Medical Laboratory Accredited to ISO15189:2012







Oncofocus® Precision Oncology



Lead Clinical Scientist: Keeda Hardisty

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Tel: +44(0)1223 785327

Pre-Reg Clinical Scientist: Katherine Benton Date: 1 of 64

Indicated Contraindicated

FINAL REPORT

Surname Requester
Forename Contact details
DOB Date requested
Gender

Histology #Tumour %90%Primary siteEsophagusTumour %-Tumour subtypeAdenocarcinoma(macrodissected)

Tissue Type Esophageal Biopsy

Comment:

The DNA and RNA extracted from this sample were of optimal quantity. The Oncofocus assay on which the sample was run met all assay specific quality metrics for DNA, but unfortunately RNA failed as reported on 23/01/2019.

Repeat RNA extraction and sequencing has been carried out. No additional variants were detected.

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:

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

Sample Cancer Type: Esophageal Cancer

Clinically Significant Biomarkers

Relevant Therapies Relevant Therapies Genomic Alteration Clinical Trials (In this cancer type) (In other cancer type) trastuzumab (Celltrion)1 trastuzumab trastuzumab (Celltrion)1 trastuzumab ERBB2 (HER2) trastuzumab (Biocon) + chemotherapy2 45 (Celltrion) + chemotherapy1 (Celltrion) + chemotherapy1 lapatinib + letrozole2 amplification trastuzumab (Samsung Bioepis)1 trastuzumab (Samsung Bioepis)1 neratinib2 trastuzumab (Samsung Bioepis) + trastuzumab (Samsung Bioepis) + trastuzumab + hormone therapy + chemotherapy1 chemotherapy1 chemotherapy trastuzumab1,2 trastuzumab1.2 trastuzumab + hormone therapy pertuzumab trastuzumab + chemotherapy1,2 adotrastuzumab + chemotherapy1,2 + trastuzumab hormone therapy trastuzumab emtansine1,2 lapatinib + trastuzumab (Biocon)2 trastuzumab lapatinib + trastuzumab + aromatase inhibitor aromatase inhibitor1 lapatinib + (Biocon) + chemotherapv2 pertuzumab + trastuzumab + hormone chemotherapy1,2 lapatinib + trastuzumab1 trastuzumab containing regimen therapy + chemotherapy trastuzumab + pertuzumab + trastuzumab + aromatase inhibitor trastuzumab + chemotherapy1,2 fulvestrant trastuzumab + tamoxifen trastuzumab (Celltrion) + anastrozole1 trastuzumab (Samsung Bioepis) + anastrozole1 trastuzumab + anastrozole1 trastuzumab (Biocon)2 Clinical trials and/or off-label Clinical trials and/or off-label 3 TP53 p.(R175H) c.524G>A

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

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

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Tier Criteria Met

Genomic Alteration	Tier Classification for Esophageal Cancer
ERBB2 amplification Tier: IA	 IA: Biomarker predicts response or resistance to EMA or FDA approved therapies in this cancer type IA: Biomarker is included in ESMO or NCCN guidelines that predict response or resistance to therapies in this cancer type IIC: Biomarker predicts response or resistance to EMA or FDA approved therapies in other cancer types IIC: Biomarker is included in ESMO or NCCN guidelines that predict response or resistance to therapies in other cancer types IIC: Biomarker is an inclusion criteria for clinical trials
TP53 p.(R175H) c.524G>A 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.

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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

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
trastuzumab + capecitabine + cisplatin	0	0	0	0	×
trastuzumab + cisplatin + fluorouracil	•	•	0	•	×
trastuzumab + paclitaxel	•	•	×	•	×
trastuzumab	•	•	×	0	(II)
trastuzumab + carboplatin + docetaxel	•	•	×	0	×
trastuzumab + cyclophosphamide + docetaxel + doxorubicin	•	•	×	×	×
trastuzumab + cyclophosphamide + doxorubicin + paclitaxel	•	0	×	×	×
trastuzumab + docetaxel	•	×	×	0	×
trastuzumab (Celltrion)	•	×	×	×	×
trastuzumab (Celltrion) + capecitabine + cisplatin	•	×	×	×	×
trastuzumab (Celltrion) + carboplatin + docetaxel	0	×	×	×	×

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

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Relevant Therapy Summary (continued)

