

Medical Laboratory
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Leading a new era of precision oncology

Oncofocus[®]

Precision Oncology

Lead Clinical Scientist: Keeda Hardisty

Pre-Reg Clinical Scientist: Katherine Benton

Date: 25 Mar 2019

1 of 13

ONC19

Surname

Forename

DOB

Gender

Female

Histology #

Primary site

Brain

Tumour subtype

Glioblastoma

Tissue Type

Parietal Tumour

Requester

Contact details

Date requested

Tumour %

-

Tumour %

90%

(macrodissected)

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.

Oncofocus currently targets 505 genes covering oncogenes, fusion genes, genes susceptible to copy number variation and tumour suppressors. Actionable genetic variants detected by Oncofocus are currently linked to 687 anti-cancer targeted therapies/therapy combinations.

The following actionable variants were detected:

Please note:

- There is limited evidence available in the literature to determine the pathogenicity of the ATRX and CREBBP variants detected. Therefore, assuming pathogenicity is confirmed, the following therapies would be applicable.
- The TP53 variant falls below our threshold for reporting, however repeat testing has confirmed its presence.

Within the 'Current Clinical Trials Information' section of this report, starting on page 5, the NCT numbers are hyperlinks to the clinicaltrials.gov webpages which should be accessed to gain further trial specific information

Sample Cancer Type: Glioblastoma

Clinically Significant Biomarkers

■ Indicated ■ Contraindicated

Genomic Alteration	Alt Allele Freq	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
ATR deletion (0.88 copies)		Clinical trials and/or off-label	Clinical trials and/or off-label	4
CDKN2A deletion (0 copies)		Clinical trials and/or off-label	Clinical trials and/or off-label	4
ATRX mutation c.5104_5107delGAAA, p.(Glu1702fs)	52.66%	Clinical trials and/or off-label	Clinical trials and/or off-label	3
NBN deletion (0.63 copies)		Clinical trials and/or off-label	Clinical trials and/or off-label	3
TP53 mutation c.743G>A, p.(Arg248Gln)	97.30%	Clinical trials and/or off-label	Clinical trials and/or off-label	2
CDKN2B deletion (0 copies)		Clinical trials and/or off-label	Clinical trials and/or off-label	2
CREBBP mutation c.3386_3399delTAAAGAATCCCATG, p.(Val1129fs)	42.81%	Clinical trials and/or off-label	Clinical trials and/or off-label	1

Sources included in relevant therapies: EMA1, FDA2, ESMO, NCCN

Hotspot variants with >10% alternate allele reads are classified as 'detected' with an assay sensitivity and positive predictive value (PPV) of 99%. Copy number variants; amplifications of CN> 6 with the 5% confidence value of ≥4 after normalization and deletions with 95% CI ≤1 are classified as present when the tumour% >50% with a sensitivity of 80% and PPV 100%. Gene Fusions are reported when occurring in >40 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. Please note this version of the Oncofocus test is an upgraded version to that accredited on our schedule

ONC19:-

Referring pathology dept:

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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.

Disclaimer: The data presented here is a result of the curation of published data sources, but may not be exhaustive. The data version is 2018.12(004).

Tier Criteria Met

Genomic Alteration	Tier Classification for Glioblastoma
<i>ATR deletion</i> Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
<i>CDKN2A deletion</i> Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
<i>ATRX mutation</i> Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
<i>NBN deletion</i> Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
<i>TP53 mutation</i> Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
<i>CDKN2B deletion</i> Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
<i>CREBBP mutation</i> Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials

Reference: Li et al. *Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists.* J Mol Diagn. 2017 Jan;19(1):4-23.

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

ATR deletion					
Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
durvalumab + olaparib	×	×	×	×	● (II)
prexasertib	×	×	×	×	● (II)
talazoparib	×	×	×	×	● (II)
BAY-1895344	×	×	×	×	● (I/II)

CDKN2A deletion					
Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
palbociclib	×	×	×	×	● (II)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

ONC19-:
Referring pathology dept:

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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 (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

CDKN2A deletion (continued)

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
ribociclib	×	×	×	×	● (II)

ATRX mutation

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
niraparib	×	×	×	×	● (II)
BAY-1895344	×	×	×	×	● (I/II)
VX-970, VX-970 + chemotherapy	×	×	×	×	● (I/II)

