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Leading a new era of precision oncology

Oncofocus®

Precision Oncology

ONCOFOCUS® TEST REPORT

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Report Highlights

6 Clinically Significant Biomarkers
0 Therapies Available
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Patient demographics

ONC20	-		
Surname	-	**Requester**	-
Forename	-	**Contact details**	-
DOB	-	**Date requested**	-
Gender	Female		
Histology #	-	**Tumour %**	-
Primary site	Not Recorded	**Tumour %**	>96%
Tumour subtype	Metastatic Melanoma	**(macrodissected)**	
Tissue Type	Jejunal Rescection		

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 738 anti-cancer targeted therapies/therapy combinations.

The clinically significant bio-markers identified in this case are summarised on page 2

The assay detected a MDM2 amplification (Copy Number 12.46). This variant meets our criteria for reporting but is not linked to any clinical trials at this time.

Within the 'Current Clinical Trials Information' section of this report, starting on page 6, the NCT numbers are hyperlinks to the clinicaltrials.gov webpages which should be accessed to gain further trial specific information

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Clinically Significant Biomarkers

Indicated **Contraindicated**

Genomic Alteration		Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
ATM deletion	(Read count 9.73)	Clinical trials and/or off-label	Clinical trials and/or off-label	7
RICTOR amplification	(Read count 0.81)	Clinical trials and/or off-label	Clinical trials and/or off-label	5
CDK4 amplification	(Read count 35)	Clinical trials and/or off-label	Clinical trials and/or off-label	4
MRE11 deletion	(Read count 0.86)	Clinical trials and/or off-label	Clinical trials and/or off-label	3
CHEK1 deletion	(Read count 0.84)	Clinical trials and/or off-label	Clinical trials and/or off-label	3
TP53 c.79C>T p.Pro27Ser	(Allele freq 30%)	Clinical trials and/or off-label	Clinical trials and/or off-label	1

Sources included in relevant therapies: EMA[1], 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%.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. Supplementary technical information is available upon request.

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Biomarker Descriptions

CDK4 (cyclin dependent kinase 4)

Background: The CDK4 gene encodes the cyclin-dependent kinase-4 protein, a homologue of CDK6. Both proteins are serine/threonine protein kinases that are involved in the regulation of the G1/S phase transition of the mitotic cell cycle[1,2]. CDK4 kinase is activated by complex formation with D-type cyclins (e.g., CCND1, CCND2, or CCND3), which leads to the phosphorylation of retinoblastoma protein (RB), followed by E2F activation, DNA replication, and cell-cycle progression[3]. Germline mutations in CDK4 are associated with familial melanoma[4,5,6].

Alterations and prevalence: Recurrent somatic mutations of CDK4 codon K22 and R24 are observed in melanoma (1-2%) and lung cancer (approximately 0.1%). Codons K22 and R24 are necessary for binding and inhibition by p16/CDKN2A[7,8,9]. CDK4 is recurrently amplified in several cancer types, most notably in sarcomas (15-20%), glioma (10-15%), adrenocortical carcinoma (5%), lung adenocarcinoma (5%), and melanoma (3%)[10,11,12,13].

Potential clinical relevance: Currently, no therapies are approved for CDK4 aberrations. Small molecule inhibitors targeting CDK4/6--including palbociclib (2015), abemaciclib (2017), and ribociclib (2017)-- are FDA approved in combination with an aromatase inhibitor or fulvestrant for the treatment of hormone receptor-positive, HER2-negative advanced or metastatic breast cancer.

TP53 (tumor protein p53)

Background: The TP53 gene encodes the p53 tumor suppressor protein that binds to DNA and activates transcription in response to diverse cellular stresses to induce cell cycle arrest, apoptosis, or DNA repair. In unstressed cells, TP53 is kept inactive by targeted degradation via MDM2, a substrate recognition factor for ubiquitin-dependent proteolysis. Alterations in TP53 is required for oncogenesis as they result in loss of protein function and gain of transforming potential[14]. Germline mutations in TP53 are the underlying cause of Li-Fraumeni syndrome, a complex hereditary cancer predisposition disorder associated with early-onset cancers[15,16].

Alterations and prevalence: TP53 is the most frequently mutated gene in the cancer genome with approximately half of all cancers experiencing TP53 mutations. Ovarian, head and neck, esophageal, and lung squamous cancers have particularly high TP53 mutation rates (60-90%)[10,11,17,18,19,20]. Approximately two-thirds of TP53 mutations are missense mutations and several recurrent missense mutations are common including substitutions at codons R158, R175, R248, R273, and R282[10,11]. Invariably, recurrent missense mutations in TP53 inactivate its ability to bind DNA and activate transcription of target genes[21,22,23,24].