In this cancer type In other cancer type

Lead Clinical Scientist: Keeda Hardisty

In this cancer type and other cancer types

Contraindicated

A Both for use and contraindicated

X No evidence

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
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) + capecitabine + cisplatin	•	×	×	×	×
trastuzumab (Samsung Bioepis) + carboplatin + docetaxel	•	×	×	×	×
trastuzumab (Samsung Bioepis) + cisplatin + fluorouracil	•	×	×	×	×
trastuzumab (Samsung Bioepis) + cyclophosphamide + docetaxel + doxorubicin	•	×	×	×	×
trastuzumab (Samsung Bioepis) + cyclophosphamide + doxorubicin + paclitaxel	•	×	×	×	×
trastuzumab (Samsung Bioepis) + docetaxel	•	×	×	×	×
trastuzumab (Samsung Bioepis) + paclitaxel	•	×	×	×	×
ado-trastuzumab emtansine	0	0	0	0	(II)
pertuzumab + trastuzumab + docetaxel	0	0	0	0	×
lapatinib + capecitabine	0	0	×	0	×
lapatinib + trastuzumab	0	×	0	0	×
lapatinib + aromatase inhibitor	0	×	×	0	×
trastuzumab (Celltrion) + anastrozole	0	×	×	×	×

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

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Relevant Therapy Summary (continued)

In this cancer type	e O In other cancer	In this cancer type and	Contraindicated	А Во
	tvpe	other cancer types		CO

A Both for use and contraindicated

× No evidence

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
trastuzumab (Samsung Bioepis) + anastrozole	0	×	×	×	×
trastuzumab + anastrozole	0	×	×	×	×
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 + chemotherapy	×	0	0	0	×
lapatinib + letrozole	×	0	×	×	×
neratinib	×	0	×	×	×
trastuzumab containing regimen	×	×		×	×
trastuzumab + chemotherapy	×	×	0	0	(II)
pertuzumab + trastuzumab + paclitaxel	×	×	0	0	×
trastuzumab + hormone therapy + chemotherapy	×	×	0	0	×
trastuzumab + vinorelbine	×	×	0	0	×
pertuzumab + trastuzumab	×	×	0	×	(II)
pertuzumab + trastuzumab + capecitabine	×	×	0	×	×
pertuzumab + trastuzumab + nab-paclitaxel	×	×	0	×	×
pertuzumab + trastuzumab + vinorelbine	×	×	0	×	×
trastuzumab + hormone therapy	×	×	0	×	×

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

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Relevant Therapy Summary (continued)

In this cancer type O In other cancer type

In this cancer type and other cancer types

Contraindicated

A Both for use and contraindicated

No evidence

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
trastuzumab + taxane	×	×	0	×	×
trastuzumab + capecitabine	×	×	×	•	×
trastuzumab + capecitabine + oxaliplatin	×	×	×	•	×
trastuzumab + carboplatin + docetaxel + fluorouracil	×	×	×	•	×
trastuzumab + carboplatin + paclitaxel	×	×	×	•	×
trastuzumab + cisplatin + docetaxel	×	×	×	•	×
trastuzumab + cisplatin + docetaxel + fluorouracil	×	×	×	•	×
trastuzumab + cisplatin + paclitaxel	×	×	×	•	×
trastuzumab + docetaxel + fluorouracil + oxaliplatin	×	×	×	•	×
trastuzumab + fluorouracil	×	×	×	•	×
trastuzumab + fluorouracil + irinotecan	×	×	×	•	×
trastuzumab + fluorouracil + oxaliplatin	×	×	×	•	×
hormone therapy	×	×	×	0	×
lapatinib + trastuzumab + aromatase inhibitor	×	×	×	0	×
pertuzumab + trastuzumab + carboplatin + docetaxel	×	×	×	0	×
pertuzumab + trastuzumab + hormone therapy + chemotherapy	×	×	×	0	×
trastuzumab + aromatase inhibitor	×	×	×	0	×
trastuzumab + chemotherapy (other)	×	×	×	0	×
trastuzumab + cyclophosphamide + docetaxel	×	×	×	0	×
trastuzumab + fulvestrant	×	×	×	0	×
trastuzumab + tamoxifen	×	×	×	0	×
afatinib + chemotherapy	×	×	×	×	(II)
ibrutinib	×	×	×	×	(II)

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

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Relevant Therapy Summary (continued)

