

Keytruda® (pembrolizumab) (Intravenous)

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I. Length of Authorization ^Δ 1-3,5,6,15-17,50,51,53,57,62,65,68,69,72,73,75-77,82,85-87,95,101,103,15e

Coverage will be provided for 6 months and may be renewed (unless otherwise specified).

- Adrenal Gland Tumors, Biliary Tract Cancer (Gallbladder Cancer or Intra-/Extra-Hepatic Cholangiocarcinoma), Bladder Cancer/Urothelial Carcinoma, Cervical Cancer, cHL, Adult CNS Cancer, Cutaneous Melanoma (in combination with ipilimumab or lenvatinib), cSCC, Endometrial Carcinoma (Uterine Neoplasms), Esophageal and Esophagogastric/Gastroesophageal Junction Cancer (first-line or subsequent therapy), Gastric Cancer (first-line therapy), HCC, MCC, MSI-H/dMMR Cancer, NSCLC (first-line or subsequent therapy), PMBCL, Primary Cutaneous Lymphomas, RCC (first-line or subsequent therapy), SCCHN, Thymic Carcinoma, Thyroid Carcinoma (Anaplastic), TMB-H Cancer, and TNBC (recurrent unresectable or metastatic disease) can be authorized up to a maximum of twenty-four (24) months of therapy.*
- Kaposi Sarcoma may not be renewed.
- Adjuvant therapy in NSCLC and RCC can be authorized up to a maximum of twelve (12) months of therapy.*
- Therapy for resectable NSCLC can be authorized for up to a maximum of twelve (12) weeks of neoadjuvant therapy and thirty-nine (39) weeks of adjuvant therapy.*
- Therapy for Cutaneous Melanoma can be authorized for up to a maximum of 8 weeks of neoadjuvant therapy (3 doses), followed by a maximum of 44 weeks (15 doses) of adjuvant therapy.
- Adjuvant therapy in Cutaneous Melanoma (*if no previous neoadjuvant pembrolizumab was used*) can be authorized up to a maximum of twelve (12) months of therapy.*
- Neoadjuvant therapy in TNBC can be authorized up to a maximum of twenty-four (24) weeks of therapy.*
- Adjuvant therapy in TNBC can be authorized up to a maximum of twenty-seven (27) weeks of therapy.*

- Reinduction therapy in Cutaneous Melanoma can be authorized up to a maximum of twelve (12) months of therapy.*

**Note: The maximum number of doses is dependent on the dosing frequency and duration of therapy. Refer to Section V for exact dosage.*

Dosing Frequency	Maximum length of therapy	Maximum number of doses
2 weeks	2 years	52 doses
3 weeks	24 weeks	8 doses
	27 weeks	9 doses
	1 year	18 doses
	2 years	35 doses
6 weeks	24 weeks	4 doses
	27 weeks	5 doses
	1 year	9 doses
	2 years	18 doses

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Keytruda 100 mg/4 mL single use vial: 12 vials per 14 day supply

B. Max Units (per dose and over time) [HCPCS Unit]:

Indication	Billable Units (BU)	Per unit time (days)
Biliary Tract Cancers, Bladder/Urothelial, Cervical, cHL, cSCC, Cutaneous Melanoma, Endometrial Carcinoma (Uterine Neoplasms), Esophageal, Esophagogastric/Gastroesophageal, Gastric, HCC, MCC, MSI-H/dMMR Cancer, PMBCL, RCC, SCCHN, TMB-H Cancer, TNBC, & Thyroid Carcinoma (Anaplastic)	400 BU	42 days
Adrenal Gland Tumors, Kaposi Sarcoma, Ovarian, Fallopian Tube, & Primary Peritoneal Cancer, Soft Tissue Sarcoma, & Thymic	200 BU	21 days
Adult CNS Cancer & NSCLC	200 BU	21 days
	1,200 BU	14 days
Primary Cutaneous Lymphomas	300 BU	21 days

III. Initial Approval Criteria ^{1,2}

Coverage is provided in the following conditions:

- Patient is at least 18 years of age (unless otherwise specified); **AND**

Universal Criteria

- Patient has not received previous therapy with a programmed death (PD-1/PD-L1)-directed therapy (e.g., cemiplimab, avelumab, nivolumab, atezolizumab, durvalumab, dostarlimab,

nivolumab/relatlimab, retifanlimab, toripalimab, tislelizumab, etc.) unless otherwise specified ^Δ;
AND

