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Leading a new era of precision oncology

Oncofocus®

Precision Oncology

ONCOFOCUS® TEST REPORT

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	-		
Surname	-	**Requester**	-
Forename	-	**Contact details**	-
DOB	-	**Date requested**	-
Gender	-		
Histology #	-	**Tumour %**	99%
Primary site	Cervix	**Tumour %**	-
Tumour subtype		**(macrodissected)**	
Tissue Type	Cervix		

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 687 anti-cancer targeted therapies/therapy combinations.

The following actionable variants were detected:
Please note; The PIK3CA variant detected falls below our normal threshold for reporting, however repeat testing has confirmed its presence.

Within the 'Current Clinical Trials Information' section of this report, starting on page 4, the NCT numbers are hyperlinks to the clinicaltrials.gov webpages which should be accessed to gain further trial specific information

Sample Cancer Type: Cervical Cancer

Clinically Significant Biomarkers

Indicated Contraindicated

Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
PIK3CA p.(E545K) c.1633G>A	Clinical trials and/or off-label	Clinical trials and/or off-label	12
CCND1 amplification	Clinical trials and/or off-label	Clinical trials and/or off-label	5
FGF19 amplification	Clinical trials and/or off-label	Clinical trials and/or off-label	4
FGF3 amplification	Clinical trials and/or off-label	Clinical trials and/or off-label	3

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.

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 Cervical Cancer
PIK3CA p.(E545K) c.1633G>A Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
CCND1 amplification Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
FGF19 amplification Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
FGF3 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

PIK3CA p.(E545K) c.1633G>A

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
MEK inhibitor + PIK3/mTOR inhibitor, PIK3/mTOR inhibitor	✖	✖	✖	✖	● (II/III)
capivasertib + olaparib	✖	✖	✖	✖	● (II)
copanlisib	✖	✖	✖	✖	● (II)
everolimus	✖	✖	✖	✖	● (II)
sirolimus	✖	✖	✖	✖	● (II)
temsirolimus	✖	✖	✖	✖	● (II)
ARQ-751	✖	✖	✖	✖	● (I)
capivasertib	✖	✖	✖	✖	● (I)
GDC-0077	✖	✖	✖	✖	● (I)
gedatolisib + palbociclib	✖	✖	✖	✖	● (I)
LY-3023414 + prexasertib	✖	✖	✖	✖	● (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.

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 (continued)

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

FGF19 amplification

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
INCB-62079	✖	✖	✖	✖	● (I/II)
TAS-120	✖	✖	✖	✖	● (I/II)
E-7090	✖	✖	✖	✖	● (I)
INCB-54828	✖	✖	✖	✖	● (I)

FGF3 amplification

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
TAS-120	✖	✖	✖	✖	● (I/II)
E-7090	✖	✖	✖	✖	● (I)
INCB-54828	✖	✖	✖	✖	● (I)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

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 Details

Current Clinical Trials Information

Clinical Trials information is current as of 2018-09-04. 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 p.(E545K) c.1633G>A

No NCT ID - see other identifier(s)
Molecular selection of therapy in metastatic colorectal cancer: a molecularly stratified randomised controlled trial programme

Cancer type: Cervical Cancer

Variant class: PIK3CA mutation

Other identifiers: 14893, CR13, CRUK/11/054, EudraCT Number: 2012-005111-12, FOCUS-4, FOCUS4, IRAS ID 119459, ISRCTN90061546, MREC N° 13/SC/0111, UKCRN ID: 14893

Population segments: First line, Stage III, Stage IV

Other inclusion criteria: PTEN underexpression

Phase: II/III

Therapies: MEK inhibitor + PIK3/mTOR inhibitor, PIK3/mTOR inhibitor

Location: United Kingdom

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: Cervical Cancer

Variant class: PIK3CA mutation

Other identifiers: 0C-14-10, 102084, 14-214, 14-430, 2014-0160, CR1322AZ, CSET 2365, D3610C00001, EudraCT Number: 2010-022167-35, IRAS ID: 62131, JapicCTI-152844, M10AZD, NCI-2014-01803, NL33755.031.10, P1TGIVEN, PRO 09