Potential clinical relevance: The FDA has granted fast track designation (2019) to APR-246 for myelodysplastic syndrome (MDS) patients harboring a TP53 mutation[25]. TP53 mutations confer poor prognosis in acute myeloid leukemia (AML), MDS, and myeloproliferative neoplasms (MPN)[26,27,28]. Similar to APR-246, other investigational therapies aimed at restoring wild-type TP53 activity, as well as compounds that induce synthetic lethality are under clinical evaluation[29,30].

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Tier Criteria Met

Genomic Alteration	Tier Classification for Melanoma
ATM deletion Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
CDK4 amplification Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
MRE11 deletion Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
RICTOR amplification Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
CHEK1 deletion Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
TP53 mutation 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

ATM deletion

Relevant Therapy	EMA	ESMO	NCCN	Clinical Trials*
durvalumab + olaparib	✖	✖	✖	● (II)
olaparib	✖	✖	✖	● (II)
talazoparib	✖	✖	✖	● (II)
avelumab, talazoparib	✖	✖	✖	● (I/II)
BAY-1895344	✖	✖	✖	● (I/II)
pamiparib, tislelizumab	✖	✖	✖	● (I)

CDK4 amplification

Relevant Therapy	EMA	ESMO	NCCN	Clinical Trials*
abemaciclib	✖	✖	✖	● (II)
palbociclib	✖	✖	✖	● (II)

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

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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

MRE11 deletion

Relevant Therapy	EMA	ESMO	NCCN	Clinical Trials*
olaparib	✖	✖	✖	● (II)
talazoparib	✖	✖	✖	● (II)
BAY-1895344	✖	✖	✖	● (I/II)
pamiparib, tislelizumab	✖	✖	✖	● (I)

RICTOR amplification

Relevant Therapy	EMA	ESMO	NCCN	Clinical Trials*
everolimus	✖	✖	✖	● (II)
atezolizumab + ipatasertib	✖	✖	✖	● (I/II)
gedatolisib + palbociclib	✖	✖	✖	● (I)

CHEK1 deletion

Relevant Therapy	EMA	ESMO	NCCN	Clinical Trials*
durvalumab + olaparib	✖	✖	✖	● (II)
olaparib	✖	✖	✖	● (II)
BAY-1895344	✖	✖	✖	● (I/II)

TP53 mutation

Relevant Therapy	EMA	ESMO	NCCN	Clinical Trials*
statin	✖	✖	✖	● (I)

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

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Relevant Therapy Details

Current Clinical Trials Information

Clinical Trials information is current as of 2019-09-09. 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'.

ATM 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: ATM 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

NCT02693535
Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Cancer type: Unspecified Solid Tumor

Variant class: ATM deletion

Other identifiers: 20170529, NCI-2017-00510, Pro00014171, TAPUR

Population segments: (N/A), Aggressive, Diffuse large B-cell lymphoma (DLBCL), Extranodal marginal zone B-cell lymphoma (MALT), First line, Follicular lymphoma (FL), Fourth line or greater, Indolent, Lymphoblastic lymphoma (LBL), Mantle cell lymphoma (MCL), Other subtype, Second line, Small lymphocytic lymphoma (SLL), Stage III, Stage IV, Third line, Waldenstrom's macroglobulinemia (WM)

Phase: II

Therapy: olaparib

Location: United States

US States: AL, AZ, CA, FL, GA, IL, MI, NC, ND, NE, OK, OR, PA, SD, TX, UT, VA, WA

Contact: Pam Mangat [pam.mangat@asco.org]

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: ATM 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

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

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ATM deletion (continued)

NCT03233204
NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice)- A Phase II Subprotocol of Olaparib in Patients With Tumors Harboring Defects in DNA Damage Repair Genes

Cancer type: Unspecified Solid Tumor

Variant class: DNA repair pathway

Other identifiers: 20170841, APEC1621H, NCI-2017-00766

Population segments: Aggressive, Indolent, Pediatric or Adolescent, Second line, Stage III, Stage IV

Phase: II

Therapy: olaparib

Locations: Puerto Rico, United States

US States: AL, AR, AZ, CA, CO, DC, FL, GA, IA, ID, IL, IN, KY, LA, MD, ME, MI, MN, MO, MS, NC, NE, NJ, NY, OH, OK, OR, PA, SC, TN, TX, UT, VA, VT, WA, WI

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

NCT03330405
A Phase Ib/II Study To Evaluate Safety And Anti Tumor Activity Of Avelumab In Combination With The Poly(Adenosine Diphosphate [Adp]-Ribose) Polymerase (Parp) Inhibitor Talazoparib In Patients With Locally Advanced Or Metastatic Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: ATM aberration