Primary Mediastinal Large B-Cell Lymphoma (PMBCL) † ‡ Φ ^{1,2,6,34,82}

- Used as single agent; **AND**
- Patient is at least 6 months of age; **AND**
- Patient has relapsed or refractory disease; **AND**
- Patient does not require urgent cytoreductive therapy; **AND**
- Used after autologous stem-cell transplant OR if ineligible for autologous stem-cell transplant, used after 2 or more prior lines of therapy

Biliary Tract Cancers (Gallbladder Cancer or Intra-/Extra-Hepatic Cholangiocarcinoma) † ‡ Φ ^{1,2,94,187e}

- Used in combination with gemcitabine and cisplatin; **AND**
- Patient has unresectable, resected gross residual (R2), or metastatic disease; **AND**
- Used as primary treatment

Urothelial Carcinoma (Bladder Cancer) † ‡ ^{1,2,8,10,35-37,88,93,99,111,54e-55e,134e,192e}

- Used in combination with enfortumab vedotin; **AND**
 - Used as first-line therapy; **AND**
 - Patient has one of the following diagnoses:
 - Locally advanced or metastatic urothelial carcinoma †
 - Muscle invasive bladder cancer with local recurrence or persistent disease in a preserved bladder treated with curative intent ‡
 - Metastatic or local bladder cancer recurrence post-cystectomy treated with curative intent ‡
 - Metastatic primary carcinoma of the urethra ‡
 - Metastatic upper genitourinary (GU) tract tumors ‡
 - Metastatic urothelial carcinoma of the prostate ‡; **OR**
- Used as a single agent; **AND**
 - Patient has Bacillus Calmette-Guerin (BCG)-unresponsive**, high-risk, non-muscle invasive bladder cancer (NMIBC) defined as one of the following †:
 - Persistent disease despite adequate BCG therapy
 - Disease recurrence after an initial tumor free state following an adequate BCG course of therapy

- T1 disease following a single induction course of BCG therapy; **AND**
- Patient has carcinoma in situ (CIS); **AND**
- Patient is ineligible for or has elected not to undergo cystectomy; **OR**
- Patient has one of the following diagnoses:
 - Locally advanced or metastatic urothelial carcinoma †
 - Muscle invasive bladder cancer with local recurrence or persistent disease in a preserved bladder treated with curative intent ‡
 - Metastatic or local bladder cancer recurrence post-cystectomy treated with curative intent ‡
 - Recurrent or metastatic primary carcinoma of the urethra (*excluding recurrence of stage T3-4 disease or palpable inguinal lymph nodes*) ‡
 - Primary carcinoma of the urethra that is stage T3-4 cN1-2 OR cN1-2 with palpable inguinal lymph nodes (*first-line therapy only*) ‡
 - Metastatic upper genitourinary (GU) tract tumors ‡; **AND**
- Used for disease that progressed during or following platinum-containing chemotherapy*; **OR**
- Used as first-line therapy in cisplatin-ineligible patients*; **AND**
 - Patient is not eligible for any platinum-containing chemotherapy (i.e., both cisplatin and carboplatin-ineligible)*

* **Note:** ^{10,71,79}

- *If patient was progression free for > 12 months after platinum therapy, consider re-treatment with platinum-based therapy if the patient is still platinum eligible (see below for cisplatin- or platinum-ineligible comorbidities).*
 - *Cisplatin-ineligible comorbidities may include the following: CrCl < 60 mL/min, ECOG PS ≥ 2 or KPS ≤ 70%, hearing loss of ≥ 25 decibels (dB) at two contiguous frequencies, grade ≥ 2 peripheral neuropathy, or NYHA Heart Failure class ≥ 3. Carboplatin may be substituted for cisplatin particularly in those patients with a CrCl < 60 mL/min or a PS of 2.*
 - *Platinum-ineligible comorbidities may include the following: CrCl < 30 mL/min, ECOG PS ≥ 3, grade ≥ 2 peripheral neuropathy, or NYHA Heart Failure class > 3, etc.*

