



[Oncofocus] Patient Test Report

ONC16-0230

Surname

Requesting clinician

Forename

DOB

Date requested

Gender

Histology #

Tumour % 70

Primary site

Bladder

Tumour %

Tumour subtype

Invasive TCC

(macrodissected)

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.

ONC16-: 0230

www.oncologica.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.

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.

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.

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]

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.

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.roche.genentechtrials@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

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.

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.

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]

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]

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

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.

PIK3CA p.(E453K) c.1357G>A (continued)**NCT02583542**

A Phase Ib/Ila 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]

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

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]

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
TSC1 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

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

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

Report Signed by

Report Checked by



Clinical Scientist



Pathologist



BMS (Senior)



BMS



Terms and Conditions

The following paragraph on Liability is an extract from the Oncologica Tests' Terms and Conditions. The extract is to draw your attention to particular terms applicable to you but nothing set out here is intended to supersede or override our Terms and Conditions, which can be found on our website at www.oncologica.com under the title Oncologica Tests' Terms and Conditions. Please read these Oncologica Test Terms and Conditions carefully before you submit an order for the Oncologica Tests, as you will be bound by these Terms and Conditions, once a contract comes into existence as per paragraph 2 of the Oncologica Test's Terms and Conditions.

6. Liability

6.1 Oncologica operates in compliance with international ISO15189:2012 standards and is regulated by UKAS. The Oncologica Tests have not been cleared or approved by the United States Food and Drug Administration; however, such clearance or approval is not required.

6.2 The Patient agrees that the Oncologica Test Report is intended for clinical use and interpretation by a physician who is experienced and skilled in the use and interpretation of clinical test data. The Oncologica Test Report is based on the Sample submitted by the Patient. The Oncologica Test Report should not be considered or its contents applied to any other patient or any other sample. Oncologica does not update an Oncologica Test Report once it has been sent.

6.3 Information compiled in the Oncologica Test Report includes is from publicly available as well as proprietary sources. By updating the source database, Oncologica makes every effort to provide the most accurate and up-to-date information. However, Oncologica does not warrant or represent that the information in the Oncologica Test Report is accurate, timely or complete.

6.4 The Oncologica Test Report contains drug and clinical trial information. However, Oncologica does not warrant or represent that any drug or clinical trial identified by the Oncologica Test will guarantee a therapeutic response for a particular Patient. The drugs listed in an Oncologica Test Report are ranked on clinical evidence as to the predicted efficacy or appropriateness for the Patient. The Patient shall ensure that its physician shall evaluate and interpret the Oncologica Test Report, along with all other available clinical information about the Patient, to determine the best treatment decisions in their own independent medical judgment. Patient management decisions should not be based on a single test, nor solely on the information contained in the Oncologica Test Report.

6.5 Subject to paragraph 6.10, Oncologica shall have no liability for any use made of the information provided in the Oncologica Test Report, including but not limited to any report prepared by Oncologica summarising the results of the Oncologica Tests, any advice supplied by Oncologica, any decisions taken, or for any costs incurred by Patient and/or the Patient's physician and/or the Agent in consequence of such use, advice or decisions. The Oncologica Test and/or the Oncologica Test Report is not a substitute for the Patient's physician's professional judgment. The use of the information provided in the Oncologica Test Report is provided as a tool for the ordering physician's use in determining the appropriate treatment for the Patient. The decision as to what course of treatment and the appropriate use of the information provided by the Oncologica Test Report is solely that of the Patient's physician.

6.6 Oncologica does not warrant or represent or guarantee that the Oncologica Tests will identify an actionable genetic alteration that is linked to anti-cancer targeted therapies. Although the Oncologica Tests are comprehensive, in a proportion of Patients, the Oncologica Test result may not identify any actionable mutations for a patient's cancer. In the event that no actionable alteration in the Sample is identified by the Oncologica Test, then the Patient is still under full obligation to pay the Charges and no refund is available to the Patient and/or Agent.

6.7 The Oncologica Test identifies genomic actionable alterations found in the submitted Sample that are linked to anti-cancer targeted agents. Also note that this test only examines tumour, and not normal tissue from the patient, and therefore cannot distinguish between somatic and germline (i.e., heritable) alterations.

6.8 Subject to Clause 6.8, Oncologica shall not be liable to the Patient whether in contract, tort (including negligence and breach of statutory duty), or otherwise for any:

- (a) Error or defect in the Oncologica Test Report as a result of any inaccurate or incomplete information supplied by the Patient;
- (b) Loss of data or materials, including the Sample and/or the Report and including any loss arising as a result of the acts or omissions of a courier;
- (c) Indirect or consequential loss arising whether or not advised of the possibility of the same.

6.9 Subject to the provisions of this Clause 6, Oncologica's total liability to the Patient in respect of all losses arising under or in connection with the Contract, whether in contract, tort (including negligence and breach of statutory duty), or otherwise, shall in no circumstances exceed the Charges paid for the Test that is the subject of the claim.

6.10 Nothing in the Contract limits or excludes the liability of Oncologica for breach of its obligations under section 12 of the Sale of Goods Act 1979 and/or section 2 of the Supply of Goods and Services Act 1982; death or personal injury resulting from negligence; or fraud or fraudulent misrepresentation.

6.11 If the Patient is a consumer (and not a business), the Patient expressly acknowledges and agrees that the Test is supplied to the Patient's specification and therefore there is no right to cancel the Test following acceptance under Clause 2.2. If the Patient is a consumer, then notwithstanding any other provisions of the Contract, none of the Patient's consumer statutory rights are affected.

