[Oncofocus] Patient Test Report

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Surname		**Requesting clinician**	
Forename			
DOB			
Gender	Male	**Date requested**	
Histology #		**Tumour %**	60
Primary site	Skin	**Tumour % (macrodissected)**	
Tumour subtype	Melanoma		
Tissue type	Skin		

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.

175 genes were targeted covering 2470 unique coding hot spots, 281 fusions and 19 CNV genes for actionable mutations linked to 484 anti-cancer targeted therapies.

The following actionable mutations were detected

Variant Summary

Sample Cancer Type: Melanoma

● 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
ALK fusion	○ (2)	○ (2)	○ (1)	○ (2)	● (8)
ERBB2 amplification	○ (10)	○ (3)	○ (5)	○ (15)	● (3)
EGFR exon 19 deletion	○ (3)	○ (2)	⚠ (3)	○ (4)	● (6)

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'. Copy number variants of a >5% confidence value of ≥4 after normalisation are classified as amplified. Gene Fusions are reported when occurring in >20 counts and meeting the thresholds of assay specific internal RNA quality control. Assay sensitivity and positive predictive value is 99% when these thresholds are met. Supplementary technical information is available upon request.

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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

ALK fusion

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
crizotinib	○	○	○	○	● (II)
ceritinib	○	○	✖	○	● (II)
crizotinib + itraconazole + midazolam + rifampicin, crizotinib + itraconazole + rifampicin	✖	✖	✖	✖	● (I/II)
entrectinib	✖	✖	✖	✖	● (I/II)
TSR-011	✖	✖	✖	✖	● (I/II)
ceritinib + chemotherapy	✖	✖	✖	✖	● (I)
crizotinib + chemotherapy, crizotinib + pazopanib, crizotinib + pazopanib + chemotherapy	✖	✖	✖	✖	● (I)
crizotinib + dasatinib	✖	✖	✖	✖	● (I)

ERBB2 amplification

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
trastuzumab	○	○	✖	○	✖
lapatinib + trastuzumab	○	✖	○	○	✖
lapatinib + capecitabine	○	✖	✖	○	✖
trastuzumab + capecitabine	○	✖	✖	○	✖
trastuzumab + docetaxel	○	✖	✖	○	✖
trastuzumab + paclitaxel	○	✖	✖	○	✖
lapatinib + aromatase inhibitor	○	✖	✖	✖	✖
trastuzumab + aromatase inhibitor	○	✖	✖	✖	✖

* 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.

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Relevant Therapy Summary (continued)

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ERBB2 amplification (continued)

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
trastuzumab + carboplatin + docetaxel	○	✖	✖	✖	✖
trastuzumab + cisplatin + fluorouracil	○	✖	✖	✖	✖
ado-trastuzumab emtansine	✖	○	○	○	✖
pertuzumab + trastuzumab + docetaxel	✖	○	✖	○	✖
pertuzumab + trastuzumab + chemotherapy	✖	✖	○	○	✖
trastuzumab + chemotherapy	✖	✖	○	○	✖
pertuzumab	✖	✖	○	✖	✖
pertuzumab + trastuzumab	✖	✖	✖	○	✖
pertuzumab + trastuzumab + paclitaxel	✖	✖	✖	○	✖
trastuzumab + chemotherapy (other)	✖	✖	✖	○	✖
trastuzumab + cisplatin + fluoropyrimidine	✖	✖	✖	○	✖
trastuzumab + vinorelbine	✖	✖	✖	○	✖
erlotinib, pertuzumab + trastuzumab, vemurafenib, vismodegib	✖	✖	✖	✖	● (II)
CART-HER-2	✖	✖	✖	✖	● (I/II)
MSC-2363318A	✖	✖	✖	✖	● (I)

EGFR exon 19 deletion

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
afatinib	○	○	○	○	✖
erlotinib	○	○	○	○	✖

* 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.

