Medical Laboratory
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oncologica®

Leading a new era of precision oncology

# Oncofocus®

## Precision Oncology

ONCOFOCUS® TEST REPORT

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## Patient demographics

| | | | |
|---|---|---|---|
| **ONC19** | | | |
| **Surname** | | **Requester** | Self Referral |
| **Forename** | | **Contact details** | |
| **DOB** | | **Date requested** | |
| **Gender** | | | |
| **Histology #** | | **Tumour %** | |
| **Primary site** | Lung | **Tumour %** | 50% |
| **Tumour subtype** | Squamous Cell Carcinoma | **(macrodissected)** | - |
| **Tissue Type** | Left Lower Lobe Biopsy (lung) | | |

## 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 748 anti-cancer targeted therapies/therapy combinations.

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

**Please note;** There is limited evidence available in the literature to determine the pathogenicity of the SMARCA4 c.710G>A p.(Gly237Asp) variant detected. Therefore, assuming pathogenicity is confirmed, the following therapies would be applicable.

*Within the 'Current Clinical Trials Information' section of this report, starting on page 14, 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 |
|---|---|---|---|
| *PIK3CA c.1633G>A p.(Glu545Lys) (Allele Freq 37.20%)* | Clinical trials and/or off-label | alpelisib + fulvestrant [2] | 9 |
| *PIK3CA amplification (CN 6)* | Clinical trials and/or off-label | Clinical trials and/or off-label | 7 |
| *BRCA2 deletion (CN 0.44)* | Clinical trials and/or off-label | Clinical trials and/or off-label | 7 |
| *ATM deletion (CN 0.52)* | Clinical trials and/or off-label | Clinical trials and/or off-label | 6 |
| *FANCD2 deletion (CN 0.36)* | Clinical trials and/or off-label | Clinical trials and/or off-label | 5 |
| *MRE11 deletion (CN 0.46)* | Clinical trials and/or off-label | Clinical trials and/or off-label | 4 |
| *PI3K/AKT/MTOR pathway PIK3CB Amplification (CN 7.1)* | Clinical trials and/or off-label | Clinical trials and/or off-label | 3 |
| *SETD2 deletion (CN 0.48)* | Clinical trials and/or off-label | Clinical trials and/or off-label | 3 |
| *BAP1 deletion (CN 0.26)* | Clinical trials and/or off-label | Clinical trials and/or off-label | 3 |
| *CHEK1 deletion (CN 0.48)* | Clinical trials and/or off-label | Clinical trials and/or off-label | 3 |
| *RB1 deletion (CN 0.74)* | Clinical trials and/or off-label | Clinical trials and/or off-label | 2 |
| *NFE2L2 c.78A>C p.(Gln26His) (Allele Freq 39.03%)* | Clinical trials and/or off-label | Clinical trials and/or off-label | 1 |
| *SMARCA4 c.710G>A p.(Gly237Asp) (Allele Freq 49.55%)* | Clinical trials and/or off-label | Clinical trials and/or off-label | 1 |

**Sources included in relevant therapies:** EMA[1], FDA[2], 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. Please note this version of the Oncofocus test is an upgraded version to that accredited on our schedule

## Other Relevant Findings

| Gene | Finding | Gene | Finding |
|---|---|---|---|
| ALK | No variants detected in the regions analysed | NTRK1 | No variants detected in the regions analysed |
| BRAF | No variants detected in the regions analysed | NTRK2 | No variants detected in the regions analysed |
| EGFR | No variants detected in the regions analysed | NTRK3 | No variants detected in the regions analysed |
| ERBB2 | No variants detected in the regions analysed | RET | No variants detected in the regions analysed |
| KRAS | No variants detected in the regions analysed | ROS1 | No variants detected in the regions analysed |
| MET | No variants detected in the regions analysed | | |

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## Biomarker Descriptions

**AKT1 (AKT serine/threonine kinase 1)**

Background: The AKT1 gene encodes Protein Kinase B, a serine/threonine kinase, that belongs to a family of closely related protein kinases that also includes AKT2 and AKT3. Growth factor signaling leads to the activation of phosphatidylinositol 3-kinase (PI3K), recruitment of AKT to the plasma membrane, and subsequent activation of downstream effectors including MTOR. The PI3K/AKT/MTOR pathway is central to the regulation of cancer cell proliferation, survival, and metabolism[1,2].

Alterations and prevalence: AKT1 encodes a proto-oncogene that is the target of recurrent somatic mutations in cancer[3]. The most common recurrent mutation is E17K, which is located in the N-terminal pleckstrin homology (PH) domain. E17K is a gain-of-function activating mutation that constitutively targets AKT1 to the plasma membrane and leads to downstream signaling[4,5]. Other recurrent activating mutations include L52H, Q79K, and D323Y/G/N, which disrupt negative regulatory interactions between the PH domain and the kinase domain[6]. AKT1 mutations in cancer are common in breast and endometrial cancers, where they occur at a prevalence of 2-5%[7]. AKT1 mutations are observed at a prevalence of 1-2% in bladder, colorectal, melanoma, and thyroid cancers[7,8]. AKT1 is overexpressed via gene amplification in ovarian cancer, lung squamous cell cancer, and sarcoma at a prevalence of 2-5%[7,8].

