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Leading a new era of precision oncology

Oncofocus®

Precision Oncology

ONCOFOCUS® TEST REPORT

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ONC19			
Surname		**Requester**	
Forename		**Contact details**	
DOB		**Date requested**	
Gender			
Histology #		**Tumour %**	-
Primary site	Stomach	**Tumour %**	95%
Tumour subtype	Adenocarcinoma	**(macrodissected)**	
Tissue Type	Total Gastrectomy		

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:

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: Gastric 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	13
EGFR amplification	Clinical trials and/or off-label	Clinical trials and/or off-label	8
TP53 p.(P278L) c.833C>T	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. *Please note this version of the Oncofocus test is an upgraded version to that accredited on our schedule*

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 Gastric Cancer
PIK3CA p.(E545K) c.1633G>A Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
EGFR amplification Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
TP53 p.(P278L) c.833C>T 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*
capivasertib + chemotherapy	✖	✖	✖	✖	● (II)
capivasertib + olaparib	✖	✖	✖	✖	● (II)
copanlisib	✖	✖	✖	✖	● (II)
everolimus	✖	✖	✖	✖	● (II)
sirolimus	✖	✖	✖	✖	● (II)
temsirolimus	✖	✖	✖	✖	● (II)
GSK-2636771 + chemotherapy	✖	✖	✖	✖	● (I/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.

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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

EGFR amplification

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
ABT-806 + chemotherapy	✖	✖	✖	✖	● (II)
erlotinib	✖	✖	✖	✖	● (II)
erlotinib, gefitinib	✖	✖	✖	✖	● (II)
gefitinib	✖	✖	✖	✖	● (II)
cetuximab + FATE-NK100	✖	✖	✖	✖	● (I)
everolimus + neratinib, neratinib + palbociclib, neratinib + trametinib	✖	✖	✖	✖	● (I)
pirotinib	✖	✖	✖	✖	● (I)
varlitinib + chemotherapy	✖	✖	✖	✖	● (I)

TP53 p.(P278L) c.833C>T

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
adavosertib + chemotherapy	✖	✖	✖	✖	● (II)
adavosertib + olaparib	✖	✖	✖	✖	● (II)
VX-970, VX-970 + chemotherapy	✖	✖	✖	✖	● (I/II)

* 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

NCT02451956
Study of AZD5363 in Combination With Paclitaxel, in Advanced Gastric Adenocarcinoma Patients Harboring PIK3CA Mutation and/or PIK3CA Amplification as a Second-line Chemotherapy

Cancer type: Gastric Cancer

Variant class: PIK3CA mutation

Other identifiers: 2014-04-128, VIKTORY

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

Exclusion criteria variant classes: ERBB2 amplification, ERBB2 overexpression

Phase: II

Therapy: capivasertib + chemotherapy

Location: Republic of Korea

NCT02615730
A Phase I-II,Open-Label, Dose Finding Study to Evaluate the Safety, Pharmacokinetics and Clinical Activity of PI3K beta Selective Inhibitor (GSK2636771) Administered in Combination With Paclitaxel in Advanced Gastric Adenocarcinoma Having Alterations in PI3K Pathway Genes

Cancer type: Gastric Cancer

Variant class: PI3K/AKT/MTOR pathway

Other identifier: 4-2015-0204

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

Phase: I/II

Therapy: GSK-2636771 + chemotherapy

Location: Republic of Korea

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

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

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

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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.

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

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: Unspecified Solid Tumor

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

Exclusion criteria variant classes: BRAF mutation, HRAS mutation, KRAS mutation, NRAS mutation

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]

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]

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)

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]

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

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)

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]

EGFR amplification

NCT02213289
PANGEA-IMBBP: Personalized Antibodies for Gastro-Esophageal Adenocarcinoma - A 1st Pilot Metastatic Trial of Biologics Beyond Progression

Cancer type: Gastric Cancer

Variant class: EGFR positive

Other identifiers: IRB14-0141, NCI-2014-02415, PANGEA-IMBBP

Population segments: First line, HER2 positive, Stage IV

Phase: II

Therapy: ABT-806 + chemotherapy

Location: United States

US State: IL

US Contact: Dr. Daniel Catenacci [dcatenac@bsd.uchicago.edu]

NCT02013089
A Pilot Study of Genomic Sequencing Guided Individualized Therapy in Gastrointestinal Cancers

Cancer type: Gastric Cancer

Variant class: EGFR aberration

Other identifiers: GIHSYSU04, GITIC

Population segments: Second line, Stage IV

Phase: II

Therapies: erlotinib, gefitinib

Location: China

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.

