Taipei Veterans General Hospital

Department of Pathology and Laboratory Medicine
No.201, Sec. 2, Shipai Rd., Beitou District, Taipei City, Taiwan
11217, R.O.C.
Tel: 02-2875-7449

Sample Information

Patient Name: 蘇登滉
Gender: Male
ID No.: Q101888459
History No.: 48012904
Age: 70

Ordering Doctor: DOC6238J 李君陽
Ordering REQ.: 0BRRWKE
Signing in Date: 2022/02/17

Path No.: S111-98427
MP No.: TM22005
Assay: Tumor Mutation Load Assay
Sample Type: FFPE
Block No.: S110-79503 (from St. Martin De Porres Hospital)
Percentage of tumor cells: 80%

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

Note:

Sample Cancer Type: Mesothelioma

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Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	*Tumor Mutational Burden* 1.69 Mut/Mb measured **Prognostic significance:** None **Diagnostic significance:** None	**pembrolizumab** [1]	pembrolizumab	2

Public data sources included in relevant therapies: FDA1, 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

*ARID1A p.(L1092Ffs*13) c.3275_3276insT, NF2 c.596_599+12delCCAGGTGAGGCCCATT*

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
ARID1A	p.(L1092Ffs*13)	c.3275_3276insT	.	chr1:27097684	29.61%	NM_006015.6	frameshift Insertion	1932
NF2	p.(?)	c.596_599+12delCCAGGTGAGGCCCATT	.	chr22:30051661	35.11%	NM_000268.4	unknown	225
PAX7	p.(S203=)	c.609G>A	.	chr1:19018270	55.90%	NM_002584.3	synonymous	542
PAX7	p.(R218=)	c.654A>C	.	chr1:19018315	48.77%	NM_002584.3	synonymous	1997
PAX7	p.(A259=)	c.777G>A	.	chr1:19018438	46.37%	NM_002584.3	synonymous	1999
ARID1A	p.(G1375A)	c.4124G>C	.	chr1:27100842	51.30%	NM_006015.6	missense	577
DDR2	p.(I751=)	c.2253C>T	.	chr1:162746130	64.32%	NM_006182.4	synonymous	1505
LTF	p.(R23dup)	c.68_69insAAG	.	chr3:46501284	100.00%	NM_002343.6	nonframeshift Insertion	87
PDGFRA	p.(P567=)	c.1701A>G	.	chr4:55141055	99.75%	NM_006206.6	synonymous	1591
IL7R	p.(A254T)	c.760G>A	.	chr5:35874604	49.07%	NM_002185.5	missense	1999
RAD50	p.(L1264F)	c.3790C>T	.	chr5:131977907	45.67%	NM_005732.4	missense	1373
DAXX	p.(L512P)	c.1535T>C	.	chr6:33287598	45.60%	NM_001141970.2	missense	2000
ADGRB3	p.(E272=)	c.816A>G	.	chr6:69640509	85.43%	NM_001704.3	synonymous	762
ADGRB3	p.(E659Kfs*14)	c.1975delG	.	chr6:69723973	45.80%	NM_001704.3	frameshift Deletion	858
SYNE1	p.(R8293Q)	c.24878G>A	.	chr6:152469278	54.11%	NM_182961.4	missense	1144
SYNE1	p.(K4785N)	c.14355G>T	.	chr6:152651465	49.47%	NM_182961.4	missense	1047
SYNE1	p.(Y4615=)	c.13845T>C	.	chr6:152651975	6.34%	NM_182961.4	synonymous	1530
SYNE1	p.(K4121S)	c.12362_12363delAGinsGT	.	chr6:152658141	52.51%	NM_182961.4	missense	1217
CARD11	p.(S116=)	c.348C>T	.	chr7:2985463	39.30%	NM_032415.6	synonymous	2000
SMO	p.(K575M)	c.1724A>T	.	chr7:128850877	52.50%	NM_005631.5	missense	2000
NCOA2	p.(A1144=)	c.3432C>T	.	chr8:71041108	46.60%	NM_006540.4	synonymous	2000
EXT1	p.(P367L)	c.1100C>T	.	chr8:118847747	3.92%	NM_000127.3	missense	51
FANCG	p.(S603F)	c.1808C>T	.	chr9:35074166	19.65%	NM_004629.2	missense	2000
ABL1	p.(T935=)	c.2805G>A	.	chr9:133760482	49.22%	NM_005157.6	synonymous	1999
CHEK1	p.(*477R)	c.1429T>C	.	chr11:125525213	47.45%	NM_001274.5	stoploss	2000
ZNF384	p.(Q501Hfs*48)	c.1503delG	.	chr12:6777110	100.00%	NM_001135734.2	frameshift Deletion	485
KMT2D	p.(P1232=)	c.3696G>A	.	chr12:49443675	49.59%	NM_003482.4	synonymous	1956
FLT1	p.(R281Q)	c.842G>A	.	chr13:29005419	53.23%	NM_002019.4	missense	1379