Potential clinical relevance: Currently no therapies are approved for AKT1 aberrations. However, in the phase II NCI-MATCH trial, the pan-AKT inhibitor capivasertib (AZD5363) demonstrated a partial response in 23% (8/35) of AKT1 E17K mutated solid tumor patients[9]. Results from a phase I clinical trial of capivasertib demonstrated partial responses in 9/52 heavily pre-treated patients with AKT1 E17K mutated solid tumors, with a median progression-free survival (PFS) of 5.5 months in ER positive breast cancer, 6.6 months in gynecologic cancers, and 4.2 months in other solid tumors[10]. In the same phase I study, an ovarian cancer patient with an AKT1 Q79K mutation demonstrated stable disease lasting 14 months[10].

**AKT2 (AKT serine/threonine kinase 2)**

Background: The AKT2 gene encodes a serine/threonine kinase that belongs to a family of closely related protein kinases that also includes AKT1 and AKT3. Growth factor signaling leads to the activation of phosphatidylinositol 3-kinase (PI3K), recruitment of AKT to the plasma membrane, and subsequent activation of downstream effectors including MTOR. The PI3K/AKT/MTOR pathway is central to the regulation of cancer cell proliferation, survival, and metabolism[1,2]. Amongst the three AKT isoforms (AKT1, AKT2, and AKT3), AKT2 is implicated in cancer cell invasion and metastasis[11,12,13].

Alterations and prevalence: AKT2 is altered by recurrent activating mutations at amino acid positions homologous to those observed in AKT1 which are found in 1-4% of melanomas, bladder, lung, uterine, and, gastric cancers[14]. In AKT2, recurrent activating mutations occur at E17K, L52R, and D324G/H[14]. AKT2 is also subject to gene amplification in ovarian cancer, lung squamous cell carcinoma, and bladder cancer at a prevalence of 3-8%[7]. A BCAM-AKT2 fusion has been identified in ovarian cancer[15].

Potential clinical relevance: Currently, no therapies are approved for AKT2 aberrations. However, the pan-AKT inhibitor capivasertib (AZD5363) is active against all AKT isoforms[16] but clinical evidence in AKT2 aberrant cancers is lacking.

**AKT3 (AKT serine/threonine kinase 3)**

Background: The AKT3 gene encodes a serine/threonine kinase that belongs to a family of closely related protein kinases that also includes AKT1 and AKT2. Growth factor signaling leads to the activation of phosphatidylinositol 3-kinase (PI3K), recruitment of AKT to the plasma membrane, and subsequent activation of downstream effectors including MTOR. The PI3K/AKT/MTOR pathway is central to the regulation of cancer cell proliferation, survival, and metabolism[1,2]. Amongst the three AKT isoforms (AKT1, AKT2, and AKT3), AKT3 is implicated in cytokinesis and activation of the DNA repair pathway[17,18].

Alterations and prevalence: AKT3 is altered by recurrent activating mutations at amino acid positions homologous to those observed in AKT1 which are found in 1-6% of melanoma, colorectal, bladder, lung, uterine, esophageal, and head and neck cancers[14]. In AKT3, recurrent activating mutations occur at E17K, L51R, Q78K, and D320H[14]. AKT3 is subject to gene amplification in breast and ovarian cancers, typically as part of broader chromosome 1q alterations. AKT3 fusions have been identified in breast and other solid cancers[7,19].

## Biomarker Descriptions (continued)

Potential clinical relevance: Currently, no therapies are approved for AKT3 aberrations. However, the pan-AKT inhibitor capivasertib (AZD5363) is active against all AKT isoforms[16], but clinical evidence in AKT3 aberrant cancers is lacking. Pre-clinical evidence suggests that AKT3 overexpression contributes to increased DNA repair and subsequent resistance to radiation and temozolomide[17].

**BRCA2 (BRCA2, DNA repair associated)**

Background: The breast cancer early onset gene 2 (BRCA2) encodes one of two BRCA proteins (BRCA1 and BRCA2) initially discovered as major hereditary breast cancer genes. Although structurally unrelated, both BRCA1 and BRCA2 exhibit tumor suppressor function and are integrally involved in the homologous recombination repair (HRR) pathway, a pathway critical in the repair of damaged DNA. Specifically, BRCA1/2 are required for repair of chromosomal double strand breaks (DSBs) which are highly unstable and compromise genome integrity[20,21]. Inherited pathogenic mutations in BRCA1/2 are known to confer increased risk in women for breast and ovarian cancer[22] and in men for breast and prostate cancer[23,24]. For individuals diagnosed with inherited pathogenic or likely pathogenic BRCA1/2 variants, estimated lifetime risks range from 41% to 90% for developing breast cancer and 8 to 62% for developing ovarian cancer[25].

Alterations and prevalence: Inherited BRCA1/2 mutations occur in 1:400 to 1:500 individuals and are observed in 10-15% of ovarian cancer and 5-10% of breast cancer[26,27,28,29,30,31,32]. Somatic alterations in BRCA2 are observed in 5-15% of melanomas, uterine, cervical, gastric, colorectal, esophageal, and lung cancers[7,8].

