[Oncofocus] Patient Test Report

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Histology #		**Tumour %**	70
Primary site	Bladder	**Tumour % (macrodissected)**	
Tumour subtype	Invasive TCC		
Tissue type	Bladder L Lateral Wall		

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.

221 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 466 anti-cancer targeted therapies.

The following actionable variants were detected:

Variant Summary

Sample Cancer Type: Bladder 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
ERBB2 p.(S310F) c.929C>T	✖	✖	✖	○ (2)	● (9)
TSC1 p.(Q55Ter) c.163C>T	✖	✖	✖	✖	● (5)
PIK3CA p.(E453K) c.1357G>A	✖	✖	✖	✖	● (9)
MDM2 amplification	✖	✖	✖	✖	● (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' with an assay sensitivity and positive predictive value of 97%. Copy number variants; amplifications of a >5% confidence value of ≥4 after normalization and deletions of ≤1 are classified as present when the tumour% >50%. Gene Fusions are reported when occurring in >20 counts and meeting the thresholds of assay specific internal RNA quality control. With a sensitivity of 99% 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

ERBB2 p.(S310F) c.929C>T

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
afatinib	✖	✖	✖	○	● (II)
trastuzumab	✖	✖	✖	○	✖
lapatinib	✖	✖	✖	✖	● (II)
neratinib	✖	✖	✖	✖	● (II)
pertuzumab + trastuzumab	✖	✖	✖	✖	● (II)
AZD-2014 + selumetinib	✖	✖	✖	✖	● (I/II)
everolimus + trastuzumab + letrozole	✖	✖	✖	✖	● (I)
MSC-2363318A	✖	✖	✖	✖	● (I)
pirotinib	✖	✖	✖	✖	● (I)
pyrotinib	✖	✖	✖	✖	● (I)

TSC1 p.(Q55Ter) c.163C>T

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
AZD-2014 + olaparib	✖	✖	✖	✖	● (II)
everolimus	✖	✖	✖	✖	● (II)
sirolimus	✖	✖	✖	✖	● (II)
temsirolimus	✖	✖	✖	✖	● (II)
MSC-2363318A	✖	✖	✖	✖	● (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.

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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

PIK3CA p.(E453K) c.1357G>A

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)
MSC-2363318A	✖	✖	✖	✖	● (I)
palbociclib + pictilisib, palbociclib + taselisib	✖	✖	✖	✖	● (I)

MDM2 amplification

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
AMG-232	✖	✖	✖	✖	● (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.

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Current US-NCCN Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated

US-NCCN information is current as of 2016-06-07. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

ERBB2 p.(S310F) c.929C>T

○ afatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ERBB2 mutation

US-NCCN Recommendation category: 2B

Population segment (Line of therapy):
- NSCLC (Not specified)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2016]

○ trastuzumab

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ERBB2 mutation

US-NCCN Recommendation category: 2B

Population segment (Line of therapy):
- NSCLC (Not specified)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2016]

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 2016-06-01. 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'.

ERBB2 p.(S310F) c.929C>T

NCT01953926

An Open-label, Multicenter, Multinational, Phase 2 Study Exploring the Efficacy and Safety of Neratinib Therapy in Patients With Solid Tumors With Activating HER2, HER3 or EGFR Mutations or With EGFR Gene Amplification.

Cancer type: Bladder Cancer

Variant class: ERBB2 activating mutation

Other identifiers: 13-140, 13-615, 2013-002872-42, BASKET, CTA733, EudraCT Number: 2013-002872-42, NCI-2014-00495, PUMA-NER-5201, REec-2014-0843, SUMMIT basket, TrialTroveID-191740

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

Phase: II

Therapy: neratinib

Countries: Australia, Finland, Israel, Italy, Spain, United States

US States: CA, MA, MO, NJ, NY, TN, TX

US Contact: Puma Biotechnology Clinical Operations [424-248-6500; ClinicalTrials@pumabiotechnology.com]

NCT02465060

Molecular Analysis for Therapy Choice (MATCH)

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 activating 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

Phase: II

Therapy: afatinib

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.

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.

ERBB2 p.(S310F) c.929C>T (continued)

NCT02091141
My Pathway: An Open Label Phase IIa Study Evaluating Trastuzumab/ Pertuzumab, Erlotinib, Vemurafenib, and Vismodegib in Patients Who Have Advanced Solid Tumors With Mutations or Gene Expression Abnormalities Predictive of Response to One of These Agents

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 activating mutation

Other identifiers: 1403013519, 2014-0459, AAAN9701, ML28897, ML28897/PRO 02, ML28897PRO/02, My Pathway, TrialTroveID-205033

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

Phase: II

Therapy: pertuzumab + trastuzumab

Country: United States

US States: AR, AZ, CA, CO, FL, GA, IL, MD, MN, NC, ND, NY, OH, OK, OR, PA, SD, TN, TX, VA, WA

US Contact: Reference Study ID Number: ML28897 [888-662-6728; global.rochegenentechtrials@roche.com]

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: ERBB2 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: lapatinib

Country: France

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

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 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

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.