NBN deletion

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
talazoparib	×	×	×	×	● (II)
BAY-1895344	×	×	×	×	● (I/II)
BGB-A317 + pamiparib	×	×	×	×	● (I)

TP53 mutation

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
adavosertib + olaparib	×	×	×	×	● (II)
VX-970, VX-970 + chemotherapy	×	×	×	×	● (I/II)

CDKN2B deletion

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
palbociclib	×	×	×	×	● (II)
ribociclib	×	×	×	×	● (II)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

ONC19-:
Referring pathology dept:

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 (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

CREBBP mutation

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
CCS-1477	×	×	×	×	● (I/II)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

ONC19-:
Referring pathology dept:

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 Details

Current Clinical Trials Information

Clinical Trials information is current as of 2018-09-04. 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'.

ATR deletion

No NCT ID - see other identifier(s)

Single Arm, Open label, Signal Seeking,
Phase IIa Trial Of The Activity Of Olaparib
In Combination With Durvalumab In
Patients With Tumours With Homologous
Recombination Repair Defects

Cancer type: Unspecified Solid Tumor**Variant class:** ATR deletion**Other identifiers:** ACTRN12617001000392, MoST Addendum 3, U1111-1182-6652**Population segments:** Second line, Stage III, Stage IV**Phase:** II**Therapy:** durvalumab + olaparib**Location:** Australia**NCT02286687**

Phase II Study of the PARP Inhibitor BMN
673 (Talazoparib Tosylate) in Advanced
Cancer Patients With Somatic Alterations
in BRCA1/2, Mutations/Deletions in
PTEN or PTEN Loss, a Homologous
Recombination Defect, Mutations/
Deletions in Other BRCA Pathway Genes
and Germline Mutation in BRCA1/2 (Not
Breast or Ovarian Cancer)

Cancer type: Unspecified Cancer**Variant class:** ATR deletion**Other identifiers:** 2013-0961, NCI-2014-02494**Population segments:** Fourth line or greater, Stage III, Stage IV**Phase:** II**Therapy:** talazoparib**Location:** United States**US State:** TX**US Contact:** Dr. Sarina Piha-Paul [713-563-1930]**NCT02873975**

A Phase II Study of the CHK1 Inhibitor
LY2606368 in Patients With Advanced
Solid Tumors Exhibiting Replicative
Stress or Homologous Recombination
Repair Deficiency

Cancer type: Unspecified Solid Tumor**Variant class:** Fanconi anemia pathway**Other identifiers:** 16-281, I4D-MC-E006, NCI-2016-01564**Population segments:** Second line, Stage III, Stage IV**Phase:** II**Therapy:** prexasertib**Location:** United States**US State:** MA**US Contact:** Dr. Geoffrey Shapiro [617-632-4942; Geoffrey_Shipiro@dfci.harvard.edu]**ONC19-:****Referring pathology dept:**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.

ATR deletion (continued)**NCT03188965**

An Open-label, First-in-human, Dose-escalation Study to Evaluate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Maximum Tolerated Dose and / or Recommended Phase II Dose of the ATR Inhibitor BAY1895344 in Patients With Advanced Solid Tumors and Lymphomas

Cancer type: Unspecified Solid Tumor

Variant class: DNA repair pathway

Other identifiers: 18594, 2017-0186, BAY1895344/18594, EudraCT Number: 2016-004484-39, IRAS ID-218516, NCI-2018-00206, Trial ID: 16754

Population segments: Adenocarcinoma, Aggressive, Diffuse large B-cell lymphoma (DLBCL), Hormone refractory, Indolent, Mantle cell lymphoma (MCL), Second line, Squamous Cell, Stage III, Stage IV

Phase: I/II

Therapy: BAY-1895344

Locations: Canada, Singapore, Switzerland, United Kingdom, United States

US State: TX

US Contact: Bayer Clinical Trials Contact [888-842-2937; clinical-trials-contact@bayer.com]

CDKN2A deletion**NCT02933736**

A Phase 0/II Study of Ribociclib (LEE011) in Preoperative Rb-Positive Recurrent High-Grade Glioma and Meningioma Patients Scheduled for Resection to Evaluate Central Nervous System (CNS) Penetration

Cancer type: Glioblastoma

Variant class: CDKN2A deletion

Other identifier: PHX-16-0116-80-12

Population segments: (N/A), Neoadjuvant

Exclusion criteria variant class: RB1 mutation

Phase: II

Therapy: ribociclib

Location: United States

US State: AZ

US Contact: Dr. Norissa Honea [602-406-6267; norissa.honea@dignityhealth.org]

ONC19-:

Referring pathology dept:

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.

