Taipei Veterans General Hospital

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## Sample Information

**Patient Name:** 張建中
**Gender:** Male
**ID No.:** A110599168
**History No.:** 37033446
**Age:** 65

**Ordering Doctor:** DOC1322F 趙毅
**Ordering REQ.:** H42L88G
**Signing in Date:** 2022/04/15

**Path No.:** S111-99031
**MP No.:** TM22006
**Assay:** Tumor Mutation Load Assay
**Sample Type:** FFPE
**Block No.:** S111-12831A
**Percentage of tumor cells:** 40%

**Reporting Doctor:** DOC5466K 葉奕成 (Phone: 8#5466)

**Note:**

## Sample Cancer Type: Gastroesophageal Junction Adenocarcinoma

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### Report Highlights

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## Relevant Gastroesophageal Junction Adenocarcinoma Variants

| Gene | Finding |
|---|---|
| ERBB2 | None detected |

## Relevant Biomarkers

| Tier | Genomic Alteration | Relevant Therapies (In this cancer type) | Relevant Therapies (In other cancer type) | Clinical Trials |
|---|---|---|---|---|
| IA | *Tumor Mutational Burden*<br>8.45 Mut/Mb measured<br>**Prognostic significance:** None<br>**Diagnostic significance:** None | **pembrolizumab** [1] | pembrolizumab | 2 |
| IIC | *ATM p.(R925Efs*7) c.2773_2774delAG*<br>ATM serine/threonine kinase<br>Allele Frequency: 27.19%<br>**Prognostic significance:** None<br>**Diagnostic significance:** None | None | **niraparib** [1]<br>**olaparib** [1]<br>bevacizumab + olaparib | 0 |
| IIC | *PTEN p.(R233*) c.697C>T*<br>phosphatase and tensin homolog<br>Allele Frequency: 44.82%<br>**Prognostic significance:** None<br>**Diagnostic significance:** None | None | **niraparib** [1]<br>bevacizumab + olaparib | 0 |

**Public data sources included in relevant therapies: FDA**1, NCCN, **EMA**2, ESMO
**Public data sources included in prognostic and diagnostic significance:** NCCN, ESMO
**Tier 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.

### Prevalent cancer biomarkers without relevant evidence based on included data sources

*TP53 p.(R342*) c.1024C>T, SMARCA4 p.(K1541Rfs*3) c.4619_4620insAA*

## Variants (Exclude variant in Taiwan BioBank with >1% allele frequency)

### DNA Sequence Variants

| Gene | Amino Acid Change | Coding | Variant ID | Locus | Allele Frequency | Transcript | Variant Effect | Coverage |
|---|---|---|---|---|---|---|---|---|
| PTEN | p.(R233*) | c.697C>T | . | chr10:89717672 | 44.82% | NM_000314.8 | nonsense | 1999 |
| ATM | p.(R925Efs*7) | c.2773_2774delAG | . | chr11:108139269 | 27.19% | NM_000051.3 | frameshift Deletion | 1979 |
| TP53 | p.(R342*) | c.1024C>T | . | chr17:7574003 | 46.05% | NM_000546.5 | nonsense | 2000 |
| SMARCA4 | p.(K1541Rfs*3) | c.4619_4620insAA | . | chr19:11169027 | 41.28% | NM_001128849.3 | frameshift Insertion | 1996 |
| BCL11A | p.(L674=) | c.2022T>C | . | chr2:60688025 | 52.55% | NM_022893.4 | synonymous | 2000 |
| BCL11A | p.(P35=) | c.105G>A | . | chr2:60773386 | 27.82% | NM_022893.4 | synonymous | 1614 |
| FN1 | p.(P1173R) | c.3518C>G | . | chr2:216261946 | 46.62% | NM_212482.3 | missense | 1731 |
| LTF | p.(R23dup) | c.68_69insAAG | . | chr3:46501284 | 100.00% | NM_002343.6 | nonframeshift Insertion | 500 |
| FOXP1 | p.(R336H) | c.1007G>A | . | chr3:71027020 | 34.92% | NM_001244815.2 | missense | 1999 |
| FGFR3 | p.(L457=) | c.1371C>T | . | chr4:1806655 | 49.72% | NM_000142.4 | synonymous | 1999 |
| PDGFRA | p.(S478Pfs*11) | c.1432delT | . | chr4:55139770 | 42.48% | NM_006206.6 | frameshift Deletion | 1994 |

