Medical Laboratory
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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

ONC18			
Surname		**Requester**	
Forename		**Contact details**	
DOB		**Date requested**	
Gender			
Histology #		**Tumour %**	>95%
Primary site	Intra-abdominal Tumour	**Tumour %**	-
Tumour subtype	Liposarcoma	**(macrodissected)**	
Tissue Type	Intra-abdominal Tumour		

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 734 anti-cancer targeted therapies/therapy combinations.

The following actionable variants were detected:

Within the 'Current Clinical Trials Information' section of this report, starting on page 3, the NCT numbers are hyperlinks to the clinicaltrials.gov webpages which should be accessed to gain further trial specific information

Clinically Significant Biomarkers

Indicated **Contraindicated**

Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
CDK4 amplification	Clinical trials and/or off-label	Clinical trials and/or off-label	7
MDM2 amplification	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 Soft Tissue Sarcoma
CDK4 amplification Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
MDM2 amplification Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials

Reference: Li et al. *Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists.* J Mol Diagn. 2017 Jan;19(1):4-23.

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

CDK4 amplification

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
abemaciclib	✖	✖	✖	✖	● (II)
palbociclib	✖	✖	✖	✖	● (II)
ribociclib	✖	✖	✖	✖	● (II)
PNT-737 + chemotherapy	✖	✖	✖	✖	● (I/II)

MDM2 amplification

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
BI 907828	✖	✖	✖	✖	● (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 Details

Current Clinical Trials Information

Clinical Trials information is current as of 2018-12-03. 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'.

CDK4 amplification

NCT03096912
A Phase II Single Arm Study Assessing Efficacy and Safety of Ribociclib in Patients With Advanced Well-Differentiated or Dedifferentiated Liposarcoma

Cancer type: Soft Tissue Sarcoma

Variant class: CDK4 amplification

Other identifiers: 243/16, CLEE011

Population segments: Line of therapy N/A, Locally advanced, Metastatic

Other inclusion criteria: RB1 positive

Phase: II

Therapy: ribociclib

Location: Israel

NCT02797977
A Phase I/II Trial of Oral SRA737 (a Chk1 Inhibitor) Given in Combination With Gemcitabine Plus Cisplatin or Gemcitabine Alone in Subjects With Advanced Cancer

Cancer type: Soft Tissue Sarcoma

Variant class: G1/S cell cycle pathway

Other identifiers: 198606, 30498, CRUKD/16/005, EudraCT Number: 2015-004467-36, PNT737-02, SRA737-02

Population segments: BRCA, Fourth line or greater, KRAS, Second line, Stage III, Stage IV, Third line

Phase: I/II

Therapy: PNT-737 + chemotherapy

Locations: Spain, United Kingdom

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: CDK4 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

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

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CDK4 amplification (continued)

NCT02693535
Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Cancer type: Unspecified Solid Tumor

Variant class: CDK4 amplification

Other identifiers: NCI-2017-00510, Pro00014171, TAPUR

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

Phase: II

Therapy: palbociclib

Location: United States

US States: AL, AZ, CA, FL, GA, IL, MI, NC, ND, NE, OK, OR, PA, SD, TX, UT, VA, WA

Contact: Pam Mangat [pam.mangat@asco.org]

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

Cancer type: Unspecified Solid Tumor

Variant class: CDK4 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

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

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

Cancer type: Unspecified Solid Tumor

Variant class: CDK4 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: palbociclib

Location: Canada

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CDK4 amplification (continued)

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

Cancer type: Unspecified Solid Tumor

Variant class: G1/S cell cycle pathway

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

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

MDM2 amplification

NCT03449381
A Phase I, Open Label, Multicenter, Dose-escalation Study of BI 907828 in Adult Patients With Wild-type TP53 Enriched Advanced Solid Tumors and Expansion in Patients With MDM2 Amplified Advanced Solid Tumors.

Cancer type: Soft Tissue Sarcoma

Variant class: MDM2 amplification

Other identifiers: 1403-0001, EudraCT Number: 2017-003210-95, JapicCTI-184058

Population segments: Adenocarcinoma, CNS mets, Large Cell, Second line, Stage III, Stage IV

Other inclusion criteria: TP53 wild type

Exclusion criteria variant class: TP53 mutation

Phase: I

Therapy: BI 907828

Locations: Canada, Japan, United States

US States: CT, FL, NY, TN

Contact: Boehringer Ingelheim [800-243-0127; clintriage.rdg@boehringer-ingelheim.com]

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Evidence Summary by Variant Class

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

CDK4 amplification

Variant Class	Evidence Items
G1/S cell cycle pathway	2
↳ CDK4 aberration	1
↳ CDK4 amplification	4

MDM2 amplification

Variant Class	Evidence Items
MDM2 amplification	1

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Variant Details

Copy Number Variations

Gene	Locus	Copy Number
CDK4	chr12:58142244	15.06
MDM2	chr12:69202190	15.31

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+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