[Oncofocus] Patient Test Report

Oncologica UK Ltd
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Surname		**Requesting clinician**	
Forename			
DOB		**Date requested**	
Gender			
Histology #		**Tumour %**	80-85%
Primary site	Breast	**Tumour % (macrodissected)**	
Tumour subtype	Adenocarcinoma		
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.

221 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 485 anti-cancer targeted therapies.

The following actionable variants were detected:

Variant Summary

Sample Cancer Type: Breast 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
CCND1 amplification	✖	✖	✖	✖	● (2)
ATM p.(L2945fs) c.8831_8832delCT	✖	✖	✖	✖	● (2)

EMA: European Medicine Agency, **US-FDA:** United States-Food and Drug Administration, **ESMO:** European Society for Medical Oncology, **US-NCCN:** United States-National Comprehensive Cancer Network. Numbers in parentheses indicate the number of relevant therapies with evidence. Hotspot variants with >10% alternate allele reads, and in >10 unique reads are classified as 'detected' with an assay sensitivity and positive predictive value of 97%. Copy number variants; amplifications of a >5% confidence value of ≥4 after normalization and deletions of ≤1 are classified as present when the tumour% >50%. Gene Fusions are reported when occurring in >20 counts and meeting the thresholds of assay specific internal RNA quality control. With a sensitivity of 99% and PPV of 99%. Supplementary technical information is available upon request.

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

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Relevant Therapy Summary

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

CCND1 amplification

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
palbociclib	✖	✖	✖	✖	● (II)
ribociclib	✖	✖	✖	✖	● (II)

ATM p.(L2945fs) c.8831_8832delCT

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

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

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Current Global Clinical Trials Information

Global Clinical Trials information is current as of 2016-09-01. For the most up-to-date information regarding a particular trial, search www.clinicaltrials.gov by NCT ID or search local clinical trials authority website by local identifier listed in 'Other identifiers'.

CCND1 amplification

NCT02187783
Modular Phase II Study to Link Targeted Therapy to Patients with Pathway Activated Tumors: Module 8 - LEE011 for Patients with CDK4/6 Pathway Activated Tumors

Cancer type: Breast Cancer

Variant class: CCND1 amplification

Other identifiers: 051501, 2014-0689, CLEE011XUS03, NCI-2014-02068, SIGNATURE, TrialTroveID-212878

Population segments: Adenocarcinoma, Aggressive, Classical, Cutaneous T-cell lymphoma (CTCL), Diffuse large B-cell lymphoma (DLBCL), Extranodal marginal zone B-cell lymphoma (MALT), Follicular lymphoma (FL), HER2 negative, Indolent, Lymphoblastic lymphoma (LBL), N/A, Nodular lymphocyte-predominant, Other subtype, Peripheral T-cell lymphoma (PTCL), Second line or greater/Refractory/Relapsed, Small lymphocytic lymphoma (SLL), Stage III, Stage IV, Triple receptor negative, Waldenstrom`s macroglobulinemia (WM)

Other inclusion criteria: ERBB2 wild type, ER negative, PR negative

Phase: II

Therapy: ribociclib

Country: United States

US State: TX

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

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

Cancer type: Unspecified Solid Tumor

Variant class: CCND1 amplification

Other identifiers: NCI-2009-01467, Study 1006, TrialTroveID-120590, UPCC 03909, UPCC03909

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

Phase: II

Therapy: palbociclib

Country: United States

US State: PA

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

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CCND1 amplification (continued)

NCT02465060
Molecular Analysis for Therapy Choice (MATCH)

Cancer type: Unspecified Solid Tumor

Variant class: CCND1 amplification

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

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

Other inclusion criteria: RB1 expression

Phase: II

Therapy: palbociclib

Country: United States

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

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

ATM p.(L2945fs) c.8831_8832delCT

NCT02401347
A Phase II Clinical Trial of BMN 673 in BRCA1 and BRCA2 Wild-Type Patients With (i) Advanced Triple-Negative Breast Cancer and Homologous Recombination Deficiency as Assessed by the HRD Assay, and (ii) Advanced HER2-Negative Breast Cancer With Either a Germline or Somatic Mutation in Homologous Recombination Pathway Genes Talazoparib Beyond BRCA (TBB) Trial

Cancer type: Breast Cancer

Variant class: ATM mutation

Other identifiers: BRS0050, NCI-2015-00036, TBB, TrialTroveID-254540

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

Other inclusion criteria: ERBB2 wild type

Phase: II

Therapy: talazoparib

Country: United States

US State: CA

US Contact: Pei Jen Chang [650-725-0866; peijenc@stanford.edu]

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ATM p.(L2945fs) c.8831_8832delCT (continued)

NCT02693535
Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Cancer type: Unspecified Solid Tumor

Variant class: ATM mutation

Other identifiers: Pro00014171, TAPUR, TrialTroveID-273941

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

Phase: II

Therapy: olaparib

Country: United States

US States: MI, NC

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

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Appendix: Evidence Summary by Variant Class

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

CCND1 amplification

Variant Class	Evidence Items
G1/S cell cycle pathway	0
↳ CCND1 amplification	3

ATM p.(L2945fs) c.8831_8832delCT

Variant Class	Evidence Items
ATM mutation	2

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Appendix: Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
ATM	p.(L2945fs)	c.8831_8832delCT	.	chr11:108225581	86.77%	NM_000051.3	frameshift Deletion

Copy Number Variations

Gene	Locus	Copy Number
CCND1	chr11:69456941	11.41

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Report Signed by		Report Checked by	
			
Clinical Scientist	☑		
Pathologist	☐	BMS	☑
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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