[Oncofocus] Patient Test Report

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Surname		**Requesting clinician**	
Forename			
DOB		**Date requested**	
Gender			
Histology #		**Tumour %**	
Primary site	Pancreas	**Tumour % (macrodissected)**	30
Tumour subtype	Adenocarcinoma		
Tissue type	Pancreas		

Comment:

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

221 genes were targeted with 2530 unique amplicons covering oncogenes, fusion genes, genes susceptible to copy number variation and tumour suppressors. Actionable genetic variants detected by Oncofocus are linked to 485 anti-cancer targeted therapies.

The following actionable variants were detected:

Variant Summary

Sample Cancer Type: Pancreatic Cancer

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

Gene Variant	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials
ERBB2 amplification	○ (12)	○ (5)	○ (6)	○ (17)	● (13)
KRAS p.(G12V) c.35G>T	⊘ (3)	⊘ (2)	⊘ (4)	⊘ (3)	● (13)
TP53 p.(G245V) c.734G>T	✖	✖	✖	✖	● (5)

EMA: European Medicine Agency, **US-FDA:** United States-Food and Drug Administration, **ESMO:** European Society for Medical Oncology, **US-NCCN:** United States-National Comprehensive Cancer Network. Numbers in parentheses indicate the number of relevant therapies with evidence. Hotspot variants with >10% alternate allele reads, and in >10 unique reads are classified as 'detected' with an assay sensitivity and positive predictive value of 92%. Copy number variants; amplifications of a >5% confidence value of ≥4 after normalization and deletions of ≤1 are classified as present when the tumour% >50%. Gene Fusions are reported when occurring in >20 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.

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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Relevant Therapy Summary

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

ERBB2 amplification

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
ado-trastuzumab emtansine	○	○	○	○	● (II)
lapatinib + capecitabine	○	○	✖	○	✖
pertuzumab + trastuzumab + docetaxel	○	○	✖	○	✖
trastuzumab	○	○	✖	✖	✖
lapatinib + trastuzumab	○	✖	○	○	✖
trastuzumab + capecitabine	○	✖	✖	○	✖
trastuzumab + docetaxel	○	✖	✖	○	✖
trastuzumab + paclitaxel	○	✖	✖	○	✖
lapatinib + aromatase inhibitor	○	✖	✖	✖	✖
trastuzumab + aromatase inhibitor	○	✖	✖	✖	✖
trastuzumab + carboplatin + docetaxel	○	✖	✖	✖	✖
trastuzumab + cisplatin + fluorouracil	○	✖	✖	✖	✖
lapatinib + letrozole	✖	○	✖	✖	✖
trastuzumab + chemotherapy	✖	✖	○	○	● (II)
pertuzumab + trastuzumab + chemotherapy	✖	✖	○	○	✖
trastuzumab + hormone therapy + chemotherapy	✖	✖	○	○	✖
pertuzumab	✖	✖	○	✖	✖
hormone therapy	✖	✖	✖	○	✖
pertuzumab + trastuzumab + paclitaxel	✖	✖	✖	○	✖
trastuzumab + carboplatin + paclitaxel	✖	✖	✖	○	✖
trastuzumab + chemotherapy (other)	✖	✖	✖	○	✖
trastuzumab + cisplatin + fluoropyrimidine	✖	✖	✖	○	✖

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available. See global clinical trials section in the pages to follow.

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

Relevant Therapy Summary (continued)

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

ERBB2 amplification (continued)

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
trastuzumab + hormone therapy	✖	✖	✖	○	✖
trastuzumab + vinorelbine	✖	✖	✖	○	✖
lapatinib	✖	✖	✖	✖	● (II)
pertuzumab + trastuzumab	✖	✖	✖	✖	● (II)
CART-HER-2	✖	✖	✖	✖	● (I/II)
selumetinib + vistusertib	✖	✖	✖	✖	● (I/II)
everolimus + trastuzumab + letrozole	✖	✖	✖	✖	● (I)
MSC-2363318A	✖	✖	✖	✖	● (I)
neratinib + pertuzumab + trastuzumab + chemotherapy	✖	✖	✖	✖	● (I)
pirotinib	✖	✖	✖	✖	● (I)
pyrotinib	✖	✖	✖	✖	● (I)
RC-48	✖	✖	✖	✖	● (I)
varlitinib + chemotherapy	✖	✖	✖	✖	● (I)

KRAS p.(G12V) c.35G>T

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
cetuximab	⊘	⊘	⊘	⊘	✖
cetuximab + oxaliplatin	⊘	✖	✖	✖	✖
panitumumab + oxaliplatin	⊘	✖	✖	✖	✖
panitumumab	✖	⊘	⊘	⊘	✖

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available. See global clinical trials section in the pages to follow.

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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Relevant Therapy Summary (continued)

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

KRAS p.(G12V) c.35G>T (continued)

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
cetuximab + chemotherapy	✖	✖	⊘	✖	✖
panitumumab + chemotherapy	✖	✖	⊘	✖	✖
tyrosine kinase inhibitors	✖	✖	✖	⊘	✖
MK-1775 + olaparib	✖	✖	✖	✖	● (II)
sorafenib	✖	✖	✖	✖	● (II)
sorafenib + chemotherapy	✖	✖	✖	✖	● (II)
afatinib + selumetinib	✖	✖	✖	✖	● (I/II)
BAL-3833	✖	✖	✖	✖	● (I/II)
dacomitinib + PD-0325901	✖	✖	✖	✖	● (I/II)
lapatinib + trametinib	✖	✖	✖	✖	● (I/II)
LNP3794	✖	✖	✖	✖	● (I/II)
palbociclib + PD-0325901	✖	✖	✖	✖	● (I/II)
selumetinib + vistusertib	✖	✖	✖	✖	● (I/II)
LXH254	✖	✖	✖	✖	● (I)
RO-5126766	✖	✖	✖	✖	● (I)
trametinib + radiation therapy, trametinib + surgical intervention	✖	✖	✖	✖	● (I)

TP53 p.(G245V) c.734G>T

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
MK-1775 + olaparib	✖	✖	✖	✖	● (II)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available. See global clinical trials section in the pages to follow.