## Variants (Exclude variant in Taiwan BioBank with >1% allele frequency) (continued)

### DNA Sequence Variants (continued)

| Gene | Amino Acid Change | Coding | Variant ID | Locus | Allele Frequency | Transcript | Variant Effect | Coverage |
|---|---|---|---|---|---|---|---|---|
| PDGFRA | p.(P567=) | c.1701A>G | . | chr4:55141055 | 99.90% | NM_006206.6 | synonymous | 1984 |
| MTRR | p.(R121W) | c.361C>T | . | chr5:7875448 | 51.22% | NM_024010.4 | missense | 1765 |
| NSD1 | p.(Q2474P) | c.7421A>C | . | chr5:176721790 | 27.33% | NM_022455.4 | missense | 1998 |
| NOTCH4 | p.(G348=) | c.1044C>T | . | chr6:32188297 | 4.41% | NM_004557.4 | synonymous | 1997 |
| HSP90AB1 | p.(S26=) | c.78C>T | . | chr6:44216444 | 45.70% | NM_001271970.1 | synonymous | 1383 |
| DST | p.(E2497K) | c.7489G>A | . | chr6:56434686 | 30.10% | NM_001144769.5 | missense | 897 |
| EGFR | p.(V819=) | c.2457G>A | . | chr7:55249159 | 50.35% | NM_005228.5 | synonymous | 2000 |
| AKAP9 | p.(T155A) | c.463A>G | . | chr7:91622256 | 19.13% | NM_005751.4 | missense | 1997 |
| ADGRA2 | p.(C380Y) | c.1139G>A | . | chr8:37690569 | 6.22% | NM_032777.10 | missense | 1544 |
| CSMD3 | p.(K2507R) | c.7520A>G | . | chr8:113326687 | 18.71% | NM_198123.2 | missense | 914 |
| TLR4 | p.(H458R) | c.1373A>G | . | chr9:120475779 | 5.57% | NM_138554.5 | missense | 1544 |
| ZNF384 | p.(Q501Hfs*48) | c.1503delG | . | chr12:6777110 | 96.21% | NM_001135734.2 | frameshift Deletion | 449 |
| EP400 | p.(V1442=) | c.4326G>A | . | chr12:132504642 | 6.25% | NM_015409.5 | synonymous | 1441 |
| TSC2 | p.(R1795H) | c.5384G>A | . | chr16:2138571 | 22.81% | NM_000548.5 | missense | 1688 |
| CDH5 | p.(I517T) | c.1550_1551delTCinsCT | . | chr16:66432423 | 27.80% | NM_001795.5 | missense | 1475 |
| ERBB2 | p.(V1128I) | c.3382G>A | . | chr17:37883770 | 4.90% | NM_004448.3 | missense | 1081 |
| SEPTIN9 | p.(G260R) | c.778G>A | . | chr17:75478282 | 29.00% | NM_001113491.2 | missense | 1569 |
| ASXL1 | p.(R323H) | c.968G>A | . | chr20:31019471 | 23.96% | NM_015338.6 | missense | 1515 |
| PTPRT | p.(A149=) | c.447A>G | . | chr20:41419874 | 29.04% | NM_133170.4 | synonymous | 971 |
| PTPRT | p.(T49=) | c.147C>T | . | chr20:41514514 | 49.65% | NM_133170.4 | synonymous | 141 |
| CHEK2 | p.(S41=) | c.123C>A | . | chr22:29130587 | 26.63% | NM_007194.4 | synonymous | 1998 |
| USP9X | p.(Q1574H) | c.4722A>C | . | chrX:41060431 | 99.40% | NM_001039590.3 | missense | 839 |

## Biomarker Descriptions

**ATM (ATM serine/threonine kinase)**

Background: The ATM gene encodes a serine/threonine kinase that belongs to the phosphatidylinositol-3-kinase related kinases (PIKKs) family of genes that also includes ATR and PRKDC (also known as DNA-PKc)[1]. ATM and ATR act as master regulators of DNA damage response. Specifically, ATM is involved in double-stranded break (DSB) repair while ATR is involved in single-stranded DNA (ssDNA) repair[2]. ATM is recruited to the DNA damage site by the MRE11/RAD50/NBN (MRN) complex that senses DSB[2,3]. Upon activation, ATM phosphorylates several downstream proteins such as the NBN, MDC1, BRCA1, CHK2 and TP53BP1 proteins[4]. ATM is a tumor suppressor gene and loss of function mutations in ATM are implicated in the BRCAness phenotype, which is characterized by a defect in homologous recombination repair (HRR), mimicking BRCA1 or BRCA2 loss[5,6]. Germline mutations in ATM often result in Ataxia-telangiectasia, a hereditary disease also referred to as DNA damage response syndrome that is characterized by chromosomal instability[7].

## Biomarker Descriptions (continued)

Alterations and prevalence: Recurrent somatic mutations in ATM are observed in 17% of endometrial carcinoma, 15% of undifferentiated stomach adenocarcinoma, 13% of bladder urothelial carcinoma, 12% of colorectal adenocarcinoma, 9% of melanoma as well as esophagogastric adenocarcinoma and 8% of non-small cell lung cancer[8,9].

Potential relevance: The PARP inhibitor, olaparib[10] is approved (2020) for metastatic castration-resistant prostate cancer (mCRPC) with deleterious or suspected deleterious, germline or somatic mutations in HRR genes that includes ATM. Consistent with other genes associated with the BRCAness phenotype, ATM mutations may aid in selecting patients likely to respond to PARP inhibitors[5,11,12]. Specifically, in a phase II trial of metastatic, castration-resistant prostate cancer, four of six patients with germline or somatic ATM mutations demonstrated clinical responses to olaparib[13]. In 2022, the FDA granted fast track designation to the small molecule inhibitor, pidnarulex[14], for BRCA1/2, PALB2, or other homologous recombination deficiency (HRD) mutations in breast and ovarian cancers.

