[Oncofocus] Patient Test Report

Oncologica UK Ltd
Suite 15-16, The Science Village
Chesterford Research Park
Cambridge, CB10 1XL, UK
Tel: +44(0)1223 785327
Email: info@oncologica.com

Histology #		**Tumour %**	
Primary site		**Tumour % (macrodissected)**	60
Tumour subtype	Renal Cell Adenocarcinoma		
Tissue type	Kidney		

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 485 anti-cancer targeted therapies.

The following actionable variants were detected:

Variant Summary

Sample Cancer Type: Kidney 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
KIT	c.1712T>A	p.(I571K)	✖	✖	✖	○ (1)	● (7)
MET	c.3742T>C	p.(Y1248H)	✖	✖	✖	✖	● (5)

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 92%. 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 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

KIT activating mutation

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
imatinib mesylate	✖	✖	✖	○	✖
dasatinib, regorafenib	✖	✖	✖	✖	● (II)
nilotinib, pazopanib	✖	✖	✖	✖	● (II)
ponatinib	✖	✖	✖	✖	● (II)
sorafenib + chemotherapy	✖	✖	✖	✖	● (II)
pexidartinib + PLX-9486, PLX-9486	✖	✖	✖	✖	● (I/II)
selumetinib + vistusertib	✖	✖	✖	✖	● (I/II)
imatinib mesylate + ipilimumab	✖	✖	✖	✖	● (I)

MET mutation

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
crizotinib	✖	✖	✖	✖	● (II)
selumetinib + vistusertib	✖	✖	✖	✖	● (I/II)
altiratinib	✖	✖	✖	✖	● (I)
bevacizumab + capmatinib	✖	✖	✖	✖	● (I)
MGCD-265	✖	✖	✖	✖	● (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.

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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 2016-09-07. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

KIT activating mutation

○ imatinib mesylate

Cancer type: Melanoma

Variant class: KIT activating mutation

US-NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic or unresectable disease, Disease progression or Maximum clinical benefit from BRAF targeted therapy (Second-line therapy)

Reference: NCCN Guidelines® - NCCN-Melanoma [Version 3.2016]

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Current Global Clinical Trials Information

Global Clinical Trials information is current as of 2016-09-01. 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'.

KIT activating mutation

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

Cancer type: Kidney Cancer

Variant class: KIT 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: selumetinib + vistusertib

Country: United Kingdom

NCT02693535
Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Cancer type: Unspecified Solid Tumor

Variant class: KIT mutation

Other identifiers: Pro00014171, TAPUR, TrialTroveID-273941

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

Phase: II

Therapies: dasatinib, regorafenib

Country: United States

US States: MI, NC

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: KIT 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

Therapies: nilotinib, pazopanib

Country: France

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KIT activating mutation (continued)

NCT02747537
Phase II Clinical Trial Treating Relapsed/ Recurrent/Refractory Pediatric Solid Tumors With the Genomically-Targeted Agent Sorafenib in Combination With Irinotecan

Cancer type: Unspecified Solid Tumor

Variant class: KIT mutation

Other identifiers: 201605006, NCI-2016-00680, TrialTroveID-277232

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

Phase: II

Therapy: sorafenib + chemotherapy

Country: United States

US State: MO

US Contact: Dr. Robert Hayashi [314-454-6018; hayashi_r@kids.wustl.edu]

NCT02272998
Phase II Study Of Ponatinib For Advanced Cancers With Genomic Alterations In Fibroblastic Growth Factor Receptor (FGFR) And Other Genomic Targets (KIT, Pdgfra, RET FLT3, ABL1)

Cancer type: Unspecified Solid Tumor

Variant class: KIT aberration

Other identifiers: 14078, 2014C0143, NCI-2014-01499, OSU-14078, TrialTroveID-219466

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

Phase: II

Therapy: ponatinib

Country: United States

US States: MI, OH

US Contact: The Ohio State University Comprehensive Cancer Center [800-293-5066]

NCT02401815
A Phase 1b Study to Assess Safety, Pharmacokinetics, Pharmacodynamics, and Preliminary Efficacy of PLX9486 as a Single Agent and in Combination With PLX3397 in Patients With Advanced Solid Tumors and Patients With Locally Advanced, Unresectable, or Metastatic Gastrointestinal Stromal Tumor (GIST) Who Have Been Previously Treated With Imatinib Mesylate, Sunitinib Malate, and Regorafenib

Cancer type: Unspecified Solid Tumor

Variant class: KIT mutation

Other identifiers: 20150108, , PLX121-01, TrialTroveID-254720

Population segments: Locally advanced, Metastatic, Second line or greater/Refractory/ Relapsed, Stage III, Stage IV, Unresectable

Phase: I/II

Therapies: pexidartinib + PLX-9486, PLX-9486

Country: United States

US States: FL, MA, MI, NY, TX

US Contact: Oscar Alcantar [oalcantar@plexxikon.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.