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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Relevant Therapy Summary (continued)

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

TP53 p.(G245V) c.734G>T (continued)

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
ixazomib + vorinostat	✖	✖	✖	✖	● (I)
MK-1775	✖	✖	✖	✖	● (I)
pembrolizumab + p53MVA	✖	✖	✖	✖	● (I)
SGT-53, SGT-53 + chemotherapy	✖	✖	✖	✖	● (I)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available. See global clinical trials section in the pages to follow.

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

Current EMA Information

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

EMA information is current as of 2016-10-03. For the most up-to-date information, search www.ema.europa.eu/ema.

ERBB2 amplification

○ ado-trastuzumab emtansine

Cancer type: Breast Cancer **Label as of:** 2016-05-19 **Variant class:** ERBB2 amplification

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002389/WC500158593.pdf

○ ado-trastuzumab emtansine

Cancer type: Breast Cancer **Label as of:** 2016-05-19 **Variant class:** ERBB2 overexpression

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002389/WC500158593.pdf

○ lapatinib + aromatase inhibitor

Cancer type: Breast Cancer **Label as of:** 2015-08-11 **Variant class:** ERBB2 amplification

Other criteria: ER positive, PR positive

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000795/WC500044957.pdf

○ lapatinib + aromatase inhibitor

Cancer type: Breast Cancer **Label as of:** 2015-08-11 **Variant class:** ERBB2 overexpression

Other criteria: ER positive, PR positive

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000795/WC500044957.pdf

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

ERBB2 amplification (continued)

lapatinib + capecitabine

Cancer type: Breast Cancer **Label as of:** 2015-08-11 **Variant class:** ERBB2 amplification

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000795/WC500044957.pdf

lapatinib + capecitabine

Cancer type: Breast Cancer **Label as of:** 2015-08-11 **Variant class:** ERBB2 overexpression

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000795/WC500044957.pdf

lapatinib + trastuzumab

Cancer type: Breast Cancer **Label as of:** 2015-08-11 **Variant class:** ERBB2 amplification

Other criteria: ER negative, PR negative

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000795/WC500044957.pdf

lapatinib + trastuzumab

Cancer type: Breast Cancer **Label as of:** 2015-08-11 **Variant class:** ERBB2 overexpression

Other criteria: ER negative, PR negative

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000795/WC500044957.pdf

pertuzumab + trastuzumab + docetaxel

Cancer type: Breast Cancer **Label as of:** 2016-05-19 **Variant class:** ERBB2 amplification

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002547/WC500140980.pdf

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

ERBB2 amplification (continued)

pertuzumab + trastuzumab + docetaxel

Cancer type: Breast Cancer **Label as of:** 2016-05-19 **Variant class:** ERBB2 overexpression

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002547/WC500140980.pdf

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

Cancer type: Breast Cancer, Esophageal Cancer, Gastric Cancer **Label as of:** 2016-10-12 **Variant class:** ERBB2 amplification

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000278/WC500074922.pdf

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

Cancer type: Breast Cancer, Esophageal Cancer, Gastric Cancer **Label as of:** 2016-10-12 **Variant class:** ERBB2 overexpression

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000278/WC500074922.pdf

KRAS p.(G12V) c.35G>T

cetuximab, cetuximab + oxaliplatin

Cancer type: Colorectal Cancer **Label as of:** 2015-02-03 **Variant class:** KRAS exon 2 mutation

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000558/WC500029119.pdf

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

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KRAS p.(G12V) c.35G>T (continued)

⊘ panitumumab + oxaliplatin

Cancer type: Colorectal Cancer **Label as of:** 2016-04-15 **Variant class:** KRAS exon 2 mutation

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000741/WC500047710.pdf

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

Current US-FDA Information

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

US-FDA information is current as of 2016-10-03. For the most up-to-date information, search www.fda.gov.

ERBB2 amplification

○ ado-trastuzumab emtansine

Cancer type: Breast Cancer **Label as of:** 2016-07-25 **Variant class:** 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:

http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/125427s096lbl.pdf

○ ado-trastuzumab emtansine

Cancer type: Breast Cancer **Label as of:** 2016-07-25 **Variant class:** ERBB2 overexpression

Indications and usage:

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

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

Reference:

http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/125427s096lbl.pdf

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

ERBB2 amplification (continued)

lapatinib + capecitabine

Cancer type: Breast Cancer **Label as of:** 2015-03-31 **Variant class:** ERBB2 overexpression

Indications and usage:

TYKERB®, a kinase inhibitor, is 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:

http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/022059s020lbl.pdf

lapatinib + letrozole

Cancer type: Breast Cancer **Label as of:** 2015-03-31 **Variant class:** ERBB2 overexpression

Other criteria: ER positive, PR positive

Indications and usage:

TYKERB®, a kinase inhibitor, is 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:

http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/022059s020lbl.pdf

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

ERBB2 amplification (continued)

pertuzumab + trastuzumab + docetaxel

Cancer type: Breast Cancer **Label as of:** 2016-03-22 **Variant class:** ERBB2 amplification

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 docetaxel 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. This indication is based on demonstration of an improvement in pathological complete response rate. No data are available demonstrating improvement in event-free survival or overall survival.

Limitations of Use:

- The safety of PERJETA® as part of a doxorubicin-containing regimen has not been established.
- The safety of PERJETA® administered for greater than 6 cycles for early breast cancer has not been established.

Reference:

http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/125409s109lbl.pdf

pertuzumab + trastuzumab + docetaxel

Cancer type: Breast Cancer **Label as of:** 2016-03-22 **Variant class:** 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 docetaxel 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. This indication is based on demonstration of an improvement in pathological complete response rate. No data are available demonstrating improvement in event-free survival or overall survival.

Limitations of Use:

- The safety of PERJETA® as part of a doxorubicin-containing regimen has not been established.
- The safety of PERJETA® administered for greater than 6 cycles for early breast cancer has not been established.

Reference:

http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/125409s109lbl.pdf

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

ERBB2 amplification (continued)

trastuzumab

Cancer type: Breast Cancer, Esophageal Cancer, Gastric Cancer **Label as of:** 2016-03-17 **Variant class:** ERBB2 amplification

Indications and usage:

Herceptin is a HER2/neu receptor antagonist indicated for:

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

Reference:

http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/103792s5330lbl.pdf

trastuzumab

Cancer type: Breast Cancer, Esophageal Cancer, Gastric Cancer **Label as of:** 2016-03-17 **Variant class:** 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.