**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[15]. 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[16,17]. In addition, PTEN has been proposed to influence RAD51 loading at double strand breaks during homologous recombination repair (HRR) and regulate the G2/M checkpoint by influencing CHEK1 localization through AKT inhibition, thereby regulating HRR efficiency[18]. 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[19]. PTEN germline mutations are also associated with inherited cancer risk in several cancer types[20].

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[8,9]. 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[17,21,22,23,24]. 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[8,9].

Potential relevance: Currently, no therapies are approved for PTEN aberrations. However, due to the role of PTEN in HRR, poly(ADP-ribose) polymerase inhibitors (PARPi) are being explored as a potential therapeutic strategy in PTEN deficient tumors[25,26]. In 2022, the FDA granted fast track designation to the small molecule inhibitor, pidnarulex[14], for BRCA1/2, PALB2, or other homologous recombination deficiency (HRD) mutations in breast and ovarian cancers.

**SMARCA4 (SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 4)**

Background: The SMARCA4 gene encodes the SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily A, member 4 protein[27]. SMARCA4, also known as BRG1, is a core member of ATP-dependent, multisubunit SWI/SNF chromatin-remodeling complex, along with SMARCB1/SNF5, SMARCC1/BAF155, SMARCC2/BAF170, and SMARCA2/BRM[28]. The SWI/SNF complex remodels chromatin at promoter and enhancer elements to alter and regulate gene expression[28,29]. SMARCA4 and SMARCA2 are highly homologous and are mutually exclusive ATPase catalytic subunits for SWI/SNF chromatin remodeling complexes[28,29]. Germline loss of function mutations in SMARCA4 are associated with atypical teratoid/rhabdoid tumors (AT/RT), and a rare form of ovarian cancer called small cell carcinoma of the ovary, hypercalcemic type (SCCOHT), which highlights the tumor suppressor function of SMARCA4.[30,31].

Alterations and prevalence: Mutations in SWI/SNF complex subunits are the most commonly mutated chromatin modulators in cancer and have been observed in 20% of all tumors[29]. Recurrent somatic mutations in SMARCA4 are observed in 10% of skin cutaneous melanoma and uterine corpus endometrial carcinoma, and 7% of esophageal adenocarcinoma[8,9].

Potential relevance: Currently, no therapies are approved for SMARCA4 aberrations. SMARCA4 mutations and deletions are considered a diagnostic marker for the SMARCA4-deficient uterine sarcoma (SDUS) subtype[32].

**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[33]. Germline mutations in TP53 are the underlying cause of Li-Fraumeni syndrome, a complex hereditary cancer predisposition disorder associated with early-onset cancers[34,35].

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

## Biomarker Descriptions (continued)

rates (60-90%)[8,9,36,37,38,39]. Approximately two-thirds of TP53 mutations are missense mutations and several recurrent missense mutations are common including substitutions at codons R158, R175, Y220, R248, R273, and R282[8,9]. Invariably, recurrent missense mutations in TP53 inactivate its ability to bind DNA and activate transcription of target genes[40,41,42,43].

Potential relevance: The small molecule p53 reactivator, PC14586, received a fast track designation (2020) by the FDA for advanced tumors harboring a TP53 Y220C mutation[44]. The FDA has granted fast track designation (2019) to the p53 reactivator, eprenetapopt,[45] and breakthrough designation[46] (2020) in combination with azacitidine or azacitidine and venetoclax for acute myeloid leukemia patients (AML) and myelodysplastic syndrome (MDS) harboring a TP53 mutation, respectively. In addition to investigational therapies aimed at restoring wild-type TP53 activity, compounds that induce synthetic lethality are also under clinical evaluation[47,48]. TP53 mutations confer poor prognosis in multiple blood cancers including AML, MDS, myeloproliferative neoplasms (MPN), and chronic lymphocytic leukemia (CLL)[49,50,51,52]. In mantle cell lymphoma, TP53 mutations are associated with poor prognosis when treated with conventional therapy including hematopoietic cell transplant[53]. Mono- and bi-allelic mutations in TP53 confer unique characteristics in MDS, with multi-hit patients also experiencing associations with complex karyotype, few co-occuring mutations, and high-risk disease presentation as well as predicted death and leukemic transformation independent of the IPSS-R staging system[54].

**Tumor Mutational Burden**

Background: Tumor mutational burden (TMB), also known as tumor mutational load (TML), is the count of somatic mutations in the DNA of cancer cells. TMB is determined by next-generation sequencing and is expressed as the number of mutations per megabase (mut/Mb) of DNA coding sequence[55]. Errors in DNA repair, including mutations in the POLE gene and in mismatch repair (MMR) genes, are associated with increased TMB[56,57,58,59,60]. High TMB is associated with increased neo-antigen burden and has been linked to response to immune checkpoint inhibitors (ICIs) that target the cytotoxic T lymphocyte antigen-4 (CTLA4), programmed death protein 1 (PD1), and programmed death-ligand 1 (PD-L1) inhibitors[61,62,63,64].