EGFR amplification (continued)

NCT02447419
Study to Evaluate the Safety and Efficacy of Gefitinib, in Subjects With EFGR Amplification Refractory Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: EGFR amplification

Other identifier: 2014-10-029

Population segments: (N/A), Second line

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

Phase: II

Therapy: gefitinib

Location: Republic of Korea

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

Cancer type: Unspecified Solid Tumor

Variant class: EGFR 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: erlotinib

Location: Canada

NCT03065387
Phase I Study of the Pan-ERBB Inhibitor Neratinib Given in Combination With Everolimus, Palbociclib or Trametinib in Advanced Cancer Subjects With EGFR Mutation/Amplification, HER2 Mutation/ Amplification or HER3/4 Mutation

Cancer type: Unspecified Solid Tumor

Variant class: EGFR amplification

Other identifiers: 2016-0430, NCI-2018-01218

Population segments: HER2 negative, HER2 positive, Second line, Stage III, Stage IV

Phase: I

Therapies: everolimus + neratinib, neratinib + palbociclib, neratinib + trametinib

Location: United States

US State: TX

US Contact: Dr. Sarina Piha-Paul [713-563-1930; spihapau@mdanderson.org]

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.

EGFR amplification (continued)

No NCT ID - see other identifier(s)
Phase I Clinical Study With Advanced Solid Tumors KBP-5209 Treatment

Cancer type: Unspecified Solid Tumor

Variant class: EGFR amplification

Other identifiers: 5209-CPK-1002, CTR20150792

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

Phase: I

Therapy: pirotinib

Location: China

NCT03319459
FATE-NK100 as Monotherapy and in Combination With Monoclonal Antibody in Subjects With Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: EGFR positive

Other identifiers: DIMENSION, NK-101

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

Phase: I

Therapy: cetuximab + FATE-NK100

Location: United States

US State: MN

US Contact: Sara Weymer [858-875-1800; clinical@fatetherapeutics.com]

NCT02435927
Phase I Study to Evaluate the Safety and Tolerability of ASLAN001 in Combination with Oxaliplatin and Capecitabine or Oxaliplatin and 5-FU with Leucovorin

Cancer type: Unspecified Solid Tumor

Variant class: EGFR aberration

Other identifier: ASLAN001-002SG

Population segments: Second line, Stage IV

Exclusion criteria variant class: EGFR T790M mutation

Phase: I

Therapy: varlitinib + chemotherapy

Location: Singapore

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.

TP53 p.(P278L) c.833C>T

NCT02448329
Study of AZD1775 in Combination With Paclitaxel, in Advanced Gastric Adenocarcinoma Patients Harboring TP53 Mutation as a Second-line Chemotherapy

Cancer type: Gastric Cancer

Variant class: TP53 mutation

Other identifiers: 2014-04-127, VIKTORY

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

Exclusion criteria variant classes: ERBB2 amplification, ERBB2 overexpression

Phase: II

Therapy: adavosertib + chemotherapy

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: TP53 mutation

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

Population segments: First line, Second line, Stage IV

Phase: II

Therapy: adavosertib + olaparib

Location: United States

US States: CT, MA, OH, TN

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

No NCT ID - see other identifier(s)
An Open-Label Study of the Safety, Tolerability, and Pharmacokinetic/ Pharmacodynamic Profile of VX-970 as a Single Agent in Combination with Carboplatin in Subjects with Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: TP53 mutation

Other identifiers: EudraCT Number: 2013-005100-34, VX13-970-002

Population segments: (N/A), Adenocarcinoma, HER2 negative, Second line or greater/ Refractory/Relapsed, Stage III, Stage IV, Triple receptor negative

Phase: I/II

Therapies: VX-970, VX-970 + chemotherapy

Location: 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.

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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	1
↳ 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

EGFR amplification

Variant Class	Evidence Items
ERBB aberration	0
↳ EGFR aberration	3
↳ EGFR positive	2
↳ EGFR amplification	3

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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.

TP53 p.(P278L) c.833C>T

Variant Class	Evidence Items
TP53 aberration	0
↳ TP53 mutation	3
↳ TP53 exon 8 mutation	0

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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	11.62%	NM_006218.3	missense	Gain of Function	Hotspot
TP53	p.(P278L)	c.833C>T	COSM10863	26.51%	NM_000546.5	missense	Loss of Function	Hotspot

Copy Number Variations

Gene	Locus	Copy Number
EGFR	chr7:55211010	6.53

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.

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Immunofocus®

PD-1/PD-L1 TESTING

IMMUNOFOCUS® TEST REPORT

Oncologica UK Ltd
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ONC19			
Surname		**Requester**	
Forename		**Contact details**	
DOB		**Date requested**	
Gender			
Histology #		**Tumour %**	-
Primary site	Stomach	**Tumour %**	95%
Tumour subtype	Adenocarcinoma	**(macrodissected)**	
Tissue Type	Total Gastrectomy		

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 heterogeneous pattern of PD-L1 expression. In some areas, particularly at the advancing margins, a high proportion (60-80%) of tumour cells show strong, moderate or weak intensity immunostaining for PD-L1 with partial and complete patterns of surface membrane expression. In other areas tumour cells show an absence of PD-L1 expression. Taken together the proportion of PD-L1 expressing tumour cells amounts to around 10% of the total tumour cell population. The tumour is associated with a marked patchy diffusely distributed PD-L1 expressing immune cell (IC) infiltrate covering 20-25% of the tumour area occupied by tumour cells, intratumoural and contiguous peritumoural stroma.

Summary; PD-L1 Tumour Proportion Score 10% ; PD-L1 positive ICs 20-25% of tumour area

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