Potential clinical relevance: Individuals possessing BRCA1/2 pathogenic germline or somatic mutations are shown to exhibit sensitivity to platinum based chemotherapy as well as treatment with poly (ADP-ribose) polymerase inhibitors (PARPi)[33]. Inhibitors targeting PARP induce synthetic lethality in recombination deficient BRCA1/2 mutant cells[34,35]. Consequently, several PARP inhibitors have been FDA approved for BRCA1/2-mutated cancers. Olaparib[36] (2014) was the first PARPi to be approved by the FDA for BRCA1/2 aberrations. Originally approved for the treatment of germline variants, olaparib is now indicated (2018) for the maintenance treatment of both germline BRCA1/2-mutated (gBRCAm) and somatic BRCA1/2-mutated (sBRCAm) epithelial ovarian, fallopian tube, or primary peritoneal cancers that are responsive to platinum-based chemotherapy. Olaparib is also indicated for the treatment of patients with gBRCAm HER2-negative metastatic breast cancer who have been treated with chemotherapy in the neoadjuvant, adjuvant, or metastatic setting. Rucaparib[37] (2016) was the first PARPi approved for the treatment of patients with either gBRCAm or sBRCAm epithelial ovarian, fallopian tube, or primary peritoneal cancers treated with two or more chemotherapies. Talazoparib[38] (2018) is indicated for the treatment of gBRCAm HER2-negative locally advanced or metastatic breast cancer. Due to efficacy in both gBRCAm and non-gBRCAm patients, Niraparib (2017) is another PARPi approved for maintenance of epithelial ovarian, fallopian tube, or primary peritoneal cancers, regardless of BRCA status[39]. Despite tolerability and efficacy, acquired resistance to PARP inhibition has been clinically reported[40]. One of the most common mechanisms of resistance includes secondary intragenic mutations that restore BRCA1/2 functionality[41].

**MTOR (mechanistic target of rapamycin kinase)**

Background: The MTOR gene encodes the mechanistic target of rapamycin kinase (also known as, mammalian target of rapamycin), which is a member of the phosphatidylinositol 3-kinase (PI3K)-related kinases family of serine/threonine protein kinases. MTOR encodes the catalytic subunit of mTOR Complex 1 (mTORC1) and 2 (mTORC2)[42]. These complexes regulate cell growth by modulating protein synthesis, autophagy, and other metabolic pathways. The mTORC1 and mTORC2 complexes are downstream effectors of the PI3K/AKT/MTOR signaling pathway and facilitate integration of the PI3K/AKT/MTOR and RAS/RAF/MEK/ERK signaling pathways[43,44,45].

Alterations and prevalence: Recurrent activating mutations differentially activate mTORC1 or mTORC2 leading to either S6K1/4EBP1 or AKT1 phosphorylation, respectively[46]. Mutations in MTOR are observed at frequencies of 5-15% in lung adenocarcinoma, clear cell renal cell carcinoma, melanoma, colorectal, gastric, and uterine cancers[7].

Potential clinical relevance: Two first generation MTOR inhibitors termed rapalogs (analogues of rapamycin) have been approved by the FDA: temsirolimus[47] (2007) for the treatment of renal cell carcinoma (RCC) and everolimus[48] (2009) for the treatment of breast, pancreatic, gastrointestinal, and lung cancers, RCC, and subependymal giant cell astrocytomas. Mutations in the FRB domain of mTOR are a potential mechanism of acquired resistance to first generation rapalogs[44,49]. While first-generation rapalogs form inhibitory

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## Biomarker Descriptions (continued)

complexes with FKBP-12, second generation mTOR inhibitors such as PF-04691502 and gedatolisib target the mTOR kinase domain directly[50].

**PIK3CA (phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha)**

Background: The PIK3CA gene encodes the phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha of the class I phosphatidylinositol 3-kinase (PI3K) enzyme[51]. PI3K is a heterodimer that contains a p85 regulatory subunit, which couples the p110α subunit (PI3K) to activated tyrosine protein kinases. PI3K catalyzes the conversion of phosphatidylinositol (4,5)-bisphosphate (PI(4,5)P2) into phosphatidylinositol (3,4,5)-trisphosphate (PI(3,4,5)P3) while the phosphatase and tensin homolog (PTEN) catalyzes the reverse reaction[52,53]. The reversible phosphorylation of inositol lipids regulates diverse aspects of cell growth and metabolism[52,53,54,55]. Recurrent somatic alterations in PIK3CA are frequent in cancer and result in activation of the PI3K/AKT/MTOR pathway, which can influence several hallmarks of cancer including cell proliferation, apoptosis, cancer cell metabolism and invasion, and genetic instability[56,57,58].

Alterations and prevalence: Recurrent somatic activating mutations in PIK3CA are common in diverse cancers and are observed in 20-30% of breast, cervical, and uterine cancers and 10-20% of bladder, gastric, head and neck, and colorectal cancers[7,8]. Activating mutations in PIK3CA commonly cluster in two regions corresponding to the exon 9 helical (codons E542/E545) and exon 20 kinase (codon H1047) domains, each having distinct mechanisms of activation[59,60,61]. PIK3CA resides in the 3q26 cytoband, a region frequently amplified (10-30%) in diverse cancers including squamous carcinomas of the lung, cervix, head and neck, and esophagus, and in serous ovarian and uterine cancers[7,8].