Population segments: (N/A), Adenocarcinoma, Estrogen receptor positive, Fourth line or greater, HER2 positive, Hormone refractory, Second line, Stage III, Stage IV, Third line

Phase: I

Therapy: capivasertib

Locations: Canada, Denmark, France, Italy, Japan, Singapore, Spain, United States

US States: CA, CO, NY, OK, PA, TN, TX

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

PIK3CA p.(E545K) c.1633G>A (continued)

NCT02688881
Study to Evaluate the Safety and Efficacy of Sirolimus, in Subject With Refractory Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: PIK3CA E545K mutation

Other identifiers: 2016-02-052, KCT0002997, SMC 2016-02-052-001

Population segments: (N/A), Second line

Phase: II

Therapy: sirolimus

Location: Republic of Korea

NCT02576444
A Phase II Study of the PARP Inhibitor Olaparib (AZD2281) Alone and in Combination With AZD1775, AZD5363, or AZD6738 in Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: PIK3CA activating mutation

Other identifiers: 1508016363, 16-314, NCI-2016-00922, OLAPCO, VICCMD1672

Population segments: First line, Second line, Stage IV

Phase: II

Therapy: capivasertib + olaparib

Location: United States

US States: CT, MA, OH, TN

US Contact: Manuel Avedissian [203-737-3669; manuel.avedissian@yale.edu]

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

Population segments: Maintenance/Consolidation, Second line, Stage III, Stage IV

Phase: II

Therapy: everolimus

Location: 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 p.(E545K) c.1633G>A (continued)

NCT02465060
Molecular Analysis for Therapy Choice (MATCH)

Cancer type: Unspecified Solid Tumor

Variant class: PIK3CA aberration

Other identifiers: 15-7002, CTSU/EAY131, EAY131, EAY131-A, EAY131-B, EAY131-C1, EAY131-C2, EAY131-E, EAY131-F, EAY131-G, EAY131-H, EAY131-I, EAY131-J, EAY131-L, EAY131-M, EAY131-MATCH, EAY131-N, EAY131-P, EAY131-Q, EAY131-R, EAY131-S1, EAY131-S2, EAY131-T, EAY131-U, EAY131-V, EAY131-W, EAY131-X, EAY131-Y, EAY131-Z1A, EAY131-Z1B, EAY131-Z1C, EAY131-Z1D, EAY131-Z1E, EAY131-Z1F, EAY131-Z1G, EAY131-Z1H, EAY131-Z1I, EAY131-Z1J, ECOGEAY131-M, MATCH, NCI-2015-00054, NCI-MATCH

Population segments: (N/A), Aggressive, Classical, Fourth line or greater, HER2 positive, Indolent, Nodular lymphocyte-predominant, Second line, Stage III, Stage IV, Third line

Phase: II

Therapy: copanlisib

Locations: Puerto Rico, 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, VT, WA, WI, WV, WY

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

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

Cancer type: Unspecified Solid Tumor

Variant class: PIK3CA 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: temsirolimus

Location: Canada

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 p.(E545K) c.1633G>A (continued)

NCT03006172
A Phase I, Open-Label, Dose-Escalation Study Evaluating the Safety, Tolerability, and Pharmacokinetics of GDC-0077 as a Single Agent in Patients With Locally Advanced or Metastatic PIK3CA-Mutant Solid Tumors and in Combination With Endocrine and Targeted Therapies in Patients With Locally Advanced or Metastatic PIK3CA-Mutant Hormone-Receptor Positive Breast Cancer

Cancer type: Unspecified Solid Tumor

Variant class: PIK3CA mutation

Other identifiers: 16-1556, EudraCT Number: 2016-003022-17, GO39374, NCI-2017-00262

Population segments: Estrogen receptor positive, HER2 negative, Line of therapy N/A, Progesterone receptor positive, Stage III, Stage IV

