[ Oncofocus ] Patient Test Report

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| | | | |
|---|---|---|---|
| **ONC17** | | | |
| **Surname** | | **Requesting Clinician** | |
| **Forename** | | | |
| **DOB** | | **Date requested** | |
| **Gender** | Female | | |
| **Histology #** | | **Tumour %** | 90% |
| **Primary site** | Thyroid | **Tumour %** | - |
| **Tumour subtype** | Metastatic | **(macrodissected)** | |
| **Tissue Type** | Adenocarcinoma Right Frontal Bone | | |

**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:** Thyroid 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 | EMA | US-FDA | ESMO | US-NCCN | Global Clinical Trials |
|---|---|---|---|---|---|
| PTEN deletion | ✖ | ✖ | ✖ | ✖ | ● (11) |
| TP53 p.(S127P) c.379T>C | ✖ | ✖ | ✖ | ✖ | ● (4) |

**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.



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

## PTEN deletion

| Relevant Therapy | EMA | US-FDA | ESMO | US-NCCN | Global Clinical Trials* |
|---|---|---|---|---|---|
| AZD-5363 + olaparib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| everolimus | ✖ | ✖ | ✖ | ✖ | ● (II) |
| GSK-2636771 | ✖ | ✖ | ✖ | ✖ | ● (II) |
| ASN-003 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| selumetinib + vistusertib | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| ARQ-751 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| AZD-5363 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| AZD8186, AZD8186 + abiraterone acetate + prednisone, AZD8186 + vistusertib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| MSC-2363318A | ✖ | ✖ | ✖ | ✖ | ● (I) |
| palbociclib + pictilisib, palbociclib + taselisib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| PQR-309 | ✖ | ✖ | ✖ | ✖ | ● (I) |

## TP53 p.(S127P) c.379T>C

| Relevant Therapy | EMA | US-FDA | ESMO | US-NCCN | Global Clinical Trials* |
|---|---|---|---|---|---|
| MK-1775 + olaparib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| ixazomib + vorinostat | ✖ | ✖ | ✖ | ✖ | ● (I) |
| MK-1775 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| SGT-53, SGT-53 + chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (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.



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'.

## PTEN deletion

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

**Cancer type:** Thyroid Cancer

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

**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:** selumetinib + vistusertib

**Location:** United Kingdom

### 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:** PTEN deletion

**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

**Location:** France

### 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:** PTEN deletion

**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

**Location:** Republic of Korea



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.

## PTEN deletion (continued)

### NCT02465060
Molecular Analysis for Therapy Choice (MATCH)

**Cancer type:** Unspecified Solid Tumor

**Variant class:** PTEN deletion

**Other identifiers:** 15-7002, 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:** (N/A), Aggressive, ALK, Classical, EGFR, HER2 positive, Indolent, Nodular lymphocyte-predominant, Second line or greater/Refractory/Relapsed, Stage III, Stage IV

**Phase:** II

**Therapy:** GSK-2636771

**Location:** 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.

### NCT02465060
Molecular Analysis for Therapy Choice (MATCH)

**Cancer type:** Unspecified Solid Tumor

**Variant class:** PTEN deletion

**Other identifiers:** 15-7002, 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:** (N/A), Aggressive, ALK, Classical, EGFR, HER2 positive, Indolent, Nodular lymphocyte-predominant, Second line or greater/Refractory/Relapsed, Stage III, Stage IV

**Other inclusion criteria:** PTEN expression

**Phase:** II

**Therapy:** GSK-2636771

**Location:** 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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## PTEN deletion (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 Solid Tumor

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

**Other identifiers:** 1508016363, OLAPCO, TrialTroveID-266161

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

**Phase:** II

**Therapy:** AZD-5363 + olaparib

**Location:** United States

**US States:** CT, MA

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

### NCT02961283
A Phase I, Open-label, Dose-finding and Cohort Expansion Study of ASN003 in Subjects With Advanced Solid Tumors

**Cancer type:** Unspecified Solid Tumor

**Variant class:** PTEN deletion

**Other identifiers:** ASN003-101, TrialTroveID-290434

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

**Phase:** I/II

**Therapy:** ASN-003

**Location:** United States

**US State:** TX

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

### 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 or PTEN-null

**Cancer type:** Unspecified Solid Tumor

**Variant class:** PTEN deletion

**Other identifiers:** ARQ 751-101, PTEN-null, TrialTroveID-272167

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

**Phase:** I

**Therapy:** ARQ-751

**Location:** United States

**US State:** NV

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



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## PTEN deletion (continued)

### NCT01884285

A Phase I, Open-label, Multicentre Study to Assess the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics and Preliminary Anti-tumour Activity of AZD8186 in Patients with Advanced Castration-resistant Prostate Cancer (CRPC), Squamous Non-Small Cell Lung Cancer (sqNSCLC), Triple Negative Breast Cancer (TNBC) and Patients with Known PTEN-deficient/mutated or PIK3CB mutated/ amplified Advanced Solid Malignancies as Monotherapy and in Combination with Abiraterone Acetate or AZD2014