ERBB2 p.(S310F) c.929C>T (continued)

NCT02152943
Combination Treatment With Everolimus, Letrozole and Trastuzumab in Hormone Receptor and HER2/Neu-positive Patients With Advanced Metastatic Breast Cancer and Other Solid Tumors: Evaluating Synergy and Overcoming Resistance

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 mutation

Other identifiers: 2014-0119, NCI-2014-01615, TrialTroveID-210119

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

Other inclusion criteria: ER positive, PR positive/negative

Phase: I

Therapy: everolimus + trastuzumab + letrozole

Country: United States

US State: TX

US Contact: Dr. Jennifer J. Wheler [713-563-1930]

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: ERBB2 mutation

Other identifiers: 5209-CPK-1002, CTR20150792, TrialTroveID-269399

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

Phase: I

Therapy: pirotinib

Country: China

NCT02500199
A Two-part Phase I, Open Label, Dose Escalation Study to Evaluate the Safety, Tolerability and Pharmacokinetics of Pyrotinib in Patients With HER2 Positive Solid Tumors Who Failed Prior HER2 Targeted Therapy

Cancer type: Unspecified Solid Tumor

Variant class: ERBB2 mutation

Other identifiers: SHRUS 1001, TrialTroveID-261429

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

Phase: I

Therapy: pyrotinib

Country: 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.

ERBB2 p.(S310F) c.929C>T (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: ERBB2 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]

TSC1 p.(Q55Ter) c.163C>T

NCT02646319
A Pilot Study of a Rapid Access Platform for Investigational Drugs (RAPID) in Advanced Cancers

Cancer type: Bladder Cancer

Variant class: TSC1 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.

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: TSC1 mutation

Other identifiers: 1508016363, OLAPCO, TrialTroveID-266161

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

Phase: II

Therapy: AZD-2014 + olaparib

Country: United States

US State: CT

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.

TSC1 p.(Q55Ter) c.163C>T (continued)

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: TSC1 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

NCT02201212
A Phase II Trial of Everolimus for Cancer Patients With Inactivating Mutations in TSC1 or TSC2

Cancer type: Unspecified Cancer

Variant class: TSC1 mutation

Other identifiers: 14-229, CRAD001MUS217T, NCI-2015-00624, TrialTroveID-213682

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

Phase: II

Therapy: everolimus

Country: United States

US State: MA

US Contact: Dr. David J Kwiatkowski [617-355-9005; dkwiatkowski@partners.org]

NCT02352844
Phase II Study of Everolimus in Patients With Advanced Solid Malignancies With TSC1 and TSC2 Mutations

Cancer type: Unspecified Solid Tumor

Variant class: TSC1 mutation

Other identifiers: 15-x018, TrialTroveID-251524

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

Phase: II

Therapy: everolimus

Country: United States

US State: MO

US Contact: Dr. Saiama Waqar [314-362-5737; swaqar@dom.wustl.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.

TSC1 p.(Q55Ter) c.163C>T (continued)

NCT02693535
Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Cancer type: Unspecified Solid Tumor

Variant class: TSC mutation

Other identifiers: Pro00014171, TAPUR, TrialTroveID-273941

Population segments: (N/A), Diffuse large B-cell lymphoma (DLBCL), Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: II

Therapy: temsirolimus

Country: United States

US States: MI, NC

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

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: TSC1 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]

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.(E453K) c.1357G>A

NCT02646319
A Pilot Study of a Rapid Access Platform for Investigational Drugs (RAPID) in Advanced Cancers

Cancer type: Bladder 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.

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 p.(E453K) c.1357G>A (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.

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.(E453K) c.1357G>A (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]

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.(E453K) c.1357G>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: 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

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

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]

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

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.(E453K) c.1357G>A (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]

MDM2 amplification

NCT01723020
A Phase I First-in-Human Study Evaluating the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of AMG 232 in Adult Subjects With Advanced Solid Tumors or Multiple Myeloma

Cancer type: Unspecified Solid Tumor

Variant class: MDM2 amplification

Other identifiers: 14-118, 15-306, 20120106, CSET 2094, EudraCT Number: 2012-002908-41, NCI-2014-02184, NL41417.078.12, TrialTroveID-177265

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

Other inclusion criteria: TP53 wild type

Phase: I

Therapy: AMG-232

Countries: France, Netherlands, United States

US States: CA, CT, MA, NJ, NY, SC

US Contact: Amgen Call Center [866-572-6436]

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.

ERBB2 p.(S310F) c.929C>T

Variant Class	Evidence Items
ERBB2 aberration	2
↳ ERBB2 mutation	6
↳ ERBB2 activating mutation	3
↳ ERBB2i sensitizing mutation	0

TSC1 p.(Q55Ter) c.163C>T

Variant Class	Evidence Items
TSC mutation	1
↳ TSC1 mutation	4
TSC1 aberration	2
↳ TSC1 mutation	4

PIK3CA p.(E453K) c.1357G>A

Variant Class	Evidence Items
PIK3CA aberration	3
↳ PIK3CA mutation	8

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 (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.

MDM2 amplification

Variant Class	Evidence Items
MDM2 amplification	1

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: Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
ERBB2	p.(S310F)	c.929C>T	COSM48358	chr17:37868208	0.0881494	NM_004448.3	missense
PIK3CA	p.(E453K)	c.1357G>A	COSM12584	chr3:178928079	0.148356	NM_006218.2	missense
TSC1	p.(Q55Ter)	c.163C>T	.	chr9:135802635	0.264495	NM_000368.4	nonsense

Copy Number Variations

Gene	Locus	Copy Number
MDM2	chr12:69207031	20.71

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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