CDKN2A deletion (continued)**NCT02693535**Targeted Agent and Profiling Utilization
Registry (TAPUR) Study**Cancer type:** Unspecified Solid Tumor**Variant class:** CDKN2A deletion**Other identifiers:** NCI-2017-00510, Pro00014171, TAPUR**Population segments:** (N/A), Aggressive, Diffuse large B-cell lymphoma (DLBCL), Extranodal marginal zone B-cell lymphoma (MALT), Follicular lymphoma (FL), Indolent, Lymphoblastic lymphoma (LBL), Mantle cell lymphoma (MCL), Other subtype, Second line, Small lymphocytic lymphoma (SLL), Stage III, Stage IV, Waldenstrom's macroglobulinemia (WM)**Phase:** II**Therapy:** palbociclib**Location:** United States**US States:** AL, AZ, CA, FL, GA, IL, MI, NC, ND, NE, OK, OR, PA, SD, TX, UT, VA, WA**US Contact:** Pam Mangat [pam.mangat@asco.org]**NCT03297606**Canadian Profiling and Targeted Agent
Utilization Trial (CAPTUR): A Phase II
Basket Trial**Cancer type:** Unspecified Solid Tumor**Variant class:** CDKN2A aberration**Other identifiers:** CA209-9DL, CAPTUR, ESR-17-12831, ML39800, PM1, WI233446**Population segments:** Aggressive, Diffuse large B-cell lymphoma (DLBCL), Extranodal marginal zone B-cell lymphoma (MALT), First line, Follicular lymphoma (FL), Indolent, Lymphoblastic lymphoma (LBL), Mantle cell lymphoma (MCL), Other subtype, Second line, Stage III, Stage IV, Waldenstrom's macroglobulinemia (WM)**Phase:** II**Therapy:** palbociclib**Location:** Canada**NCT01037790**Phase II Trial of the Cyclin-Dependent
Kinase Inhibitor PD 0332991 in Patients
With Cancer**Cancer type:** Unspecified Solid Tumor**Variant class:** G1/S cell cycle pathway**Other identifiers:** NCI-2009-01467, Study 1006, UPCC 03909, UPCC03909**Population segments:** Estrogen receptor positive, Fourth line or greater, HER2 negative, HER2 positive, Metastatic, Progesterone receptor positive, Second line, Stage III, Stage IV, Third line, Triple receptor negative**Phase:** II**Therapy:** palbociclib**Location:** United States**US State:** PA**US Contact:** Dr. Peter O. Dwyer [855-216-0098; PennCancerTrials@emergingmed.com]**ONC19-:****Referring pathology dept:**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.

ATRX mutation

NCT03207347

A Phase II Trial of the PARP Inhibitor, Niraparib, in BAP1 and Other DNA Damage Response (DDR) Pathway Deficient Neoplasms (UF-STO-ETI-001)

Cancer type: Unspecified Cancer

Variant class: ATRX mutation

Other identifier: UF-STO-ETI-001

Population segments: (N/A), Second line

Phase: II

Therapy: niraparib

Location: United States

US State: FL

US Contact: Ashton Monismith [352-265-0680 ext 87657; amonismith@ufl.edu]

No NCT ID - see other identifier(s)

An Open-Label Study of the Safety, Tolerability, and Pharmacokinetic/ Pharmacodynamic Profile of VX-970 as a Single Agent in Combination with Carboplatin in Subjects with Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: DNA repair mutation

Other identifiers: EudraCT Number: 2013-005100-34, VX13-970-002

Population segments: (N/A), Adenocarcinoma, HER2 negative, Second line or greater/ Refractory/Relapsed, Stage III, Stage IV, Triple receptor negative

Phase: I/II

Therapies: VX-970, VX-970 + chemotherapy

Location: United Kingdom

NCT03188965

An Open-label, First-in-human, Dose-escalation Study to Evaluate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Maximum Tolerated Dose and / or Recommended Phase II Dose of the ATR Inhibitor BAY1895344 in Patients With Advanced Solid Tumors and Lymphomas