Alterations and prevalence: In one study of over 100,000 tumor samples, the median TMB value was 3.6 mut/Mb although TMB values vary widely across cancers[65]. Certain childhood cancers, leukemia, glioblastoma, and neuroblastoma typically have low mutation burden and median TMB values <1 mut/Mb[62,65]. In comparison, cancers that experience genotoxic insults including skin cancer and lung cancer have higher median TMB values of approximately 10 mut/Mb[62,65]. For example, within non-small cell lung cancer (NSCLC), higher TMB was observed in former/current smokers (10.5 mut/Mb) relative to never smokers (0.6 mut/Mb)[62,65,66]. There is no consensus around the definition of high and low TMB that could be applied universally to all tumor types, instead multiple sources suggest that TMB status is a cancer type specific attribute[65,67,68]. In NSCLC, several studies have suggested establishing a threshold between low and high TMB of 10 +/- 1 mut/Mb[69,70,71,72].

Potential relevance: ICIs stimulate a patient's own T-cells to kill tumors and have exhibited benefits in some patients. The first ICI to be approved by the FDA was ipilimumab (2011), an anti-CTLA4 antibody indicated for the treatment of metastatic melanoma. In 2014, anti-PD-1 antibodies, nivolumab (2014) and pembrolizumab (2014), were subsequently approved for the treatment of metastatic melanoma. Pembrolizumab was also approved (2014) for advanced esophageal squamous cell carcinoma. In 2020, the indication for pembrolizumab[73] was expanded to include TMB-H (>/= 10 mut/Mb) solid tumors that have progressed on prior therapy. Indications have been expanded for these ICIs to include several other cancer types including NSCLC, advanced renal cell carcinoma, classical Hodgkin lymphoma, recurrent or metastatic squamous cell carcinoma of the head and neck, urothelial carcinoma, microsatellite instability (MSI)-High or mismatch repair deficient (dMMR) colorectal cancer, and hepatocellular carcinoma. Atezolizumab (2016), avelumab (2017), and durvalumab (2017), that target programmed death-ligand 1 (PD-L1), were subsequently approved by the FDA. However, the predictive biomarkers that underlie the clinical benefits of these approved immunotherapies, including TMB, are under active investigation. Several published studies including the CheckMate 586 and CheckMate 817 clinical trials have concluded that high TMB was associated with improved response to FDA approved checkpoint inhibitors[70,74,75]. In contrast, several promising previous trials failed to show an improvement in survival outcomes between high and low TMB including CheckMate 227 (ipilimumab + nivolumab vs. chemotherapy), CheckMate 026 (nivolumab vs. chemotherapy), KEYNOTE 189 (pembrolizumab vs. chemotherapy), KEYNOTE 021 (pembrolizumab vs. pembrolizumab + chemotherapy), and Lung-MAP (nivolumab + ipilimumab vs. nivolumab). In response, suggestions to combine TMB score with PD-L1 expression as a way to increase the predictive power for patient stratification have been reported[76]. Nivolumab alone or in combination with ipilimumab is recommended for use in NSCLC with evidence of high TMB[77]. Pembrolizumab is indicated for use in various cancer types with evidence of metastasis including Ewing sarcoma, salivary gland neoplasms, cervical cancer, uterine sarcoma, endometrial carcinoma, thyroid cancer, ovarian cancer, esophageal cancer, esophagogastric junction cancer, breast cancer, and germ cell tumors with high TMB[32,78,79,80,81,82,83,84,85]. TMB score estimation is affected by the utilized assays, therefore efforts are underway to develop a standardized approach for score calculation with the aim to support consistent reporting of TMB values across laboratories[86,87,88,89].

## Relevant Therapy Summary

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ✖ No evidence

### Tumor Mutational Burden

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

### ATM p.(R925Efs*7) c.2773_2774delAG

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| niraparib | ○ | ○ | ✖ | ○ | ✖ |
| olaparib | ○ | ○ | ✖ | ✖ | ✖ |
| bevacizumab + olaparib | ✖ | ✖ | ✖ | ○ | ✖ |

### PTEN p.(R233*) c.697C>T

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| niraparib | ○ | ○ | ✖ | ○ | ✖ |
| bevacizumab + olaparib | ✖ | ✖ | ✖ | ○ | ✖ |

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

# Relevant Therapy Details

## Current FDA Information

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

FDA information is current as of 2022-02-16. For the most up-to-date information, search www.fda.gov.

## Tumor Mutational Burden

### ● pembrolizumab

**Cancer type:** Solid Tumor **Label as of:** 2022-02-04 **Variant class:** Tumor Mutational Burden

**Indications and usage:**

KEYTRUDA® is a programmed death receptor-1 (PD-1)-blocking antibody indicated:

Melanoma

- for the treatment of patients with unresectable or metastatic melanoma.
- for the adjuvant treatment of adult and pediatric (12 years and older) patients with Stage IIB, IIC, or III melanoma following complete resection.

Non-Small Cell Lung Cancer (NSCLC)

- in combination with pemetrexed and platinum chemotherapy, as first-line treatment of patients with metastatic nonsquamous NSCLC, with no EGFR or ALK genomic tumor aberrations.
- in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, as first-line treatment of patients with metastatic squamous NSCLC.
- as a single agent for the first-line treatment of patients with NSCLC expressing PD-L1 [Tumor Proportion Score (TPS) ≥ 1%] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is:
  - stage III where patients are not candidates for surgical resection or definitive chemoradiation, or
  - metastatic.
- as a single agent for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥1%) as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving KEYTRUDA®.