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Relevant Therapy Summary (continued)

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EGFR exon 19 deletion (continued)

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
gefitinib	○	✖	⚠	✖	✖
erlotinib + chemotherapy	✖	✖	✖	○	● (I)
afatinib + chemotherapy	✖	✖	✖	○	✖
erlotinib, pertuzumab + trastuzumab, vemurafenib, vismodegib	✖	✖	✖	✖	● (II)
CLR-457	✖	✖	✖	✖	● (I/II)
EGF-816	✖	✖	✖	✖	● (I/II)
epitinib	✖	✖	✖	✖	● (I)
MSC-2363318A	✖	✖	✖	✖	● (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.

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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 2015-07-01. For the most up-to-date information, search www.ema.europa.eu/ema.

ALK fusion

○ crizotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2015-06-08 **Variant class:** ALK fusion

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002489/WC500134759.pdf

○ ceritinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2015-07-09 **Variant class:** ALK positive

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/003819/WC500187504.pdf

ERBB2 amplification

○ lapatinib + aromatase inhibitor, lapatinib + capecitabine, lapatinib + trastuzumab

Cancer type: Breast Cancer **Label as of:** 2015-07-02 **Variant class:** ERBB2 amplification

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000795/WC500044957.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:** 2015-06-30 **Variant class:** ERBB2 amplification

Reference:

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

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EGFR exon 19 deletion

afatinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2014-11-06 **Variant class:** EGFR exon 19 deletion

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002280/WC500152392.pdf

erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2014-02-03 **Variant class:** EGFR activating mutation

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000618/WC500033994.pdf

gefitinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2014-11-11 **Variant class:** EGFR activating mutation

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/001016/WC500036358.pdf

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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 2015-07-01. For the most up-to-date information, search www.fda.gov.

ALK fusion

○ crizotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2015-03-20 **Variant class:** ALK fusion

Indications and usage:
XALKORI® is a kinase inhibitor indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic kinase (ALK)-positive as detected by an FDA-approved test.

Reference:

http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/202570s013lbl.pdf

○ ceritinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2014-04-29 **Variant class:** ALK positive

Indications and usage:
ZYKADIA™ is a kinase inhibitor indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to crizotinib. This indication is approved under accelerated approval based on tumor response rate and duration of response. An improvement in survival or disease-related symptoms has not been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Reference:

http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/205755s000lbl.pdf

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ERBB2 amplification

ado-trastuzumab emtansine

Cancer type: Breast Cancer **Label as of:** 2015-05-29 **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/2015/125427s087lbl.pdf

pertuzumab + trastuzumab + docetaxel

Cancer type: Breast Cancer **Label as of:** 2015-05-29 **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/2015/125409s105lbl.pdf

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ERBB2 amplification (continued)

trastuzumab

Cancer type: Breast Cancer, Esophageal Cancer, Gastric Cancer **Label as of:** 2015-04-23 **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/2015/103792s5327lbl.pdf

EGFR exon 19 deletion

afatinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2013-11-21 **Variant class:** EGFR exon 19 deletion

Indications and usage:

GILOTRIF™ is a kinase inhibitor indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test.

Limitation of Use: Safety and efficacy of GILOTRIF have not been established in patients whose tumors have other EGFR mutations

Reference:

http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/201292s002lbl.pdf

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EGFR exon 19 deletion (continued)

○ erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2015-04-27 **Variant class:** EGFR exon 19 deletion

Indications and usage:

TARCEVA® is a kinase inhibitor indicated for:

- First-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test.
- Maintenance treatment of patients with locally advanced or metastatic NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy.
- Treatment of locally advanced or metastatic NSCLC after failure of at least one prior chemotherapy regimen.
- First-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer, in combination with gemcitabine.

Limitations of Use:

- TARCEVA® is not recommended for use in combination with platinum-based chemotherapy.
- Safety and efficacy of TARCEVA® have not been evaluated as first-line treatment in patients with metastatic NSCLC whose tumors have EGFR mutations other than exon 19 deletions or exon 21 (L858R) substitution.