In this cancer type O In other cancer

type

In this cancer type and other cancer types

Contraindicated

A Both for use and contraindicated

X No evidence

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
ipilimumab + nivolumab + trastuzumab, nivolumab + trastuzumab + chemotherapy	×	×	×	×	(II)
lapatinib	×	×	×	×	(II)
olaparib + chemotherapy	×	×	×	×	(II)
pembrolizumab + chemotherapy	×	×	×	×	(II)
pembrolizumab + trastuzumab + chemotherapy	×	×	×	×	(II)
pertuzumab + trastuzumab + chemotherapy, trastuzumab + chemotherapy	×	×	×	×	(II)
poziotinib	×	×	×	×	(II)
trastuzumab (Celltrion) + chemotherapy	×	×	×	×	(II)
trastuzumab deruxtecan	×	×	×	×	(II)
CART-HER-2	×	×	×	×	(1/11)
margetuximab + pembrolizumab	×	×	×	×	(1/11)
MCLA-128	×	×	×	×	(1/11)
TAS0728	×	×	×	×	(1/11)
AdHER-2	×	×	×	×	(I)
aldesleukin, HER2Bi-armed activated T cells	×	×	×	×	(I)
ARX-788	×	×	×	×	(I)
atezolizumab + PRS-343	×	×	×	×	(I)
BAT-8001	×	×	×	×	(I)
BTRC-4017A	×	×	×	×	(I)
dacomitinib + gedatolisib	×	×	×	×	(I)
everolimus + neratinib, neratinib + palbociclib, neratinib + trametinib	×	×	×	×	(l)
everolimus + trastuzumab + letrozole	×	×	×	×	(I)

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

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Relevant Therapy Summary (continued)

In this cancer type O In other cancer

In this cancer type and other cancer types

Contraindicated

A Both for use and contraindicated

X No evidence

ERBB2 amplification (continued)

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
FATE-NK100 + trastuzumab	×	×	×	×	(I)
GBR 1302	×	×	×	×	(I)
MP-0274	×	×	×	×	(I)
pirotinib	×	×	×	×	(I)
PRS-343	×	×	×	×	(I)
pyrotinib	×	×	×	×	(I)
pyrotinib, pyrotinib + chemotherapy	×	×	×	×	(I)
RC-48	×	×	×	×	(I)
varlitinib + chemotherapy	×	×	×	×	(I)
ZW-25 + chemotherapy	×	×	×	×	(I)

TP53 p.(R175H) c.524G>A

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

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

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Relevant Therapy Details

Lead Clinical Scientist: Keeda Hardisty

Current EMA Information

In	this	cancer	type
Ш	uns	cancer	type

O 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

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), 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, 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

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ERBB2 amplification (continued)

O ado-trastuzumab emtansine

Lead Clinical Scientist: Keeda Hardisty

Label as of: 2018-09-19 Cancer type: Breast Cancer Variant class: ERBB2 overexpression or

ERBB2 amplification

Reference:

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

O lapatinib + aromatase inhibitor

Variant class: ERBB2 overexpression or Cancer type: Breast Cancer Label as of: 2018-09-07

ERBB2 amplification

Other criteria: ER positive, PR positive

Reference:

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

O 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

O 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

O pertuzumab + trastuzumab + docetaxel

Label as of: 2018-10-05 Cancer type: Breast Cancer Variant class: ERBB2 overexpression or

ERBB2 amplification

Reference:

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

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ERBB2 amplification (continued)

O 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

O 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

O 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

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Lead Clinical Scientist: Keeda Hardisty

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Date:

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Current FDA Information

In this cancer type	O In other cancer type	In this cancer type and	Contraindicated	Not recommended	U
		other cancer types			

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

ERBB2 amplification

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

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

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ERBB2 amplification (continued)

O ado-trastuzumab emtansine

Lead Clinical Scientist: Keeda Hardisty

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

O 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

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ERBB2 amplification (continued)

O 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

O 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

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ERBB2 amplification (continued)

O 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

O 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

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ERBB2 amplification (continued)

O 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

O trastuzumab, trastuzumab + carboplatin + docetaxel, trastuzumab + cyclophosphamide + docetaxel + doxorubicin, trastuzumab + cyclophosphamide + doxorubicin + paclitaxel

Label as of: 2018-10-17

ERBB2 overexpression

Variant class: ERBB2 amplification or

Other criteria: ER negative, PR negative

Indications and usage:

Cancer type: Breast Cancer

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

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Current ESMO Information

■ In this cancer type
O In other cancer type
O In this cancer type and O Contraindicated other cancer types
O Contraindicated other cancer types

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

ERBB2 amplification

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.]

O 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.]

O 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.]

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ERBB2 amplification (continued)

O trastuzumab + chemotherapy

Lead Clinical Scientist: Keeda Hardisty

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.]

O 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.]

O 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.]

O 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.]

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

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ERBB2 amplification (continued)

O ado-trastuzumab emtansine

Lead Clinical Scientist: Keeda Hardisty

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.]

O 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.]

O 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.]

O 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.]

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ERBB2 amplification (continued)

O 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.]

O 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.]

O 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.]

O 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.]

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ERBB2 amplification (continued)

O 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.]

O 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.]

O 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.]

O 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.]

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

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ERBB2 amplification (continued)

O 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.]

O 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.]