Potential clinical relevance: The PI3K inhibitor, alpelisib[62], is FDA approved (2019) in combination with fulvestrant for the treatment of patients with PIK3CA-mutated, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, advanced or metastatic breast cancer. Additionally, a phase Ib study of alpelisib with letrozole in patients with metastatic estrogen receptor (ER)-positive breast cancer, the clinical benefit rate, defined as lack of disease progression ≥ 6 months, was 44% (7/16) in PIK3CA-mutated tumors and 20% (2/20) in PIK3CA wild-type tumors[63]. Specifically, exon 20 H1047R mutations were associated with more durable clinical responses in comparison to exon 9 E545K mutations[63]. However, alpelisib did not improve response when administered with letrozole in patients with ER+ early breast cancer with PIK3CA mutations[64]. Case studies with MTOR inhibitors sirolimus and temsirolimus report isolated cases of clinical response in PIK3CA mutated refractory cancers[65,66].

**PTEN (phosphatase and tensin homolog)**

Background: The PTEN gene encodes the phosphatase and tensin homolog, a tumor suppressor protein with lipid and protein phosphatase activities[67]. PTEN antagonizes PI3K/AKT signaling by catalyzing the dephosphorylation of phosphatidylinositol (3,4,5)-trisphosphate (PIP3) to PIP2 at the cell membrane, which inhibits the activation of AKT[68,68,69]. Germline mutations in PTEN are linked to hamartoma tumor syndromes, including Cowden disease, which are defined by uncontrolled cell growth and benign or malignant tumor formation[70]. PTEN germline mutations are also associated with inherited cancer risk in several cancer types[71].

Alterations and prevalence: PTEN is frequently altered in cancer by inactivating loss-of-function mutations and by gene deletion. PTEN mutations are frequently observed in 50%-60% of uterine cancer[7,8]. Nearly half of somatic mutations in PTEN are stop-gain or frame-shift mutations that result in truncation of the protein reading frame. Recurrent missense or stop-gain mutations at codons R130, R173, and R233 result in loss of phosphatase activity and inhibition of wild-type PTEN[69,72,73,74,75]. PTEN gene deletion is observed in 15% of prostate cancer, 9% of squamous lung cancer, 9% of glioblastoma, and 1-5% of melanoma, sarcoma, and ovarian cancer[7,8].

Potential clinical relevance: Currently, no therapies are approved for PTEN aberrations. However, due to the role of PTEN in genome stability, poly(ADP-ribose) polymerase inhibitors (PARPi) are being explored as a potential therapeutic strategy in PTEN deficient tumors[76,77].

**RB1 (RB transcriptional corepressor 1)**

Background: The RB1 gene encodes the retinoblastoma protein (pRB) and is an early molecular hallmark of cancer. RB1 belongs to the family of pocket proteins that also includes p107 and p130, which play a crucial role in the cell proliferation, apoptosis, and differentiation[78,79]. RB1 is well characterized as a tumor suppressor gene that restrains cell cycle progression from G1 phase to S phase[80]. Specifically, RB1 binds and represses the E2F family of transcription factors that regulate the expression of genes involved in

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## Biomarker Descriptions (continued)

the G1/S cell cycle regulation[78,79,81]. Germline mutations in RB1 are associated with retinoblastoma (a rare childhood tumor) as well as other cancer types such as osteosarcoma, soft tissue sarcoma, and melanoma[82].

Alterations and prevalence: Recurrent somatic alterations in RB1, including mutations and biallelic loss, lead to the inactivation of the RB1 protein. RB1 mutations are observed in urothelial carcinoma (approximately 16%), endometrial cancer (approximately 12%), and sarcomas (approximately 9%)[8]. Similarly, biallelic loss of RB1 is observed in sarcomas (approximately 13%), urothelial carcinoma (approximately 6%), and endometrial cancer (approximately 1%)[8]. Biallelic loss of the RB1 gene is also linked to the activation of chemotherapy-induced acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL)[83,84,85].

Potential clinical relevance: Currently, there are no therapies approved for RB1 aberrations.

**STK11 (serine/threonine kinase 11)**

Background: The STK11 gene, also known as liver kinase B1 (LKB1), encodes the serine/threonine kinase 11 protein. STK11 is a tumor suppressor with multiple substrates including AMP-activated protein kinase (AMPK) that regulates cell metabolism, growth, and tumor suppression[86]. Germline mutations in STK11 are associated with Peutz-Jeghers syndrome, an autosomal dominant disorder, characterized by gastrointestinal polyp formation and elevated risk of neoplastic development[87,88].

Alterations and prevalence: Somatic mutations in STK11 have been reported in 10% of lung cancer, 4% of cervical cancer, and up to 3% of cholangiocarcinoma and uterine cancer[7,8,89,90]. Copy number deletion leads to inactivation of STK11 in cervical, ovarian, and lung cancers, among others[7,8,87,90,91].

