[Oncofocus] Patient Test Report

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Histology #		**Tumour %**	80
Primary site	Eye	**Tumour % (macrodissected)**	
Tumour subtype	Uveal Melanoma		
Tissue type			

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:

Please note: No variants were identified at BRAF codon 600

Variant Summary

Sample Cancer Type: Melanoma

● 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
BAP1 p.(L230fs) c.688_688delC	✖	✖	✖	✖	● (1)
GNAQ p.(Q209P) c.626A>C	✖	✖	✖	✖	● (4)
MYC 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

BAP1 p.(L230fs) c.688_688delC

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
vorinostat	✖	✖	✖	✖	● (II)

GNAQ p.(Q209P) c.626A>C

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
trametinib	✖	✖	✖	✖	● (II)
vorinostat	✖	✖	✖	✖	● (II)
selumetinib + vistusertib	✖	✖	✖	✖	● (I/II)
LXH254	✖	✖	✖	✖	● (I)

MYC amplification

Relevant Therapy	EMA	US-FDA	ESMO	US-NCCN	Global Clinical Trials*
INCB-54329	✖	✖	✖	✖	● (I/II)

* 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 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'.

BAP1 p.(L230fs) c.688_688delC

NCT01587352
A Phase II Study of Vorinostat (NSC 701852) in Metastatic Uveal Melanoma

Cancer type: Melanoma

Variant class: BAP1 mutation

Other identifiers: 12-027, 9111, AAAO5917, CUMC-IRBAAAO5917, MSKCC-12-027, NCI-2012-00860, NCI9111, TrialTroveID-166837, VICCMEL1351

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

Phase: II

Therapy: vorinostat

Country: United States

US States: NY, TN

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

GNAQ p.(Q209P) c.626A>C

NCT01587352
A Phase II Study of Vorinostat (NSC 701852) in Metastatic Uveal Melanoma

Cancer type: Melanoma

Variant class: GNAQ mutation

Other identifiers: 12-027, 9111, AAAO5917, CUMC-IRBAAAO5917, MSKCC-12-027, NCI-2012-00860, NCI9111, TrialTroveID-166837, VICCMEL1351

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

Phase: II

Therapy: vorinostat

Country: United States

US States: NY, TN

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

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GNAQ p.(Q209P) c.626A>C (continued)

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

Cancer type: Melanoma

Variant class: RAS/RAF/MEK/ERK pathway

Other identifiers: 009896QM, EudraCT Number: 2014-002613-31, IRAS ID 172356, Torcmek, TrialTroveID-265019, UKCRN ID:18725

Population segments: EGFR, FGFR, HER2 negative, HER2 positive, KRAS, Second line or greater/Refractory/Relapsed, Squamous Cell, Stage III, Stage IV, Triple receptor negative

Phase: I/II

Therapy: selumetinib + vistusertib

Country: United Kingdom

NCT02465060
Molecular Analysis for Therapy Choice (MATCH)

Cancer type: Unspecified Solid Tumor

Variant class: GNAQ 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: ALK, EGFR, HER2 positive, Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Exclusion criteria variant class: BRAF V600 mutation

Phase: II

Therapy: trametinib

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.

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GNAQ p.(Q209P) c.626A>C (continued)

NCT02607813
A Phase I Dose Finding Study of Oral LXH254 in Adult Patients With Advanced Solid Tumors Harboring MAPK Pathway Alterations

Cancer type: Unspecified Solid Tumor

Variant class: RAS/RAF/MEK/ERK pathway

Other identifiers: 2015-0913, CLXH254X2101, EudraCT Number: 2015-003421-33, NCI-2015-02280, REec-2016-2132, TrialTroveID-268216

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

Phase: I

Therapy: LXH254

Countries: Canada, Germany, Japan, Netherlands, Spain, United States

US States: NY, TX

US Contact: Novartis Pharmaceuticals [888-669-6682]

MYC amplification

NCT02431260
A Phase I, Open-Label, Dose-Escalation, Safety and Tolerability Study of INCB054329 in Subjects With Advanced Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: MYC aberration

Other identifiers: 2015-0054, INCB 54329-101, NCI-2015-00936, TrialTroveID-252118, UMCC 2015.032, UW15024

Population segments: Aggressive, Classical, Diffuse large B-cell lymphoma (DLBCL), Hormone refractory, Indolent, Nodular lymphocyte-predominant, Other subtype, Second line or greater/Refractory/Relapsed, Stage III, Stage IV

Phase: I/II

Therapy: INCB-54329

Country: United States

US States: CA, CO, IL, IN, MI, MO, TN, TX, WA

US Contact: Incyte Corporation Call Center [855-463-3463]

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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.

BAP1 p.(L230fs) c.688_688delC

Variant Class	Evidence Items
BAP1 mutation	1

GNAQ p.(Q209P) c.626A>C

Variant Class	Evidence Items
RAS/RAF/MEK/ERK pathway	2
↳ GNAQ mutation	2

MYC amplification

Variant Class	Evidence Items
MYC aberration	1
↳ MYC amplification	0

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Appendix: Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
BAP1	p.(L230fs)	c.688_688delC	.	chr3:52440363	27.35%	NM_004656.3	frameshift Deletion
GNAQ	p.(Q209P)	c.626A>C	COSM28758	chr9:80409488	22.05%	NM_002072.4	missense

Copy Number Variations

Gene	Locus	Copy Number
MYC	chr8:128748884	4.74

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