Head and Neck Squamous Cell Cancer (HNSCC)

- in combination with platinum and FU for the first-line treatment of patients with metastatic or with unresectable, recurrent HNSCC.
- as a single agent for the first-line treatment of patients with metastatic or with unresectable, recurrent HNSCC whose tumors express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by an FDA-approved test.
- as a single agent for the treatment of patients with recurrent or metastatic HNSCC with disease progression on or after platinum-containing chemotherapy.

Classical Hodgkin Lymphoma (cHL)

- for the treatment of adult patients with relapsed or refractory cHL.
- for the treatment of pediatric patients with refractory cHL, or cHL that has relapsed after 2 or more lines of therapy.

Primary Mediastinal Large B-Cell Lymphoma (PMBCL)

- for the treatment of adult and pediatric patients with refractory PMBCL, or who have relapsed after 2 or more prior lines of therapy.
- Limitations of Use: KEYTRUDA® is not recommended for treatment of patients with PMBCL who require urgent cytoreductive therapy.

Urothelial Carcinoma

- for the treatment of patients with locally advanced or metastatic urothelial carcinoma who:
  - are not eligible for any platinum-containing chemotherapy, or

## Tumor Mutational Burden (continued)

- who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy

- for the treatment of patients with Bacillus Calmette-Guerin (BCG)-unresponsive, high-risk, non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy.

Microsatellite Instability-High or Mismatch Repair Deficient Cancer

- for the treatment of adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options.[1]
- Limitations of Use: The safety and effectiveness of KEYTRUDA® in pediatric patients with MSI-H central nervous system cancers have not been established.

Microsatellite Instability-High or Mismatch Repair Deficient Colorectal Cancer (CRC)

- for the treatment of patients with unresectable or metastatic MSI-H or dMMR colorectal cancer (CRC).

Gastric Cancer

- in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy, for the first-line treatment of patients with locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma.

Esophageal Cancer

- for the treatment of patients with locally advanced or metastatic esophageal or gastroesophageal junction (GEJ) (tumors with epicenter 1 to 5 centimeters above the GEJ) carcinoma that is not amenable to surgical resection or definitive chemoradiation either:
  - in combination with platinum- and fluoropyrimidine-based chemotherapy, or
  - as a single agent after one or more prior lines of systemic therapy for patients with tumors of squamous cell histology that express PD-L1 (CPS ≥10) as determined by an FDA-approved test.

Cervical Cancer

- in combination with chemotherapy, with or without bevacizumab, for the treatment of patients with persistent, recurrent, or metastatic cervical cancer whose tumors express PD-L1 (CPS ≥1) as determined by an FDA-approved test.
- as a single agent for the treatment of patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumors express PD-L1 (CPS ≥1) as determined by an FDA-approved test.

Hepatocellular Carcinoma (HCC)

- for the treatment of patients with HCC who have been previously treated with sorafenib.[1]

Merkel Cell Carcinoma (MCC)

- for the treatment of adult and pediatric patients with recurrent locally advanced or metastatic Merkel cell carcinoma.[1]

Renal Cell Carcinoma (RCC)

- in combination with axitinib, for the first-line treatment of adult patients with advanced RCC.
- in combination with lenvatinib, for the first-line treatment of adult patients with advanced RCC.
- for the adjuvant treatment of patients with RCC at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions.

Endometrial Carcinoma

- in combination with lenvatinib, for the treatment of patients with advanced endometrial carcinoma that is not MSI-H or dMMR, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.

Tumor Mutational Burden-High (TMB-H) Cancer

- for the treatment of adult and pediatric patients with unresectable or metastatic tumor mutational burden-high (TMB-H) [≥10 mutations/megabase (mut/Mb)] solid tumors, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options.[1]
- Limitations of Use: The safety and effectiveness of KEYTRUDA® in pediatric patients with TMB-H central nervous system cancers have not been established.

Cutaneous Squamous Cell Carcinoma (cSCC)and description of clinical benefit in the confirmatory trial

## Tumor Mutational Burden (continued)

- for the treatment of patients with recurrent or metastatic cSCC or locally advanced cSCC that is not curable by surgery or radiation.

Triple-Negative Breast Cancer (TNBC)

- for the treatment of patients with high-risk early-stage TNBC in combination with chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery.
- in combination with chemotherapy, for the treatment of patients with locally recurrent unresectable or metastatic TNBC whose tumors express PD-L1 (CPS ≥10) as determined by an FDA approved test.

Adult Indications: Additional Dosing Regimen of 400 mg Every 6 Weeks

- for use at an additional recommended dosage of 400 mg every 6 weeks for all approved adult indications.[2]

[1] This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

[2] This indication is approved under accelerated approval based on pharmacokinetic data, the relationship of exposure to efficacy, and the relationship of exposure to safety. Continued approval for this dosing may be contingent upon verification and description of clinical benefit in the confirmatory trials.

**Reference:**

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/125514s125lbl.pdf

## ATM p.(R925Efs*7) c.2773_2774delAG

### olaparib

**Cancer type:** Castration-Resistant Prostate Cancer **Label as of:** 2022-01-31 **Variant class:** ATM mutation

**Indications and usage:**

LYNPARZA® is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated:

Ovarian cancer

- for the maintenance treatment of adult patients with deleterious or suspected deleterious germline or somatic BRCA-mutated advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA®.
- in combination with bevacizumab for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy and whose cancer is associated with homologous recombination deficiency (HRD)-positive status defined by either:
  - a deleterious or suspected deleterious BRCA mutation, and/or
  - genomic instability.

Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA®.

- for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, who are in complete or partial response to platinum-based chemotherapy.
- for the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA®.

Breast cancer

- for the treatment of adult patients with deleterious or suspected deleterious gBRCAm, HER2-negative metastatic breast cancer who have been treated with chemotherapy in the neoadjuvant, adjuvant or metastatic setting. Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine therapy. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA®.

Pancreatic cancer

- for the maintenance treatment of adult patients with deleterious or suspected deleterious gBRCAm metastatic pancreatic adenocarcinoma whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA®.

Prostate cancer

- for the treatment of adult patients with deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC) who have progressed following prior treatment with enzalutamide or abiraterone. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA®.

**Reference:**

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/208558s021lbl.pdf

## ATM p.(R925Efs*7) c.2773_2774delAG (continued)

### niraparib

**Cancer type:** Ovarian Cancer **Label as of:** 2021-07-27 **Variant class:** HR Deficient

**Indications and usage:**

ZEJULA® is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated:

- for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy.
- for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.
- for the treatment of adult patients with advanced ovarian, fallopian tube, or primary peritoneal cancer who have been treated with 3 or more prior chemotherapy regimens and whose cancer is associated with homologous recombination deficiency (HRD) positive status defined by either:
  - a deleterious or suspected deleterious BRCA mutation, or
  - genomic instability and who have progressed more than 6 months after response to the last platinum-based chemotherapy.

Select patients for therapy based on an FDA-approved companion diagnostic for ZEJULA®.

**Reference:**

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/208447s022s024lbl.pdf

## PTEN p.(R233*) c.697C>T

### niraparib

**Cancer type:** Ovarian Cancer **Label as of:** 2021-07-27 **Variant class:** HR Deficient

**Indications and usage:**

ZEJULA® is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated:

- for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy.
- for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.
- for the treatment of adult patients with advanced ovarian, fallopian tube, or primary peritoneal cancer who have been treated with 3 or more prior chemotherapy regimens and whose cancer is associated with homologous recombination deficiency (HRD) positive status defined by either:
  - a deleterious or suspected deleterious BRCA mutation, or
  - genomic instability and who have progressed more than 6 months after response to the last platinum-based chemotherapy.

Select patients for therapy based on an FDA-approved companion diagnostic for ZEJULA®.

**Reference:**

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/208447s022s024lbl.pdf

## Current NCCN Information

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

NCCN information is current as of 2022-02-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

# Tumor Mutational Burden

### ◑ pembrolizumab

**Cancer type:** Esophageal Cancer, Gastroesophageal Junction Adenocarcinoma

**Variant class:** Tumor Mutational Burden

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Adenocarcinoma, Squamous Cell; Unresectable, Locally Advanced, Recurrent, Metastatic (Second-line therapy, Subsequent therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 1.2022]

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### ○ pembrolizumab

**Cancer type:** Chondrosarcoma, Ewing Sarcoma, Osteosarcoma

**Variant class:** Tumor Mutational Burden

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Unresectable, Metastatic, Progression (Subsequent therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Bone Cancer [Version 2.2022]

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### ○ pembrolizumab

**Cancer type:** Breast Cancer

**Variant class:** Tumor Mutational Burden

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Stage IV; Invasive, Unresectable, Metastatic, Progression (Line of therapy not specified); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2022]

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### ○ pembrolizumab

**Cancer type:** Cervical Small Cell Neuroendocrine Carcinoma

**Variant class:** Tumor Mutational Burden

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Recurrent, Metastatic (Second-line therapy, Subsequent therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Cervical Cancer [Version 1.2022]

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## Tumor Mutational Burden (continued)

### pembrolizumab

**Cancer type:** Cervical Cancer **Variant class:** Tumor Mutational Burden

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Squamous Cell, Adenocarcinoma, Adenosquamous; Recurrent, Metastatic, Progression (Second-line therapy, Subsequent therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Cervical Cancer [Version 1.2022]

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### pembrolizumab

**Cancer type:** Gastric Cancer **Variant class:** Tumor Mutational Burden

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Unresectable, Locally Advanced, Recurrent, Metastatic (Second-line therapy, Subsequent therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Gastric Cancer [Version 2.2022]

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### pembrolizumab

**Cancer type:** Head and Neck Cancer **Variant class:** Tumor Mutational Burden

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Nasopharyngeal; Recurrent, Unresectable, Metastatic (Subsequent therapy); Useful in certain circumstances
- Salivary Gland Neoplasm; Recurrent, Unresectable, Metastatic (Line of therapy not specified); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 1.2022]

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### pembrolizumab

**Cancer type:** Extrahepatic Cholangiocarcinoma, Gallbladder Carcinoma, Intrahepatic Cholangiocarcinoma **Variant class:** Tumor Mutational Burden

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Unresectable, Metastatic, Progression (Subsequent therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Hepatobiliary Cancers [Version 5.2021]

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## Tumor Mutational Burden (continued)

### pembrolizumab

**Cancer type:** Large Cell Neuroendocrine Carcinoma, Small Cell Neuroendocrine Carcinoma

**Variant class:** Tumor Mutational Burden

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Poorly Differentiated; Unresectable, Metastatic, Progression (Line of therapy not specified); Consider