Potential clinical relevance: Currently, no therapies are approved for STK11 aberrations. However, the presence of STK11 may be a mechanism of resistance to immunotherapies. In a phase III clinical trial of nivolumab in lung adenocarcinoma, patients with KRAS-STK11 co-mutations demonstrated a worse (0/6) objective response rate (ORR) in comparison to patients with KRAS-TP53 co-mutations (4/7) or KRAS mutations only (2/11) (ORR= 0% vs 57.1% vs 18.25%, respectively)[92].

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## Tier Criteria Met

| Genomic Alteration | Tier Classification for Non-Small Cell Lung Cancer |
|---|---|
| *PIK3CA mutation*<br>Tier: IIC | IIC: Biomarker predicts response or resistance to EMA or FDA approved therapies in other cancer types<br>IIC: Biomarker is included in ESMO or NCCN guidelines that predict response or resistance to therapies in other cancer types<br>IIC: Biomarker is an inclusion criteria for clinical trials |
| *PIK3CA amplification*<br>Tier: IIC | IIC: Biomarker is an inclusion criteria for clinical trials |
| *BRCA2 deletion*<br>Tier: IIC | IIC: Biomarker is an inclusion criteria for clinical trials |
| *ATM deletion*<br>Tier: IIC | IIC: Biomarker is an inclusion criteria for clinical trials |
| *FANCD2 deletion*<br>Tier: IIC | IIC: Biomarker is an inclusion criteria for clinical trials |
| *MRE11 deletion*<br>Tier: IIC | IIC: Biomarker is an inclusion criteria for clinical trials |
| *PI3K/AKT/MTOR pathway*<br>Tier: IIC | IIC: Biomarker is an inclusion criteria for clinical trials |
| *SETD2 deletion*<br>Tier: IIC | IIC: Biomarker is an inclusion criteria for clinical trials |
| *BAP1 deletion*<br>Tier: IIC | IIC: Biomarker is an inclusion criteria for clinical trials |
| *CHEK1 deletion*<br>Tier: IIC | IIC: Biomarker is an inclusion criteria for clinical trials |
| *RB1 deletion*<br>Tier: IIC | IIC: Biomarker is an inclusion criteria for clinical trials |
| *NFE2L2 mutation*<br>Tier: IIC | IIC: Biomarker is an inclusion criteria for clinical trials |
| *SMARCA4 mutation*<br>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.

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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

### PIK3CA mutation

| Relevant Therapy | EMA | FDA | ESMO | NCCN | Clinical Trials* |
|---|---|---|---|---|---|
| alpelisib + fulvestrant | ✖ | ○ | ✖ | ○ | ✖ |
| capivasertib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| capivasertib, olaparib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| everolimus | ✖ | ✖ | ✖ | ✖ | ● (II) |
| LY-3023414 | ✖ | ✖ | ✖ | ✖ | ● (II) |
| sirolimus | ✖ | ✖ | ✖ | ✖ | ● (II) |
| temsirolimus | ✖ | ✖ | ✖ | ✖ | ● (II) |
| atezolizumab + ipatasertib | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| GDC-0077 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| gedatolisib + palbociclib | ✖ | ✖ | ✖ | ✖ | ● (I) |

### PIK3CA amplification

| Relevant Therapy | EMA | FDA | ESMO | NCCN | Clinical Trials* |
|---|---|---|---|---|---|
| capivasertib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| capivasertib, olaparib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| everolimus | ✖ | ✖ | ✖ | ✖ | ● (II) |
| sirolimus | ✖ | ✖ | ✖ | ✖ | ● (II) |
| temsirolimus | ✖ | ✖ | ✖ | ✖ | ● (II) |
| atezolizumab + ipatasertib | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| gedatolisib + palbociclib | ✖ | ✖ | ✖ | ✖ | ● (I) |

### BRCA2 deletion

| Relevant Therapy | EMA | FDA | ESMO | NCCN | Clinical Trials* |
|---|---|---|---|---|---|
| durvalumab + olaparib | ✖ | ✖ | ✖ | ✖ | ● (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

### BRCA2 deletion (continued)

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

### ATM deletion

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

### FANCD2 deletion

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

### PI3K/AKT/MTOR pathway

| Relevant Therapy | EMA | FDA | ESMO | NCCN | Clinical Trials* |
|---|---|---|---|---|---|
| capivasertib, olaparib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| atezolizumab + ipatasertib | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| gedatolisib + palbociclib | ✖ | ✖ | ✖ | ✖ | ● (I) |

### SETD2 deletion

| Relevant Therapy | EMA | FDA | ESMO | NCCN | Clinical Trials* |
|---|---|---|---|---|---|
| adavosertib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| avelumab + talazoparib | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| BAY-1895344 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |

### BAP1 deletion

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

### CHEK1 deletion

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

### RB1 deletion

| Relevant Therapy | EMA | FDA | ESMO | NCCN | Clinical Trials* |
|---|---|---|---|---|---|
| palbociclib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| prexasertib | ✖ | ✖ | ✖ | ✖ | ● (II) |

### NFE2L2 mutation

| Relevant Therapy | EMA | FDA | ESMO | NCCN | Clinical Trials* |
|---|---|---|---|---|---|
| sapanisertib | ✖ | ✖ | ✖ | ✖ | ● (II) |

### SMARCA4 mutation

| Relevant Therapy | EMA | FDA | ESMO | NCCN | Clinical Trials* |
|---|---|---|---|---|---|
| tazemetostat | ✖ | ✖ | ✖ | ✖ | ● (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 Details

## Current FDA Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated 👎 Not recommended 🛡 Resistance

FDA information is current as of 2019-08-23. For the most up-to-date information, search www.fda.gov.