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Current NCCN Information

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

ERBB2 amplification

trastuzumab + 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 + cisplatin + fluorouracil

Cancer type: Esophageal Cancer Variant class: ERBB2 overexpression

NCCN Recommendation category: 1

Population segment (Line of therapy):

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

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

trastuzumab + 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]

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

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ERBB2 amplification (continued)

trastuzumab + capecitabine + oxaliplatin

Cancer type: Esophageal Cancer Variant class: ERBB2 overexpression

NCCN Recommendation category: 2B

Population segment (Line of therapy):

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

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

trastuzumab + 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 + 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 + 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]

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

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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]

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 + 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 + 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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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.

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Pre-Reg Clinical Scientist: Katherine Benton Date:

ERBB2 amplification (continued)

trastuzumab + fluorouracil

Lead Clinical Scientist: Keeda Hardisty

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: 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: 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 + 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]

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

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Lead Clinical Scientist: Keeda Hardisty Pre-Reg Clinical Scientist: Katherine Benton Date:

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ERBB2 amplification (continued)

O 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]

O 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]

O 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]

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ERBB2 amplification (continued)

O trastuzumab + chemotherapy

Lead Clinical Scientist: Keeda Hardisty

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]

O 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]

O 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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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.

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Pre-Reg Clinical Scientist: Katherine Benton Date: 29 of 64

ERBB2 amplification (continued)

O 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]

O 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]

O 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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Pre-Reg Clinical Scientist: Katherine Benton Date:

ERBB2 amplification (continued)

O ado-trastuzumab emtansine

Lead Clinical Scientist: Keeda Hardisty

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]

O 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]

O 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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ERBB2 amplification (continued)

O 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]

O 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]

O 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]

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

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Lead Clinical Scientist: Keeda Hardisty Pre-Reg Clinical Scientist: Katherine Benton Date:

ERBB2 amplification (continued)

O 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]

O 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]

O 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]

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ERBB2 amplification (continued)

O 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]

O 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]

O 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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ERBB2 amplification (continued)

O 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]

O 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]

O 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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Lead Clinical Scientist: Keeda Hardisty Pre-Reg Clinical Scientist: Katherine Benton Date:

ERBB2 amplification (continued)

O 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]

O 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]

O 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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ERBB2 amplification (continued)

O 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]

O 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]

O 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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ERBB2 amplification (continued)

O trastuzumab + fulvestrant

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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]

O 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]

O 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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ERBB2 amplification (continued)

O trastuzumab + paclitaxel

Lead Clinical Scientist: Keeda Hardisty

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]

O 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]

O 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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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.

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Pre-Reg Clinical Scientist: Katherine Benton Date: 39 of 64

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ERBB2 amplification (continued)

O trastuzumab + capecitabine

Lead Clinical Scientist: Keeda Hardisty

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]

O 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]

O 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]

O 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]

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ERBB2 amplification (continued)

O 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]

O 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]

O 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]

O 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]

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ERBB2 amplification (continued)

O 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]

O 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]

O 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]

O 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]

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Lead Clinical Scientist: Keeda Hardisty Pre-Reg Clinical Scientist: Katherine Benton Date:

ERBB2 amplification (continued)

O 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]

O 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]

O 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]

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Lead Clinical Scientist: Keeda Hardisty Pre-Reg Clinical Scientist: Katherine Benton Date: 43 of 64

ERBB2 amplification (continued)

O 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]

O 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]

O 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]

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]

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

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Lead Clinical Scientist: Keeda Hardisty

Pre-Reg Clinical Scientist: Katherine Benton

Date:

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ERBB2 amplification (continued)

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 + 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 + 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]

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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Lead Clinical Scientist: Keeda Hardisty

Pre-Reg Clinical Scientist: Katherine Benton

Date:

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ERBB2 amplification (continued)

📭 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]

👎 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: Gastric Cancer Variant class: ERBB2 overexpression

Summary:

 $\label{eq:nccn} \textbf{NCCN Guidelines} \textbf{@ include the following supporting statement} (\textbf{s}) :$

"Trastuzumab is not recommended for use with anthracyclines"

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

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ERBB2 amplification (continued)

trastuzumab + cyclophosphamide + docetaxel + doxorubicin

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

Summary:

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

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

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

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]

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Current Clinical Trials Information

Lead Clinical Scientist: Keeda Hardisty

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

NCT01522768

A Phase II Study of Afatinib and Paclitaxel in Patients With Advanced HER2-Positive Trastuzumab Refractory Advanced Esophagogastric Cancer

Cancer type: Esophageal Cancer

Variant class: ERBB2 amplification or

ERBB2 overexpression

Other identifiers: 11-166, 3G-15-6, NCI-2012-00414

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

line

Phase: II

Therapy: afatinib + chemotherapy

Location: United States

US States: CA, MA, NJ, NY

US Contact: Dr. Yelena Janjigian [646-888-4186]

NCT02884453

Proof-of-concept study of ibrutinib in c-MYC and HER2 amplified gastrooesophageal carcinoma

