Medical Laboratory
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oncologica®

Leading a new era of precision oncology

# Oncofocus®

## Precision Oncology

ONCOFOCUS® TEST REPORT

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**Lead Clinical Scientist:** - **Pre-Reg Clinical Scientist:** -

| | | | |
|---|---|---|---|
| **Surname** | - | **Requester** | - |
| **Forename** | - | **Contact details** | - |
| **DOB** | - | **Date requested** | - |
| **Gender** | - | | |
| **Histology #** | - | **Tumour %** | - |
| **Primary site** | Vulva | **Tumour %** | - |
| **Tumour subtype** | Malignant Pecoma | **(macrodissected)** | |
| **Tissue Type** | Vulva | | |

**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 3, the NCT numbers are hyperlinks to the clinicaltrials.gov webpages which should be accessed to gain further trial specific information*

## **Sample Cancer Type:** Soft Tissue Sarcoma

## Clinically Significant Biomarkers

**Indicated** **Contraindicated**

| Genomic Alteration | copy number | Reads | Relevant Therapies (In this cancer type) | Relevant Therapies (In other cancer type) | Clinical Trials |
|---|---|---|---|---|---|
| TBL1XR1-PIK3CA fusion | | 248 | Clinical trials and/or off-label | Clinical trials and/or off-label | 7 |
| SMARCB1 deletion | 0.34 | | Clinical trials and/or off-label | Clinical trials and/or off-label | 1 |

**Sources included in relevant therapies:** EMA[1], FDA[2], 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 Soft Tissue Sarcoma |
|---|---|
| *PIK3CA aberration*<br>Tier: IIC | IIC: Biomarker is an inclusion criteria for clinical trials |
| *SMARCB1 deletion*<br>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 aberration

| Relevant Therapy | EMA | FDA | ESMO | NCCN | Clinical Trials* |
|---|---|---|---|---|---|
| capivasertib + olaparib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| copanlisib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| sapanisertib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| temsirolimus | ✖ | ✖ | ✖ | ✖ | ● (II) |
| capivasertib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| gedatolisib + palbociclib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| palbociclib + pictilisib, palbociclib + taselisib | ✖ | ✖ | ✖ | ✖ | ● (I) |

### SMARCB1 deletion

| Relevant Therapy | EMA | FDA | ESMO | NCCN | Clinical Trials* |
|---|---|---|---|---|---|
| pembrolizumab | ✖ | ✖ | ✖ | ✖ | ● (II) |

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



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# 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 aberration

### NCT02987959
Phase II Study of TAK-228 (MLN0128) in Soft Tissue Sarcomas With Dysregulation of the mTOR Pathway

**Cancer type:** Soft Tissue Sarcoma

**Variant class:** PI3K/AKT/MTOR pathway

**Other identifiers:** 16-1047, SAR-081

**Population segments:** Locally advanced, Metastatic, Second line, Stage IV, Unresectable

**Phase:** II

**Therapy:** sapanisertib

**Location:** United States

**US State:** PA

**US Contact:** Dr. Sujana Movva [888-369-2427; sujana.movva@fccc.edu]

### 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.



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## PIK3CA aberration (continued)

### 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

### 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:** PI3K/AKT/MTOR pathway

**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]

### 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:** PI3K/AKT/MTOR pathway

**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]



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## PIK3CA aberration (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:** PI3K/AKT/MTOR pathway

**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]

### 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:** PI3K/AKT/MTOR pathway

**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

## SMARCB1 deletion

### NCT03012620
Secured Access to Pembrolizumab for Adult Patients With Selected Rare Cancer Types

**Cancer type:** Soft Tissue Sarcoma

**Variant class:** SMARCB1 deletion

**Other identifiers:** EudraCT Number: 2016-002260-14, UC0105/1612

**Population segments:** Aggressive, Anaplastic, Follicular, Fourth line or greater, Locally advanced, Medullary, Metastatic, Papillary, Recurrent, Stage III, Stage IV, Third line, Unresectable

**Phase:** II

**Therapy:** pembrolizumab

**Location:** France



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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 aberration

| Variant Class | Evidence Items |
|---|---|
| PI3K/AKT/MTOR pathway | 5 |
| ↳ PIK3CA aberration | 2 |

### SMARCB1 deletion

| Variant Class | Evidence Items |
|---|---|
| SMARCB1 deletion | 1 |



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