Reference:

http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/021743s021lbl.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 2015-07-06. For the most up-to-date information, search www.esmo.org.

ALK fusion

○ crizotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ALK fusion

ESMO Recommendation category: I, A

Population segment (Line of therapy):
- Metastatic NSCLC (First or second-line therapy)

Reference: ESMO Clinical Practice Guidelines - Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2014) 25 (suppl 3): iii27-iii39.]

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 - Primary Breast Cancer [Ann Oncol 2013; 24 (Suppl 6): vi7-vi23.]

○ 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.]

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ERBB2 amplification (continued)

○ 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.]

○ 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.]

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ERBB2 amplification (continued)

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.]

EGFR exon 19 deletion

afatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

ESMO Recommendation category: I, A

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

Reference: ESMO Clinical Practice Guidelines - Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2014) 25 (suppl 3): iii27-iii39.]

erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

ESMO Recommendation category: I, A

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

Reference: ESMO Clinical Practice Guidelines - Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2014) 25 (suppl 3): iii27-iii39.]

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EGFR exon 19 deletion (continued)

○ gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

ESMO Recommendation category: I, A

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

Reference: ESMO Clinical Practice Guidelines - Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2014) 25 (suppl 3): iii27-iii39.]

⊘ gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR mutation

ESMO Recommendation category: II, A

Population segment (Line of therapy):
- Postoperative, early stages I or II in adjuvant setting (Not specified)

Reference: ESMO Clinical Practice Guidelines - Early-Stage and Locally Advanced (non-metastatic) Non-Small-Cell Lung Cancer [Ann Oncol 2013; 24 (Suppl 6): vi89-vi98.]

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-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 2015-07-06. For the most up-to-date information, search www.nccn.org.

ALK fusion

○ crizotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ALK fusion

US-NCCN Recommendation category: 1

Population segment (Line of therapy):
- Adenocarcinoma, Large cell, NSCLC (NOS), Squamous cell carcinoma; Rearrangement discovered prior to first-line chemotherapy (First-line therapy)

Reference: NCCN Guidelines® - Non-Small Cell Lung Cancer [Version 7.2015]

○ ceritinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ALK fusion

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large cell, NSCLC (NOS), Squamous cell carcinoma; Progression after first-line therapy (Subsequent therapy)

Reference: NCCN Guidelines® - Non-Small Cell Lung Cancer [Version 7.2015]

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ALK fusion (continued)

crizotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ALK fusion

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large cell, NSCLC (NOS), Squamous cell carcinoma; Progression after first-line therapy (Subsequent therapy)
- Adenocarcinoma, Large cell, NSCLC (NOS), Squamous cell carcinoma; Rearrangement discovered during first-line chemotherapy (First-line therapy)

Reference: NCCN Guidelines® - Non-Small Cell Lung Cancer [Version 7.2015]

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® - Breast Cancer [Version 2.2015]

trastuzumab + chemotherapy

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

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® - Breast Cancer [Version 2.2015]

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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® - Breast Cancer [Version 2.2015]

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® - Breast Cancer [Version 2.2015]

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® - Breast Cancer [Version 2.2015]

pertuzumab + trastuzumab

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

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Disease progression after treatment with trastuzumab-based therapy without pertuzumab (Not specified)

Reference: NCCN Guidelines® - Breast Cancer [Version 2.2015]

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

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® - Breast Cancer [Version 2.2015]

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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® - Breast Cancer [Version 2.2015]

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trastuzumab

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® - Breast Cancer [Version 2.2015]

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ERBB2 amplification (continued)

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® - Breast Cancer [Version 2.2015]

trastuzumab + chemotherapy

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

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Tumors 0.6-1.0cm, node-negative (Not specified)
- Smaller tumors that have less than or equal to 2mm axillary node metastases (Not specified)
- Metastatic breast cancer (First-line therapy)
- Metastatic breast cancer previously treated with a trastuzumab-based regimen (Not specified)
- Inflammatory breast cancer (Not specified)