Cancer type: Esophageal Cancer

Variant class: ERBB2 amplification

Other identifiers: 4449, CCR4449, EudraCT Number: 2015-005525-39, iMYC

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

Phase: II

Therapy: ibrutinib

Location: United Kingdom

NCT03409848

Ipilimumab or FOLFOX in Combination With Nivolumab and Trastuzumab in Previously Untreated HER2 Positive Locally Advanced or Metastatic EsophagoGastric Adenocarcinoma

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

Other identifiers: AIO-STO-0217, EudraCT Number:2017-000624-10, INTEGA

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

Phase: II

Therapies: ipilimumab + nivolumab + trastuzumab, nivolumab + trastuzumab +

chemotherapy

Location: Germany

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ERBB2 amplification (continued)

NCT02954536

Phase II Trial of Pembrolizumab in Combination With Trastuzumab, Fluoropyrimidine, and Platinum Chemotherapy in First Line Stage IV HER2-positive Metastatic Esophagogastric (EG) Cancer

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression or

ERBB2 amplification

Other identifiers: 16-937, NCI-2016-01716

Population segments: First line, HER2 positive, Stage IV

Phase: II

Therapy: pembrolizumab + trastuzumab + chemotherapy

Location: United States

US States: NJ, NY

US Contact: Dr. Yelena Janjigian [646-888-4186]

NCT02205047

Integration of Trastuzumab, With or Without Pertuzumab, Into perioperative chemotherApy of HER-2 Positive stomach cancer: the INNOVATION-TRIAL

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

Other identifiers: 1203-GITCG, EORTC-1203, EORTC-1203-GITCG, EudraCT Number:

2014-000722-38, INNOVATION, IRAS ID: 177557, MO28922

Population segments: HER2 positive, Neoadjuvant, Stage II, Stage III

Phase: II

Therapies: pertuzumab + trastuzumab + chemotherapy, trastuzumab + chemotherapy

Locations: Belgium, Estonia, France, Germany, Israel, Italy, Norway, Portugal, Republic of

Korea, Spain, Switzerland, United Kingdom

NCT02678182

PLATFORM: Planning treatment of oesophago-gastric (OG) cancer#A randomised maintenance therapy trial.

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

Other identifiers: 3804, EudraCT Number: 2014-002169-30, PLATFORM

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

Phase: II

Therapy: trastuzumab

Location: United Kingdom

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

Lead Clinical Scientist: Keeda Hardisty Pre-Reg Clinical Scientist: Katherine Benton Date:

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ERBB2 amplification (continued)

NCT03588533

Safety and Efficacy Evaluation of Capecitabine, Cisplatin, and Herzuma Combination Chemotherapy for the First Line Treatment of Advanced Gastric or Gastroesophageal Junction Adenocarcinoma Patients.

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression or

ERBB2 amplification

Other identifiers: DAUHIRB-18-121, HERZUMA-GC

Population segments: First line, HER2 positive, Stage IV

Phase: II

Therapy: trastuzumab (Celltrion) + chemotherapy

Location: Republic of Korea

No NCT ID - see other identifier(s)

A randomized phase II study of systemic chemotherapy with and without trastuzumab followed by surgery in HER2 positive advanced gastric or esophagogastric junction adenocarcinoma with extensive lymph node metastasis (JCOG1301:Trigger

Study)

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

Other identifiers: JCOG1301, JCOG1301C, Trigger Study, UMIN000016920

Population segments: Adjuvant, Neoadjuvant, Other mets, Stage III, Stage IV

Phase: II

Therapy: trastuzumab + chemotherapy

Location: Japan

NCT02250209

Trastuzumab Plus XELOX for HER2positive Stage III Gastric Cancer After D2 Gastrectomy:Prospective Observational Study.

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

Other identifier: CGOG20130101005

Population segments: Adjuvant, HER2 positive, Stage III

Phase: II

Therapy: trastuzumab + chemotherapy

Location: China

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ERBB2 amplification (continued)

NCT02725424

A Randomized, Multicenter, Controlled Phase II Study to Compare Preoperative Chemotherapy of SOX Versus SOXT or DOS in Locally Advanced Gastric/ Gastroesophageal Cancer

Cancer type: Esophageal Cancer

Variant class: ERBB2 amplification or

ERBB2 overexpression

Other identifiers: CH-GI-071, MATCH

Population segments: Adjuvant, Neoadjuvant, Second line, Stage III

Phase: II

Therapy: trastuzumab + chemotherapy

Location: China

No NCT ID - see other identifier(s)

A Randomised, double-blind, placebo controlled, multi-centre phase II study to assess the Efficacy and safety of 2nd line Olaparib in combination with Paclitaxel, in Western patients with advanced gastric and gastro-oesophageal junction cancer

Cancer type: Esophageal Cancer

Variant class: ERBB2 positive

Other identifiers: CCR4309, EudraCT Number: 2015-001605-14, OPERa

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

Phase: II

Therapy: olaparib + chemotherapy

Location: United Kingdom

NCT03342937

A Single Arm, Phase II Study of Pembrolizumab, Oxaliplatin, and Capecitabine in the First Line Treatment of Patients With Gastro-esophageal

Cancer.