Reference:

http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/103792s5330lbl.pdf

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

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KRAS p.(G12V) c.35G>T

⊘ cetuximab

Cancer type: Colorectal Cancer **Label as of:** 2015-04-10 **Variant class:** KRAS G12 mutation

Indications and usage:

Erbitux® is an epidermal growth factor receptor (EGFR) antagonist indicated for treatment of:

Head and Neck Cancer

- Locally or regionally advanced squamous cell carcinoma of the head and neck in combination with radiation therapy.
- Recurrent locoregional disease or metastatic squamous cell carcinoma of the head and neck in combination with platinum-based therapy with 5-FU.
- Recurrent or metastatic squamous cell carcinoma of the head and neck progressing after platinum-based therapy.

Colorectal Cancer

K-Ras wild-type, EGFR-expressing, metastatic colorectal cancer as determined by FDA-approved tests

- in combination with FOLFIRI for first-line treatment,
- in combination with irinotecan in patients who are refractory to irinotecan-based chemotherapy,
- as a single agent in patients who have failed oxaliplatin- and irinotecan-based chemotherapy or who are intolerant to irinotecan.

Limitation of Use: Erbitux® is not indicated for treatment of *Ras*-mutant colorectal cancer.

Reference:

http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/125084s262lbl.pdf

⊘ panitumumab

Cancer type: Colorectal Cancer **Label as of:** 2015-03-11 **Variant class:** KRAS G12 mutation

Indications and usage:

Vectibix® is an epidermal growth factor receptor (EGFR) antagonist indicated for the treatment of wild-type KRAS (exon 2) metastatic colorectal cancer (mCRC) as determined by an FDA-approved test for this use:

- In combination with FOLFOX for first-line treatment.
- As monotherapy following disease progression after prior treatment with fluoropyrimidine, oxaliplatin, and irinotecan-containing chemotherapy.

Limitation of Use: Vectibix® is not indicated for the treatment of patients with *RAS*-mutant mCRC or for whom *RAS* mutation status is unknown.

Reference:

http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/125147s200lbl.pdf

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Current ESMO Information

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

ESMO information is current as of 2016-09-07. For the most up-to-date information, search www.esmo.org.

ERBB2 amplification

○ trastuzumab + chemotherapy

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

ESMO Recommendation category: I, A

Population segment (Line of therapy):
- Primary breast cancer (Not specified)

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

○ trastuzumab + hormone therapy + chemotherapy

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

Other criteria: ER positive

ESMO Recommendation category: I, A

Population segment (Line of therapy):
- Not specified

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

○ trastuzumab + chemotherapy

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

Other criteria: ER negative

ESMO Recommendation category: IV, B

Population segment (Line of therapy):
- Not specified

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

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

ERBB2 amplification (continued)

ado-trastuzumab emtansine

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

ESMO Recommendation category: I, A

Population segment (Line of therapy):
- Progression after trastuzumab based therapy (Second-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESO-ESMO Advanced Breast Cancer [Ann Oncol (2014) doi: 10.1093/annonc/mdu385 and The Breast 2014, doi: 10.1016/j.breast.2014.08.009.]

pertuzumab + trastuzumab + chemotherapy

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

ESMO Recommendation category: I, A

Population segment (Line of therapy):
- Previously untreated metastatic breast cancer (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESO-ESMO Advanced Breast Cancer [Ann Oncol (2014) doi: 10.1093/annonc/mdu385 and The Breast 2014, doi: 10.1016/j.breast.2014.08.009.]

trastuzumab + chemotherapy

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

ESMO Recommendation category: I, A

Population segment (Line of therapy):
- Metastatic breast cancer previously treated in the adjuvant setting (First-line therapy)
- Metastatic breast cancer untreated with trastuzumab (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESO-ESMO Advanced Breast Cancer [Ann Oncol (2014) doi: 10.1093/annonc/mdu385 and The Breast 2014, doi: 10.1016/j.breast.2014.08.009.]

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

ERBB2 amplification (continued)

lapatinib + trastuzumab

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

ESMO Recommendation category: I, B

Population segment (Line of therapy):
- Progression on trastuzumab (Not specified)

Reference: ESMO Clinical Practice Guidelines - ESO-ESMO Advanced Breast Cancer [Ann Oncol (2014) doi: 10.1093/annonc/mdu385 and The Breast 2014, doi: 10.1016/j.breast.2014.08.009.]

pertuzumab

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

ESMO Recommendation category: II, C

Population segment (Line of therapy):
- Metastatic breast cancer previously untreated with pertuzumab (After first-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESO-ESMO Advanced Breast Cancer [Ann Oncol (2014) doi: 10.1093/annonc/mdu385 and The Breast 2014, doi: 10.1016/j.breast.2014.08.009.]

KRAS p.(G12V) c.35G>T

cetuximab

Cancer type: Colorectal Cancer **Variant class:** KRAS exon 2 mutation

ESMO Recommendation category: II, A

Population segment (Line of therapy):
- Metastatic colorectal cancer (All treatment lines)

Reference: ESMO Clinical Practice Guidelines - Metastatic Colorectal Cancer [Ann Oncol (2014) 25 (suppl 3): iii1-iii9.]

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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KRAS p.(G12V) c.35G>T (continued)

cetuximab + chemotherapy

Cancer type: Colorectal Cancer **Variant class:** KRAS exon 2 mutation

ESMO Recommendation category: II, A

Population segment (Line of therapy):
- Metastatic colorectal cancer (All treatment lines)

Reference: ESMO Clinical Practice Guidelines - Metastatic Colorectal Cancer [Ann Oncol (2014) 25 (suppl 3): iii1-iii9.]

panitumumab

Cancer type: Colorectal Cancer **Variant class:** KRAS exon 2 mutation

ESMO Recommendation category: II, A

Population segment (Line of therapy):
- Metastatic colorectal cancer (All treatment lines)

Reference: ESMO Clinical Practice Guidelines - Metastatic Colorectal Cancer [Ann Oncol (2014) 25 (suppl 3): iii1-iii9.]

panitumumab + chemotherapy

Cancer type: Colorectal Cancer **Variant class:** KRAS exon 2 mutation

ESMO Recommendation category: II, A

Population segment (Line of therapy):
- Metastatic colorectal cancer (All treatment lines)

Reference: ESMO Clinical Practice Guidelines - Metastatic Colorectal Cancer [Ann Oncol (2014) 25 (suppl 3): iii1-iii9.]

cetuximab

Cancer type: Colorectal Cancer **Variant class:** KRAS mutation

ESMO Recommendation category: II, A

Population segment (Line of therapy):
- Metastatic disease (Not specified)

Reference: ESMO Clinical Practice Guidelines - Rectal Cancer [Ann Oncol 2013; 24 (Suppl 6): vi81-vi88.]