Reference: NCCN Guidelines® - Breast Cancer [Version 2.2015]

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® - Breast Cancer [Version 2.2015]

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 + 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® - Breast Cancer [Version 2.2015]

○ 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® - Breast Cancer [Version 2.2015]

○ trastuzumab + cisplatin + fluoropyrimidine

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

US-NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - Esophageal and Esophagogastric Junction Cancers [Version 3.2015]

○ trastuzumab + cisplatin + fluoropyrimidine

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

US-NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - Gastric Cancer [Version 3.2015]

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ERBB2 amplification (continued)

○ trastuzumab + chemotherapy (other)

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

US-NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Locally advanced or metastatic adenocarcinoma (Not specified)

Reference: NCCN Guidelines® - Esophageal and Esophagogastric Junction Cancers [Version 3.2015]

○ trastuzumab + chemotherapy (other)

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

US-NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Locally advanced or metastatic gastric cancer (Not specified)

Reference: NCCN Guidelines® - Gastric Cancer [Version 3.2015]

EGFR exon 19 deletion

○ afatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

US-NCCN Recommendation category: 1

Population segment (Line of therapy):
- Adenocarcinoma, Large cell, NSCLC (NOS), Squamous cell carcinoma; Mutation discovered prior to First-line chemotherapy (First-Line therapy)

Reference: NCCN Guidelines® - Non-Small Cell Lung Cancer [Version 7.2015]

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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EGFR exon 19 deletion (continued)

erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

US-NCCN Recommendation category: 1

Population segment (Line of therapy):
- Adenocarcinoma, Large cell, NSCLC (NOS), Squamous cell carcinoma; Mutation discovered prior to First-line chemotherapy (First-Line therapy)

Reference: NCCN Guidelines® - Non-Small Cell Lung Cancer [Version 7.2015]

afatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large cell, NSCLC (NOS), Squamous cell carcinoma; Progression after first-line therapy (Subsequent therapy)
- Adenocarcinoma, Large cell, NSCLC (NOS), Squamous cell carcinoma; Mutation discovered during first-line chemotherapy (First-line therapy)

Reference: NCCN Guidelines® - Non-Small Cell Lung Cancer [Version 7.2015]

erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large cell, NSCLC (NOS), Squamous cell carcinoma; Progression after first-line therapy (Subsequent therapy)
- Adenocarcinoma, Large cell, NSCLC (NOS), Squamous cell carcinoma; Mutation discovered during first-line chemotherapy (First-line therapy)

Reference: NCCN Guidelines® - Non-Small Cell Lung Cancer [Version 7.2015]

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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EGFR exon 19 deletion (continued)

○ afatinib + chemotherapy

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

US-NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Adenocarcinoma, Large cell, NSCLC (NOS), Squamous cell carcinoma; Mutation discovered during first-line chemotherapy (First-Line therapy)

Reference: NCCN Guidelines® - Non-Small Cell Lung Cancer [Version 7.2015]

○ erlotinib + chemotherapy

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

US-NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Adenocarcinoma, Large cell, NSCLC (NOS), Squamous cell carcinoma; Mutation discovered during first-line chemotherapy (First-Line therapy)

Reference: NCCN Guidelines® - Non-Small Cell Lung Cancer [Version 7.2015]

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 Global Clinical Trials Information

Global Clinical Trials information is current as of 2015-08-03. 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'.

