



[Oncofocus] Patient Test Report

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

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	<input type="radio"/> (1)	<input type="radio"/> (1)	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/> (4)
CDKN2A deletion	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/> (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.

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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.

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	<input type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/> (II)
rucaparib	<input checked="" type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>
prexasertib	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/> (II)
BGB-290 + BGB-A317	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/> (I)
talazoparib + chemotherapy	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/> (I)

CDKN2A deletion

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
ilorasertib	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/> (II)
palbociclib	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/> (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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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'.

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](tel:617-632-4942); Geoffrey_Shapiro@dfci.harvard.edu]

ONC17-:www.oncologica.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.

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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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.

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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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)**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]**ONC17-:**www.oncologica.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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