KIT activating mutation (continued)

NCT01738139
A Phase I Trial of Ipilimumab (Immunotherapy) and Imatinib Mesylate (c-Kit Inhibitor) in Patients With Advanced Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: KIT mutation

Other identifiers: 2012-0784, NCI-2013-00030, TrialTroveID-178427

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

Phase: I

Therapy: imatinib mesylate + ipilimumab

Country: United States

US State: TX

US Contact: Dr. David S. Hong [713-563-1930]

MET mutation

NCT02034981
AcSé CRIZOTINIB : Secured Access to Crizotinib for Patients With Tumors Harboring a Genomic Alteration on One of the Biological Targets of the Drug

Cancer type: Kidney Cancer

Variant class: MET mutation

Other identifiers: AcSé, AcSé CRIZOTINIB, EudraCT Number: 2013-000885-13, FSCA-crizotinib, TrialTroveID-200633, UC-0105/1303

Population segments: Aggressive, Anaplastic, Follicular, Line of therapy N/A, Medullary, Papillary, Pediatric or Adolescent, Peripheral T-cell lymphoma (PTCL), Stage III, Stage IV

Phase: II

Therapy: crizotinib

Country: France

NCT01524926
Cross-tumoral Phase II Clinical Trial Exploring Crizotinib (PF-02341066) in Patients With Advanced Tumors Induced by Causal Alterations of ALK and/or MET ("CREATE")

Cancer type: Kidney Cancer

Variant class: MET aberration

Other identifiers: 90101, CREATE, CREATE 90101, CSET 1934, CTBE2013000249, EORTC-90101, EORTC-90101-NOCI, EudraCT number: 2011-001988-52, IRAS ID: 108771, NL40334.058.12, RECF1932, TrialTroveID-161601, UKCRN ID: 14490

Population segments: Cutaneous T-cell lymphoma (CTCL), Indolent, Locally advanced, Metastatic, Pediatric or Adolescent, Peripheral T-cell lymphoma (PTCL), Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: II

Therapy: crizotinib

Countries: Belgium, France, Germany, Italy, Netherlands, Norway, Poland, Slovakia, Slovenia, United Kingdom

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MET mutation (continued)

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

Cancer type: Kidney Cancer

Variant class: MET 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: selumetinib + vistusertib

Country: United Kingdom

NCT02386826
Phase Ib Study Evaluating the c-Met Inhibitor INC280 in Combination With Bevacizumab in Glioblastoma Multiforme (GBM), Metastatic Colorectal Cancer (mCRC) and Metastatic Renal Cell Carcinoma (mRCC) Patients

Cancer type: Kidney Cancer

Variant class: MET mutation

Other identifiers: SCRI REFMAL 365, TrialTroveID-253602

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

Phase: I

Therapy: bevacizumab + capmatinib

Country: United States

US States: CO, CT, TN

US Contact: Sarah Cannon Research Institute [877-691-7274; asksarah@scresearch.net]

NCT02693535
Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Cancer type: Unspecified Solid Tumor

Variant class: MET mutation

Other identifiers: Pro00014171, TAPUR, TrialTroveID-273941

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

Phase: II

Therapy: crizotinib

Country: United States

US States: MI, NC

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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MET mutation (continued)

NCT00697632
Open-Label Dose-Escalation Trial to Evaluate the Safety, Pharmacokinetics, and Pharmacodynamics of Daily Oral MGCD265 Administered Without Interruption to Subjects With Advanced Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: MET mutation

Other identifiers: 00005540, 00009948, 2012-0741, 20142263, 265-101, AAAP0559, DFCI 08-007, MGCD265-101, MIRATI265-101, NCI-2010-00030, P1TMG265, Trial 101, TrialTroveID-081814, UCI-13-49, UW13036

Population segments: Advanced, Hormone refractory, Second line or greater/ Refractory/Relapsed, Stage II, Stage III, Stage IV, Unresectable

Phase: I

Therapy: MGCD-265

Countries: Canada, Republic of Korea, United States

US States: CA, IL, MA, MO, NC, NY, PA, TX, UT, WA

US Contact: Mirati Therapeutics Study Locator Services [844-356-0895; miratistudylocator@emergingmed.com]

NCT02228811
A Multicenter Phase I Ascending Dose Study of DCC-2701 To Assess Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics in Patients With Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: MET aberration

Other identifiers: 14-031, 2014-0878, DCC-2701-01-001, NCI-2014-02040, TrialTroveID-201122, VICCPHI13113

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

Phase: I

Therapy: altiratinib

Country: United States

US States: CO, MA, PA, TN, TX

US Contact: Jama Pitman [785-830-2100; jpitman@deciphera.com]

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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.

KIT activating mutation

Variant Class	Evidence Items
KIT aberration	2
↳ KIT mutation	5
↳ KIT activating mutation	1

MET mutation

Variant Class	Evidence Items
MET aberration	3
↳ MET positive	0
↳ MET mutation	4

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