** *Adequate BCG therapy is defined as administration of at least five of six doses of an initial induction course AND at least two of three doses of maintenance therapy or at least two of six doses of a second induction course.*

Triple-Negative Breast Cancer (TNBC) † ‡ Ψ ^{1,2,69}

- Used as first-line therapy for recurrent unresectable or metastatic disease; **AND**
 - Used in combination with albumin-bound paclitaxel, paclitaxel, or gemcitabine with carboplatin; **AND**

- Tumor expresses PD-L1 (combined positive score [CPS] ≥ 10) as determined by an FDA-approved or CLIA-compliant test❖; **OR**
- Patient has high-risk early-stage (i.e., stage II-III) disease; **AND**
 - Used as neoadjuvant therapy in combination with carboplatin and paclitaxel, then in combination with cyclophosphamide and either doxorubicin or epirubicin; **OR**
 - Used as adjuvant therapy as a single agent following use as neoadjuvant therapy in combination with chemotherapy

Adult Central Nervous System (CNS) Cancer ‡^{2,47,49,50}

- Used as a single agent; **AND**
- Primary tumor is due to BRAF non-specific melanoma or PD-L1 positive (TPS $\geq 1\%$) non-small cell lung cancer (NSCLC); **AND**
 - Used as initial treatment in patients with small asymptomatic brain metastases; **OR**
 - Used for relapsed limited brain metastases with either stable systemic disease or reasonable systemic treatment options; **OR**
 - Used for recurrent limited brain metastases; **OR**
 - Used for recurrent extensive brain metastases with stable systemic disease or reasonable systemic treatment options

Cervical Cancer † ‡^{1,2,42,70,100}

- Patient has FIGO 2014 Stage III-IVA disease; **AND**
 - Used in combination with platinum-containing chemoradiotherapy (CRT); **OR**
- Tumor expresses PD-L1 (CPS ≥ 1) as determined by an FDA-approved or CLIA-compliant test❖; **AND**
 - Used as a single agent; **AND**
 - Used as subsequent therapy for recurrent or metastatic disease; **OR**
 - Used in combination with cisplatin or carboplatin AND paclitaxel (with or without bevacizumab)[^]; **AND**
 - Patient has persistent, recurrent, or metastatic disease; **AND**
 - Used as first-line therapy; **AND**
 - Disease is not amenable to curative treatment (i.e., surgery and/or radiation)

[^]Pembrolizumab may be continued as maintenance therapy

Esophageal Cancer and Esophagogastric/Gastroesophageal Junction Cancer † ‡ Φ

1,2,39-41,66,67,95,98,101

- Patient is not a surgical candidate or has unresectable locally advanced, recurrent, or metastatic disease; **AND**
 - Used as first-line therapy; **AND**
 - Patient has HER2-positive esophagogastric/gastroesophageal junction adenocarcinoma; **AND**
 - Used in combination with trastuzumab, fluorouracil or capecitabine, and oxaliplatin or cisplatin; **AND**
 - Tumor expresses PD-L1 (CPS ≥ 1) as determined by an FDA-approved or CLIA compliant test²; **OR**
 - Patient has HER2-negative adenocarcinoma; **AND**
 - Used in combination with oxaliplatin or cisplatin AND either fluorouracil or capecitabine; **AND**
 - Tumor expresses PD-L1 (CPS ≥ 10) as determined by an FDA-approved or CLIA compliant test²; **OR**
 - Patient has squamous cell carcinoma; **AND**
 - Used in combination with oxaliplatin or cisplatin AND either fluorouracil or capecitabine; **AND**
 - Tumor expresses PD-L1 (CPS ≥ 10) as determined by an FDA-approved or CLIA compliant test²; **OR**
 - Used as subsequent therapy; **AND**
 - Used as a single agent; **AND**
 - Patient has esophageal squamous cell carcinoma †; **AND**
 - Tumor expresses PD-L1 (CPS ≥ 10) as determined by an FDA-approved or CLIA compliant test²; **AND**
 - Patients with HER2-positive disease must have previously received HER2-directed therapy (e.g., trastuzumab, etc.)

