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Leading a new era of precision oncology

Oncofocus®

Precision Oncology

ONCOFOCUS® TEST REPORT

Oncologica UK Ltd
Suite 2, The Newnham Building
Chesterford Research Park, Little Chesterford
Cambridge, CB10 1XL
Tel: +44(0)1223 785327
Email: info@oncologica.com

ONC19			
Surname		**Requester**	
Forename		**Contact details**	
DOB		**Date requested**	
Gender			
Histology #		**Tumour %**	70%
Primary site	Unknown	**Tumour %**	-
Tumour subtype	Metastatic Carcinoma	**(macrodissected)**	
Tissue Type	Liver		

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

Oncofocus currently targets 505 genes covering oncogenes, fusion genes, genes susceptible to copy number variation and tumour suppressors. Actionable genetic variants detected by Oncofocus are currently linked to 687 anti-cancer targeted therapies/ therapy combinations.

The following actionable variants were detected:

Please note; The KRAS amplifiifcation falls below our normal threshold for reporting, however, the quality of the assay metrics support the reporting of the variant at this lower sensitivity.

Within the 'Current Clinical Trials Information' section of this report, starting on page 6, the NCT numbers are hyperlinks to the clinicaltrials.gov webpages which should be accessed to gain further trial specific information

Sample Cancer Type: Unknown Primary Origin

Clinically Significant Biomarkers

Indicated **Contraindicated**

Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
MET exon 14 skipping mutation (2928 reads)	Clinical trials and/or off-label	crizotinib	4
KRAS amplification (5 copies)	Clinical trials and/or off-label	Clinical trials and/or off-label	6
AKT3 amplification (6 copies)	Clinical trials and/or off-label	Clinical trials and/or off-label	6
NTRK1 amplification (6 copies)	Clinical trials and/or off-label	Clinical trials and/or off-label	5
CCND2 amplification (6 copies)	Clinical trials and/or off-label	Clinical trials and/or off-label	3
MYC amplification (14 copies)	Clinical trials and/or off-label	Clinical trials and/or off-label	1
FANCI deletion (0.9 copies)	Clinical trials and/or off-label	Clinical trials and/or off-label	3
ARID1A deletion (0.8 copies)	Clinical trials and/or off-label	Clinical trials and/or off-label	1

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

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

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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Tier Criteria Met

Genomic Alteration	Tier Classification for Unknown Primary Origin
MET exon 14 skipping mutation Tier IIC	IIC: Biomarker is included in ESMO or NCCN guidelines that predict response or resistance to therapies in other cancer types IIC: Biomarker is an inclusion criteria for clinical trials
KRAS amplification Tier IIC	IIC: Biomarker is an inclusion criteria for clinical trials
AKT3 amplification Tier IIC	IIC: Biomarker is an inclusion criteria for clinical trials
NTRK1 amplification Tier IIC	IIC: Biomarker is an inclusion criteria for clinical trials
CCND2 amplification Tier IIC	IIC: Biomarker is an inclusion criteria for clinical trials
MYC amplification Tier IIC	IIC: Biomarker is an inclusion criteria for clinical trials
FANC deletion Tier IIC	IIC: Biomarker is an inclusion criteria for clinical trials
ARID1A deletion Tier IIC	IIC: Biomarker is an inclusion criteria for clinical trials

Reference: Li et al. Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American

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

MET exon 14 skipping mutation

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
crizotinib	✖	✖	✖	○	● (II)
AMG-337	✖	✖	✖	✖	● (II)
ABBV-399, ABBV-399 + erlotinib, ABBV-399 + nivolumab	✖	✖	✖	✖	● (I)

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

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Relevant Therapy Summary (continued)

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

KRAS amplification

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
sorafenib	✖	✖	✖	✖	● (II)
ASTX029	✖	✖	✖	✖	● (I/II)
cobimetinib	✖	✖	✖	✖	● (I/II)
abemaciclib + LY3214996 , LY3214996 , LY3214996 + chemotherapy, LY3214996 + midazolam	✖	✖	✖	✖	● (I)
LTT-462	✖	✖	✖	✖	● (I)
LXH254 , LXH254 + spartalizumab	✖	✖	✖	✖	● (I)

AKT3 amplification

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

NTRK1 amplification

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
entrectinib	✖	✖	✖	✖	● (I/II)
LOXO-195	✖	✖	✖	✖	● (I/II)
larotrectinib	✖	✖	✖	✖	● (I)
sitravatinib	✖	✖	✖	✖	● (I)
VMD-928	✖	✖	✖	✖	● (I)

