[Oncofocus] Patient Test Report

Oncologica UK Ltd
Suite 15-16, The Science Village
Chesterford Research Park
Cambridge, CB10 1XL, UK
Tel: +44(0)1223 785327
Email: info@oncologica.com

ONC17			
Surname		**Requesting Clinician**	
Forename			
DOB		**Date requested**	
Gender	Female		
Histology #	02689/A1 Lung	**Tumour %**	20-25%
Primary site	Adenocarcinoma	**Tumour %**	-
Tumour subtype	Soft Tissue	**(macrodissected)**	
Tissue Type			

Comment:

237 genes were targeted using 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 582 anti-cancer targeted therapies.

The RNA extracted from this sample was of optimal quality. The DNA extracted form the sample was of borderline quality. The Oncofocus assay on which the sample was run met all assay specific quality metrics for detecting oncogenes, fusion genes and tumour suppressors, however, copy number variation analysis was not possible.

The following actionable variants were detected:

Variant Summary

Sample Cancer Type: Non-Small Cell Lung 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 **p.(Ala775_Gly776insYVMA) c.2313_2324dup** (also known as p.(E770_A771insAYVM) c.2324_2325insATACGTGATGGC)	✖	✖	✖	● (2)	● (15)

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(PPV) of 92%. Copy number variants; amplifications of CN> 6 with the 5% confidence value of ≥4 after normalization and deletions with 95% CI ≤1 are classified as present when the tumour% >50% with a sensitivity of 80% and PPV 100%. Gene Fusions are reported when occurring in >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.

Oncologica UK Ltd
Suite 15-16, The Science Village
Chesterford Research Park
Cambridge, CB10 1XL, UK
Tel: +44(0)1223 785327
Email: info@oncologica.com

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 p.(E770_A771insAYVM) c.2324_2325insATACGTGATGGC

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
afatinib	✖	✖	✖	●	● (II)
trastuzumab	✖	✖	✖	●	✖
ado-trastuzumab emtansine	✖	✖	✖	✖	● (II)
afatinib + chemotherapy	✖	✖	✖	✖	● (II)
AZD-8931, erlotinib + chemotherapy	✖	✖	✖	✖	● (II)
erlotinib + chemotherapy	✖	✖	✖	✖	● (II)
lapatinib	✖	✖	✖	✖	● (II)
luminespib	✖	✖	✖	✖	● (II)
neratinib	✖	✖	✖	✖	● (II)
pertuzumab + trastuzumab	✖	✖	✖	✖	● (II)
pyrotinib	✖	✖	✖	✖	● (II)
AP32788	✖	✖	✖	✖	● (I/II)
pirotinib	✖	✖	✖	✖	● (I/II)
selumetinib + vistusertib	✖	✖	✖	✖	● (I/II)
everolimus + trastuzumab + letrozole	✖	✖	✖	✖	● (I)
varlitinib + 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.

Oncologica UK Ltd
Suite 15-16, The Science Village
Chesterford Research Park
Cambridge, CB10 1XL, UK
Tel: +44(0)1223 785327
Email: info@oncologica.com

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 2016-12-01. 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 p.(E770_A771insAYVM) c.2324_2325insATACGTGATGGC

● afatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ERBB2 mutation

US-NCCN Recommendation category: 2B

Population segment (Line of therapy):
- NSCLC (Not specified)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2017]

● trastuzumab

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ERBB2 mutation

US-NCCN Recommendation category: 2B

Population segment (Line of therapy):
- NSCLC (Not specified)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2017]

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 2016-12-01. 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 p.(E770_A771insAYVM) c.2324_2325insATACGTGATGGC

No NCT ID - see other identifier(s)
A Study of Trastuzumab Emtansine in Patients With HER2-Positive, Recurrent Metastatic Non-Small Cell Lung Cancer

Cancer type: Non-Small Cell Lung Cancer

Variant class: ERBB2 exon 20 insertion

Other identifiers: HER2-CS-2, TrialTroveID-258506, UMIN000017709

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

Phase: II

Therapy: ado-trastuzumab emtansine

Location: Japan

NCT02369484
Afatinib in Pretreated Patients With Advanced NSCLC Harbouring HER2 Exon 20 Mutations

