[Oncofocus] Patient Test Report

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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.

175 genes were targeted covering 2470 unique coding hot spots, 281 fusions and 19 CNV genes for actionable mutations linked to 484 anti-cancer targeted therapies.

The following actionable mutations were detected.

Variant Summary

Sample Cancer Type: Endometrial 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		Alt allele freq	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials
PIK3CA	c.1634A>G	p.(Glu545Gly)	27%	✖	✖	✖	✖	● (10)
PIK3CA	c.3139C>T	p.(His1047Tyr)	30%	✖	✖	✖	✖	● (10)
ESR1	c.1613A>G	p.(Asp538Gly)	30%	✖	✖	✖	✖	● (1)

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'. Copy number variants of a >5% confidence value of ≥4 after normalisation are classified as amplified. Gene Fusions are reported when occurring in >20 counts and meeting the thresholds of assay specific internal RNA quality control. Assay sensitivity and positive predictive value is 99% when these thresholds are met. 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

PIK3CA/ESR1 mutation

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
AZD-5363	✖	✖	✖	✖	● (I)

PIK3CA mutation

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
AZD-5363 + olaparib	✖	✖	✖	✖	● (II)
everolimus	✖	✖	✖	✖	● (II)
sirolimus	✖	✖	✖	✖	● (II)
taselisib	✖	✖	✖	✖	● (II)
AZD-2014 + selumetinib	✖	✖	✖	✖	● (I/II)
alpelisib + infigratinib	✖	✖	✖	✖	● (I)
AZD-5363	✖	✖	✖	✖	● (I)
copanlisib	✖	✖	✖	✖	● (I)
MSC-2363318A	✖	✖	✖	✖	● (I)
palbociclib + pictilisib, palbociclib + taselisib	✖	✖	✖	✖	● (I)

* 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 2016-06-01. 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'.

PIK3CA/ESR1 mutation

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: Endometrial Cancer

Variant class: PIK3CA mutation

Other identifiers: 102084, 14-214, 14-430, 2014-0160, CR1322AZ, D3610C00001, EudraCT Number: 2010-022167-35, IRAS ID: 62131, JapicCTI-152844, M10AZD, NCI-2014-01803, NL33755.031.10, P1TGIVEN, TrialTroveID-136773

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

Phase: I

Therapy: AZD-5363

Countries: Canada, France, Italy, Japan, Netherlands, Singapore, Spain, United Kingdom, United States

US States: CA, CO, CT, NY, OK, OR, SC, TN, TX

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

PIK3CA mutation

NCT02646319

A Pilot Study of a Rapid Access Platform for Investigational Drugs (RAPID) in Advanced Cancers

Cancer type: Endometrial Cancer

Variant class: PIK3CA aberration

Other identifiers: MC1313, NCI-2015-02151, RAPID, TrialTroveID-270911

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

Phase: II

Therapy: sirolimus

Country: United States

US States: AZ, MN

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

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PIK3CA mutation (continued)

NCT02155582
A Phase I Pharmacodynamic Study of Copanlisib (BAY 80-6946) as Monotherapy in Patients with Non-Hodgkin`s Lymphoma and Solid Tumors

Cancer type: Endometrial Cancer

Variant class: PIK3CA aberration

Other identifiers: 16790, BAYER 16790, EudraCT Number: 2013-004746-42, TrialTroveID-210261

Population segments: Aggressive, Diffuse large B-cell lymphoma (DLBCL), Follicular lymphoma (FL), Indolent, Mantle cell lymphoma (MCL), Other subtype, Peripheral T-cell lymphoma (PTCL), Second line or greater/Refractory/Relapsed, Squamous Cell, Stage III, Stage IV, Waldenstrom`s macroglobulinemia (WM)

Phase: I

Therapy: copanlisib

Countries: Belgium, France

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 Solid Tumor

Variant class: PIK3CA mutation

Other identifiers: 1508016363, OLAPCO, TrialTroveID-266161

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

Phase: II

Therapy: AZD-5363 + olaparib

Country: United States

US State: CT

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

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: PIK3CA mutation

Other identifiers: ET12-081, EudraCT number: 2012-004510-34, MOST, ProfiLER, TrialTroveID-200294

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

Phase: II

Therapy: everolimus

Country: 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.