Phase: I

Therapy: GDC-0077

Locations: Canada, France, Spain, United Kingdom, United States

US States: MA, NY, TN

US Contact: Reference Study ID Number: GO39374 [888-662-6728; global-roche-genentech-trials@gene.com]

NCT03065062
Phase I Study of the CDK4/6 Inhibitor Palbociclib (PD-0332991) in Combination With the PI3K/mTOR Inhibitor Gedatolisib (PF-05212384) for Patients With Advanced Squamous Cell Lung, Pancreatic, Head & Neck and Other Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: PIK3CA mutation

Other identifiers: 16-499, NCI-2017-00434

Population segments: Second line, Squamous Cell, Stage III, Stage IV

Phase: I

Therapy: gedatolisib + palbociclib

Location: United States

US State: MA

US Contact: Dr. Nicole Chau [617-632-3090]

NCT02124148
A Phase Ib Trial of LY2606368 in Combination With Chemotherapy or Targeted Agents in Advanced and/or Metastatic Tumors

Cancer type: Unspecified Cancer

Variant class: PIK3CA mutation

Other identifiers: 15295, 2014-0193, I4D-MC-JTJF, NCI-2014-01348

Population segments: Second line, Stage III, Stage IV

Phase: I

Therapy: LY-3023414 + prexasertib

Location: United States

US States: FL, OK, TN, TX

US Contact: Eli Lilly and Company [877-285-4559]

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 p.(E545K) c.1633G>A (continued)

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

Population segments: Estrogen receptor positive, Fourth line or greater, HER2 negative, HER2 positive, KRAS, Stage III, Stage IV, Triple receptor negative

Phase: I

Therapies: palbociclib + pictilisib, palbociclib + taselisib

Location: United Kingdom

NCT02761694
A Phase I Dose Escalation Study of ARQ 751 in Adult Subjects With Advanced Solid Tumors With AKT1, 2, 3 Genetic Alterations, Activating PI3K Mutations, PTEN-null, or Other Known Actionable PTEN Mutations

Cancer type: Unspecified Solid Tumor

Variant class: PI3K activating mutation

Other identifiers: 2016-0212, ARQ 751-101, PTEN-null

Population segments: Second line, Stage III, Stage IV

Phase: I

Therapy: ARQ-751

Location: United States

US State: TX

US Contact: ArQule [781-994-0300; ClinicalTrials@arqule.com]

CCND1 amplification

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: Cervical Cancer

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

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.

CCND1 amplification (continued)

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: CCND1 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

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

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, 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

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

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

Cancer type: Unspecified Solid Tumor

Variant class: CCND1 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

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

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.

CCND1 amplification (continued)

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

Cancer type: Unspecified Solid Tumor

Variant class: CCND1 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

FGF19 amplification

NCT02052778
Phase I/II Study of TAS-120 in Patients With Advanced Solid Tumors Harboring FGF/FGFR Aberrations

Cancer type: Unspecified Solid Tumor

Variant class: FGF19 amplification

Other identifiers: 121062, 14-135, 17-23, 17084, 2014-0069, CSET 2107, CT680, EudraCT Number: 2013-004810-16, IND Number 121062, IRAS ID 143913, IRAS ID 143913, MC# 17-23, NCI-2014-01148, NL 20171130, NL64142.056.17, P 47317, REFMAL 340, TPU-TAS-120-101, UW18036

Population segments: FGFR, Second line, Stage III, Stage IV

Phase: I/II

Therapy: TAS-120

Locations: Australia, France, Hong Kong, Spain, United Kingdom, United States

US States: AZ, CA, FL, MA, MN, NM, NY, PA, SC, TX, WA

US Contact: Dr. Jerry Huang [jhuang@taihooncology.com]

NCT03144661
A Phase I, Open-Label, Dose-Escalation and Expansion, Safety and Tolerability Study of INCB062079 in Subjects With Advanced Hepatocellular Carcinoma and Other Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: FGF19 aberration

Other identifiers: 18-006, INCB 62079-101, INCB62079-101, NCI-2017-02493, UMCC 2017.041

Population segments: Second line, Stage III, Stage IV

Phase: I/II

Therapy: INCB-62079

Locations: Belgium, United States

US States: AL, AZ, IN, MI, NY

US Contact: Incyte Corporation Call Center (US) [855-463-3463; medinfo@incyte.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.

