Squamous Cell, Stage III, Stage IV, Triple receptor negative

Phase: I

Therapy: LY3143921

Location: United Kingdom

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.

TP53 p.(S314fs) c.940delT (continued)

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

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.

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

AKT2 amplification

Variant Class	Evidence Items
PI3K/AKT/MTOR pathway	4
↳ AKT aberration	1
↳ AKT2 aberration	2
↳ AKT2 amplification	1

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.

Oncologica UK Ltd
Suite 2, The Newnham Building,
Chesterford Research Park
Little Chesterford, Cambridge, CB10 1XL

Tel: +44(0)1223 785327
Email: info@oncologica.com

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.

CCNE1 amplification

Variant Class	Evidence Items
G1/S cell cycle pathway	1
↳ CCNE1 aberration	1
↳ CCNE1 amplification	3

TP53 p.(S314fs) c.940delT

Variant Class	Evidence Items
TP53 aberration	1
↳ TP53 mutation	3
↳ TP53 deleterious mutation	0

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Email: info@oncologica.com

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Allele Frequency	Transcript	Variant Effect	Gene Class	Variant Class
TP53	p.(S314fs)	c.940delT	.	86.98%	NM_000546.5	frameshift Deletion	Loss of Function	Deleterious

Copy Number Variations

Gene	Locus	Copy Number
ERBB2	chr17:37868168	12.14
CCNE1	chr19:30303882	8.78
AKT2	chr19:40739755	13.45

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Suite 2, The Newnham Building, Chesterford Research Park,
Little Chesterford, Cambridge, CB10 1XL

+44 (0) 1223 785 327 - info@oncologica.com

Ireland

Bymac Centre, Northwest
Business Park, Blanchardstow, Dublin 15

+353 1 8604204

Italy

Parco Tecnologico della Sardegna
Pula, Località Piscinamanna

+39 02 808 88210