ALK fusion

NCT01634763
A Phase I, Multicenter, Open-label Dose Escalation Study of LDK378, Administered Orally in Japanese Patients with Tumors Characterized by Genetic Alterations in ALK

Cancer type: Melanoma

Variant class: ALK aberration

Other identifiers: CLDK378X1101, JapicCTI-121897, TrialTroveID-170968

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

Phase: I

Therapy: ceritinib

Country: Japan

NCT02186821
Modular Phase II Study to Link Targeted Therapy to Patients With Pathway Activated Tumors: Module - 7 Ceritinib (LDK378) for Patients Whose Tumors Have Aberrations in ALK or ROS1

Cancer type: Unspecified Solid Tumor

Variant class: ALK fusion

Other identifiers: 2014-0669, CLDK378AUS23, SIGNATURE, TrialTroveID-212790

Population segments: Aggressive, Classical, Diffuse large B-cell lymphoma (DLBCL), Follicular lymphoma (FL), Indolent, Mantle cell lymphoma (MCL), Nodular lymphocyte-predominant, Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: II

Therapy: ceritinib

Country: United States

US States: CO, IL, NM, OR, PA, RI, TX, WA

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

NCT02034981
AcSé CRIZOTINIB : Secured Access to Crizotinib for Patients With Tumors Harboring a Genomic Alteration on One of the Biological Targets of the Drug

Cancer type: Unspecified Solid Tumor

Variant class: ALK aberration

Other identifiers: AcSé, AcSé CRIZOTINIB, EudraCT Number: 2013-000885-13, FSCA-crizotinib, TrialTroveID-200633, UC-0105/1303

Population segments: Aggressive, Anaplastic, Follicular, Line of therapy N/A, Medullary, Papillary, Pediatric or Adolescent, Peripheral T-cell lymphoma (PTCL), Stage III, Stage IV

Phase: II

Therapy: crizotinib

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.

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ALK fusion (continued)

NCT00939770
A Phase I/II Study of PF-02341066, an Oral Small Molecule Inhibitor of Anaplastic Lymphoma Kinase (ALK) and c-Met, in Children With Relapsed/ Refractory Solid Tumors, Primary CNS Tumors, and Anaplastic Large Cell Lymphoma

Cancer type: Unspecified Solid Tumor

Variant class: ALK fusion

Other identifiers: 10-C-0178, 100178, AAAE7196, ADV912, ADVL0912, COG-ADVL0912, HUM00034160, PROFILE 912, TrialTroveID-112357

Population segments: (N/A), ALK, Indolent, Pediatric or Adolescent, Peripheral T-cell lymphoma (PTCL), Second line or greater/Refractory/Relapsed

Phase: I/II

Therapy: crizotinib

Countries: Canada, United States

US States: AL, CA, CO, DC, GA, IL, IN, MA, MD, MI, MN, MO, NY, OH, OR, PA, TN, TX, WA, WI

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

NCT00585195
Phase I/II Safety, Pharmacokinetic and Pharmacodynamic Study of Pf-02341066, A C-met/Hgfr Selective Tyrosine Kinase Inhibitor, Administered Orally To Patients with Advanced Cancer

Cancer type: Unspecified Solid Tumor

Variant class: ALK fusion

Other identifiers: 06068, 14473B, A8081001, A8081001_PF-02341066, BIDMC 06-068, COMIRB 06-0155, CT316, DFHCC 06-068, MSKCC 07-157, PRMC 06-23, PROFILE 1001, Study 1001, TrialTroveID-052471, UCI 07-40, UCI-07-40, UCIRB 14473, VICCPHI1255

Population segments: Adenocarcinoma, Aggressive, ALK, First line, Large Cell, Locally advanced, Metastatic, Other subtype, Peripheral T-cell lymphoma (PTCL), Second line or greater/Refractory/Relapsed, Squamous Cell, Stage II, Stage III, Stage IV

Phase: I/II

Therapies: crizotinib + itraconazole + midazolam + rifampicin, crizotinib + itraconazole + rifampicin

Countries: Australia, Republic of Korea, United States

US States: CA, CO, IL, MA, MI, NC, NY, OH, PA, TN

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

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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ALK fusion (continued)

NCT02048488
A Phase I/IIa Open-Label, Dose Escalation and Cohort Expansion Trial of Oral TSR-011 in Patients With Advanced Solid Tumors and Lymphomas