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

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Relevant Therapy Summary (continued)

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

CCND2 amplification

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
abemaciclib	✖	✖	✖	✖	● (II)
palbociclib	✖	✖	✖	✖	● (II)

MYC amplification

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
prexasertib	✖	✖	✖	✖	● (II)

FANC deletion

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

ARID1A deletion

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
talazoparib	✖	✖	✖	✖	● (II)

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

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Relevant Therapy Details

Current NCCN Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated 👎 Not recommended 🛡 Resistance

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

MET exon 14 skipping mutation

○ crizotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** MET exon 14 skipping mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Non-Small Cell Lung Cancer; Emerging targeted agents

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer Version 6.2018]

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Current Clinical Trials Information

Clinical Trials information is current as of 2018-09-04. For the most up-to-date information regarding a particular trial, search www.clinicaltrials.gov by NCT ID or search local clinical trials authority website by local identifier listed in 'Other identifiers'.

MET exon 14 skipping mutation

NCT03147976
A Phase II Study of AMG 337 in Subjects With Advanced or Metastatic Solid Tumors That Overexpress Mesenchymal Epithelial Transition (MET) or Harbor MET Exon 14 Skipping (METex14del) Mutations

Cancer type: Unspecified Solid Tumor

Variant class: MET exon 14 skipping mutation

Other identifier: QUILT-3.036

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

Phase: II

Therapy: AMG-337

Location: United States

US State: CA

US Contact: NantPharma Clinical Review Team 310-853-7562; clinical.trials@NantKwest.com]

NCT02465060
Molecular Analysis for Therapy Choice (MATCH)

Cancer type: Unspecified Solid Tumor

Variant class: MET exon 14 skipping mutation

Other identifiers: 15-7002, CTSU/EAY131, EAY131, EAY131-A, EAY131-B, EAY131-C1, EAY131-C2, EAY131-E, EAY131-F, EAY131-G, EAY131-H, EAY131-I, EAY131-J, EAY131-L, EAY131-M, EAY131-MATCH, EAY131-N, EAY131-P, EAY131-Q, EAY131-R, EAY131-S1, EAY131-S2, EAY131-T, EAY131-U, EAY131-V, EAY131-W, EAY131-X, EAY131-Y, EAY131-Z1A, EAY131-Z1B, EAY131-Z1C, EAY131-Z1D, EAY131-Z1E, EAY131-Z1F, EAY131-Z1G, EAY131-Z1H, EAY131-Z1I, EAY131-Z1J, ECOGEAY131-M, MATCH, NCI-2015-00054, NCI-MATCH

Population segments: (N/A), Aggressive, Classical, Fourth line or greater, HER2 positive, Indolent, Nodular lymphocyte-predominant, Second line, Stage III, Stage IV, Third line

Phase: II

Therapy: crizotinib

Locations: Puerto Rico, United States

US States: AK, AL, AR, AZ, CA, CO, CT, DC, DE, FL, GA, HI, IA, ID, IL, IN, KS, KY, LA, MA, MD, ME, MI, MN, MO, MS, MT, NC, ND, NE, NH, NJ, NM, NV, NY, OH, OK, OR, PA, RI, SC, SD, TN, TX, UT, VA, VT, WA, WI, WV, WY

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

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.

MET exon 14 skipping mutation (continued)

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

Cancer type: Unspecified Solid Tumor

Variant class: MET aberration

Other identifiers: CA209-9DL, CAPTUR, ESR-17-12831, ML39800, PM1, WI233446

Population segments: Aggressive, Diffuse large B-cell lymphoma (DLBCL), Extranodal marginal zone B-cell lymphoma (MALT), First line, Follicular lymphoma (FL), Indolent, Lymphoblastic lymphoma (LBL), Mantle cell lymphoma (MCL), Other subtype, Second line, Stage III, Stage IV, Waldenstrom`s macroglobulinemia (WM)

Phase: II

Therapy: crizotinib

Location: Canada

NCT02099058
A Multicenter, Phase I/Ib, Open-Label, Dose-Escalation Study of ABBV-399, an Antibody Drug Conjugate, in Subjects With Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: MET exon 14 skipping mutation

Other identifiers: 00052355, 14-438, 201506075, 2016-0618, EudraCT Number: 2014-003154-14, M14-237, NCI-2014-00926

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

Phase: I

Therapies: ABBV-399, ABBV-399 + erlotinib, ABBV-399 + nivolumab

Locations: Finland, France, Italy, Taiwan, United States

US States: CA, CO, IL, MA, MI, MO, NC, TN, TX, VA

US Contact: ABBVIE CALL CENTER 847-283-8955; abbvieclinicaltrials@abbvie.com]

KRAS amplification

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 amplification

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

Population segments: Maintenance/Consolidation, Second line, Stage III, Stage IV

Exclusion criteria variant class: BRAF V600 mutation (Unspecified Solid Tumor)

Phase: II

Therapy: sorafenib

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.