Cancer type: Unspecified Solid Tumor

Variant class: DNA repair pathway

Other identifiers: 18594, 2017-0186, BAY1895344/18594, EudraCT Number: 2016-004484-39, IRAS ID-218516, NCI-2018-00206, Trial ID: 16754

Population segments: Adenocarcinoma, Aggressive, Diffuse large B-cell lymphoma (DLBCL), Hormone refractory, Indolent, Mantle cell lymphoma (MCL), Second line, Squamous Cell, Stage III, Stage IV

Phase: I/II

Therapy: BAY-1895344

Locations: Canada, Singapore, Switzerland, United Kingdom, United States

US State: TX

US Contact: Bayer Clinical Trials Contact [888-842-2937; clinical-trials-contact@bayer.com]

ONC19-:

Referring pathology dept:

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.

NBN deletion

NCT02286687

Phase II Study of the PARP Inhibitor BMN 673 (Talazoparib Tosylate) in Advanced Cancer Patients With Somatic Alterations in BRCA1/2, Mutations/Deletions in PTEN or PTEN Loss, a Homologous Recombination Defect, Mutations/Deletions in Other BRCA Pathway Genes and Germline Mutation in BRCA1/2 (Not Breast or Ovarian Cancer)

Cancer type: Unspecified Cancer

Variant class: NBN deletion

Other identifiers: 2013-0961, NCI-2014-02494

Population segments: Fourth line or greater, Stage III, Stage IV

Phase: II

Therapy: talazoparib

Location: United States

US State: TX

US Contact: Dr. Sarina Piha-Paul [713-563-1930]

NCT03188965

An Open-label, First-in-human, Dose-escalation Study to Evaluate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Maximum Tolerated Dose and / or Recommended Phase II Dose of the ATR Inhibitor BAY1895344 in Patients With Advanced Solid Tumors and Lymphomas

Cancer type: Unspecified Solid Tumor

Variant class: DNA repair pathway

Other identifiers: 18594, 2017-0186, BAY1895344/18594, EudraCT Number: 2016-004484-39, IRAS ID-218516, NCI-2018-00206, Trial ID: 16754

Population segments: Adenocarcinoma, Aggressive, Diffuse large B-cell lymphoma (DLBCL), Hormone refractory, Indolent, Mantle cell lymphoma (MCL), Second line, Squamous Cell, Stage III, Stage IV

Phase: I/II

Therapy: BAY-1895344

Locations: Canada, Singapore, Switzerland, United Kingdom, United States

US State: TX

US Contact: Bayer Clinical Trials Contact [888-842-2937; clinical-trials-contact@bayer.com]

NCT02660034

A Phase I/Ib, Open Label, Multiple Dose, Dose Escalation and Expansion Study to Investigate the Safety, Pharmacokinetics and Antitumor Activity of the Anti-PD-1 Monoclonal Antibody BGB-A317 in Combination With the PARP Inhibitor BGB-290 in Subjects With Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: HRR pathway

Other identifiers: 16-183, A317/290, BGB-A317/BGB-290_Study_001, CT783, NCI-2018-00791

Population segments: HER2 negative, Second line, Stage III, Stage IV, Triple receptor negative

Phase: I

Therapy: BGB-A317 + pamiparib

Locations: Australia, New Zealand, Spain, United States

US States: AZ, CA, CO, FL, MA, NY, PA, TN, TX, VA

US Contact: Dr. Ginny Paton [clinicaltrials@beigene.com]

ONC19-:

Referring pathology dept:

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.

TP53 mutation

NCT02576444

A Phase II Study of the PARP Inhibitor Olaparib (AZD2281) Alone and in Combination With AZD1775, AZD5363, or AZD6738 in Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: TP53 mutation

Other identifiers: 1508016363, 16-314, NCI-2016-00922, OLAPCO, VICCMD1672

Population segments: First line, Second line, Stage IV

Phase: II

Therapy: adavosertib + olaparib

Location: United States

US States: CT, MA, OH, TN

US Contact: Manuel Avedissian [203-737-3669; manuel.avedissian@yale.edu]

No NCT ID - see other identifier(s)

An Open-Label Study of the Safety, Tolerability, and Pharmacokinetic/ Pharmacodynamic Profile of VX-970 as a Single Agent in Combination with Carboplatin in Subjects with Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: TP53 mutation