Other identifiers: 17-687, 18-1008, 2017-0524, 34807, B9991025, EudraCT Number: 2017-001509-33, IRAS ID 235395, JAVELIN PARP MEDLEY, NCI-2017-02385, P 60917, s17-01353, S17-01353

Population segments: Estrogen receptor positive, HER2 negative, Hormone refractory, Progesterone receptor positive, Second line, Stage III, Stage IV, Triple receptor negative

Phase: I/II

Therapies: avelumab, talazoparib

Locations: Australia, Canada, Denmark, Hungary, Russian Federation, United Kingdom, United States

US States: AR, DC, MA, MN, NY, OH, TX

Contact: Pfizer CT.gov Call Center [800-718-1021; ClinicalTrials.gov_Inquiries@pfizer.com]

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ATM 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: 18-441, 18594, 2017-0186, BAY1895344/18594, EudraCT Number: 2016-004484-39, IRAS ID-218516, JapicCTI-183998, NCI-2018-00206

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

Phase: I/II

Therapy: BAY-1895344

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

US States: FL, GA, MA, NY, OH, PA, TX, UT

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, 18-009, A317/290, BGB-A317/BGB-290, BGB-A317/BGB-290_Study_001, CT783, NCI-2018-00791, P 55217, VICCPHI1814

Population segments: Fourth line or greater, HER2 negative, Pulmonary, Second line, Stage III, Stage IV, Third line, Triple receptor negative

Phase: I

Therapies: pamiparib, tislelizumab

Locations: Australia, France, New Zealand, Spain, United Kingdom, United States

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

Contact: Rob Stewart [clinicaltrials@beigene.com]

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CDK4 amplification

NCT01037790
Phase II Trial of the Cyclin-Dependent Kinase Inhibitor PD 0332991 in Patients With Cancer

Cancer type: Melanoma

Variant class: CDK4 amplification

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

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

NCT02896335
A Phase II Study of Palbociclib in Progressive Brain Metastases Harboring Alterations in the CDK Pathway

Cancer type: Melanoma

Variant class: CDK4 amplification

Other identifiers: 16-254, NCI-2016-02025

Population segments: CNS mets, Second line, Stage IV

Phase: II

Therapy: palbociclib

Location: United States

US State: MA

Contact: Dr. Priscilla Brastianos [617-724-8770; PBRASTIANOS@mgh.harvard.edu]

NCT03310879
A Phase II Study of the CDK4/6 Inhibitor Abemaciclib in Patients With Solid Tumors Harboring Genetic Alterations in Genes Encoding D-type Cyclins or Amplification of CDK4 or CDK6

Cancer type: Unspecified Solid Tumor

Variant class: CDK4 amplification

Other identifiers: 17-343, NCI-2017-02359

Population segments: First line, Stage III, Stage IV

Phase: II

Therapy: abemaciclib

Location: United States

US State: MA

Contact: Dr. Geoffrey Shapiro [617-632-4942; geoffrey_shapiro@dfci.harvard.edu]

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CDK4 amplification (continued)

NCT02693535
Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Cancer type: Unspecified Solid Tumor

Variant class: CDK4 amplification

Other identifiers: 20170529, NCI-2017-00510, Pro00014171, TAPUR

Population segments: (N/A), Aggressive, Diffuse large B-cell lymphoma (DLBCL), Extranodal marginal zone B-cell lymphoma (MALT), First line, Follicular lymphoma (FL), Fourth line or greater, Indolent, Lymphoblastic lymphoma (LBL), Mantle cell lymphoma (MCL), Other subtype, Second line, Small lymphocytic lymphoma (SLL), Stage III, Stage IV, Third line, 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

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: CDK4 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

MRE11 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: MRE11 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

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

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MRE11 deletion (continued)

NCT03233204
NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice)- A Phase II Subprotocol of Olaparib in Patients With Tumors Harboring Defects in DNA Damage Repair Genes

Cancer type: Unspecified Solid Tumor

Variant class: DNA repair pathway

Other identifiers: 20170841, APEC1621H, NCI-2017-00766

Population segments: Aggressive, Indolent, Pediatric or Adolescent, Second line, Stage III, Stage IV

Phase: II

Therapy: olaparib

Locations: Puerto Rico, United States

US States: AL, AR, AZ, CA, CO, DC, FL, GA, IA, ID, IL, IN, KY, LA, MD, ME, MI, MN, MO, MS, NC, NE, NJ, NY, OH, OK, OR, PA, SC, TN, TX, UT, VA, VT, WA, WI

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

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: 18-441, 18594, 2017-0186, BAY1895344/18594, EudraCT Number: 2016-004484-39, IRAS ID-218516, JapicCTI-183998, NCI-2018-00206