KRAS amplification (continued)

NCT03520075
A Phase I/II Study of the Safety, Pharmacokinetics, and Activity of ASTX029 in Subjects With Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: RAS/RAF/MEK/ERK pathway

Other identifier: ASTX029-01

Population segments: Second line, Stage III, Stage IV

Phase: I/II

Therapy: ASTX029

Location: United States

US States: CT, TX, VA

US Contact: Richard J. Morishige 925-560-2882; Richard.Morishige@astx.com]

NCT02639546
A Phase I/II, Multicenter, Open-Label, Dose-Escalation Study of The Safety And Pharmacokinetics of Cobimetinib In Pediatric And Young Adult Patients With Previously Treated Solid Tumors - iMATRIX Cobi

Cancer type: Unspecified Solid Tumor

Variant class: RAS/RAF/MEK/ERK pathway

Other identifiers: 15-524, 16-041, 2015-0929, CTRC#15-0005, DRKS00010690, EudraCT Number: 2014-004685-25, GO29665, iMATRIX Cobi, iMATRIXcobi, IRAS ID: 174562, NCI-2016-00541, NL52503.078.16

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

Phase: I/II

Therapy: cobimetinib

Locations: Canada, France, Germany, Israel, Italy, Spain, United Kingdom, United States

US States: AR, AZ, CA, FL, MA, NY, PA, TX

US Contact: Reference Study ID Number: GO29665 888-662-6728; global-roche-genentech-trials@gene.com]

NCT02857270
A Phase I Study of an ERK1/2 Inhibitor (LY3214996) Administered Alone or in Combination With Other Agents in Advanced Cancer

Cancer type: Unspecified Solid Tumor

Variant class: RAS/RAF/MEK/ERK pathway

Other identifiers: 16419, EudraCT Number: 2016-001907-21, I8S-MC-JUAB, JUAB, NCI-2017-00039

Population segments: Second line, Stage III, Stage IV

Phase: I

Therapies: abemaciclib + LY3214996 , LY3214996 , LY3214996 + chemotherapy, LY3214996 + midazolam

Locations: Australia, France, United States

US States: FL, MA, TN, TX

US Contact: Eli Lilly and Company 877-285-4559]

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 amplification (continued)

NCT02711345
A Phase I Dose Finding Study of Oral LTT462 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: CLTT462X2101, EudraCT number: 2015-003614-24, JapicCTI-163207, NCI-2016-00539, NL57739.031.16

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

Phase: I

Therapy: LTT-462

Locations: Germany, Italy, Japan, Netherlands, Singapore, Spain, Switzerland, United States

US States: NY, TX

US Contact: Novartis Pharmaceuticals 888-669-6682; Novartis.email@novartis.com]

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: 16-225, 2015-0913, CLXH254X2101, EudraCT Number: 2015-003421-33, NCI-2015-02280, NL55506.078.15, Nov RAFi (CLXH254X2101), REec-2016-2132, SNCTP000002708

Population segments: Second line, Stage III, Stage IV

Phase: I

Therapies: LXH254 , LXH254 + spartalizumab

Locations: Canada, France, Germany, Japan, Netherlands, Republic of Korea, Spain, Switzerland, United States

US States: NY, TX

US Contact: Novartis Pharmaceuticals 888-669-6682; Novartis.email@novartis.com]

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AKT3 amplification

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

Cancer type: Unspecified Solid Tumor

Variant class: AKT3 aberration

Other identifiers: CA209-9DL, CAPTUR, ESR-17-12831, ML39800, PM1, WI233446

Population segments: Aggressive, Diffuse large B-cell lymphoma (DLBCL), Extranodal marginal zone B-cell lymphoma (MALT), First line, Follicular lymphoma (FL), Indolent, Lymphoblastic lymphoma (LBL), Mantle cell lymphoma (MCL), Other subtype, Second line, Stage III, Stage IV, Waldenstrom`s macroglobulinemia (WM)