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
LAMP1	p.(G187Efs*38)	c.556_557delCGinsA	.	chr13:113965176	100.00%	NM_005561.4	frameshift Block Substitution	1472
NTRK3	p.(V432I)	c.1294G>A	.	chr15:88669604	38.48%	NM_001012338.2	missense	1211
NF1	p.(K2456=)	c.7368A>G	.	chr17:29677247	52.20%	NM_001042492.3	synonymous	1998
SEPTIN9	p.(D484E)	c.1452C>G	.	chr17:75488774	49.32%	NM_001113491.2	missense	1997
BCL2	p.(A42Pfs*54)	c.124delG	.	chr18:60985775	83.67%	NM_000633.2	frameshift Deletion	251
BCL2	p.(P40Rfs*112)	c.119_127delCGGGGGCCGinsGGGGCCA	.	chr18:60985773	16.33%	NM_000633.2	frameshift Block Substitution	251
TCF3	p.(G431S)	c.1291_1293delGGCinsAGT	.	chr19:1619348	53.94%	NM_001136139.4	missense	432
CEBPA	p.(H195_P196dup)	c.589_590insACCCGC	.	chr19:33792731	15.79%	NM_004364.4	nonframeshift Insertion	
KDM6A	p.(E860K)	c.2578G>A	.	chrX:44929478	98.95%	NM_021140.3	missense	572

Biomarker Descriptions

ARID1A (AT-rich interaction domain 1A)

Background: The ARID1A gene encodes the AT-rich interaction domain 1A tumor suppressor protein[1]. ARID1A, also known as BAF250A, belongs to the ARID1 subfamily that also includes AR1D1B[1,2]. ARID1A and ARID1B are mutually exclusive subunits of the BAF variant of the SWI/SNF chromatin-remodeling complex[2,3]. The BAF complex is a multisubunit protein that consists of SMARCB1/IN1, SMARCC1/BAF155, SMARCC2/BAF170, SMARCA4/BRG1, and SMARCA2/BRM[3]. The BAF complex remodels chromatin at promoter and enhancer elements to alter and regulate gene expression[3,4]. ARID1A binds to transcription factors and coactivator/corepressor complexes to alter transcription[2]. Recurrent inactivating mutations in BAF complex subunits, including ARID1A, lead to transcriptional dysfunction thereby, altering its tumor suppressor function[2].

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[4]. The majority of ARID1A inactivating mutations are nonsense or frameshift mutations[2]. Somatic mutations in ARID1A have been identified in 50% of ovarian clear cell carcinoma, 30% of endometrioid carcinoma, and 24-43% of uterine corpus endometrial carcinoma, bladder urothelial carcinoma, and stomach adenocarcinoma[3,5,6]. In microsatellite stable (MSS) colorectal cancer, mutations in ARID1A have been observed to correlate with increased tumor mutational burden (TMB) and expression of genes involved in the immune response[7].

Potential relevance: Currently, no therapies are approved for ARID1A aberrations.