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

Phase: I/II

Therapy: BAY-1895344

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

US States: FL, GA, MA, NY, OH, PA, TX, UT

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, 18-009, A317/290, BGB-A317/BGB-290, BGB-A317/BGB-290_Study_001, CT783, NCI-2018-00791, P 55217, VICCPHI1814

Population segments: Fourth line or greater, HER2 negative, Pulmonary, Second line, Stage III, Stage IV, Third line, Triple receptor negative

Phase: I

Therapies: pamiparib, tislelizumab

Locations: Australia, France, New Zealand, Spain, United Kingdom, United States

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

Contact: Rob Stewart [clinicaltrials@beigene.com]

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RICTOR amplification

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: RICTOR amplification

Other identifiers: ET12-081, EudraCT number: 2012-004510-34, MOST, ProfiLER

Population segments: Maintenance/Consolidation, Second line, Stage III, Stage IV, Third line

Phase: II

Therapy: everolimus

Location: France

NCT03673787
Ice-CAP: A Phase I Trial of Ipatasertib in Combination With Atezolizumab in Patients With Advanced Solid Tumours With PI3K Pathway Hyperactivation

Cancer type: Unspecified Solid Tumor

Variant class: PI3K/AKT/MTOR pathway

Other identifiers: CCR4720, EudraCT Number: 2017-003005-18, Ice-CAP, IceCAP, IRAS ID 233461

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

Phase: I/II

Therapy: atezolizumab + ipatasertib

Location: United Kingdom

NCT03065062
Phase I Study of the CDK4/6 Inhibitor Palbociclib (PD-0332991) in Combination With the PI3K/mTOR Inhibitor Gedatolisib (PF-05212384) for Patients With Advanced Squamous Cell Lung, Pancreatic, Head & Neck and Other Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: PI3K/AKT/MTOR pathway

Other identifiers: 16-499, NCI-2017-00434

Population segments: Second line, Squamous Cell, Stage III, Stage IV

Phase: I

Therapy: gedatolisib + palbociclib

Location: United States

US State: MA

Contact: Dr. Nicole Chau [617-632-3090]

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CHEK1 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: CHEK1 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

NCT03233204
NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice)- A Phase II Subprotocol of Olaparib in Patients With Tumors Harboring Defects in DNA Damage Repair Genes

Cancer type: Unspecified Solid Tumor

Variant class: DNA repair pathway

Other identifiers: 20170841, APEC1621H, NCI-2017-00766

Population segments: Aggressive, Indolent, Pediatric or Adolescent, Second line, Stage III, Stage IV

Phase: II

Therapy: olaparib

Locations: Puerto Rico, United States

US States: AL, AR, AZ, CA, CO, DC, FL, GA, IA, ID, IL, IN, KY, LA, MD, ME, MI, MN, MO, MS, NC, NE, NJ, NY, OH, OK, OR, PA, SC, TN, TX, UT, VA, VT, WA, WI

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

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: 18-441, 18594, 2017-0186, BAY1895344/18594, EudraCT Number: 2016-004484-39, IRAS ID-218516, JapicCTI-183998, NCI-2018-00206

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

Phase: I/II

Therapy: BAY-1895344

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

US States: FL, GA, MA, NY, OH, PA, TX, UT

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

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TP53 mutation

NCT03560882
A Pilot Trial of Atorvastatin in p53-Mutant and p53 Wild-Type Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: TP53 mutation

Other identifiers: IIT-2018-p53Atorva, NCI-2019-00374

Population segments: (N/A), Second line, Untreated

Phase: I

Therapy: statin

Location: United States

US State: KS

Contact: Kerry Hepler [913-945-7552; ctnursenav@kumc.edu]

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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.

ATM deletion

Variant Class	Evidence Items
DNA repair pathway	6
↳ ATM aberration	1
↳ ATM deletion	3
↳ DNA repair deletion	0
↳ ATM deletion	3
HRR pathway	2
↳ ATM aberration	1
↳ ATM deletion	3

CDK4 amplification

Variant Class	Evidence Items
G1/S cell cycle pathway	0
↳ CDK4 aberration	1
↳ CDK4 amplification	4

MRE11 deletion

Variant Class	Evidence Items
DNA repair pathway	6
↳ DNA repair deletion	0
↳ MRE11 deletion	1
HRR pathway	2
↳ MRE11 deletion	1

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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.

RICTOR amplification

Variant Class	Evidence Items
PI3K/AKT/MTOR pathway	2
↳ RICTOR amplification	1

CHEK1 deletion

Variant Class	Evidence Items
DNA repair pathway	6
↳ DNA repair deletion	0
↳ CHEK1 deletion	1

TP53 mutation

Variant Class	Evidence Items
TP53 aberration	0
↳ TP53 mutation	1

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