**Cancer type:** Unspecified Solid Tumor

**Variant class:** PTEN deletion

**Other identifiers:** 13-300, 20131275, D4620C00001, EudraCT Number: 2013-000703-17, IRAS ID: 129536, NCI-2013-02191, TrialTroveID-189056

**Population segments:** HER2 negative, Hormone refractory, Second line or greater/ Refractory/Relapsed, Squamous Cell, Stage III, Stage IV, Triple receptor negative

**Phase:** I

**Therapies:** AZD8186, AZD8186 + abiraterone acetate + prednisone, AZD8186 + vistusertib

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

**US States:** MA, MI, WA, WI

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

### 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:** PTEN 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

**Exclusion criteria variant classes:** AKT2 amplification, AKT2 mutation

**Phase:** I

**Therapy:** MSC-2363318A

**Location:** United States

**US States:** AL, CA, FL, MI, NY, TX, VT

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



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.

## PTEN deletion (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:** PI3K/AKT/MTOR pathway

**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:** Adenocarcinoma, Estrogen receptor positive, HER2 positive, Hormone refractory, Second line or greater/Refractory/Relapsed, Stage III, Stage IV

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

**Phase:** I

**Therapy:** AZD-5363

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

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

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

### NCT02338622
A Phase I Multi-centre Trial of the Combination of Olaparib (PARP Inhibitor) and AZD5363 (AKT Inhibitor) in Patients With Advanced Solid Tumours

**Cancer type:** Unspecified Solid Tumor

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

**Other identifiers:** 14/LO/0103, CCR4058, ComPAKT, CRUKD/14/004, EudraCT number: 2013-004692-13, TrialTroveID-213474, UKCRN ID 16550

**Population segments:** HER2 negative, Hormone refractory, Second line or greater/Refractory/Relapsed, Stage III, Stage IV, Triple receptor negative

**Phase:** I

**Therapy:** AZD-5363 + olaparib

**Location:** United Kingdom

### 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, TrialTroveID-253778

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

**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.

## PTEN deletion (continued)

### NCT02483858
Phase I Study of Oral PQR309 in Patients With Advanced Solid Tumors.

**Cancer type:** Unspecified Solid Tumor

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

**Other identifiers:** EudraCT Number: 2015-003919-38, I 258914, IRAS ID: 193390, PQR309-003, REec-2016-2264, TrialTroveID-260655

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

**Phase:** I

**Therapy:** PQR-309

**Location:** United States

**US State:** NY

**US Contact:** Dr. Alex Adjei [Alex.Adjei@RoswellPark.org]

## TP53 p.(S127P) c.379T>C

### 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:** TP53 mutation

**Other identifiers:** 1508016363, OLAPCO, TrialTroveID-266161

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

**Phase:** II

**Therapy:** MK-1775 + olaparib

**Location:** United States

**US States:** CT, MA

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

### NCT02042989
A Phase I Study of MLN9708 and Vorinostat to Target Autophagy in Patients With Advanced p53 Mutant Malignancies

**Cancer type:** Unspecified Solid Tumor

**Variant class:** TP53 mutation

**Other identifiers:** 2013-0511, NCI-2014-01091, TrialTroveID-201319

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

**Phase:** I

**Therapy:** ixazomib + vorinostat

**Location:** United States

**US State:** TX

**US Contact:** Dr. Siqing Fu [713-563-1930]



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## TP53 p.(S127P) c.379T>C (continued)

### NCT02610075
A Phase Ib Study to Determine the Maximum Tolerated Dose (MTD) of AZD1775 Monotherapy in Patients With Locally Advanced or Metastatic Solid Tumours.

**Cancer type:** Unspecified Solid Tumor

**Variant class:** TP53 mutation

**Other identifiers:** D6015C00003, REFMAL 398, TrialTroveID-268385

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

**Phase:** I

**Therapy:** MK-1775

**Location:** United States

**US States:** CO, TN

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

### NCT02354547
A Phase I Study of SGT-53, a TfRscFv-Liposome-p53 Complex, in Children with Refractory or Recurrent Solid Tumors

**Cancer type:** Unspecified Solid Tumor

**Variant class:** TP53 mutation

**Other identifiers:** 1405-1316, SGT53-01-2, TrialTroveID-251586

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

**Phase:** I

**Therapies:** SGT-53, SGT-53 + chemotherapy

**Location:** United States

**US State:** TX

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



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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# 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.

## PTEN deletion

| Variant Class | Evidence Items |
|---|---|
| PI3K/AKT/MTOR pathway | 6 |
| ↳ PTEN aberration | 1 |
| ↳ PTEN deletion | 7 |

## TP53 p.(S127P) c.379T>C

| Variant Class | Evidence Items |
|---|---|
| TP53 mutation | 4 |



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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 |
|---|---|---|---|---|---|---|---|---|
| TP53 | p.(S127P) | c.379T>C | COSM44687 | 58.81% | NM_000546.5 | missense | Loss of Function | Hotspot |

## Copy Number Variations

| Gene | Locus | Copy Number |
|---|---|---|
| PTEN | chr10:89624207 | 0.42 |



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