## PIK3CA mutation

### ○ alpelisib + fulvestrant

**Cancer type:** Breast Cancer **Label as of:** 2019-05-24 **Variant class:** PIK3CA mutation

**Other criteria:** ERBB2 negative, Hormone receptor positive

**Indications and usage:**
PIQRAY® is a kinase inhibitor indicated in combination with fulvestrant for the treatment of postmenopausal women, and men, with hormone receptor (HR)- positive, human epidermal growth factor receptor 2 (HER2)-negative, PIK3CA-mutated, advanced or metastatic breast cancer as detected by an FDA-approved test following progression on or after an endocrine-based regimen.

**Reference:**

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212526s000lbl.pdf

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## Current NCCN Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated 👎 Not recommended 🛡 Resistance

NCCN information is current as of 2019-05-15. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

## PIK3CA mutation

### ○ alpelisib + fulvestrant

**Cancer type:** Breast Cancer

**Variant class:** PIK3CA mutation

**Other criteria:** ERBB2 negative

**NCCN Recommendation category:** 1

**Population segment (Line of therapy):**
- Recurrent or Stage IV Invasive Breast Cancer; No prior endocrine therapy within 1 year; Postmenopausal (First-line therapy) (Preferred)

**Reference:** NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2019]

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## Current Clinical Trials Information

Clinical Trials information is current as of 2019-06-05. 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'.

## PIK3CA mutation

### NCT02664935
National Lung Matrix Trial: Multi-drug, Genetic Marker-directed, Non-comparative, Multi-centre, Multi-arm Phase II Trial in Non-small Cell Lung Cancer

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** PIK3CA mutation

**Other inclusion criteria:** BRAF wild type, HRAS wild type, KRAS wild type, NF1 wild type, NRAS wild type

**Other identifiers:** EudraCT Number: 2014-000814-73, IRAS ID: 151280, ISRCTN38344105, MREC N°: 14/SC/1346, National Lung Matrix trial, RG_14-072, UKCRN ID: 17746

**Population segments:** Adenocarcinoma, ALK, EGFR, FGFR, Second line, Squamous Cell, Stage III, Stage IV

**Exclusion criteria variant classes:** BRAF aberration, HRAS aberration, KRAS aberration, NF1 aberration, NRAS aberration

**Phase:** II

**Therapy:** capivasertib

**Location:** United Kingdom

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### 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:** Non-Small Cell Lung Cancer

**Variant class:** PIK3CA mutation

**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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### 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:** PIK3CA mutation

**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

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## PIK3CA mutation (continued)

### NCT02688881
Study to Evaluate the Safety and Efficacy of Sirolimus, in Subject With Refractory Solid Tumors

**Cancer type:** Unspecified Solid Tumor

**Variant class:** PIK3CA mutation

**Other identifiers:** 2016-02-052, KCT0002997, SMC 2016-02-052-001

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

**Phase:** II

**Therapy:** sirolimus

**Location:** Republic of Korea

### NCT03155620
NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice) Screening Protocol

**Cancer type:** Unspecified Solid Tumor

**Variant class:** PI3K/AKT/MTOR mutation

**Other identifiers:** 17-729, APEC1621SC, COGAPEC1621SC, N 55017 SC, NCI-2017-01251, NCI-COG Pediatric MATCH, Pediatric MATCH

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

**Phase:** II

**Therapy:** LY-3023414

**Locations:** Puerto Rico, United States

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

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

### NCT03297606
Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial

**Cancer type:** Unspecified Solid Tumor

**Variant class:** PIK3CA 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:** temsirolimus

**Location:** Canada

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## PIK3CA mutation (continued)

### 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:** PI3K/AKT/MTOR pathway

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

**Population segments:** First line, Second line, Stage IV

**Phase:** II

**Therapies:** capivasertib, olaparib

**Location:** United States

**US States:** CT, MA, OH, TN

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

### 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

### NCT03006172
A Phase I, Open-Label, Dose-Escalation Study Evaluating the Safety, Tolerability, and Pharmacokinetics of GDC-0077 as a Single Agent in Patients With Locally Advanced or Metastatic PIK3CA-Mutant Solid Tumors and in Combination With Endocrine and Targeted Therapies in Patients With Locally Advanced or Metastatic PIK3CA-Mutant Hormone-Receptor Positive Breast Cancer

**Cancer type:** Unspecified Solid Tumor

**Variant class:** PIK3CA mutation

**Other identifiers:** 16-1556, EudraCT Number: 2016-003022-17, GO39374, NCI-2017-00262

**Population segments:** Estrogen receptor positive, HER2 negative, Progesterone receptor positive, Second line, Stage III, Stage IV

**Phase:** I

**Therapy:** GDC-0077

**Locations:** Canada, France, Spain, United Kingdom, United States

**US States:** MA, NY, TN

**Contact:** Reference Study ID Number: GO39374 [888-662-6728; global-roche-genentech-trials@gene.com]

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## PIK3CA amplification

### NCT02664935
National Lung Matrix Trial: Multi-drug, Genetic Marker-directed, Non-comparative, Multi-centre, Multi-arm Phase II Trial in Non-small Cell Lung Cancer

