[Oncofocus] Patient Test Report

Oncologica UK Ltd
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Gender	Male		
Histology #		**Tumour %**	80
Primary site	Olfactory Neuroblastoma	**Tumour % (macrodissected)**	
Tumour subtype	Metastatic Neuroblastoma		
Tissue type	Liver		

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: Other Cancer Type

● 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
BRCA2 copy number deletion	○ (1)	✖	✖	✖	○ (3)
IDH2 p.(R172T) c.515G>C	✖	✖	✖	✖	○ (2)
KIT p.(D820Y) c.2458G>T	✖	✖	✖	✖	○ (7)
TP53 p.(H179R) c.536A>G	✖	✖	✖	✖	○ (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 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

BRCA2 mutation

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
olaparib	○	✖	✖	✖	○ (II)
rucaparib	✖	✖	✖	✖	○ (I/II)
talazoparib + chemotherapy	✖	✖	✖	✖	○ (I)

IDH2 mutation

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
AG-881	✖	✖	✖	✖	○ (I)
CB-839	✖	✖	✖	✖	○ (I)

KIT exon 17 mutation

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
dasatinib, regorafenib	✖	✖	✖	✖	○ (II)
imatinib mesylate	✖	✖	✖	✖	○ (II)
nilotinib, pazopanib	✖	✖	✖	✖	○ (II)
ponatinib	✖	✖	✖	✖	○ (II)
AZD-2014 + selumetinib	✖	✖	✖	✖	○ (I/II)
pexidartinib + PLX-9486, PLX-9486	✖	✖	✖	✖	○ (I/II)
imatinib mesylate + ipilimumab	✖	✖	✖	✖	○ (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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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

TP53 mutation

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.

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Current EMA Information

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

EMA information is current as of 2016-07-01. For the most up-to-date information, search www.ema.europa.eu/ema.

BRCA2 mutation

○ olaparib

Cancer type: Ovarian Cancer **Label as of:** 2016-04-13 **Variant class:** BRCA mutation

Reference:

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/003726/WC500180151.pdf

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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'.

BRCA2 mutation

NCT02693535
Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Cancer type: Unspecified Solid Tumor

Variant class: BRCA2 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: olaparib

Country: United States

US States: MI, NC

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

NCT01482715
A Phase I/II, Open-Label, Safety, Pharmacokinetic, and Preliminary Efficacy Study of Oral Rucaparib in Patients With gBRCA Mutation Ovarian Cancer or Other Solid Tumor

Cancer type: Unspecified Solid Tumor

Variant class: BRCA mutation

Other identifiers: 12-048, CO-338-010, EudraCT Number: 2011-004250-26, NCRN365, REFMAL 259 IST, Study 10, TrialTroveID-149555

Population segments: Aggressive, Classical, Indolent, Nodular lymphocyte-predominant, Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: I/II

Therapy: rucaparib

Countries: United Kingdom, United States

US State: TN

US Contact: Clovis Oncology Clinical Trial Information [855-262-3040; clovistrials@emergingmed.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.

BRCA2 mutation (continued)

NCT02317874
A Phase I Study of BMN 673 in Combination with Carboplatin and Paclitaxel in Patients with Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: BRCA2 mutation

Other identifiers: 051513, 9782, NCI 9782, NCI-2014-02474, TrialTroveID-248774

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

Phase: I

Therapy: talazoparib + chemotherapy

Country: United States

US States: NJ, WI

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

IDH2 mutation

NCT02481154
A Phase I, Multicenter, Open-Label, Dose-Escalation and Expansion, Safety, Pharmacokinetic, Pharmacodynamic, and Clinical Activity Study of Orally Administered AG-881 in Patients With Advanced Solid Tumors, Including Gliomas, With an IDH1 and/or IDH2 Mutation

Cancer type: Unspecified Solid Tumor

Variant class: IDH2 mutation

Other identifiers: 00063389, 15-268, 2015-0310, AG881-C-002, TrialTroveID-260347

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

Phase: I

Therapy: AG-881

Country: United States

US States: CA, MA, NC, NY, TN, TX

US Contact: Dr. Susan Pandya [617-844-6430; susan.pandya@agios.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.

IDH2 mutation (continued)

NCT02071862
PhI Study of the Safety, PK, and PDn of Escalating Oral Doses of the Glutaminase Inhibitor CB-839, as a Single Agent and in Combination With Standard Chemotherapy in Patients With Advanced and/or Treatment-Refractory Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: IDH2 mutation

Other identifiers: 14-111, 14-455, 14951, 2014-0605, AAAO1854, CX-839-001, NCI-2014-01059, RM 320, TrialTroveID-197872

Population segments: Adenocarcinoma, Advanced, EGFR, First line, HER2 negative, KRAS, Locally advanced, Metastatic, Second line or greater/Refractory/Relapsed, Stage III, Stage IV, Triple receptor negative, Untreated

Phase: I

Therapy: CB-839

Country: United States

US States: CA, FL, GA, MA, NY, PA, TN, TX

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

KIT exon 17 mutation

NCT02461849
A Phase II, Open-label, Study in Patients With Refractory, Metastatic Cancer Harboring KIT Mutation or Amplification to Investigate the Clinical Efficacy and Safety of Imatinib Therapy.

Cancer type: Unspecified Cancer

Variant class: KIT exon 17 mutation

Other identifiers: 2013-12-074, TrialTroveID-258736

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

Phase: II

Therapy: imatinib mesylate

Country: Republic of Korea

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), 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.

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 exon 17 mutation (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: 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

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

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KIT exon 17 mutation (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: 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: AZD-2014 + selumetinib

Country: United Kingdom

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: David S. Hong [713-563-1930]

TP53 mutation

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

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.

TP53 mutation (continued)

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

Country: United States

US State: TX

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

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

Country: 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

Country: United States

US State: TX

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

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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.

BRCA2 mutation

Variant Class	Evidence Items
BRCA mutation	2
↳ BRCA2 mutation	2

IDH2 mutation

Variant Class	Evidence Items
IDH2 mutation	2

KIT exon 17 mutation

Variant Class	Evidence Items
KIT aberration	2
↳ KIT mutation	4
↳ KIT exon 17 mutation	1

TP53 mutation

Variant Class	Evidence Items
TP53 aberration	0
↳ TP53 mutation	4

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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.


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