[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

Surname			
Forename DOB		**Requesting Clinician**	
Gender	Male		
Histology #	H3480/16	**Date requested**	
Primary site	Bone/soft Tissue		
Tumour subtype	High Grade Sarcoma	**Tumour %**	90%
Tissue Type	Bone Left Inferior Pubic Ramus	**Tumour % (macrodissected)**	-

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.

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 following actionable variants were detected:

Variant Summary

Sample Cancer Type: Soft Tissue Sarcoma

● 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
BRCA1 p.(L668fs) c.2001_2002insA	○ (1)	○ (1)	✖	✖	● (4)
CDKN2A deletion	✖	✖	✖	✖	● (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(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.

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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

BRCA1 p.(L668fs) c.2001_2002insA

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
olaparib	○	✖	✖	✖	● (II)
rucaparib	✖	○	✖	✖	✖
prexasertib	✖	✖	✖	✖	● (II)
BGB-290 + BGB-A317	✖	✖	✖	✖	● (I)
talazoparib + chemotherapy	✖	✖	✖	✖	● (I)

CDKN2A deletion

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
ilorasertib	✖	✖	✖	✖	● (II)
palbociclib	✖	✖	✖	✖	● (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 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 2017-01-03. For the most up-to-date information, search www.ema.europa.eu/ema.

BRCA1 p.(L668fs) c.2001_2002insA

○ olaparib

Cancer type: Ovarian Cancer **Label as of:** 2016-11-03 **Variant class:** BRCA mutation

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/003726/WC500180151.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 2017-01-03. For the most up-to-date information, search www.fda.gov.

BRCA1 p.(L668fs) c.2001_2002insA

○ rucaparib

Cancer type: Ovarian Cancer **Label as of:** 2016-12-19 **Variant class:** BRCA mutation

Indications and usage:

RUBRACA™ is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated as monotherapy for the treatment of patients with deleterious BRCA mutation (germline and/or somatic) associated advanced ovarian cancer who have been treated with two or more chemotherapies. Select patients for therapy based on an FDA-approved companion diagnostic for RUBRACA™.

This indication is approved under accelerated approval based on objective response rate and duration of response. 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/2016/209115s000lbl.pdf

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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'.

BRCA1 p.(L668fs) c.2001_2002insA

NCT02693535
Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Cancer type: Unspecified Solid Tumor

Variant class: BRCA1 mutation

Other identifiers: Pro00014171, TAPUR, TrialTroveID-273941

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 or greater/Refractory/Relapsed, Small lymphocytic lymphoma (SLL), Stage III, Stage IV, Waldenstrom`s macroglobulinemia (WM)

Phase: II

Therapy: olaparib

Location: United States

US States: IL, MI, NC, PA, SD

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

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: BRCA1 mutation

Other identifiers: 16-281, TrialTroveID-284902

Population segments: Second line or greater/Refractory/Relapsed, 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]

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BRCA1 p.(L668fs) c.2001_2002insA (continued)

NCT02576444
A Phase II Study of the PARP Inhibitor Olaparib (AZD2281) Alone and in Combination With AZD1775, AZD5363, or AZD2014 in Advanced Solid Tumors

Cancer type: Unspecified Cancer

Variant class: DNA repair pathway

Other identifiers: 1508016363, OLAPCO, TrialTroveID-266161

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

Phase: II

Therapy: olaparib

Location: United States

US States: CT, MA

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

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: HRR pathway

Other identifiers: 16-281, TrialTroveID-284902

Population segments: Second line or greater/Refractory/Relapsed, 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]

NCT02317874
A Phase I Study of BMN 673 in Combination with Carboplatin and Paclitaxel in Patients with Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: BRCA1 mutation

Other identifiers: 051513, 9782, NCI 9782, NCI-2014-02474, NCI9782, TrialTroveID-248774

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

Phase: I

Therapy: talazoparib + chemotherapy

Location: United States

US States: NJ, WI

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

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BRCA1 p.(L668fs) c.2001_2002insA (continued)

NCT02660034
A Phase 1b, Open Label, Multiple Dose, Dose Escalation and Expansion Study to Investigate the Safety, Pharmacokinetics and Antitumor Activity of the Anti-PD-1 Monoclonal Antibody BGB-A317 in Combination With the PARP Inhibitor BGB-290 in Subjects With Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: HRR pathway

Other identifiers: BGB-A317/BGB-290_Study_001, TrialTroveID-271778

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

Phase: I

Therapy: BGB-290 + BGB-A317

Location: Australia

CDKN2A deletion

NCT02478320
A Proof-of-Concept Study for Ilorasertib (ABT-348) Activity in Patients With CDKN2A-Deficient Advanced Solid Cancers: a Phase II Basket Trial

Cancer type: Unspecified Solid Tumor

Variant class: CDKN2A deletion

Other identifiers: 2014-0920, NCI-2015-01251, TrialTroveID-260223

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

Phase: II

Therapy: ilorasertib

Location: United States

US State: TX

US Contact: Dr. David S. Hong [713-563-1930]

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CDKN2A deletion (continued)

NCT02693535
Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Cancer type: Unspecified Solid Tumor

Variant class: CDKN2A deletion

Other identifiers: Pro00014171, TAPUR, TrialTroveID-273941

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 or greater/Refractory/Relapsed, Small lymphocytic lymphoma (SLL), Stage III, Stage IV, Waldenstrom`s macroglobulinemia (WM)

Phase: II

Therapy: palbociclib

Location: United States

US States: IL, MI, NC, PA, SD

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

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, TrialTroveID-120590, UPCC 03909, UPCC03909

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

Phase: II

Therapy: palbociclib

Location: United States

US State: PA

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

CDKN2A deletion (continued)

NCT02540876

A Pilot Study for Ilorasertib (ABT-348) in Patients With CDKN2A-deficient Advanced Solid Cancers: A Series of Individual Patient Cross-Over Studies With Growth Trajectory Assessment

Cancer type: Unspecified Solid Tumor

Variant class: CDKN2A deletion

Other identifiers: AbbVie IIS-10750, IRB15-0083, NCI-2015-01328, P30CA014599, TrialTroveID-264142

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

Phase: I

Therapy: ilorasertib

Location: United States

US State: IL

US Contact: Linda L. Janisch [773-702-1612; ljanisch@medicine.bsd.uchicago.edu]

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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.

BRCA1 p.(L668fs) c.2001_2002insA

Variant Class	Evidence Items
DNA repair pathway	1
↳ BRCA mutation	2
↳ BRCA1 mutation	3
HRR pathway	2
↳ BRCA mutation	2
↳ BRCA1 mutation	3
Fanconi anemia pathway	0
↳ BRCA mutation	2
↳ BRCA1 mutation	3

CDKN2A deletion

Variant Class	Evidence Items
G1/S cell cycle pathway	1
↳ CDKN2A negative	0
↳ CDKN2A deletion	3

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Appendix: Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Allele Frequency	Transcript	Variant Effect	Gene Class	Variant Class
BRCA1	p.(L668fs)	c.2001_2002insA	.	23.04%	NM_007300.3	frameshift Insertion	Loss of Function	Deleterious

Copy Number Variations

Gene	Locus	Copy Number
CDKN2A	chr9:21968185	0.54

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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.

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


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