**Reference:** NCCN Guidelines® - NCCN-Neuroendocrine and Adrenal Tumors [Version 4.2021]

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### pembrolizumab

**Cancer type:** Neuroendocrine Tumor

**Variant class:** Tumor Mutational Burden

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Well Differentiated; G3; Locally Advanced, Metastatic, Progression (Line of therapy not specified)

**Reference:** NCCN Guidelines® - NCCN-Neuroendocrine and Adrenal Tumors [Version 4.2021]

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### pembrolizumab

**Cancer type:** Ovarian Cancer

**Variant class:** Tumor Mutational Burden

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Epithelial, Less Common Ovarian Cancers, Fallopian Tube, Primary Peritoneal; Recurrent (Recurrence therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2022]

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### pembrolizumab

**Cancer type:** Castration-Resistant Prostate Cancer

**Variant class:** Tumor Mutational Burden

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Adenocarcinoma; Metastatic, Progression (Subsequent therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Prostate Cancer [Version 3.2022]

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### pembrolizumab

**Cancer type:** Testicular Cancer

**Variant class:** Tumor Mutational Burden

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Germ Cell Tumor; Metastatic, Recurrent (Third-line therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Testicular Cancer [Version 2.2022]

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## Tumor Mutational Burden (continued)

### pembrolizumab

**Cancer type:** Thyroid Gland Follicular Carcinoma, Thyroid Gland Hurthle Cell Carcinoma, Thyroid Gland Papillary Carcinoma

**Variant class:** Tumor Mutational Burden

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Locally Recurrent, Advanced, Metastatic (Line of therapy not specified); Consider

**Reference:** NCCN Guidelines® - NCCN-Thyroid Carcinoma [Version 3.2021]

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### pembrolizumab

**Cancer type:** Thyroid Gland Medullary Carcinoma

**Variant class:** Tumor Mutational Burden

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Recurrent, Persistent, Local, Distant Metastases, Regional (Line of therapy not specified); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Thyroid Carcinoma [Version 3.2021]

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### pembrolizumab

**Cancer type:** Thyroid Gland Anaplastic Carcinoma

**Variant class:** Tumor Mutational Burden

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Stage IVC; Metastatic (Second-line therapy); Useful in certain circumstances, Consider

**Reference:** NCCN Guidelines® - NCCN-Thyroid Carcinoma [Version 3.2021]

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### pembrolizumab

**Cancer type:** Endometrial Carcinoma, Endometrial Clear Cell Adenocarcinoma, Endometrial Serous Adenocarcinoma, Undifferentiated and Dedifferentiated Carcinomas of the Uterine Corpus, Uterine Corpus Carcinosarcoma

**Variant class:** Tumor Mutational Burden

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Unresectable, Metastatic, Progression (Second-line therapy); Preferred intervention

**Reference:** NCCN Guidelines® - NCCN-Uterine Neoplasms [Version 1.2022]

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## Tumor Mutational Burden (continued)

### pembrolizumab

**Cancer type:** Uterine Sarcoma **Variant class:** Tumor Mutational Burden

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Unresectable, Metastatic, Progression (Second-line therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Uterine Neoplasms [Version 1.2022]

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### pembrolizumab

**Cancer type:** Neuroendocrine Tumor **Variant class:** Tumor Mutational Burden

**NCCN Recommendation category:** 2B

**Population segment (Line of therapy):**
- Well Differentiated; G3; Locally Advanced, Metastatic, Progression, Unresectable (Line of therapy not specified)

**Reference:** NCCN Guidelines® - NCCN-Neuroendocrine and Adrenal Tumors [Version 4.2021]

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### pembrolizumab

**Cancer type:** Castration-Resistant Prostate Cancer **Variant class:** Tumor Mutational Burden

**NCCN Recommendation category:** 2B

**Population segment (Line of therapy):**
- Adenocarcinoma; Visceral Metastases, Progression (Subsequent therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Prostate Cancer [Version 3.2022]

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## ATM p.(R925Efs*7) c.2773_2774delAG

### olaparib

**Cancer type:** Castration-Resistant Prostate Cancer **Variant class:** ATM mutation

**NCCN Recommendation category:** 1

**Population segment (Line of therapy):**
- Adenocarcinoma; Metastatic (Subsequent therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Prostate Cancer [Version 3.2022]

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## ATM p.(R925Efs*7) c.2773_2774delAG (continued)

### olaparib

**Cancer type:** Castration-Resistant Prostate Cancer **Variant class:** ATM mutation

**NCCN Recommendation category:** 2B

**Population segment (Line of therapy):**
- Adenocarcinoma; Visceral Metastases (Subsequent therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Prostate Cancer [Version 3.2022]

### niraparib

**Cancer type:** Ovarian Cancer **Variant class:** HR Deficient

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Epithelial, Less Common Ovarian Cancers, Fallopian Tube, Primary Peritoneal; Recurrent (Recurrence therapy); Preferred intervention

**Reference:** NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2022]

## PTEN p.(R233*) c.697C>T

### niraparib

**Cancer type:** Ovarian Cancer **Variant class:** HR Deficient

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Epithelial, Less Common Ovarian Cancers, Fallopian Tube, Primary Peritoneal; Recurrent (Recurrence therapy); Preferred intervention

**Reference:** NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2022]

## Current ESMO Information

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

ESMO information is current as of 2022-02-01. For the most up-to-date information, search www.esmo.org.