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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KRAS p.(G12V) c.35G>T (continued)

⊘ panitumumab

Cancer type: Colorectal Cancer **Variant class:** KRAS mutation

ESMO Recommendation category: II, A

Population segment (Line of therapy):
- Metastatic disease (Not specified)

Reference: ESMO Clinical Practice Guidelines - Rectal Cancer [Ann Oncol 2013; 24 (Suppl 6): vi81-vi88.]

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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Current US-NCCN Information

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

US-NCCN information is current as of 2016-09-07. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

ERBB2 amplification

○ pertuzumab + trastuzumab + docetaxel

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

US-NCCN Recommendation category: 1

Population segment (Line of therapy):
- Metastatic breast cancer (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2016]

○ trastuzumab + chemotherapy

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

Other criteria: ER negative and/or PR negative

US-NCCN Recommendation category: 1

Population segment (Line of therapy):
- Tumors >1cm (Not specified)
- One or more > 2mm ipsilateral axillary lymph node metastases (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2016]

○ trastuzumab + cisplatin + fluoropyrimidine

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

US-NCCN Recommendation category: 1

Population segment (Line of therapy):
- Locally advanced or metastatic adenocarcinoma (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2016]

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

ERBB2 amplification (continued)

trastuzumab + cisplatin + fluoropyrimidine

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

US-NCCN Recommendation category: 1

Population segment (Line of therapy):
- Locally advanced or metastatic adenocarcinoma (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2016]

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trastuzumab + cisplatin + fluoropyrimidine

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

US-NCCN Recommendation category: 1

Population segment (Line of therapy):
- Locally advanced or metastatic gastric cancer (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2016]

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trastuzumab + cisplatin + fluoropyrimidine

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

US-NCCN Recommendation category: 1

Population segment (Line of therapy):
- Locally advanced or metastatic adenocarcinoma (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2016]

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trastuzumab + hormone therapy + chemotherapy

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

Other criteria: ER positive and/or PR positive

US-NCCN Recommendation category: 1

Population segment (Line of therapy):
- Node positive, Ductal, Lobular, Mixed, Metaplasic tumors greater than 1 mm to one or more ipsilateral axillary lymph node (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2016]

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

ERBB2 amplification (continued)

ado-trastuzumab emtansine

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

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic breast cancer previously treated with trastuzumab-based regimen (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2016]

hormone therapy

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

Other criteria: ER positive and/or PR positive

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Ductal, Lobular, Mixed, Metaplasic tumors less than or equal to 0.5cm (pT1, PT2, pT3 and pN0) (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2016]

lapatinib + capecitabine

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

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic breast cancer previously treated with trastuzumab-based regimen (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2016]

lapatinib + trastuzumab

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

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic breast cancer previously treated with trastuzumab-based regimen (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2016]

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)

○ pertuzumab + trastuzumab + chemotherapy

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

Other criteria: ER negative and PR negative, ER positive and/or PR positive

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Did not receive pertuzumab as part of neoadjuvant therapy (Neoadjuvant/adjuvant therapy)
- Disease progression after treatment with trastuzumab-based therapy without pertuzumab (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2016]

○ pertuzumab + trastuzumab + paclitaxel

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

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic breast cancer (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2016]

○ trastuzumab + capecitabine

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

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic breast cancer (First-line therapy)
- Metastatic breast cancer previously treated with trastuzumab-based regimen (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2016]

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

ERBB2 amplification (continued)

trastuzumab + carboplatin + paclitaxel

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

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic breast cancer (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2016]

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trastuzumab + chemotherapy

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

Other criteria: ER positive and/or PR positive

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Ductal, Lobular, Mixed, Metaplasic tumors less than or equal to 0.5cm (pT1, PT2, pT3 and pN1mi) (Not specified)
- Recurrent or stage IV, Endocrine refractory (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2016]

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trastuzumab + chemotherapy

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

Other criteria: ER negative and/or PR negative

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Recurrent or stage IV, Endocrine refractory (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2016]

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 + docetaxel

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

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic breast cancer (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2016]

○ trastuzumab + hormone therapy

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

Other criteria: ER positive and/or PR positive

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Ductal, Lobular, Mixed, Metaplasic tumors 0.6-1.0 cm (pT1, PT2, pT3 and pN1mi) (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2016]

○ trastuzumab + hormone therapy + chemotherapy

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

Other criteria: ER positive and/or PR positive

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Ductal, Lobular, Mixed, Metaplasic tumors 0.6-1.0 cm (pT1, PT2, pT3 and pN1mi) (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2016]

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

ERBB2 amplification (continued)

trastuzumab + paclitaxel

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

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Low-risk stage I disease (Neoadjuvant/adjuvant therapy)
- Metastatic breast cancer (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2016]

trastuzumab + vinorelbine

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

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic breast cancer (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2016]

trastuzumab + chemotherapy (other)

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

US-NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Locally advanced or metastatic adenocarcinoma (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2016]

trastuzumab + chemotherapy (other)

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

US-NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Locally advanced or metastatic adenocarcinoma (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2016]

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

ERBB2 amplification (continued)

trastuzumab + chemotherapy (other)

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

US-NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Locally advanced or metastatic gastric cancer (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2016]

trastuzumab + chemotherapy (other)

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

US-NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Locally advanced or metastatic adenocarcinoma (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 3.2016]

trastuzumab + hormone therapy

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

Other criteria: ER positive and/or PR positive

US-NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Ductal, Lobular, Mixed, Metaplasic tumors less than or equal to 0.5cm (pT1, PT2, pT3 and pN0) (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2016]

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 + hormone therapy + chemotherapy