Cancer type: Esophageal Cancer

Variant class: ERBB2 positive

Other identifiers: KeyLargo, NCI-2018-00083, Pro00080566

Population segments: First line, Stage IV

Phase: II

Therapy: pembrolizumab + chemotherapy

Location: United States

US State: NC

US Contact: Taylor Kennedy Frenchi [919-668-1861; taylor.kennedy.frenchi@duke.edu]

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

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ERBB2 amplification (continued)

NCT02213289

PANGEA-IMBBP: Personalized Antibodies for Gastro-Esophageal Adenocarcinoma - A 1st Pilot Metastatic Trial of Biologics Beyond Progression

Cancer type: Esophageal Cancer Variant class: ERBB2 positive Other identifiers: IRB14-0141, NCI-2014-02415, PANGEA-IMBBP

Population segments: First line, HER2 positive, Stage IV

Phase: II

Therapy: trastuzumab + chemotherapy

Location: United States

US State: IL

US Contact: Dr. Daniel Catenacci [dcatenac@bsd.uchicago.edu]

NCT03329690

A Phase II, Multicenter, Open-label Study of DS-8201a in Subjects With HER2-expressing Advanced Gastric or Gastroesophageal Junction Adenocarcinoma

Cancer type: Esophageal Cancer

Variant class: ERBB2 positive

Other identifiers: DESTINY-Gastric01, DS8201-A-J202, JapicCTI-173727

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

Phase: II

Therapy: trastuzumab deruxtecan

Locations: Japan, Republic of Korea

NCT03292250

Public-interest Multicenter Umbrella Trial Based on Genetic Analysis in Korean Head and Neck Cancer and Esophageal Cancer Patient - Part 1 (HNSCC)] A Biomarker-driven, Open Label, Single Arm, Multicentre Phase II Study of Abemaciclib in Patients With Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma Who Failed to Platinumbased Therapy

Cancer type: Esophageal Cancer Variant class: ERBB aberration Other identifiers: 13Y-MC-E011, KCSG-TRIUMPH

Population segments: Second line, Stage IV

Phase: II

Therapy: poziotinib

Location: Republic of Korea

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

Lead Clinical Scientist: Keeda Hardisty Pre-I

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ERBB2 amplification (continued)

NCT02689284

A Phase Ib/II, Open Label, Dose Escalation Study of Margetuximab in Combination With Pembrolizumab in Patients With Relapsed/Refractory Advanced HER2+ Gastroesophageal Junction or Gastric Cancer

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression or

ERBB2 amplification

Other identifiers: 1510016618, 16-258, CP-MGAH22-05, NCI-2016-00290

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

Phase: I/II

Therapy: margetuximab + pembrolizumab

Locations: Canada, Republic of Korea, Singapore, Taiwan, United States

US States: CT, DC, IL, MA, MD, MI, MO, NC, PA, TN, WA

US Contact: Alice Drumheller [drumhellera@MacroGenics.com]

NCT02912949

A Phase I/II Study of MCLA-128, a Full Length IgG1 Bispecific Antibody Targeting HER2 and HER3, in Patients With Solid Tumors

Cancer type: Esophageal Cancer

Variant class: ERBB2 amplification

Other identifiers: EudraCT Number: 2014-003277-42, MCLA-128-CL01, NL51045.031.14

Population segments: Adenocarcinoma, ALK, EGFR, Estrogen receptor positive, Fourth line or greater, HER2 positive, Large Cell, Second line, Squamous Cell, Stage III, Stage IV, Third line

Phase: I/II

Therapy: MCLA-128

Locations: France, Italy, Netherlands, Spain

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: Esophageal 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]

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

Lead Clinical Scientist: Keeda Hardisty Pre-Reg Clinical Scientist: Katherine Benton

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ERBB2 amplification (continued)

NCT02662348

T Cell Mediated Adaptive Therapy for Her2-positive Neoplasms of Digestive

System

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression

Other identifier: 2013-SR-116.F1

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

Phase: I

Therapies: aldesleukin, HER2Bi-armed activated T cells

Location: China

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: Esophageal Cancer

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]

No NCT ID - see other identifier(s)

A Phase I Open Single-center Dose

A Phase I, Open, Single-center Dose Escalation To Evaluate Safety, Tolerability and Pharmacokinetic Characteristics of BAT8001 Injection In Patients With HER2

Positive Solid Tumors.