Phase: II

Therapy: temsirolimus

Location: Canada

NCT02576444
A Phase II Study of the PARP Inhibitor Olaparib (AZD2281) Alone and in Combination With AZD1775, AZD5363, or AZD6738 in Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: PI3K/AKT/MTOR pathway

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

Population segments: First line, Second line, Stage IV

Phase: II

Therapy: capivasertib + olaparib

Location: United States

US States: CT, MA, OH, TN

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

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

Cancer type: Unspecified Solid Tumor

Variant class: AKT3 aberration

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

Population segments: Second line, Stage III, Stage IV

Phase: I

Therapy: ARQ-751

Location: United States

US State: TX

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

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AKT3 amplification (continued)

NCT01226316

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

Cancer type: Unspecified Solid Tumor

Variant class: PI3K/AKT/MTOR pathway

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

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

Exclusion criteria variant classes: BRAF mutation (Bladder Cancer, Colorectal Cancer, Esophageal Cancer, Gastric Cancer, Gastrointestinal Stromal Tumor, Glioblastoma, Head and Neck Cancer, Kidney Cancer, Liver Cancer, Melanoma, Mesothelioma, Non-Small Cell Lung Cancer, Osteosarcoma, Pancreatic Cancer, Prostate Cancer, Skin Basal Cell Carcinoma, Small Cell Lung Cancer, Soft Tissue Sarcoma, Testicular Cancer, Thyroid Cancer), HRAS mutation (Bladder Cancer, Colorectal Cancer, Esophageal Cancer, Gastric Cancer, Gastrointestinal Stromal Tumor, Glioblastoma, Head and Neck Cancer, Kidney Cancer, Liver Cancer, Melanoma, Mesothelioma, Non-Small Cell Lung Cancer, Osteosarcoma, Pancreatic Cancer, Prostate Cancer, Skin Basal Cell Carcinoma, Small Cell Lung Cancer, Soft Tissue Sarcoma, Testicular Cancer, Thyroid Cancer), KRAS mutation (Bladder Cancer, Colorectal Cancer, Esophageal Cancer, Gastric Cancer, Gastrointestinal Stromal Tumor, Glioblastoma, Head and Neck Cancer, Kidney Cancer, Liver Cancer, Melanoma, Mesothelioma, Non-Small Cell Lung Cancer, Osteosarcoma, Pancreatic Cancer, Prostate Cancer, Skin Basal Cell Carcinoma, Small Cell Lung Cancer, Soft Tissue Sarcoma, Testicular Cancer, Thyroid Cancer), NRAS mutation (Bladder Cancer, Colorectal Cancer, Esophageal Cancer, Gastric Cancer, Gastrointestinal Stromal Tumor, Glioblastoma, Head and Neck Cancer, Kidney Cancer, Liver Cancer, Melanoma, Mesothelioma, Non-Small Cell Lung Cancer, Osteosarcoma, Pancreatic Cancer, Prostate Cancer, Skin Basal Cell Carcinoma, Small Cell Lung Cancer, Soft Tissue Sarcoma, Testicular Cancer, Thyroid Cancer)

Phase: I

Therapy: capivasertib

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

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

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

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AKT3 amplification (continued)

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

Cancer type: Unspecified Solid Tumor

Variant class: PI3K/AKT/MTOR pathway

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

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

Phase: I

Therapy: gedatolisib + palbociclib

Location: United States

US State: MA

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

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

Cancer type: Unspecified Solid Tumor

Variant class: PI3K/AKT/MTOR pathway

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

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

Phase: I

Therapies: palbociclib + pictilisib, palbociclib + taselisib

Location: United Kingdom

NTRK1 amplification

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: NTRK1 aberration

Other identifiers: ALKA-372-001, EudraCT Number: 2012-000148-88

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

Phase: I/II

Therapy: entrectinib

Location: Italy

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

NTRK1 amplification (continued)

NCT03215511
A Phase I/II Study of the TRK Inhibitor LOXO-195 in Adult and Pediatric Subjects With Previously Treated NTRK Fusion Cancers

Cancer type: Unspecified Solid Tumor

Variant class: NTRK aberration

Other identifiers: 2017-0418, EudraCT Number: 2017-004246-20, LOXO-EXT-17005

Population segments: Second line, Stage III, Stage IV

Phase: I/II

Therapy: LOXO-195

Locations: Denmark, United States

US States: CA, MA, NY, OR, TN, TX

US Contact: Patient Advocacy 855-687-5123; clinicaltrials@loxooncology.com]