Cancer type: Unspecified Solid Tumor

Variant class: ALK positive

Other identifiers: EudraCT Number: 2013-000686-37, PR-20-5006-C, REFMAL 290 IST, TrialTroveID-175362

Population segments: Aggressive, ALK, Classical, First line, Indolent, Locally advanced, Metastatic, Nodular lymphocyte-predominant, Papillary, Second line or greater/Refractory/Relapsed, Stage II, Stage III, Stage IV

Phase: I/II

Therapy: TSR-011

Countries: Poland, Spain, Taiwan, United Kingdom, United States

US States: AZ, CA, TN, VA

US Contact: Clinical Trial Management Group [TSR011@tesarobio.com]

No NCT ID - see other identifier(s)
A Phase I/II Dose Escalation Study of RXDX-101 in Patients with Solid Tumors with Activating Alterations in the TrkA, ROS1 or ALK Tyrosine Kinase Receptors

Cancer type: Unspecified Solid Tumor

Variant class: ALK aberration

Other identifiers: ALKA-372-001, TrialTroveID-188328

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

Phase: I/II

Therapy: entrectinib

Country: Italy

NCT02097810
A Phase I/IIa, Multicenter, Open-Label Study of Oral RXDX-101 in Adult Patients with Locally Advanced or Metastatic Cancer Confirmed to be Positive for TrkA, TrkB, TrkC, ROS1, or ALK Molecular Alterations Study Targeting ALK, ROS1 or TRKA/B/C (STARTRK-1)

Cancer type: Unspecified Solid Tumor

Variant class: ALK aberration

Other identifiers: 14-131, 14-271, 2014-0512, EudraCT Number: 2014-001326-15, REec-2014-1210, RXDX-101-01, STARTRK-1, TrialTroveID-203930, UCI 14-01

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

Phase: I/II

Therapy: entrectinib

Countries: Republic of Korea, Spain, United States

US States: CA, CO, DC, FL, MA, NY, TN, TX

US Contact: Ignyta, Inc. [858-255-5959]

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.

ALK fusion (continued)

NCT02227940
A Phase I Study of Ceritinib (LDK378), a Novel ALK Inhibitor, in Combination With Gemcitabine-Based Chemotherapy in Patients With Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: ALK fusion

Other identifiers: I 248813, NCI-2014-01766, TrialTroveID-215704

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

Phase: I

Therapy: ceritinib + chemotherapy

Country: United States

US State: NY

US Contact: Roswell Park [877-275-7724; ASKRPCI@roswellpark.org]

NCT01548144
A Two Steps Phase I Trial of Pazopanib or Pemetrexed in Combination With Crizotinib Followed by the Triplet, Crizotinib Plus Pazopanib Plus Pemetrexed in Patients With Advanced Malignancies

Cancer type: Unspecified Cancer

Variant class: ALK fusion

Other identifiers: 2011-1142, NCI-2012-00324, TrialTroveID-163762

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

Phase: I

Therapies: crizotinib + chemotherapy, crizotinib + pazopanib, crizotinib + pazopanib + chemotherapy

Country: United States

US State: TX

US Contact: Dr Ralph Zinner [800-392-1611]

NCT01744652
A Phase I Trial of Dasatinib in Combination With Crizotinib in Patients With Advanced Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: ALK fusion

Other identifiers: 2012-0721, NCI-2013-00071, TrialTroveID-178941

Population segments: Aggressive, Classical, Hormone refractory, Indolent, Metastatic, Nodular lymphocyte-predominant, Second line or greater/Refractory/Relapsed, Stage IV, Unresectable

Phase: I

Therapy: crizotinib + dasatinib

Country: United States

US State: TX

US Contact: Dr. David S. Hong [800-392-1611]

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

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, ML28897, ML28897PRO/02, My Pathway, TrialTroveID-205033

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

Exclusion criteria variant classes: RAS mutation, BRAF activating mutation, EGFR exon 20 mutation

Phase: II

Therapies: erlotinib, pertuzumab + trastuzumab, vemurafenib, vismodegib

Country: United States

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

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

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

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, 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, MN, 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.