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

Other criteria: ER positive and/or PR positive

US-NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Ductal, Lobular, Mixed, Metaplasic tumors less than or equal to 0.5cm (pT1, PT2, pT3 and pN0) (Not specified)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2016]

KRAS p.(G12V) c.35G>T

⊘ cetuximab

Cancer type: Colorectal Cancer **Variant class:** KRAS mutation

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic colorectal cancer (Not specified)

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 2.2016]

⊘ cetuximab

Cancer type: Colorectal Cancer **Variant class:** KRAS mutation

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic colorectal cancer (Not specified)

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 2.2016]

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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KRAS p.(G12V) c.35G>T (continued)

panitumumab

Cancer type: Colorectal Cancer **Variant class:** KRAS mutation

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic colorectal cancer (Not specified)

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 2.2016]

panitumumab

Cancer type: Colorectal Cancer **Variant class:** KRAS mutation

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic colorectal cancer (Not specified)

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 2.2016]

tyrosine kinase inhibitors

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

Summary:

NCCN Guidelines® do not contain a recommendation regarding KRAS mutations and tyrosine kinase inhibitor (TKI) therapy in non-small cell lung cancer, but include the following evidentiary statements:

- "KRAS mutations are associated with intrinsic EGFR TKI resistance, and KRAS gene sequencing could be useful for the selection of patients as candidates for EGFR TKI therapy. KRAS testing may identify patients who may not benefit from further molecular diagnostic testing."
- "KRAS mutations are also predictive of lack of benefit from platinum/vinorelbine chemotherapy or EGFR TKI therapy."
- "TKI therapy is not effective in patients with KRAS mutations and ALK gene rearrangements."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2016]

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

Current Global Clinical Trials Information

Global Clinical Trials information is current as of 2016-09-01. 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

No NCT ID - see other identifier(s)
The IMPaCT Trial: Individualised Molecular Pancreatic Cancer Therapy. A Pilot, Randomized, Open label Phase II Trial Assessing First Line Treatment With Gemcitabine or Personalized Treatment Based on Tumour Molecular Signatures in Patients With Metastatic Pancreatic Cancer

Cancer type: Pancreatic Cancer

Variant class: ERBB2 overexpression

Other identifiers: ACTRN12612000777897, IMPaCT, TrialTroveID-196354

Population segments: First line, Stage III, Stage IV

Phase: II

Therapy: trastuzumab + chemotherapy

Country: Australia

NCT02713984
A Clinical Research of CAR T Cells Targeting HER2 Positive Cancer

Cancer type: Pancreatic Cancer

Variant class: ERBB2 positive

Other identifiers: TMMU-BTC-005, TrialTroveID-275196

Population segments: (N/A), HER2 positive, Second line or greater/Refractory/Relapsed

Phase: I/II

Therapy: CART-HER-2

Country: China

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

Cancer type: Pancreatic Cancer

Variant class: ERBB2 aberration

Other identifiers: 009896QM, EudraCT Number: 2014-002613-31, IRAS ID 172356, Torcmek, TrialTroveID-265019, UKCRN ID:18725

Population segments: EGFR, FGFR, HER2 negative, HER2 positive, KRAS, Second line or greater/Refractory/Relapsed, Squamous Cell, Stage III, Stage IV, Triple receptor negative

Phase: I/II

Therapy: selumetinib + vistusertib

Country: United Kingdom

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

ERBB2 amplification (continued)

NCT02465060
Molecular Analysis for Therapy Choice (MATCH)

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 amplification

Other identifiers: CTSU/EAY131, EAY131, EAY131-A, EAY131-B, EAY131-E, EAY131-F, EAY131-G, EAY131-H, EAY131-I, EAY131-MATCH, EAY131-N, EAY131-P, EAY131-Q, EAY131-R, EAY131-S1, EAY131-S2, EAY131-T, EAY131-U, EAY131-V, EAY131-X, ECOGEAY131-M, MATCH, NCI-2015-00054, NCI-MATCH, TrialTroveID-258747

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

Phase: II

Therapy: ado-trastuzumab emtansine

Country: 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, WA, WI, WV, WY

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

NCT02675829
A Phase II Trial of Ado-Trastuzumab Emtansine for Patients With HER2 Amplified or Mutant Cancers

Cancer type: Unspecified Cancer

Variant class: ERBB2 amplification

Other identifiers: 15-335, TrialTroveID-256389

Population segments: First line, Stage III, Stage IV

Phase: II

Therapy: ado-trastuzumab emtansine

Country: United States

US State: NY

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

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, TrialTroveID-200294

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

Phase: II

Therapy: lapatinib

Country: France

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

ERBB2 amplification (continued)

NCT02091141
My Pathway: An Open Label Phase IIa Study Evaluating Trastuzumab/ Pertuzumab, Erlotinib, Vemurafenib, and Vismodegib in Patients Who Have Advanced Solid Tumors With Mutations or Gene Expression Abnormalities Predictive of Response to One of These Agents

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 amplification

Other identifiers: 1403013519, 2014-0459, AAAN9701, J1480, ML28897, ML28897/PRO 02, ML28897PRO/02, My Pathway, NCI-2014-01811, TrialTroveID-205033

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

Phase: II

Therapy: pertuzumab + trastuzumab

Country: United States

US States: AR, AZ, CA, CO, FL, GA, IL, MD, MN, NC, ND, NY, OH, OK, OR, PA, SD, TN, TX, VA, WA

US Contact: Reference Study ID Number: ML28897 [888-662-6728; global.rochegenentechtrials@roche.com]

NCT02091141
My Pathway: An Open Label Phase IIa Study Evaluating Trastuzumab/ Pertuzumab, Erlotinib, Vemurafenib, and Vismodegib in Patients Who Have Advanced Solid Tumors With Mutations or Gene Expression Abnormalities Predictive of Response to One of These Agents

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 overexpression

Other identifiers: 1403013519, 2014-0459, AAAN9701, J1480, ML28897, ML28897/PRO 02, ML28897PRO/02, My Pathway, NCI-2014-01811, TrialTroveID-205033