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** PIK3CA amplification

**Other inclusion criteria:** BRAF wild type, HRAS wild type, KRAS wild type, NF1 wild type, NRAS wild type

**Other identifiers:** EudraCT Number: 2014-000814-73, IRAS ID: 151280, ISRCTN38344105, MREC N°: 14/SC/1346, National Lung Matrix trial, RG_14-072, UKCRN ID: 17746

**Population segments:** Adenocarcinoma, ALK, EGFR, FGFR, Second line, Squamous Cell, Stage III, Stage IV

**Exclusion criteria variant classes:** BRAF aberration, HRAS aberration, KRAS aberration, NF1 aberration, NRAS aberration

**Phase:** II

**Therapy:** capivasertib

**Location:** United Kingdom

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### 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:** Non-Small Cell Lung Cancer

**Variant class:** PIK3CA amplification

**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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### 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:** PIK3CA 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

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## PIK3CA amplification (continued)

### NCT02688881
Study to Evaluate the Safety and Efficacy of Sirolimus, in Subject With Refractory Solid Tumors

**Cancer type:** Unspecified Solid Tumor

**Variant class:** PIK3CA amplification

**Other identifiers:** 2016-02-052, KCT0002997, SMC 2016-02-052-001

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

**Phase:** II

**Therapy:** sirolimus

**Location:** Republic of Korea

### NCT03297606
Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial

**Cancer type:** Unspecified Solid Tumor

**Variant class:** PIK3CA 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:** temsirolimus

**Location:** Canada

### 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:** PI3K/AKT/MTOR pathway

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

**Population segments:** First line, Second line, Stage IV

**Phase:** II

**Therapies:** capivasertib, olaparib

**Location:** United States

**US States:** CT, MA, OH, TN

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

### 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

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## BRCA2 deletion

### 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:** Non-Small Cell Lung Cancer

**Variant class:** BRCA 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, 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

**Therapy:** 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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**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:** BRCA2 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

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### 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:** BRCA2 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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## BRCA2 deletion (continued)

### NCT03297606
Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial

**Cancer type:** Unspecified Solid Tumor

**Variant class:** BRCA2 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:** olaparib

**Location:** Canada

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### 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

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

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### 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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## BRCA2 deletion (continued)

### 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:** HER2 negative, Pulmonary, Second line, Stage III, Stage IV, Third line, Triple receptor negative

**Phase:** I

**Therapy:** pamiparib + tislelizumab

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

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

**Contact:** Rob Stewart [clinicaltrials@beigene.com]

## ATM deletion

### 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:** Non-Small Cell Lung Cancer

**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, 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

**Therapy:** 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]

### 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

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## ATM deletion (continued)

### 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]

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### 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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### 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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## ATM deletion (continued)

### 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:** HER2 negative, Pulmonary, Second line, Stage III, Stage IV, Third line, Triple receptor negative

**Phase:** I

**Therapy:** pamiparib + tislelizumab

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

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

**Contact:** Rob Stewart [clinicaltrials@beigene.com]

## FANCD2 deletion

### 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:** Non-Small Cell Lung Cancer

**Variant class:** DNA repair pathway

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

**Therapy:** 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]

**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:** FANC 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

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## FANCD2 deletion (continued)

### 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

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

### 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:** Fanconi anemia pathway

**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]

### 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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## MRE11 deletion

### 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:** Non-Small Cell Lung Cancer

**Variant class:** DNA repair pathway

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

**Therapy:** 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]

### 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]

### 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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## MRE11 deletion (continued)

### 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:** HER2 negative, Pulmonary, Second line, Stage III, Stage IV, Third line, Triple receptor negative

**Phase:** I

**Therapy:** pamiparib + tislelizumab

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

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

**Contact:** Rob Stewart [clinicaltrials@beigene.com]

## PI3K/AKT/MTOR pathway

### 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:** Non-Small Cell Lung Cancer

**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]

### 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:** PI3K/AKT/MTOR pathway

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

**Population segments:** First line, Second line, Stage IV

**Phase:** II

**Therapies:** capivasertib, olaparib

**Location:** United States

**US States:** CT, MA, OH, TN

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

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## PI3K/AKT/MTOR pathway (continued)

### 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

## SETD2 deletion

### 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:** Non-Small Cell Lung Cancer

**Variant class:** DNA repair pathway

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

**Therapy:** 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]

### NCT03284385
A Phase II Study of AZD1775 in SETD2-Deficient Advanced Solid Tumor Malignancies

**Cancer type:** Unspecified Solid Tumor

**Variant class:** SETD2 deletion

**Other identifiers:** 10170, NCI-2017-01670

**Population segments:** Second line, Stage III, Stage IV

**Phase:** II

**Therapy:** adavosertib

**Location:** United States

**US States:** CA, DC, MA, MD, MO, PA

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

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## SETD2 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]

## BAP1 deletion

### 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:** Non-Small Cell Lung Cancer

**Variant class:** DNA repair pathway

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

**Therapy:** 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]

**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:** BAP1 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

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## BAP1 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]