FGF19 amplification (continued)

NCT03235570
A Phase I, Open-Label, Dose-Escalation, Dose-Expansion, Safety and Tolerability Study of INCB054828 in Japanese Subjects With Advanced Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: FGF aberration

Other identifier: INCB 54828-102

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

Phase: I

Therapy: INCB-54828

Location: Japan

NCT02275910
A Phase I Study of E7090 in Subjects With Solid Tumor

Cancer type: Unspecified Solid Tumor

Variant class: FGF pathway

Other identifiers: E7090-J081-101, JapicCTI-142740

Population segments: Fourth line or greater, Stage III, Stage IV

Phase: I

Therapy: E-7090

Location: Japan

FGF3 amplification

NCT02052778
Phase I/II Study of TAS-120 in Patients With Advanced Solid Tumors Harboring FGF/FGFR Aberrations

Cancer type: Unspecified Solid Tumor

Variant class: FGF aberration

Other identifiers: 121062, 14-135, 17-23, 17084, 2014-0069, CSET 2107, CT680, EudraCT Number: 2013-004810-16, IND Number 121062, IRAS ID 143913, IRAS ID 143913, MC# 17-23, NCI-2014-01148, NL 20171130, NL64142.056.17, P 47317, REFMAL 340, TPU-TAS-120-101, UW18036

Population segments: FGFR, Second line, Stage III, Stage IV

Phase: I/II

Therapy: TAS-120

Locations: Australia, France, Hong Kong, Spain, United Kingdom, United States

US States: AZ, CA, FL, MA, MN, NM, NY, PA, SC, TX, WA

US Contact: Dr. Jerry Huang [jhuang@taihooncology.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.

FGF3 amplification (continued)

NCT03235570
A Phase I, Open-Label, Dose-Escalation, Dose-Expansion, Safety and Tolerability Study of INCB054828 in Japanese Subjects With Advanced Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: FGF aberration

Other identifier: INCB 54828-102

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

Phase: I

Therapy: INCB-54828

Location: Japan

NCT02275910
A Phase I Study of E7090 in Subjects With Solid Tumor

Cancer type: Unspecified Solid Tumor

Variant class: FGF pathway

Other identifiers: E7090-J081-101, JapicCTI-142740

Population segments: Fourth line or greater, Stage III, Stage IV

Phase: I

Therapy: E-7090

Location: Japan

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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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 p.(E545K) c.1633G>A

Variant Class	Evidence Items
PI3K/AKT/MTOR pathway	0
↳ PI3K activating mutation	1
↳ PIK3CA activating mutation	1
↳ PIK3CA E545 mutation	0
↳ PIK3CA E545K mutation	1
↳ PIK3CA aberration	2
↳ PIK3CA mutation status	0
↳ PIK3CA mutation	7
↳ PIK3CA exon 9 mutation	0
↳ PIK3CA E545 mutation	0
↳ PIK3CA E545K mutation	1
↳ PIK3CA activating mutation	1
↳ PIK3CA E545 mutation	0
↳ PIK3CA E545K mutation	1

CCND1 amplification

Variant Class	Evidence Items
G1/S cell cycle pathway	1
↳ CCND1 aberration	1
↳ CCND1 amplification	3

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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Evidence Summary by Variant Class (continued)

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.