NCT03556228
An Open-Label, Multiple-Dose, Dose-Escalation Study to Investigate the Safety, Pharmacokinetics, and Pharmacodynamics of VMD-928 in Subjects With Solid Tumors or Lymphoma

Cancer type: Unspecified Solid Tumor

Variant class: NTRK1 amplification

Other identifiers: 18029, VMO-01C

Population segments: Aggressive, Classical, HER2 negative, Indolent, Nodular lymphocyte-predominant, Second line, Stage III, Stage IV, Triple receptor negative

Phase: I

Therapy: VMD-928

Location: United States

US State: CA

US Contact: VM Oncology 510-661-6770; om@vmoncology.com]

NCT02122913
A Phase I Study of the Oral TRK Inhibitor LOXO-101 in Adult Patients With Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: NTRK amplification

Other identifiers: 14-189, 2014-1056, LOXO-TRK-14001, NCI-2014-02044

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

Phase: I

Therapy: larotrectinib

Location: United States

US States: CO, MA, OH, OR, PA, TN, TX

US Contact: Patient Advocacy clinicaltrials@loxooncology.com]

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

Oncologica UK Ltd
Suite 2, The Newnham Building
Chesterford Research Park, Little Chesterford
Cambridge, CB10 1XL
Tel: +44(0)1223 785327
Email: info@oncologica.com

NTRK1 amplification (continued)

NCT02219711
A Phase I/Ib Study of MGCD516 in Patients With Advanced Solid Tumor Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: NTRK amplification

Other identifiers: 14-308, 16071502, 2014-1005, 20150094, 516-001, 76853, AAAO0006, NCI-2014-01866, UMCC 2015.040, UW15054

Population segments: Adenocarcinoma, EGFR, Hormone refractory, Line of therapy N/A, Second line, Stage III, Stage IV, Third line, Unresectable

Phase: I

Therapy: sitravatinib

Locations: Republic of Korea, United States

US States: AL, CA, CO, FL, IL, MA, MD, MI, NE, NM, NY, OH, PA, SC, TN, TX, UT, VA, WA, WI

US Contact: Mirati Therapeutics Study Locator Services 844-893-5530; miratistudylocator@emergingmed.com]

CCND2 amplification

NCT03310879
A Phase II Study of the CDK4/6 Inhibitor Abemaciclib in Patients With Solid Tumors Harboring Genetic Alterations in Genes Encoding D-type Cyclins or Amplification of CDK4 or CDK6

Cancer type: Unspecified Solid Tumor

Variant class: CCND2 amplification

Other identifiers: 17-343, NCI-2017-02359

Population segments: First line, Stage III, Stage IV

Phase: II

Therapy: abemaciclib

Location: United States

US State: MA

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

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

Cancer type: Unspecified Solid Tumor

Variant class: CCND2 amplification

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

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

Phase: II

Therapy: palbociclib

Location: United States

US State: PA

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

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Oncologica UK Ltd
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Chesterford Research Park, Little Chesterford
Cambridge, CB10 1XL
Tel: +44(0)1223 785327
Email: info@oncologica.com

CCND2 amplification (continued)

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

Cancer type: Unspecified Solid Tumor

Variant class: CCND2 amplification

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

Population segments: CNS mets, Second line, Stage IV

Phase: II

Therapy: palbociclib

Location: United States

US State: MA

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

MYC amplification

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

Cancer type: Unspecified Solid Tumor

Variant class: MYC amplification

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

Population segments: Second line, Stage III, Stage IV

Phase: II

Therapy: prexasertib

Location: United States

US State: MA

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

FANC deletion

No NCT ID - see other identifier(s)
Single Arm, Open label, Signal Seeking, Phase IIa Trial Of The Activity Of Olaparib In Combination With Durvalumab In Patients With Tumours With Homologous Recombination Repair Defects

Cancer type: Unspecified Solid Tumor

Variant class: FANC deletion

Other identifiers: ACTRN12617001000392, MoST Addendum 3, U1111-1182-6652

Population segments: Second line, Stage III, Stage IV

Phase: II

Therapy: durvalumab + olaparib

Location: Australia

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Oncologica UK Ltd
Suite 2, The Newnham Building
Chesterford Research Park, Little Chesterford
Cambridge, CB10 1XL
Tel: +44(0)1223 785327
Email: info@oncologica.com

FANC deletion (continued)