EGFR exon 19 deletion

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: EGFR activating mutation

Other identifiers: 1403013519, 2014-0459, ML28897, ML28897PRO/02, My Pathway, TrialTroveID-205033

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

Exclusion criteria variant classes: RAS mutation, BRAF activating mutation, EGFR exon 20 mutation

Phase: II

Therapies: erlotinib, pertuzumab + trastuzumab, vemurafenib, vismodegib

Country: United States

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

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

NCT02189174
A Phase I/II Multicenter, Open-label Study of CLR457, Administered Orally in Adult Patients With Advanced Solid Malignancies.

Cancer type: Unspecified Solid Tumor

Variant class: EGFR mutation

Other identifiers: 14-155, 14-282, CCLR457X2101, EudraCT number: 2014-000316-34, JapicCTI-152791, NCI-2014-02051, TrialTroveID-212988

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

Phase: I/II

Therapy: CLR-457

Countries: Canada, Japan, Singapore, Spain, United States

US States: MA, NY, TN

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.

EGFR exon 19 deletion (continued)

NCT02108964
A Phase I/II, Multicenter, Open-label Study of EGFRmut-TKI EGF816, Administered Orally in Adult Patients with EGFRmut Solid Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: EGFR mutation

Other identifiers: 14-112, 14-249, CEGF816X2101, EudraCT Number: 2013-004482-14, TrialTroveID-206746

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

Phase: I/II

Therapy: EGF-816

Countries: Canada, Germany, Japan, Republic of Korea, Singapore, Spain, Taiwan, United States

US States: MA, NY

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

NCT01532011
A Phase I Dose-Escalation Study of Erlotinib in Combination With Pralatrexate in Subjects With Advanced Cancer

Cancer type: Unspecified Cancer

Variant class: EGFR exon 19 deletion

Other identifiers: 2011-0916, TrialTroveID-162206

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

Phase: I

Therapy: erlotinib + chemotherapy

Country: United States

US State: TX

US Contact: Dr. Jennifer J. Wheler [713-745-9246]

No NCT ID - see other identifier(s)
A Phase I First-in-Human, Safety, Efficacy and Tolerability Study of HMPL-813 for the Treatment of Various Tumours Including Tumours Carrying Activating EGFR Mutations that Have Metastasized to the Brain from Non-Small Cell Lung Cancer.

Cancer type: Unspecified Cancer

Variant class: EGFR activating mutation

Other identifiers: 2010-813-00CH1, CTR20130972, TrialTroveID-132127

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

Phase: I

Therapy: epitinib

Country: China

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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EGFR exon 19 deletion (continued)

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: EGFR positive

Other identifiers: 2013-0525, CHRMS 14-081, EMR100018-001, 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, MN, 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.

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.

ALK fusion

Variant Class	Evidence Items
ALK aberration	4
↳ ALK positive	3
↳ ALK fusion	12

ERBB2 amplification

Variant Class	Evidence Items
ERBB2 aberration	1
↳ ERBB2 positive	10
↳ ERBB2 amplification	21

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.

EGFR exon 19 deletion

Variant Class	Evidence Items
EGFR positive	1
↳ EGFR mutation	3
↳ EGFR exon 19 mutation	0
↳ EGFR exon 19 activating mutation	0
↳ EGFR exon 19 sensitizing mutation	0
↳ EGFR exon 19 deletion	13
↳ EGFR activating mutation	4
↳ EGFR exon 19 activating mutation	0
↳ EGFR exon 19 sensitizing mutation	0
↳ EGFR exon 19 deletion	13
↳ EGFRi sensitizing mutation	0
↳ EGFR exon 19 sensitizing mutation	0
↳ EGFR exon 19 deletion	13

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.

Report Signed by		Report Checked by	
			
Clinical Scientist	☑	BMS	☐
Pathologist	☐	BMS (Senior)	☑
BMS (Senior)	☐		

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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