Cancer type: Non-Small Cell Lung Cancer

Variant class: ERBB2 exon 20 mutation

Other identifiers: 1200.230, ETOP 7-14, ETOP 7-14 - NICHE, EudraCT Number: 2014-005098-35, NICHE, REec-2015-1543, TrialTroveID-252749

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

Phase: II

Therapy: afatinib

Locations: Germany, Netherlands, Spain, Switzerland

NCT01922583
A Multi-center Phase II Study of AUY922 in Patients with Stage IV Non-small Cell Lung Cancer (NSCLC) With Driver Molecular Alterations Other Than Sensitive EGFR Mutation, Who have Progressed after one Line of Systemic Therapy

Cancer type: Non-Small Cell Lung Cancer

Variant class: ERBB2 exon 20 mutation

Other identifiers: 1020009413, CAUY922ATW02T(201302063MIPD), TrialTroveID-192154

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

Phase: II

Therapy: luminespib

Location: Taiwan

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 p.(E770_A771insAYVM) c.2324_2325insATACGTGATGGC (continued)

NCT01953926
An Open-label, Multicenter, Multinational, Phase II Study Exploring the Efficacy and Safety of Neratinib Therapy in Patients With Solid Tumors With Activating HER2, HER3 or EGFR Mutations or With EGFR Gene Amplification.

Cancer type: Non-Small Cell Lung Cancer

Variant class: ERBB2 activating mutation

Other identifiers: 13-140, 13-615, CTA733, EudraCT Number: 2013-002872-42, IRAS ID: 171670, NCI-2014-00495, PUMA-NER-5201, REec-2014-0843, SUMMIT, SUMMIT basket, TrialTroveID-191740

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

Phase: II

Therapy: neratinib

Locations: Australia, Finland, Israel, Italy, Republic of Korea, Spain, United Kingdom, United States

US States: CA, FL, MA, MO, MS, NJ, NY, TN, TX

US Contact: Puma Biotechnology Clinical Operations [424-248-6500; ClinicalTrials@pumabiotechnology.com]

NCT02597946
A Phase II Study of Afatinib in Patients With Advanced NSCLC Harboring HER2 Mutations, Previously Treated With Chemotherapy

Cancer type: Non-Small Cell Lung Cancer

Variant class: ERBB2 mutation

Other identifiers: CTR20160453, 1200.222, TrialTroveID-267515

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

Phase: II

Therapy: afatinib + chemotherapy

Location: Malaysia

NCT02535507
Single Arm Phase II Clinical Trial to Investigate the Efficacy and Safety of Pyrotinib as a Single Agent in HER2 Mutation Advanced Non-small Cell Lung Cancer Patients Who Failed to Previous at Least 2nd Line Treatments

Cancer type: Non-Small Cell Lung Cancer

Variant class: ERBB2 mutation

Other identifiers: FK1406, TrialTroveID-263775

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

Phase: II

Therapy: pyrotinib

Location: 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.

Oncologica UK Ltd
Suite 15-16, The Science Village
Chesterford Research Park
Cambridge, CB10 1XL, UK
Tel: +44(0)1223 785327
Email: info@oncologica.com

ERBB2 p.(E770_A771insAYVM) c.2324_2325insATACGTGATGGC (continued)

NCT02117167
Intergroup Trial UNICANCER UC 0105-1305/ IFCT 1301: SAFIR02_Lung - Evaluation of the Efficacy of High Throughput Genome Analysis as a Therapeutic Decision Tool for Patients With Metastatic Non-small Cell Lung Cancer

Cancer type: Non-Small Cell Lung Cancer

Variant class: ERBB2 aberration

Other identifiers: EudraCT Number: 2013-001653-27, IFCT-1301 SAFIR02 Lung, SAFIR02 Lung ITTC-1301, SAFIR02_Lung, TrialTroveID-207256, UC 0105-1305 / IFCT 1301

Population segments: Adenocarcinoma, First line, Large Cell, Maintenance/ Consolidation, Second line or greater/Refractory/Relapsed, Squamous Cell, Stage III, Stage IV