Other identifiers: EudraCT Number: 2013-005100-34, VX13-970-002

Population segments: (N/A), Adenocarcinoma, HER2 negative, Second line or greater/ Refractory/Relapsed, Stage III, Stage IV, Triple receptor negative

Phase: I/II

Therapies: VX-970, VX-970 + chemotherapy

Location: United Kingdom

CDKN2B deletion

NCT02933736

A Phase 0/II Study of Ribociclib (LEE011) in Preoperative Rb-Positive Recurrent High-Grade Glioma and Meningioma Patients Scheduled for Resection to Evaluate Central Nervous System (CNS) Penetration

Cancer type: Glioblastoma

Variant class: CDKN2B deletion

Other identifier: PHX-16-0116-80-12

Population segments: (N/A), Neoadjuvant

Exclusion criteria variant class: RB1 mutation

Phase: II

Therapy: ribociclib

Location: United States

US State: AZ

US Contact: Dr. Norissa Honea [602-406-6267; norissa.honea@dignityhealth.org]

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Referring pathology dept:

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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.

CDKN2B deletion (continued)**NCT01037790**

Phase II Trial of the Cyclin-Dependent Kinase Inhibitor PD 0332991 in Patients With Cancer

Cancer type: Unspecified Solid Tumor

Variant class: G1/S cell cycle pathway

Other identifiers: NCI-2009-01467, Study 1006, UPCC 03909, UPCC03909

Population segments: Estrogen receptor positive, Fourth line or greater, HER2 negative, HER2 positive, Metastatic, Progesterone receptor positive, Second line, Stage III, Stage IV, Third line, Triple receptor negative

Phase: II

Therapy: palbociclib

Location: United States

US State: PA

US Contact: Dr. Peter O. Dwyer [855-216-0098; PennCancerTrials@emergingmed.com]

CREBBP mutation**NCT03568656**

An Open-label Phase I/IIa Study to Evaluate the Safety and Efficacy of CCS1477 as Monotherapy and in Combination, in Patients With Advanced Solid/Metastatic Tumours.

Cancer type: Unspecified Solid Tumor

Variant class: CREBBP mutation

Other identifier: CCS1477-01

Population segments: Hormone refractory, Second line, Stage III, Stage IV

Phase: I/II

Therapy: CCS-1477

Location: United Kingdom

ONC19-:

Referring pathology dept:

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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.

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.

ATR deletion

Variant Class	Evidence Items
DNA repair pathway	3
↳ ATR deletion	2
Fanconi anemia pathway	1
↳ ATR deletion	2

CDKN2A deletion

Variant Class	Evidence Items
G1/S cell cycle pathway	2
↳ CDKN2A aberration	1
↳ CDKN2A negative	0
↳ CDKN2A deletion	2

ATRX mutation

Variant Class	Evidence Items
DNA repair pathway	3
↳ DNA repair mutation	1
↳ ATRX mutation	1

ONC19-:
Referring pathology dept:

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.

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.

NBN deletion

Variant Class	Evidence Items
DNA repair pathway	3
↳ NBN deletion	1
HRR pathway	1
↳ NBN deletion	1

TP53 mutation

Variant Class	Evidence Items
TP53 aberration	0
↳ TP53 mutation	2

CDKN2B deletion

Variant Class	Evidence Items
G1/S cell cycle pathway	2
↳ CDKN2B deletion	1

CREBBP mutation

Variant Class	Evidence Items
CREBBP mutation	1

ONC19-:
Referring pathology dept:

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.

Quality Metric	Controlled parameters	Sample
Chip loading	≥60%	95%
Total reads	>45 million reads	93,309,824
Enrichment	100% ideal	100%
Clonal: Polyclonal ratio	Up to 55% polyclonal	29%
Low Quality	≤26% approximately.	7%
Usable reads	≥30%	65%
Aligned bases	≥80% Can be less if base coverage, and % reads on target is high	88%
Unaligned bases	≤20%	12%
Mean raw accuracy	This value should be as close to 100% as possible	99%
Overall read length histogram	Median read length 98-115bp for DNA only, 65-90bp RNA only, DNA & RNA 100bp ±20	111