## ATM p.(R925Efs*7) c.2773_2774delAG

### ○ bevacizumab + olaparib

**Cancer type:** Ovarian Cancer **Variant class:** HR Deficient

**ESMO Level of Evidence/Grade of Recommendation:** I / A

**Population segment (Line of therapy):**
- Epithelial; Relapsed (Maintenance therapy); ESMO-MCBS v1.1 score: 3

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Newly Diagnosed and Relapsed Epithelial Ovarian Carcinoma [Ann Oncol 2013; 24 (Suppl 6): vi24-vi32. (eUpdate: 19 July 2021, 01 April 2020, 21 September 2016; Corrigendum: 03 October 2018)]

### ○ niraparib

**Cancer type:** Ovarian Cancer **Variant class:** HR Deficient

**ESMO Level of Evidence/Grade of Recommendation:** I / A

**Population segment (Line of therapy):**
- Epithelial; Relapsed (Maintenance therapy); ESMO-MCBS v1.1 score: 3

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Newly Diagnosed and Relapsed Epithelial Ovarian Carcinoma [Ann Oncol 2013; 24 (Suppl 6): vi24-vi32. (eUpdate: 19 July 2021, 01 April 2020, 21 September 2016; Corrigendum: 03 October 2018)]

## PTEN p.(R233*) c.697C>T

### ○ bevacizumab + olaparib

**Cancer type:** Ovarian Cancer **Variant class:** HR Deficient

**ESMO Level of Evidence/Grade of Recommendation:** I / A

**Population segment (Line of therapy):**
- Epithelial; Relapsed (Maintenance therapy); ESMO-MCBS v1.1 score: 3

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Newly Diagnosed and Relapsed Epithelial Ovarian Carcinoma [Ann Oncol 2013; 24 (Suppl 6): vi24-vi32. (eUpdate: 19 July 2021, 01 April 2020, 21 September 2016; Corrigendum: 03 October 2018)]

### ○ niraparib

**Cancer type:** Ovarian Cancer **Variant class:** HR Deficient

**ESMO Level of Evidence/Grade of Recommendation:** I / A

**Population segment (Line of therapy):**
- Epithelial; Relapsed (Maintenance therapy); ESMO-MCBS v1.1 score: 3

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Newly Diagnosed and Relapsed Epithelial Ovarian Carcinoma [Ann Oncol 2013; 24 (Suppl 6): vi24-vi32. (eUpdate: 19 July 2021, 01 April 2020, 21 September 2016; Corrigendum: 03 October 2018)]

## Clinical Trials in Taiwan region:

## Clinical Trials Summary

### Tumor Mutational Burden

| NCT ID | Title | Phase |
|---|---|---|
| NCT04589845 | Tumor-Agnostic Precision Immunooncology and Somatic Targeting Rational for You (TAPISTRY) Phase II Platform Trial | II |
| NCT02628067 | A Clinical Trial of Pembrolizumab (MK-3475) Evaluating Predictive Biomarkers in Subjects With Advanced Solid Tumors (KEYNOTE 158). | II |

## Alerts Informed By Public Data Sources

### Current FDA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

FDA information is current as of 2022-02-16. For the most up-to-date information, search www.fda.gov.

### ATM p.(R925Efs*7) c.2773_2774delAG

#### pidnarulex

**Cancer type:** Breast Cancer, Ovarian Cancer **Variant class:** HR Deficient

**Supporting Statement:**
The FDA has granted Fast Track Designation to the small molecule inhibitor, pidnarulex for BRCA1/2, PALB2, or other HRD mutations in breast and ovarian cancers.

**Reference:**

https://www.senhwabio.com//en/news/20220125

### PTEN p.(R233*) c.697C>T

#### pidnarulex

**Cancer type:** Breast Cancer, Ovarian Cancer **Variant class:** HR Deficient

**Supporting Statement:**
The FDA has granted Fast Track Designation to the small molecule inhibitor, pidnarulex for BRCA1/2, PALB2, or other HRD mutations in breast and ovarian cancers.

**Reference:**

https://www.senhwabio.com//en/news/20220125

## Current NCCN Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

NCCN information is current as of 2022-02-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

## Tumor Mutational Burden

### pembrolizumab

**Cancer type:** Giant Cell Tumor of Soft Tissue **Variant class:** Tumor Mutational Burden

**NCCN Recommendation category:** 2A

**Summary:**

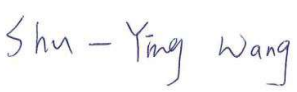
NCCN Guidelines® include the following supporting statement(s):

- "NCCN does not recommend this systemic treatment for GCTB since it is not technically a malignant tumor."

**Reference:** NCCN Guidelines® - NCCN-Bone Cancer [Version 2.2022]

## Signatures

**Testing Personnel:**



2022.04.18
10:14:37 +08'00'

**Laboratory Supervisor:**

2022.04.18
10:14:54 +08'00'

**Pathologist:**

2022.04.18
10:15:08 +08'00'

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