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

Phase: II

Therapy: pertuzumab + trastuzumab

Country: United States

US States: AR, AZ, CA, CO, FL, GA, IL, MD, MN, NC, ND, NY, OH, OK, OR, PA, SD, TN, TX, VA, WA

US Contact: Reference Study ID Number: ML28897 [888-662-6728; global.rochegenentechtrials@roche.com]

NCT02693535
Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 amplification

Other identifiers: Pro00014171, TAPUR, TrialTroveID-273941

Population segments: (N/A), Aggressive, Diffuse large B-cell lymphoma (DLBCL), Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: II

Therapy: pertuzumab + trastuzumab

Country: United States

US States: MI, NC

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

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

ERBB2 amplification (continued)

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 identifiers: CHN-PLAGH-BT-009, TrialTroveID-193409

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

Phase: I/II

Therapy: CART-HER-2

Country: China

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, TrialTroveID-210119

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

Other inclusion criteria: ER positive and/or PR positive

Phase: I

Therapy: everolimus + trastuzumab + letrozole

Country: United States

US State: TX

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

NCT02593708
Phase I Study to Evaluate the Safety of Neratinib in Combination With Paclitaxel, Trastuzumab and Pertuzumab in Women and Men With Advanced or Metastatic HER2+ Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 amplification

Other identifiers: 149517, TrialTroveID-267207

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

Phase: I

Therapy: neratinib + pertuzumab + trastuzumab + chemotherapy

Country: United States

US State: CA

US Contact: Michelle Melisko [415-353-7070; Michelle.Melisko@ucsf.edu]

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

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ERBB2 amplification (continued)

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

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 amplification

Other identifiers: 5209-CPK-1002, CTR20150792, TrialTroveID-269399

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

Phase: I

Therapy: pirotinib

Country: China

NCT02500199
A Two-part Phase I, Open Label, Dose Escalation Study to Evaluate the Safety, Tolerability and Pharmacokinetics of Pyrotinib in Patients Whose Disease Progressed on Prior HER2 Targeted Therapy

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 overexpression

Other identifiers: SHRUS 1001, TrialTroveID-261429

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

Phase: I

Therapy: pyrotinib

Country: United States

US State: TX

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

NCT02500199
A Two-part Phase I, Open Label, Dose Escalation Study to Evaluate the Safety, Tolerability and Pharmacokinetics of Pyrotinib in Patients Whose Disease Progressed on Prior HER2 Targeted Therapy

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 amplification

Other identifiers: SHRUS 1001, TrialTroveID-261429

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

Phase: I

Therapy: pyrotinib

Country: United States

US State: TX

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

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)

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, TrialTroveID-271028

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

Phase: I

Therapy: RC-48

Country: China

NCT02881190
A Tolerance, Safety and Pharmacokinetic Ascending Dose Phase I Study of RC48-ADC Administered Subcutaneously 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, TrialTroveID-270499

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

Phase: I

Therapy: RC-48

Country: China

NCT01971515
A Phase I, First-in-Human, Dose Escalation Trial of MSC2363318A, a Dual p70S6K/Akt Inhibitor, in Subjects With Advanced Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 aberration

Other identifiers: 2013-0525, CHRMS 14-081, EMR100018-001, NCI-2013-02370, TrialTroveID-196334

Population segments: Aggressive, Classical, EGFR, HER2 positive, Indolent, Nodular lymphocyte-predominant, Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: I

Therapy: MSC-2363318A

Country: United States

US States: CA, MI, TX, VT

US Contact: US Medical Information [888-275-7376]

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

ERBB2 amplification (continued)

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 identifiers: ASLAN001-002SG, TrialTroveID-254374

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

Exclusion criteria variant class: EGFR T790M mutation

Phase: I

Therapy: varlitinib + chemotherapy

Country: Singapore

KRAS p.(G12V) c.35G>T

NCT02450656
Phase I/II study with the combination of afatinib and selumetinib in advanced KRAS mutant positive and PIK3CA wildtype colorectal, non-small cell lung and pancreatic cancer

Cancer type: Pancreatic Cancer

Variant class: KRAS exon 2 mutation

Other identifiers: EudraCT Number: 2014-001855-22, M14AFS, NL49983.031.14, TrialTroveID-251759

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

Other inclusion criteria: PIK3CA wild type

Phase: I/II

Therapy: afatinib + selumetinib

Country: Netherlands

NCT02039336
Phase I/II Study With the Combination of Dacomitinib and PD-0325901 in Metastatic KRAS Mutation Positive Colorectal, Non-small Cell Lung and Pancreatic Cancer

Cancer type: Pancreatic Cancer

Variant class: KRAS exon 2 mutation

Other identifiers: EudraCT Number: 2013-003299-10, M13DAP, NL45985.031.13, TrialTroveID-200856

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

Phase: I/II

Therapy: dacomitinib + PD-0325901

Country: Netherlands

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.

KRAS p.(G12V) c.35G>T (continued)

NCT02230553
Phase I/II study with lapatinib plus trametinib in patients with metastatic KRAS mutant colorectal, non-small cell lung and pancreatic cancer

Cancer type: Pancreatic Cancer

Variant class: KRAS exon 2 mutation

Other identifiers: EudraCT Number: 2014-002209-39, M14LTK, NL49551.031.14, TrialTroveID-214278

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

Other inclusion criteria: PIK3CA wild type

Phase: I/II

Therapy: lapatinib + trametinib

Country: Netherlands

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

Cancer type: Pancreatic Cancer

Variant class: RAS/RAF/MEK/ERK pathway

Other identifiers: 009896QM, EudraCT Number: 2014-002613-31, IRAS ID 172356, Torcmek, TrialTroveID-265019, UKCRN ID:18725

Population segments: EGFR, FGFR, HER2 negative, HER2 positive, KRAS, Second line or greater/Refractory/Relapsed, Squamous Cell, Stage III, Stage IV, Triple receptor negative

Phase: I/II

Therapy: selumetinib + vistusertib

Country: United Kingdom

NCT02576444
A Phase II Study of the PARP Inhibitor Olaparib (AZD2281) Alone and in Combination With AZD1775, AZD5363, or AZD2014 in Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant classes: KRAS & TP53 mutation

Other identifiers: 1508016363, OLAPCO, TrialTroveID-266161

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

Phase: II

Therapy: MK-1775 + olaparib

Country: United States

US State: CT

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

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.