Gastric Cancer † ‡ Φ 1,2,39,67,95,98,103

- Patient is not a surgical candidate or has unresectable locally advanced, recurrent, or metastatic disease; **AND**
- Used as first-line therapy; **AND**
 - Patient has HER2-positive adenocarcinoma; **AND**

- Used in combination with trastuzumab, fluorouracil or capecitabine, and oxaliplatin or cisplatin; **AND**
- Tumor expresses PD-L1 (CPS \geq 1) as determined by an FDA-approved or CLIA compliant test²; **OR**
- Patient has HER2-negative adenocarcinoma; **AND**
 - Used in combination with oxaliplatin or cisplatin AND either fluorouracil or capecitabine; **AND**
 - Tumor expresses PD-L1 (CPS \geq 10) as determined by an FDA-approved or CLIA compliant test²

Squamous Cell Carcinoma of the Head and Neck (SCCHN) † ‡ ^{1,2,31,32,106,42e,188e}

- Patient has Very Advanced Head and Neck Cancer*; **AND**
- Patient has NON-nasopharyngeal cancer; **AND**
- Patient has unresectable, recurrent, persistent, or metastatic disease; **AND**
 - Used as a single agent; **AND**
 - Tumor expresses PD-L1 (CPS \geq 1) as determined by an FDA-approved or CLIA-compliant test²; **AND**
 - Used as first-line therapy †; **OR**
 - Used as subsequent therapy for disease that has progressed on or after platinum-containing chemotherapy; **OR**
 - Used in combination with cetuximab; **AND**
 - Patient has a performance status 0-1; **AND**
 - Patient has platinum-resistant disease or is platinum-ineligible; **OR**
 - Used in combination with carboplatin or cisplatin AND either fluorouracil, docetaxel, paclitaxel; **AND**
 - Patient has a performance status 0-1; **AND**
 - Used as first-line therapy

* Very Advanced Head and Neck Cancer includes: Newly diagnosed locally advanced T4b (M0) disease; newly diagnosed unresectable regional nodal disease (typically N3); metastatic disease at initial presentation (M1); or recurrent or persistent disease.

Hepatocellular Carcinoma (HCC) † ‡ ^{1,2,43,107}

- Used as a single agent; **AND**
- Patient has Child-Pugh Class A liver impairment (*i.e.*, excluding Child-Pugh Class B and C); **AND**
 - Disease is secondary to hepatitis B †; **AND**
 - Patient has received prior systemic therapy other than a PD-1/PD-L1- containing regimen; **OR**

- Used as subsequent therapy for progressive disease ‡; **AND**
 - Patient has liver-confined, unresectable disease and deemed ineligible for transplant; **OR**
 - Patient has extrahepatic/metastatic disease and deemed ineligible for resection, transplant, or locoregional therapy

Adult Classical Hodgkin Lymphoma (cHL) † ‡ Φ^{1,2,33,61,96,97}

- Patient has relapsed or refractory disease; **AND**
 - Used as a single agent; **OR**
 - Used in combination with GVD (gemcitabine, vinorelbine, liposomal doxorubicin) or ICE (ifosfamide, carboplatin, etoposide); **AND**
 - Patient is ≤ 60 years of age

Pediatric Classical Hodgkin Lymphoma † ‡ Φ^{1,2,33,61}

- Patient is at least 6 months of age*; **AND**
- Used as a single agent; **AND**
 - Patient has refractory disease †; **OR**
 - Patient has relapsed disease; **AND**
 - Used after two (2) or more prior lines of therapy †; **OR**
 - Used as subsequent therapy in patients heavily pretreated with platinum or anthracycline-based chemotherapy ‡; **OR**
 - Used as subsequent therapy in patients with an observed decrease in cardiac function ‡

** Pediatric Classical Hodgkin Lymphoma may be applicable to adolescent and young adult (AYA) patients up to the age of 39 years.*

Kaposi Sarcoma ‡^{2,85,86}

- Used as a single agent as subsequent therapy; **AND**
- Patient has endemic or classic disease; **AND**
- Used for relapsed/refractory advanced cutaneous disease; **AND**
- Disease has progressed on or has not responded to first-line systemic therapy; **AND**
- Disease has progressed on alternate first-line systemic therapy; **AND**
- Patient does not have multicentric Castleman disease (MCD) or KSHV–associated inflammatory cytokine syndrome (KICS)