NF2 (NF2, moesin-ezrin-radixin like (MERLIN) tumor suppressor)

Background: The NF2 gene encodes the cytoskeletal Merlin (Moesin-ezrin-radixin-like) protein. NF2 is also known as Schwannomin due to its prevalence in neuronal Schwann cells. NF2 is structurally and functionally related to the Ezrin, Radixin, Moesin (ERM) family which is known to control plasma membrane function, thereby influencing cell shape, adhesion, and growth[8,9,10]. NF2 regulates several cellular pathways including the RAS/RAF/MEK/ERK, PI3K/AKT, and Hippo-YAP pathways, thus impacting cell motility, adhesion, invasion, proliferation, and apoptosis[8,9,10,11]. NF2 functions as a tumor suppressor wherein loss of function mutations are shown to confer a predisposition to tumor development[9,10,12]. Specifically, deleterious germline mutations or deletion of NF2 leading to loss of heterozygosity (LOH) is causal of neurofibromatosis type 2, a tumor prone disorder characterized by early age onset of multiple Schwannomas and meningiomas[9,10,12].

Biomarker Descriptions (continued)

Alterations and prevalence: Somatic mutations in NF2 are predominantly misssense or truncating and are observed in about 23% of mesothelioma, 5% of cholangiocarcinoma and uterine cancer, and about 3% of papillary renal cell carcinoma (pRCC), bladder, and cervical cancers[5]. Biallelic loss of NF2 is also observed in approximately 8% of mesothelioma cases[5].

Potential relevance: Currently, no therapies are approved for NF2 aberrations.

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[13]. Errors in DNA repair, including mutations in the POLE gene and in mismatch repair (MMR) genes, are associated with increased TMB[14,15,16,17,18]. 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[19,20,21,22].

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[23]. Certain childhood cancers, leukemia, glioblastoma, and neuroblastoma typically have low mutation burden and median TMB values <1 mut/Mb[20,23]. In comparison, cancers that experience genotoxic insults including skin cancer and lung cancer have higher median TMB values of approximately 10 mut/Mb[20,23]. 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)[20,23,24]. 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[23,25,26]. In NSCLC, several studies have suggested establishing a threshold between low and high TMB of 10 +/- 1 mut/Mb[27,28,29,30].

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[31] 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[28,32,33]. 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[34]. Nivolumab alone or in combination with ipilimumab is recommended for use in NSCLC with evidence of high TMB[35]. 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[36,37,38,39,40,41,42,43,44]. 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[45,46,47,48].

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)

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

Relevant Therapy Summary (continued)

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

Tumor Mutational Burden (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
atezolizumab	✖	✖	✖	✖	● (II)

* 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 2021-11-17. For the most up-to-date information, search www.fda.gov.

Tumor Mutational Burden

● pembrolizumab

Cancer type: Solid Tumor **Label as of:** 2021-11-17 **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 patients with melanoma with involvement of lymph node(s) 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
  - who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy

Tumor Mutational Burden (continued)

- 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.[1]
- as a single agent for the treatment of patients with recurrent locally advanced or metastatic gastric or GEJ adenocarcinoma whose tumors express PD-L1 (CPS ≥1) as determined by an FDA-approved test, with disease progression on or after 2 or more prior lines of therapy including fluoropyrimidine- and platinum-containing chemotherapy and if appropriate, HER2/neu-targeted therapy.[1]

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/2021/125514s113lbl.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 2021-11-01. 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: 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]

○ 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 8.2021]

○ 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]

○ 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]

Tumor Mutational Burden (continued)

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 4.2021]

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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 5.2021]

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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 3.2021]

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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]

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 (Line of therapy not specified); Consider

Reference: NCCN Guidelines® - NCCN-Neuroendocrine and Adrenal Tumors [Version 3.2021]

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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 (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Neuroendocrine and Adrenal Tumors [Version 3.2021]

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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 3.2021]

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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 1.2022]

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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 1.2022]

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

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 4.2021]

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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 4.2021]

Tumor Mutational Burden (continued)

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 3.2021]

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 1.2022]

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 NCCN Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

NCCN information is current as of 2021-11-01. 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:

Laboratory Supervisor:

Pathologist:

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