Cancer type: Esophageal Cancer

Variant class: ERBB2 overexpression or

ERBB2 amplification

Other identifiers: BAT-8001-001-CR, CTR20170072

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

III, Stage IV

Phase: I

Therapy: BAT-8001

Location: China

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

Cancer type: Esophageal Cancer

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

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

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

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Lead Clinical Scientist: Keeda Hardisty Pre-Reg Clinical Scientist: Katherine Benton

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ERBB2 amplification (continued)

NCT02892123

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

Cancer type: Esophageal Cancer

Variant class: ERBB2 amplification or

ERBB2 overexpression

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 + chemotherapy

Locations: Canada, United States

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

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

NCT03650348

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

Cancer type: Esophageal Cancer

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]

NCT01920061

A Phase Ib Open-label Three-arm Multicenter Study To Assess The Safety And Tolerability Of Pf-05212384 (pi3k/Mtor Inhibitor) In Combination With Other Antitumor Agents

Cancer type: Esophageal Cancer

Variant class: ERBB2 positive

Other identifiers: 101938, 13-382, 133229, B2151002, EudraCT Number: 2013-001390-24, NCI-2013-01814, P1TB21502, Pro00027912

Population segments: EGFR, First line, HER2 negative, HER2 positive, Hormone refractory, Second line or greater/Refractory/Relapsed, Stage III, Stage IV, Triple receptor negative

Phase: I

Therapy: dacomitinib + gedatolisib

Locations: Italy, Spain, United Kingdom, United States

US States: AL, CA, MA, MI, SC

US Contact: Pfizer CT.gov Call Center [800-718-1021;

ClinicalTrials.gov_Inquiries@pfizer.com]

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

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ERBB2 amplification (continued)

NCT02378389

A Phase I Study of Pyrotinib In Combination with Docetaxel In Patients with HER2 Positive Advanced Gastric Cancer

Cancer type: Esophageal Cancer

Variant class: ERBB2 positive

Other identifiers: BLTN-Id, CTR20150178

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

Phase: I

Therapies: pyrotinib, pyrotinib + chemotherapy

Location: China

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

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

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ERBB2 amplification (continued)

NCT02465060

Molecular Analysis for Therapy Choice (MATCH)

Cancer type: Unspecified Solid Tumor Variant class: ERBB2 amplification 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

Other identifiers: 15-7002, CTSU/EAY131, EAY131, EAY131-A, EAY131-B, EAY131-C1,

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]

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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

NCT01935843

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

Cancer type: Unspecified Solid Tumor

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

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

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ERBB2 amplification (continued)

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]

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]

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

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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]

NCT02500199

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

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 overexpression or

ERBB2 amplification

Other identifiers: NCI-2017-00491, SHRUS 1001

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

III, Stage IV

Phase: I

Therapy: pyrotinib

Location: United States

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

US Contact: Dr. Ewa Matczak [609-423-2155 ext 215;

ewa.matczak@hengruitherapeutics.com]

NCT02881138

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

Malignant Solid Tumors.

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 overexpression

Other identifiers: C001 CANCER, CTR20150876

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

Phase: I

Therapy: RC-48

Location: China

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

Lead Clinical Scientist: Keeda Hardisty

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ERBB2 amplification (continued)

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

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

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]

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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 HER2positive Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 positive

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

Date:

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

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

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TP53 p.(R175H) c.524G>A

NCT03096054

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

Cancer type: Esophageal 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

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

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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	1
➡ ERBB2 status	0
► ERBB2 aberration	3
➡ ERBB2 positive	27
► ERBB2 amplification	80
ERBB aberration	1
➡ ERBB2 status	0
► ERBB2 aberration	3
➡ ERBB2 positive	27
► ERBB2 overexpression	124