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

Cancer type: Unspecified Solid Tumor

Variant class: Fanconi anemia pathway

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

Population segments: Second line, Stage III, Stage IV

Phase: II

Therapy: prexasertib

Location: United States

US State: MA

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

NCT02286687
Phase II Study of the PARP Inhibitor BMN 673 (Talazoparib Tosylate) in Advanced Cancer Patients With Somatic Alterations in BRCA1/2, Mutations/Deletions in PTEN or PTEN Loss, a Homologous Recombination Defect, Mutations/ Deletions in Other BRCA Pathway Genes and Germline Mutation in BRCA1/2 (Not Breast or Ovarian Cancer)

Cancer type: Unspecified Cancer

Variant class: Fanconi anemia pathway

Other identifiers: 2013-0961, NCI-2014-02494

Population segments: Fourth line or greater, Stage III, Stage IV

Phase: II

Therapy: talazoparib

Location: United States

US State: TX

US Contact: Dr. Sarina Piha-Paul 713-563-1930]

ARID1A deletion

NCT02286687
Phase II Study of the PARP Inhibitor BMN 673 (Talazoparib Tosylate) in Advanced Cancer Patients With Somatic Alterations in BRCA1/2, Mutations/Deletions in PTEN or PTEN Loss, a Homologous Recombination Defect, Mutations/ Deletions in Other BRCA Pathway Genes and Germline Mutation in BRCA1/2 (Not Breast or Ovarian Cancer)

Cancer type: Unspecified Cancer

Variant class: ARID1A deletion

Other identifiers: 2013-0961, NCI-2014-02494

Population segments: Fourth line or greater, Stage III, Stage IV

Phase: II

Therapy: talazoparib

Location: United States

US State: TX

US Contact: Dr. Sarina Piha-Paul 713-563-1930]

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Oncologica UK Ltd
Suite 2, The Newnham Building
Chesterford Research Park, Little Chesterford
Cambridge, CB10 1XL
Tel: +44(0)1223 785327
Email: info@oncologica.com

Evidence Summary by Variant Class

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.

MET exon 14 skipping mutation

Variant Class	Evidence Items
MET aberration	1
↳ MET positive	0
↳ MET exon 14 skipping mutation	4

KRAS amplification

Variant Class	Evidence Items
RAS/RAF/MEK/ERK pathway	5
↳ RAS amplification	0
↳ KRAS amplification	1
↳ KRAS aberration	0
↳ KRAS positive	0
↳ KRAS amplification	1

AKT3 amplification

Variant Class	Evidence Items
PI3K/AKT/MTOR pathway	4
↳ AKT aberration	0
↳ AKT3 aberration	2

NTRK1 amplification

Variant Class	Evidence Items
NTRK aberration	1
↳ NTRK amplification	2
↳ NTRK1 amplification	1
↳ NTRK1 aberration	1
↳ NTRK1 positive	0
↳ NTRK1 amplification	1

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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.

CCND2 amplification

Variant Class	Evidence Items
G1/S cell cycle pathway	0
↳ CCND2 amplification	3

MYC amplification

Variant Class	Evidence Items
MYC aberration	0
↳ MYC amplification	1

FANC deletion

Variant Class	Evidence Items
Fanconi anemia pathway	2
↳ FANC aberration	0
↳ FANC deletion	1

ARID1A deletion

Variant Class	Evidence Items
ARID1A deletion	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.

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

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

Ireland

Bymac Centre, Northwest
Business Park, Blanchardstow, Dublin 15

+353 1 8604204

Italy

Parco Tecnologico della Sardegna
Pula, Località Piscinamanna

+39 02 808 88210

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PD-1/PD-L1 TESTING

IMMUNOFOCUS® TEST REPORT

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Suite 2, The Newnham Building
Chesterford Research Park, Little Chesterford
Cambridge, CB10 1XL
Tel: +44(0)1223 785327
Email: info@oncologica.com

ONC19			
Surname		**Requester**	
Forename		**Contact details**	
DOB		**Date requested**	
Gender			
Histology #		**Tumour %**	70%
Primary site	Unknown	**Tumour %**	-
Tumour subtype	Metastatic Carcinoma	**(macrodissected)**	
Tissue Type	Liver		

PD-L1 test

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

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

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

PD-L1 Result

No significant PD-L1 immunostaining of tumour cells is observed. The tumour is associated with a focal sparse PD-L1 expressing immune cell (IC) infiltrate. The PD-L1 expressing tumour infiltrating immune cells (ICs) cover <1% of the tumour area occupied by tumour cells, intratumoural and contiguous peritumoural stroma.

Summary; PD-L1 Tumour Proportion Score 0%; PD-L1 positive ICs <1% of tumour area

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