PIK3CA mutation (continued)

NCT02449538
Study to Evaluate the Safety and Efficacy of Everolimus, in Subjects With PIK3CA Amplification, PTEN Loss and PIK3CA Mutation Refractory Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: PIK3CA mutation

Other identifiers: 2015-01-117, TrialTroveID-257722

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

Exclusion criteria variant classes: BRAF V600 mutation, KRAS G12 mutation, KRAS G13 mutation

Phase: II

Therapy: everolimus

Country: Republic of Korea

NCT02449564
The Pilot Study Evaluate the Safety and Efficacy of Sirolimus in Patients With PIK3CA Mutation and/or PIK3CA Amplification Refractory Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: PIK3CA mutation

Other identifiers: 2014-10-030, TrialTroveID-257741

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

Phase: II

Therapy: sirolimus

Country: Republic of Korea

NCT02465060
Molecular Analysis for Therapy Choice (MATCH)

Cancer type: Unspecified Solid Tumor

Variant class: PIK3CA mutation

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

Exclusion criteria variant classes: PTEN deletion, RAS mutation

Phase: II

Therapy: taselisib

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.

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PIK3CA mutation (continued)

NCT02583542
A Phase Ib/IIa Study of AZD2014 in Combination With Selumetinib in Patients With Advanced Cancers.

Cancer type: Unspecified Solid Tumor

Variant class: PIK3CA aberration

Other identifiers: 009896QM, EudraCT Number: 2014-002613-31, IRAS ID 172356, Torcmek, TrialTroveID-265019, UKCRN ID:18725

Population segments: EGFR, FGFR, HER2 negative, HER2 positive, KRAS, Second line or greater/Refractory/Relapsed, Squamous Cell, Stage III, Stage IV, Triple receptor negative

Phase: I/II

Therapy: AZD-2014 + selumetinib

Country: United Kingdom

NCT01928459
A Phase Ib, Open-label Study of Oral BGJ398 in Combination with Oral BYL719 in Adult Patients with Select Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: PIK3CA mutation

Other identifiers: 13-246, CBGJ398X2102, CT610, CTBE2014000264, EudraCT Number: 2013-001018-14, NCI-2013-01763, NL47080.031.13, SAKK 69/13, TrialTroveID-192837

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

Other inclusion criteria: FGFR1 wild type, FGFR2 wild type, FGFR3 wild type

Phase: I

Therapy: alpelisib + infigratinib

Countries: Australia, Belgium, France, Germany, Italy, Republic of Korea, Spain, Switzerland, United States

US States: FL, MI, MO, NY, TN, TX

US Contact: Novartis Pharmaceuticals [888-669-6682]

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: PIK3CA mutation

Other identifiers: CCR4191, EudraCT Number: 2014-002658-37, IRAS ID 159997, PIPA, TrialTroveID-253778

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

Phase: I

Therapies: palbociclib + pictilisib, palbociclib + taselisib

Country: United Kingdom

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PIK3CA mutation (continued)

NCT01971515

A Phase I, First-in-Human, Dose Escalation Trial of MSC2363318A, a Dual p70S6K/Akt Inhibitor, in Subjects With Advanced Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: PIK3CA aberration

Other identifiers: 2013-0525, CHRMS 14-081, EMR100018-001, NCI-2013-02370, TrialTroveID-196334

Population segments: Aggressive, Classical, EGFR, HER2 positive, Indolent, Nodular lymphocyte-predominant, Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: I

Therapy: MSC-2363318A

Country: United States

US States: CA, MI, TX, VT

US Contact: US Medical Information [888-275-7376]

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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.

PIK3CA mutation

Variant Class	Evidence Items
PIK3CA aberration	4
↳ PIK3CA mutation	8

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

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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.

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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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