DNA

Quality Metric	Controlled parameters	Sample
Number of mapped reads	>4.5 million	6,786,910
Percent reads on target	>90%	95.12%
Average base coverage depth	>1200	1,904
Uniformity of amplicon (base) coverage	>90% (degraded 85-90%)	94.68%
Percent assigned amplicon reads	>90%	95.12%
Amplicons with no strand bias	>90%	98.60%
Amplicons reading end to end	>80%	94.50%
% base reads on target	>85%	91.72%
coverage at 1X	>90% coverage is required at 500X for samples with tumour percentages below 40%	99.94%
coverage at 20X		98.25%
coverage at 100X		98.25%
coverage at 500X		92.47%
MAPD value	In the presence of a copy number variant, this value should be <0.5	0.245

RNA

Quality Metric	Controlled parameters	Test specific figures
Mapped reads	>40,000 for software to call a fusion, (should be over 500,000)	3,099,964
Expression Control Genes MYC	>15 read counts indicates the gene is present (5 out of 6 genes should be present to accept the presence of a fusion)	11408
Expression Control Genes HMBS		6992
Expression Control Genes TBP		399562
Expression Control Genes LRP1		194556
Expression Control Genes ITGB7		4916
Expression Control Genes MRPL13		388215



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Oncologica UK Ltd, Suite 2, The Newnham Building,
Chesterford Research Park, Little Chesterford,
Cambridge, CB10 1XL

+44 (0) 1223 785 327 - info@oncologica.com

Ireland

Bymac Centre, Northwest
Business Park, Blanchardstown, Dublin 15

+353 1 8604204

Italy

Parco Tecnologico della Sardegna
Pula, Località Piscinamanna

+39 02 808 88210

Medical Laboratory
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PD-1/PD-L1 TESTING

ONC19**Surname****Forename****DOB****Gender**

Female

Histology #**Primary site**

Brain

Tumour subtype

Glioblastoma

Tissue Type

Parietal Tumour

Requester**Contact details****Date requested****Tumour %**

-

Tumour %

90%

(macrodissected)**PD-L1 test**

PD-L1 IHC assays are used to help identify those patients most likely to benefit from anti-PD-1/PD-L1 directed immunotherapies. Assessment involves the determination of a range of cut-off/threshold values for PD-L1 positive tumour cells and PD-L1 positive immune cells. These cut off values are identified as predictors of response to anti-PD-L1 directed therapies used in the treatment of a range of different cancer types and include pembrolizumab, atezolizumab, avelumab, nivolumab, and durvalumab. The established cut off values for tumour proportion scores (>1%, >25%, >50%) and PD-L1 positive immune cells (10%), which vary according to immunotherapy, tumour type and whether first or second line therapy is to be used.

The Oncologica® Immunofocus PD-L1 immunocytochemistry assay quantifies the proportion of tumour cells that express PD-L1 (Tumour Proportion Score) and the area occupied by tumour infiltrating PD-L1 positive immune cells.

The Oncologica® Immunofocus PD-L1 immunocytochemistry assay is a Laboratory Developed Test utilising the RUO rabbit monoclonal antibody clone E1L3N (Cell Signalling Technologies) and Leica Bond III instrumentation. The performance of the Immunofocus assay is continually assessed by involvement in recognised External Quality Assessment schemes and returns performance levels commensurate with approved the PD-L1 diagnostic assays. All Immunofocus assay testing is performed within the scope of UKAS/ISO 15189:2012 accreditation. Clone E1L3N is not licensed and approved for use in clinical testing to direct the use of PD-1/PD-L1 therapies. The PD-L1 protein expression levels in tumour cells generated by the Immunofocus PD-L1 assay should therefore be interpreted within the context of these facts.

PD-L1 Result

No significant PD-L1 immunostaining of tumour cells is observed. There is an absence of a tumour associated PD-L1 expressing immune cell (IC) infiltrate.

Summary; PD-L1 Tumour Proportion Score 0%; PD-L1 positive ICs 0% of tumour area



oncologica®



Oncologica UK Ltd, Suite 2, The Newnham Building,
Chesterford Research Park, Little Chesterford,
Cambridge, CB10 1XL

+44 (0) 1223 785 327 - info@oncologica.com

Ireland

Bymac Centre, Northwest
Business Park, Blanchardstown, Dublin 15

+353 1 8604204

Italy

Parco Tecnologico della Sardegna
Pula, Località Piscinamanna

+39 02 808 88210