## CHEK1 deletion

### 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:** Non-Small Cell Lung Cancer

**Variant class:** DNA repair pathway

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

**Therapy:** 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]

**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

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## CHEK1 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]

## RB1 deletion

### 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:** RB1 deletion

**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

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

### 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

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

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## NFE2L2 mutation

### NCT02417701
A Phase II Study of MLN0128 (TAK-228) in Patients With Advanced Non-Small Cell Lung Cancers Harboring NFE2L2 and KEAP-1 Mutations

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** NFE2L2 mutation

**Other identifiers:** 15-249, 2015-00500, 9780, NCI-2015-00545

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

**Phase:** II

**Therapy:** sapanisertib

**Location:** United States

**US States:** NJ, NY

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

## SMARCA4 mutation

### NCT03155620
NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice) Screening Protocol

**Cancer type:** Unspecified Solid Tumor

**Variant class:** SMARCA4 mutation

**Other identifiers:** 17-729, APEC1621SC, COGAPEC1621SC, N 55017 SC, NCI-2017-01251, NCI-COG Pediatric MATCH, Pediatric MATCH

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

**Phase:** II

**Therapy:** tazemetostat

**Locations:** Puerto Rico, United States

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

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

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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.

### PIK3CA mutation

| Variant Class | Evidence Items |
|---|---|
| PI3K/AKT/MTOR pathway | 7 |
| ↳ PI3K/AKT/MTOR mutation | 1 |
| ↳ PIK3CA mutation | 7 |
| ↳ PIK3CA aberration | 2 |
| ↳ PIK3CA mutation | 7 |

### PIK3CA amplification

| Variant Class | Evidence Items |
|---|---|
| PI3K/AKT/MTOR pathway | 7 |
| ↳ PIK3CA aberration | 2 |
| ↳ PIK3CA amplification | 4 |

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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.

### BRCA2 deletion

| Variant Class | Evidence Items |
|---|---|
| DNA repair pathway | 12 |
| ↳ BRCA aberration | 1 |
| ↳ BRCA2 aberration | 1 |
| ↳ BRCA2 deletion | 2 |
| ↳ DNA repair deletion | 0 |
| ↳ BRCA2 deletion | 2 |
| HRR pathway | 3 |
| ↳ BRCA aberration | 1 |
| ↳ BRCA2 aberration | 1 |
| ↳ BRCA2 deletion | 2 |
| Fanconi anemia pathway | 3 |
| ↳ FANC deletion | 1 |
| ↳ BRCA2 deletion | 2 |
| ↳ BRCA aberration | 1 |
| ↳ BRCA2 aberration | 1 |
| ↳ BRCA2 deletion | 2 |

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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.

### ATM deletion

| Variant Class | Evidence Items |
|---|---|
| DNA repair pathway | 12 |
| ↳ ATM aberration | 1 |
| ↳ ATM deletion | 3 |
| ↳ DNA repair deletion | 0 |
| ↳ ATM deletion | 3 |
| HRR pathway | 3 |
| ↳ ATM aberration | 1 |
| ↳ ATM deletion | 3 |

### FANCD2 deletion

| Variant Class | Evidence Items |
|---|---|
| DNA repair pathway | 12 |
| ↳ DNA repair deletion | 0 |
| ↳ FANCD2 deletion | 0 |
| Fanconi anemia pathway | 3 |
| ↳ FANC deletion | 1 |
| ↳ FANCD2 deletion | 0 |

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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.

### MRE11 deletion

| Variant Class | Evidence Items |
|---|---|
| DNA repair pathway | 12 |
| ↳ DNA repair deletion | 0 |
| ↳ MRE11 deletion | 1 |
| HRR pathway | 3 |
| ↳ MRE11 deletion | 1 |

### PI3K/AKT/MTOR pathway

| Variant Class | Evidence Items |
|---|---|
| PI3K/AKT/MTOR pathway | 7 |

### SETD2 deletion

| Variant Class | Evidence Items |
|---|---|
| DNA repair pathway | 12 |
| ↳ DNA repair deletion | 0 |
| ↳ SETD2 deletion | 1 |

### BAP1 deletion

| Variant Class | Evidence Items |
|---|---|
| DNA repair pathway | 12 |
| ↳ DNA repair deletion | 0 |
| ↳ BAP1 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.

### CHEK1 deletion

| Variant Class | Evidence Items |
|---|---|
| DNA repair pathway | 12 |
| ↳ DNA repair deletion | 0 |
| ↳ CHEK1 deletion | 1 |

### RB1 deletion

| Variant Class | Evidence Items |
|---|---|
| G1/S cell cycle pathway | 1 |
| ↳ RB1 aberration | 0 |
| ↳ RB1 deletion | 1 |

### NFE2L2 mutation

| Variant Class | Evidence Items |
|---|---|
| NFE2L2 mutation | 1 |

### SMARCA4 mutation

| Variant Class | Evidence Items |
|---|---|
| SMARCA4 mutation | 1 |

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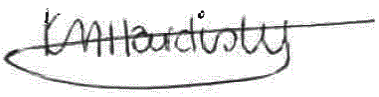
| Signed |  | Signed |  |
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