Phase: II

Therapies: AZD-8931, erlotinib + chemotherapy

Location: France

NCT02716116
A Phase I/II Study Of The Safety, Pharmacokinetics, And Anti-Tumor Activity Of The Oral EGFR/HER2 Inhibitor AP32788 In Non-Small Cell Lung Cancer

Cancer type: Non-Small Cell Lung Cancer

Variant class: ERBB2 exon 20 insertion

Other identifiers: 16-143, AP32788-15-101, NCI-2016-00587, TrialTroveID-262671

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

Phase: I/II

Therapy: AP32788

Location: United States

US States: CA, CO, MA, NY, TN, VA

US Contact: Dr. Shuanglian Li [617-503-7148; Shuanglian.Li@ariad.com]

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

Cancer type: Non-Small Cell Lung 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

Location: United Kingdom

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

ERBB2 p.(E770_A771insAYVM) c.2324_2325insATACGTGATGGC (continued)

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

Cancer type: Lung Cancer

Variant class: ERBB2 activating mutation

Other identifiers: 15-335, TrialTroveID-256389

Population segments: First line, Stage III, Stage IV

Phase: II

Therapy: ado-trastuzumab emtansine

Location: United States

US State: NY

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

NCT02465060
Molecular Analysis for Therapy Choice (MATCH)

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 activating mutation

Other identifiers: 15-7002, 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: (N/A), Aggressive, ALK, Classical, EGFR, HER2 positive, Indolent, Nodular lymphocyte-predominant, Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: II

Therapy: afatinib

Location: 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.

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 p.(E770_A771insAYVM) c.2324_2325insATACGTGATGGC (continued)

NCT02091141
My Pathway: An Open Label Phase IIa Study Evaluating Trastuzumab/ Pertuzumab, Erlotinib, Vemurafenib/ Cobimetinib, 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 activating mutation

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

Location: 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: Hoffmann-La Roche, Study Director [888-662-6728; global.rochegenentechtrials@roche.com]

NCT02689336
Phase II Clinical Trial Treating Relapsed/ Recurrent/Refractory Pediatric Solid Tumors With the Genomically-Targeted Agent Erlotinib in Combination With Temozolomide

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 mutation

Other identifiers: 201604002, NCI-2016-00549, TrialTroveID-273560

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

Phase: II

Therapy: erlotinib + chemotherapy

Location: United States

US State: MO

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

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 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

Phase: II

Therapy: lapatinib

Location: France

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

ERBB2 p.(E770_A771insAYVM) c.2324_2325insATACGTGATGGC (continued)

NCT02442414
A Phase 1 Study of KBP-5209 in Patients With Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: ERBB aberration

Other identifiers: 2014-0891, 5209-CPK-1001, NCI-2015-00881, TrialTroveID-195201

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

Phase: I/II

Therapy: pirotinib

Location: United States

US States: IN, TX, UT

US Contact: Matthew S. Hunt [608-332-8641; Matthew.hunt2@covance.com]

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 mutation

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

Location: United States

US State: TX

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

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 mutation

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

Location: 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.

Oncologica UK Ltd
Suite 15-16, The Science Village
Chesterford Research Park
Cambridge, CB10 1XL, UK
Tel: +44(0)1223 785327
Email: info@oncologica.com

ERBB2 p.(E770_A771insAYVM) c.2324_2325insATACGTGATGGC (continued)

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 mutation

Other identifiers: SHRUS 1001, TrialTroveID-261429

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

Phase: I

Therapy: pyrotinib

Location: United States

US State: TX

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

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

Location: Singapore

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

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 p.(E770_A771insAYVM) c.2324_2325insATACGTGATGGC

Variant Class	Evidence Items
ERBB aberration	1
↳ ERBB2 aberration	3
↳ ERBB2 mutation	9
↳ ERBB2 activating mutation	4
↳ ERBB2 exon 20 insertion	2
↳ ERBB2 exon 20 mutation	2
↳ ERBB2 exon 20 insertion	2

Appendix: Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Allele Frequency	Transcript	Variant Effect	Gene Class	Variant Class
ERBB2	p.(E770_A771insAYVM)	c.2324_2325insATACGTGATGGC	COSM682	11.43%	NM_004448.3	nonframeshift Insertion	Gain of Function	Hotspot

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


oncologica