Renal Cell Carcinoma (RCC) † ‡^{1,2,45,74-76}

- Patient has clear cell histology; **AND**
 - Used in combination with axitinib or lenvatinib; **AND**

- Used as first-line therapy for advanced, relapsed, or stage IV disease; **OR**
 - Used as a single agent; **AND**
 - Used as adjuvant therapy †; **AND**
 - Patient has undergone a nephrectomy prior to receiving treatment; **AND**
 - Patient has stage II disease with grade 4 tumors (with or without sarcomatoid features); **OR**
 - Patient has stage III disease; **OR**
 - Patient has undergone a metastasectomy with complete resection of disease within one year of nephrectomy for relapsed or stage IV disease; **OR**
- Patient has non-clear cell histology; **AND**
 - Used as a single agent as first-line therapy for relapsed or stage IV disease ‡

Cutaneous Melanoma † ‡ Φ ^{1,2,22-24,65,68,87,112,15e}

- Used as first-line therapy as a single agent for unresectable or metastatic* disease; **OR**
- Used as subsequent therapy; **AND**
 - Used for metastatic* or unresectable disease with progression or relapse following treatment with anti-PD-1 therapy; **AND**
 - Used as a single agent; **AND**
 - Used as re-induction therapy in patients who experienced stable disease or better **after** at least 24 months of pembrolizumab therapy OR a complete response after at least 6 months of pembrolizumab, but subsequently have disease progression after treatment discontinuation; **OR**
 - Used for metastatic* or unresectable disease with progression, intolerance, and/or projected risk of progression with BRAF-targeted therapy (e.g., dabrafenib/trametinib, vemurafenib/cobimetinib, encorafenib/binimetinib, etc.); **AND**
 - Used as a single agent; **AND**
 - Anti-PD-1 therapy was not previously used; **OR**
 - Used as re-induction therapy in patients who experienced stable disease or better **after** at least 24 months of pembrolizumab therapy OR a complete response after at least 6 months of pembrolizumab, but subsequently have disease progression after treatment discontinuation; **OR**
 - Used in combination with ipilimumab; **AND**
 - Used after progression on single-agent anti-PD-1 therapy and combination ipilimumab/anti-PD-1 therapy was not previously used; **OR**
- Used as a single agent for neoadjuvant treatment; **AND**
 - Patient has stage III disease; **AND**

- Used as primary treatment for clinically positive, resectable nodal disease; **OR**
 - Used for limited resectable disease with clinical satellite/in-transit metastases; **OR**
- Patient has limited resectable local satellite/in-transit recurrence; **OR**
- Patient has resectable disease limited to nodal recurrence; **OR**
- Used as a single agent for adjuvant treatment; **AND**
 - Patient has stage IIB, IIC, or III melanoma following complete resection; **AND**
 - Patient is at least 12 years of age

**Metastatic disease includes stage III unresectable/borderline resectable disease with clinically positive node(s) or clinical satellite/in-transit metastases, as well as unresectable local satellite/in-transit recurrence, unresectable nodal recurrence, and widely disseminated distant metastatic disease.*

Merkel Cell Carcinoma (MCC) † ‡ ☐ ^{1,2,9,44,22e}

- Patient is at least 6 months of age; **AND**
- Used as first-line therapy as a single agent; **AND**
 - Patient has primary or recurrent locally advanced disease † ‡; **AND**
 - Both curative surgery and curative radiation therapy are not feasible; **OR**
 - Patient has distant metastatic disease †; **OR**
 - Patient has recurrent regional disease †; **AND**
 - Both curative surgery and curative radiation therapy are not feasible

Adrenal Gland Tumors ‡ ^{2,62,63,77,128e,129e,203e}

- Patient has locoregional unresectable or metastatic adrenocortical carcinoma (ACC); **AND**
- Used as a single agent

Non-Small Cell Lung Cancer (NSCLC) † ‡ ^{1,2,11,25-29,120e,133e,136e,196e}

- Used for stage III disease †; **AND**
 - Used as first-line therapy as a single-agent in patients who are not candidates for surgical resection or definitive chemoradiation; **AND**
 - Used in patients with tumors expressing PD-L1 (TPS ≥1%) as determined by an FDA-approved or CLIA compliant test❖ and with no EGFR or ALK genomic tumor aberrations; **OR**
- Used as neoadjuvant therapy †; **AND**
 - Patient has resectable stage II, IIIA, or IIIB (N2) disease (tumors ≥4 cm or node positive); **AND**
 - Used in combination with platinum-containing chemotherapy, and then continued as a single agent as adjuvant treatment after surgery; **OR**
- Used as adjuvant therapy; **AND**