KRAS p.(G12V) c.35G>T (continued)

NCT02029001
A Two-period, Multicenter, Randomized, Open-label, Phase II Study Evaluating the Clinical Benefit of a Maintenance Treatment Targeting Tumor Molecular Alterations in Patients With Progressive Locally-advanced or Metastatic Solid Tumors MOST: My own specific treatment

Cancer type: Unspecified Solid Tumor

Variant class: KRAS mutation

Other identifiers: ET12-081, EudraCT number: 2012-004510-34, MOST, ProfiLER, TrialTroveID-200294

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

Exclusion criteria variant class: BRAF V600 mutation

Phase: II

Therapy: sorafenib

Country: France

NCT02747537
Phase II Clinical Trial Treating Relapsed/Recurrent/Refractory Pediatric Solid Tumors With the Genomically-Targeted Agent Sorafenib in Combination With Irinotecan

Cancer type: Unspecified Solid Tumor

Variant class: RAS mutation

Other identifiers: 201605006, NCI-2016-00680, TrialTroveID-277232

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

Phase: II

Therapy: sorafenib + chemotherapy

Country: United States

US State: MO

US Contact: Dr. Robert Hayashi [314-454-6018; hayashi_r@kids.wustl.edu]

NCT02022982
Phase I/II Study of the CDK4/6 Inhibitor Palbociclib (PD-0332991) in Combination With the MEK Inhibitor PD-0325901 for Patients with KRAS Mutant Non-Small Cell Lung Cancer and Other Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: KRAS mutation

Other identifiers: 13-506, NCI-2014-00940, TrialTroveID-200043

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

Phase: I/II

Therapy: palbociclib + PD-0325901

Country: United States

US State: MA

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

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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KRAS p.(G12V) c.35G>T (continued)

NCT02437227
A Phase 1, First in Man, Dual Centre, Open-label Dose Escalation Study With Expansion to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of CCT3833 (BAL3833), a panRAF Inhibitor, Given Orally in Patients With Advanced Solid Tumours, Including Metastatic Melanoma

Cancer type: Unspecified Solid Tumor

Variant class: RAS mutation

Other identifiers: 4232, PanRAF, TrialTroveID-257046

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

Phase: I/II

Therapy: BAL-3833

Country: United Kingdom

No NCT ID - see other identifier(s)
A Phase I/II Study of LNP3794 in Patients with Advanced Solid Tumors having RAS/BRAF Mutations

Cancer type: Unspecified Solid Tumor

Variant class: RAS mutation

Other identifier: TrialTroveID-250171

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

Phase: I/II

Therapy: LNP3794

Country: United Kingdom

NCT02407509
A Phase I Trial of RO5126766 (a Dual RAF/MEK Inhibitor) Exploring Intermittent, Oral Dosing Regimens in Patients With Solid Tumours or Multiple Myeloma

Cancer type: Unspecified Solid Tumor

Variant class: KRAS mutation

Other identifiers: CCR3808, DDU RAF/MEK, EudraCT Number: 2012-001040-22, TrialTroveID-206542

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

Phase: I

Therapy: RO-5126766

Country: United Kingdom

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

KRAS p.(G12V) c.35G>T (continued)

NCT02015117
A Phase 1 Study of Trametinib in Combination With Radiation Therapy for Brain Metastases

Cancer type: Unspecified Cancer

Variant class: KRAS mutation

Other identifiers: 2013C0115, 9458, NCI-2013-02343, OSU 13197, OSU-13197, TrialTroveID-199440

Population segments: CNS mets, First line, Line of therapy N/A, Stage IV

Phase: I

Therapies: trametinib + radiation therapy, trametinib + surgical intervention

Country: United States

US States: IL, OH

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

NCT02607813
A Phase I Dose Finding Study of Oral LXH254 in Adult Patients With Advanced Solid Tumors Harboring MAPK Pathway Alterations

Cancer type: Unspecified Solid Tumor

Variant class: RAS/RAF/MEK/ERK pathway

Other identifiers: 2015-0913, CLXH254X2101, EudraCT Number: 2015-003421-33, NCI-2015-02280, REec-2016-2132, TrialTroveID-268216

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

Phase: I

Therapy: LXH254

Countries: Canada, Germany, Japan, Netherlands, Spain, United States

US States: NY, TX

US Contact: Novartis Pharmaceuticals [888-669-6682]

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

TP53 p.(G245V) c.734G>T

NCT02432963
A Phase I Study of a p53MVA Vaccine in Combination With Pembrolizumab

Cancer type: Pancreatic Cancer

Variant class: TP53 mutation

Other identifiers: 116634, 122284, 122771, 124524, 15002, NCI-2015-00653, TrialTroveID-256830

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

Phase: I

Therapy: pembrolizumab + p53MVA

Country: United States

US State: CA

US Contact: Vincent Chung [800-826-4673]

NCT02576444
A Phase II Study of the PARP Inhibitor Olaparib (AZD2281) Alone and in Combination With AZD1775, AZD5363, or AZD2014 in Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant classes: KRAS & TP53 mutation

Other identifiers: 1508016363, OLAPCO, TrialTroveID-266161

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

Phase: II

Therapy: MK-1775 + olaparib

Country: United States

US State: CT

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

NCT02042989
A Phase I Study of MLN9708 and Vorinostat to Target Autophagy in Patients With Advanced p53 Mutant Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: TP53 mutation

Other identifiers: 2013-0511, NCI-2014-01091, TrialTroveID-201319

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

Phase: I

Therapy: ixazomib + vorinostat

Country: United States

US State: TX

US Contact: Dr. Siqing Fu [713-563-1930]

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

TP53 p.(G245V) c.734G>T (continued)

NCT02610075
A Phase Ib Study to Determine the Maximum Tolerated Dose (MTD) of AZD1775 Monotherapy in Patients With Locally Advanced or Metastatic Solid Tumours.