FGF19 amplification

Variant Class	Evidence Items
FGF pathway	2
↳ FGF aberration	3
↳ FGF19 aberration	1
↳ FGF19 amplification	1

FGF3 amplification

Variant Class	Evidence Items
FGF pathway	2
↳ FGF aberration	3

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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Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Allele Frequency	Transcript	Variant Effect	Gene Class	Variant Class
PIK3CA	p.(E545K)	c.1633G>A	COSM763	49.06%	NM_006218.3	missense	Gain of Function	Hotspot

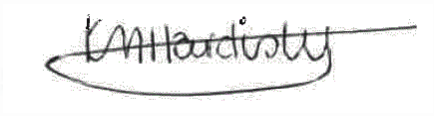
Copy Number Variations

Gene	Locus	Copy Number
CCND1	chr11:69455971	6.8
FGF19	chr11:69513953	7.31
FGF3	chr11:69624975	8.53

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.

Report Authorised by

Signed



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Keeda Hardisty

Clinical Scientist [X]

Pathologist [ ]

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Katherine Benton

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Immunofocus®

PD-1/PD-L1 TESTING

IMMUNOFOCUS® TEST REPORT

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	-		
Surname	-	**Requester**	-
Forename	-	**Contact details**	-
DOB	-	**Date requested**	-
Gender	-		
Histology #	-	**Tumour %**	99%
Primary site	Cervix	**Tumour %** (macrodissected)	-
Tumour subtype			
Tissue Type	Cervix		

PD-L1 test

PD-L1 IHC assays are used to help identify those patients most likely to benefit from anti-PD-1/PD-L1 directed immunotherapies. Assessment involves the determination of a range of cut-off/threshold values for PD-L1 positive tumour cells and PD-L1 positive immune cells. These cut off values are identified as predictors of response to anti-PD-L1 directed therapies used in the treatment of a range of different cancer types and include pembrolizumab, atezolizumab, avelumab, nivolumab, and durvalumab. The established cut off values for tumour proportion scores (>1%,>25%, >50%) and PD-L1 positive immune cells (10%), which vary according to immunotherapy, tumour type and whether first or second line therapy is to be used.

The Oncologica® Immunofocus PD-L1 immunocytochemistry assay quantifies the proportion of tumour cells that express PD-L1 (Tumour Proportion Score) and the area occupied by tumour infiltrating PD-L1 positive immune cells.

The Oncologica® Immunofocus PD-L1 immunocytochemistry assay is a Laboratory Developed Test utilising the RUO rabbit monoclonal antibody clone E1L3N (Cell Signalling Technologies) and Leica Bond III instrumentation. The performance of the Immunofocus assay is continually assessed by involvement in recognised External Quality Assessment schemes and returns performance levels commensurate with approved the PD-L1 diagnostic assays. All Immunofocus assay testing is performed within the scope of UKAS/ISO 15189:2012 accreditation. Clone E1L3N is not licensed and approved for use in clinical testing to direct the use of PD-1/PD-L1 therapies. The PD-L1 protein expression levels in tumour cells generated by the Immunofocus PD-L1 assay should therefore be interpreted within the context of these facts.

PD-L1 Result

The tumour shows a markedly heterogeneous pattern of PD-L1 expression. At the advancing margins the majority of tumour cells (80-90%) show strong or moderate intensity immunostaining for PD-L1 with complete patterns of surface membrane expression. In other areas of the tumour a smaller proportion of tumour cells show PD-L1 expression. Taken together the proportion of PD-L1 expressing tumour cells amounts to around 20-25% of the total tumour cell population . The tumour is associated with a focal sparse PD-L1 expressing immune cell (IC) infiltrate. PD-L1 expressing tumour infiltrating immune cells (ICs) cover around 4-5% of the tumour area occupied by tumour cells, intratumoural and contiguous peritumoural stroma.

Summary; PD-L1 Tumour Proportion Score 20-25%; PD-L1 positive ICs 4-5% of tumour area

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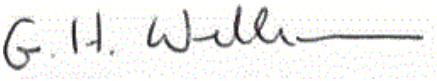

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Professor Gareth Williams

Clinical Scientist	☐
Pathologist	☑
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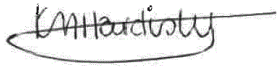

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