- Used as a single agent; **AND**
 - Used following resection and previous adjuvant platinum-based chemotherapy; **AND**
 - Patient has stage IB (T2a \geq 4 cm), II, or IIIA disease †; **OR**
 - Used following previous neoadjuvant pembrolizumab plus chemotherapy and resection for stage II, IIIA, or IIIB (N2) disease; **OR**
- Used for recurrent, advanced, or metastatic disease (excluding locoregional recurrence or symptomatic local disease without evidence of disseminated disease) or mediastinal lymph node recurrence with prior radiation therapy; **AND**
- Used as first-line therapy; **AND**
 - Used for one of the following:
 - PD-L1 expression-positive (TPS \geq 1%) tumors, as detected by an FDA-approved or CLIA compliant test❖, that are negative for actionable molecular biomarkers*¥
 - Patients with performance status (PS) 0-1 who have tumors that are negative for actionable molecular biomarkers*¥ and PD-L1 expression <1%
 - Patients with PS 0-1 who are positive for one of the following molecular biomarkers: EGFR exon 20, BRAF V600E, NTRK1/2/3 gene fusion, MET exon 14 skipping, RET rearrangement, or ERBB2 (HER2); **AND**
 - Used in combination with pemetrexed AND either carboplatin or cisplatin for non-squamous cell histology; **OR**
 - Used in combination with carboplatin AND either paclitaxel or albumin-bound paclitaxel for squamous cell histology; **OR**
 - Used as a single agent (*for PD-L1 expression-positive tumors ONLY*) †; **OR**
- Used as subsequent therapy; **AND**
 - Used in patients with tumors expressing PD-L1 (TPS \geq 1%) as determined by an FDA-approved or CLIA compliant test❖ in patients with disease progression on or after platinum-containing chemotherapy (patients with EGFR or ALK genomic tumor aberrations should also have disease progression on FDA-approved therapy§); **AND**
 - Used as a single agent; **OR**
 - Used for one of the following:
 - Patients with PS 0-1 who are positive for one of the following molecular biomarkers* and have received prior targeted therapy§: EGFR exon 19 deletion or L858R tumors, EGFR S768I, L861Q and/or G719X, ALK rearrangement, or ROS1 rearrangement

- Patients with PS 0-1 who are positive for one of the following molecular biomarkers*: BRAF V600E, NTRK1/2/3 gene fusion, MET exon 14 skipping, or RET rearrangement; **AND**
- Used in combination with carboplatin **AND** either paclitaxel or albumin-bound paclitaxel for squamous cell histology; **OR**
- Used in combination with pemetrexed **AND** either carboplatin or cisplatin for non-squamous cell histology; **OR**
- Used as continuation maintenance therapy in patients who have achieved tumor response or stable disease following initial systemic therapy; **AND**
 - Used in combination with pemetrexed following a first-line pembrolizumab/pemetrexed/(carboplatin or cisplatin) regimen for non-squamous cell histology; **OR**
 - Used as a single agent following a first-line pembrolizumab/carboplatin/ (paclitaxel or albumin-bound paclitaxel) regimen for squamous cell histology; **OR**
 - Used as a single agent following a first-line pembrolizumab monotherapy regimen

**Note: Actionable molecular genomic biomarkers include EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 (HER2). Complete genotyping for EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 (HER2), via biopsy and/or plasma testing. If a clinically actionable marker is found, it is reasonable to start therapy based on the identified marker. Treatment is guided by available results and, if unknown, these patients are treated as though they do not have driver oncogenes.*

‡ May also be used for patients with KRAS G12C mutation positive tumors.