Cancer type: Unspecified Solid Tumor

Variant class: TP53 mutation

Other identifiers: D6015C00003, REFMAL 398, TrialTroveID- 268385

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

Phase: I

Therapy: MK-1775

Country: United States

US States: CO, TN

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

NCT02354547
A Phase I Study of SGT-53, a TfRscFv-Liposome-p53 Complex, in Children with Refractory or Recurrent Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: TP53 mutation

Other identifiers: 1405-1316, SGT53-01-2, TrialTroveID-251586

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

Phase: I

Therapies: SGT-53, SGT-53 + chemotherapy

Country: United States

US State: TX

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

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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Appendix: 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
ERBB2 aberration	3
↳ ERBB2 positive	7
↳ ERBB2 overexpression	21
ERBB2 aberration	3
↳ ERBB2 positive	7
↳ ERBB2 amplification	44

KRAS p.(G12V) c.35G>T

Variant Class	Evidence Items
RAS/RAF/MEK/ERK pathway	2
↳ RAS mutation	3
↳ RAS activating mutation	0
↳ KRAS activating mutation	0
↳ KRAS G12 mutation	2
↳ KRAS mutation	13
↳ KRAS activating mutation	0
↳ KRAS G12 mutation	2
↳ KRAS exon 2 mutation	9
↳ KRAS G12 mutation	2

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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Appendix: Evidence Summary by Variant Class (continued)

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

TP53 p.(G245V) c.734G>T

Variant Class	Evidence Items
TP53 mutation	6

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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Appendix: Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
KRAS	p.(G12V)	c.35G>T	COSM520	chr12:25398284	20.19%	NM_033360.3	missense
TP53	p.(G245V)	c.734G>T	COSM11196	chr17:7577547	25.58%	NM_000546.5	missense

Copy Number Variations

Gene	Locus	Copy Number
ERBB2	chr17:37845133	5.1

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

TERMS AND CONDITIONS

The following paragraph on Liability is an extract from the Oncologica Tests' Terms and Conditions. The extract is to draw your attention to particular terms applicable to you but nothing set out here is intended to supersede or override our Terms and Conditions, which can be found on our website at www.oncologica.com under the title Oncologica Tests' Terms and Conditions. Please read these Oncologica Test Terms and Conditions carefully before you submit an order for the Oncologica Tests, as you will be bound by these Terms and Conditions, once a contract comes into existence as per paragraph 2 of the Oncologica Test's Terms and Conditions.

6. Liability

6.1 Oncologica operates in compliance with international ISO15189:2012 standards and is regulated by UKAS. The Oncologica Tests have not been cleared or approved by the United States Food and Drug Administration; however, such clearance or approval is not required.

6.2 The Patient agrees that the Oncologica Test Report is intended for clinical use and interpretation by a physician who is experienced and skilled in the use and interpretation of clinical test data. The Oncologica Test Report is based on the Sample submitted by the Patient. The Oncologica Test Report should not be considered or its contents applied to any other patient or any other sample. Oncologica does not update an Oncologica Test Report once it has been sent.

6.3 Information compiled in the Oncologica Test Report includes is from publicly available as well as proprietary sources. By updating the source database, Oncologica makes every effort to provide the most accurate and up-to-date information. However, Oncologica does not warrant or represent that the information in the Oncologica Test Report is accurate, timely or complete.

6.4 The Oncologica Test Report contains drug and clinical trial information. However, Oncologica does not warrant or represent that any drug or clinical trial identified by the Oncologica Test will guarantee a therapeutic response for a particular Patient. The drugs listed in an Oncologica Test Report are ranked on clinical evidence as to the predicted efficacy or appropriateness for the Patient. The Patient shall ensure that its physician shall evaluate and interpret the Oncologica Test Report, along with all other available clinical information about the Patient, to determine the best treatment decisions in their own independent medical judgment. Patient management decisions should not be based on a single test, nor solely on the information contained in the Oncologica Test Report.

6.5 Subject to paragraph **6.10**, Oncologica shall have no liability for any use made of the information provided in the Oncologica Test Report, including but not limited to any report prepared by Oncologica summarising the results of the Oncologica Tests, any advice supplied by Oncologica, any decisions taken, or for any costs incurred by Patient and/or the Patient's physician and/or the Agent in consequence of such use, advice or decisions. The Oncologica Test and/or the Oncologica Test Report is not a substitute for the Patient's physician's professional judgment. The use of the information provided in the Oncologica Test Report is provided as a tool for the ordering physician's use in determining the appropriate treatment for the Patient. The decision as to what course of treatment and the appropriate use of the information provided by the Oncologica Test Report is solely that of the Patient's physician.

6.6 Oncologica does not warrant or represent or guarantee that the Oncologica Tests will identify an actionable genetic alteration that is linked to anti-cancer targeted therapies. Although the Oncologica Tests are comprehensive, in a proportion of Patients, the Oncologica Test result may not identify any actionable mutations for a patient's cancer. In the event that no actionable alteration in the Sample is identified by the Oncologica Test, then the Patient is still under full obligation to pay the Charges and no refund is available to the Patient and/or Agent.

6.7 The Oncologica Test identifies genomic actionable alterations found in the submitted Sample that are linked to anti-cancer targeted agents. Also note that this test only examines tumour, and not normal tissue from the patient, and therefore cannot distinguish between somatic and germline (i.e., heritable) alterations.

6.8 Subject to Clause **6.8**, Oncologica shall not be liable to the Patient whether in contract, tort (including negligence and breach of statutory duty), or otherwise for any:

(a) Error or defect in the Oncologica Test Report as a result of any inaccurate or incomplete information supplied by the Patient;

(b) Loss of data or materials, including the Sample and/or the Report and including any loss arising as a result of the acts or omissions of a courier;

(c) Indirect or consequential loss arising whether or not advised of the possibility of the same.

6.9 Subject to the provisions of this Clause 6, Oncologica' s total liability to the Patient in respect of all losses arising under or in connection with the Contract, whether in contract, tort (including negligence and breach of statutory duty), or otherwise, shall in no circumstances exceed the Charges paid for the Test that is the subject of the claim.

6.10 Nothing in the Contract limits or excludes the liability of Oncologica for breach of its obligations under section 12 of the Sale of Goods Act 1979 and/or section 2 of the Supply of Goods and Services Act 1982; death or personal injury resulting from negligence; or fraud or fraudulent misrepresentation.

6.11 If the Patient is a consumer (and not a business), the Patient expressly acknowledges and agrees that the Test is supplied to the Patient's specification and therefore there is no right to cancel the Test following acceptance under Clause 2.2. If the Patient is a consumer, then notwithstanding any other provisions of the Contract, none of the Patient's consumer statutory rights are affected.


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