TP53 p.(R175H) c.524G>A

Variant Class	Evidence Items
TP53 aberration	0
→ TP53 mutation	3

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Variant Details

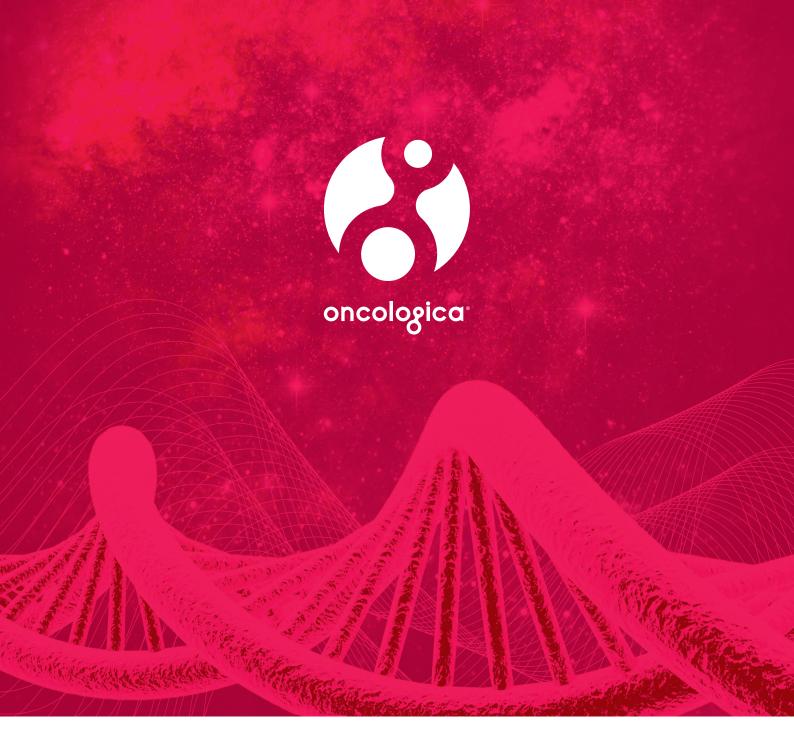
DNA Sequence Variants

				Allele				
Gene	Amino Acid Change	Coding	Variant ID	Frequency	Transcript	Variant Effect	Gene Class	Variant Class
TP53	p.(R175H)	c.524G>A	COSM10648	54.28%	NM_000546.5	missense	Loss of Function	Hotspot

Copy Number Variations		
Gene	Locus	Copy Number
ERBB2	chr17:37868168	73.02

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Report Authorised by	Report reviewed by	
Signed Renth	Signed	ly —
printed Katherine Benton	printed Keeda Hardist	ty
Adams a		
Pre-Reg Clinical Scientist Pathologist BMS [Senior]	BMS Clinical Scientist	





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Immunofocus®

PD-1/PD-L1 TESTING



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Date: 1 of 2

Surname
Forename DOB
Gender
Histology #
Primary site
Tumour subtype

Tissue Type

Esophagus Adenocarcinoma Esophageal Biopsy Requester Contact details Date requested

Tumour % 90%
Tumour % (macrodissected)

PD-L1 test

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

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

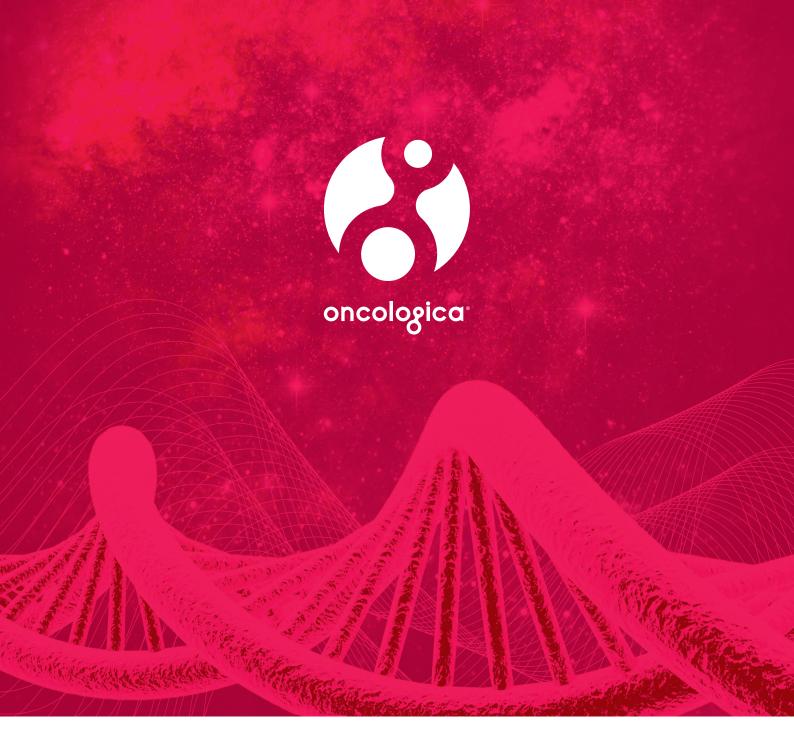
The Oncologica® Immunofocus PD-L1 immunocytochemistry assay is a Laboratory Developed Test utilising the RUO rabbit monoclonal antibody clone E1L3N (Cell Signalling Technologies) and Leica Bond III instrumentation. The performance of the Immunofocus assay is continually assessed by involvement in recognised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

PD-L1 Result

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

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

Report Authorised by	/	Report reviewed by		
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Printed		Printed		
Professor Gareth Wil	liams	Katherine Benton		
Clinical Scientist		Clinical S	cientist	\checkmark
Pathologist	\square	Pathologi	st	
BMS (Senior)		BMS (Ser	nior)	





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