Ovarian, Fallopian Tube, and Primary Peritoneal Cancer ‡^{2,104,105,197e,198e,204e,205e}

- Patient has epithelial* ovarian, fallopian tube, or primary peritoneal cancer; **AND**
- Used in combination with oral cyclophosphamide and bevacizumab; **AND**
- Patient has platinum-resistant disease; **AND**
 - Patient has persistent or recurrent disease; **AND**
 - Patient is not experiencing an immediate biochemical relapse (i.e., rising CA-125 without radiographic evidence of disease); **OR**
 - Patient has recurrent disease (*low-grade serous carcinoma only*)

** Epithelial subtypes include serous, endometrioid, carcinosarcoma (malignant mixed Müllerian tumors [MMMTs] of the ovary), clear cell, mucinous, and borderline epithelial tumors (also known as low malignant potential [LMP] tumors).*

Primary Cutaneous Lymphomas ‡^{2,15,102e,104e,117e}

- Used as a single agent systemic therapy; **AND**

- Patient has Mycosis Fungoides/Sezary Syndrome; **AND**
 - Used as subsequent therapy for relapsed or persistent disease; **AND**
 - Patient has one of the following:
 - Stage III Mycosis Fungoides
 - Stage IV Sezary Syndrome; **OR**
 - Used as subsequent therapy for disease refractory to multiple previous therapies (*excluding use in patients with stage IA Mycosis Fungoides*)

Soft Tissue Sarcoma ‡ ^{2,56,83,89,90}

- Used in combination with axitinib; **AND**
 - Patient has alveolar soft part sarcoma (ASPS); **OR**
- Used as a single agent; **AND**
 - Patient has undifferentiated pleomorphic sarcoma (UPS); **AND**
 - Used as subsequent therapy for advanced/metastatic disease with disseminated metastases (*Note: only applies to Extremity/Body Wall, Head/Neck**); **OR**
 - Used as alternative systemic therapy for unresectable or progressive disease after initial therapy for unresectable localized disease (*Note: only applies to Retroperitoneal/Intra-Abdominal***); **OR**
 - Used as subsequent therapy for stage IV disease with disseminated metastases (*Note: only applies to Retroperitoneal/Intra-Abdominal***)

**For atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDLPS) of the extremity, abdominal wall, trunk that was initially diagnosed as ALT/WDLPS and shows evidence of de-differentiation, treat as other soft tissue sarcomas.*

***For well-differentiated liposarcoma (WDLPS-retroperitoneum, paratesticular) with or without evidence of de-differentiation, treat as other soft tissue sarcomas.*

Cutaneous Squamous Cell Carcinoma (cSCC) † ‡ ^{1,2,58,125e}

- Used as a single agent; **AND**
- Patient has locally advanced, recurrent or metastatic disease that is not curable by surgery or radiation

Thymic Carcinoma ‡ ^{2,16,17}

- Used as a single agent; **AND**
- Used as second-line therapy; **AND**
- Patient has unresectable or metastatic disease

Thyroid Carcinoma (Anaplastic Carcinoma) ‡ ^{2,108,109,206e}

- Used in combination with lenvatinib; **AND**

- Patient has stage IVC disease; **AND**
 - Used as aggressive first-line therapy; **OR**
 - Used as second-line therapy

Endometrial Carcinoma (Uterine Neoplasms) † ‡ ^{1,2,46,80,91}

- Used in combination with lenvatinib; **AND**
 - Disease is mismatch repair proficient (pMMR) as determined by an FDA-approved or CLIA-compliant test❖ or NOT microsatellite instability-high (MSI-H); **AND**
 - Patient received prior platinum-based therapy in any setting (including neoadjuvant or adjuvant therapy); **AND**
 - Used as first-line therapy for recurrent disease (*excluding use in patients with isolated metastases*); **OR**
 - Used as subsequent therapy for advanced, recurrent, or metastatic disease; **OR**
- Used in combination with carboplatin and paclitaxel, followed by single agent maintenance therapy; **AND**
 - Used as adjuvant treatment; **AND**
 - Patient has Stage III or IV endometrioid adenocarcinoma; **OR**
 - Used as primary treatment (*excluding use in patients with carcinosarcoma*); **AND**
 - Patient has Stage III or IV disease; **OR**
 - Used for recurrent disease (*excluding use in patients with carcinosarcoma*); **OR**
- Used as a single agent as maintenance therapy following treatment with pembrolizumab in combination with carboplatin and paclitaxel

Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Cancer † ‡

^{1,2,4,38,51,110,113-115}

- Patient is at least 6 months of age; **AND**
- Patient has microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors, as determined by an FDA-approved or CLIA compliant test❖; **AND**
- Patient has unresectable or medically inoperable, advanced, recurrent, persistent, or metastatic solid tumors; **AND**
 - Used as a single agent; **AND**
 - Used for disease progression following prior treatment †; **AND**
 - Patient has Colorectal Cancer and was previously treated with a fluoropyrimidine AND either oxaliplatin or irinotecan; **OR**
 - Patient has no satisfactory alternative treatment options; **OR**
 - Used as initial therapy † ‡; **AND**

- Patient has one of the following cancers:
 - Colorectal Cancer
 - Esophagogastric/Gastroesophageal Junction Cancer
 - Gastric Cancer; **OR**
- Used as neoadjuvant therapy ‡; **AND**
 - Patient has Colorectal Cancer; **OR**
- Used in combination with oxaliplatin **AND** either fluorouracil or capecitabine; **AND**
 - Patient has Esophagogastric/Gastroesophageal Junction Cancer; **AND**
 - Used as first-line therapy; **OR**
 - Patient has Gastric Cancer; **AND**
 - Used as first-line therapy

Tumor Mutational Burden-High (TMB-H) Cancer † ‡^{1,2,57}

- Patient is at least 6 months of age; **AND**
- Patient has tumor mutational burden-high (TMB-H) [≥ 10 mutations/megabase (mut/Mb)] solid tumors, as determined by an FDA-approved or CLIA-compliant test ❖; **AND**
- Used as a single agent; **AND**
- Pediatric patients must not have a diagnosis of TMB-H central nervous system cancer; **AND**
- Patient does not have melanoma or non-small cell lung cancer (NSCLC); **AND**
- Patient has unresectable or medically inoperable, advanced, recurrent, persistent, or metastatic solid tumors; **AND**
- Used for disease progression following prior treatment †; **AND**
- Patient has no satisfactory alternative treatment options

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

❖ If confirmed using an FDA-approved assay – <http://www.fda.gov/companiondiagnostics>

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

Ψ ER Scoring Interpretation (following ER testing by validated IHC assay) ¹¹⁶	
Results	Interpretation
– 0% – <1% of nuclei stain	– ER-negative

– 1%–10% of nuclei stain	– ER-low–positive*
– >10% of nuclei stain	– ER-positive

**Note: Invasive cancers with between 1%–10% ER positivity are considered ER-low–positive. However, this group is noted to be heterogeneous and the biologic behavior of ER-low–positive cancers may be more similar to ER-negative cancers. This should be considered in decision making for other adjuvant therapy and overall treatment pathway.*

§ Genomic Aberration/Mutational Driver Targeted Therapies ¹¹ (Note: not all inclusive, refer to guidelines for appropriate use)			
<i>EGFR</i> exon 19 deletion or exon 21 L858R tumors	<i>EGFR</i> S768I, L861Q, and/or G719X mutation positive tumors	<i>EGFR</i> exon 20 insertion mutation positive tumors	<i>NTRK1/2/3</i> gene fusion positive tumors
– Afatinib – Erlotinib – Dacomitinib – Gefitinib – Osimertinib – Amivantamab	– Afatinib – Erlotinib – Dacomitinib – Gefitinib – Osimertinib – Amivantamab	– Amivantamab	– Larotrectinib – Entrectinib
<i>ALK</i> rearrangement-positive tumors	<i>ROS1</i> rearrangement-positive tumors	<i>BRAF</i> V600E-mutation positive tumors	<i>ERBB2 (HER2)</i> mutation positive tumors
– Alectinib – Brigatinib – Ceritinib – Crizotinib – Lorlatinib	– Ceritinib – Crizotinib – Entrectinib – Lorlatinib – Repotrectinib	– Dabrafenib ± trametinib – Encorafenib + binimetinib – Vemurafenib	– Fam-trastuzumab deruxtecan-nxki – Ado-trastuzumab emtansine
PD-L1 tumor expression ≥ 1%	<i>MET</i> exon-14 skipping mutations	<i>RET</i> rearrangement-positive tumors	<i>KRAS G12C</i> mutation positive tumors
– Pembrolizumab – Atezolizumab – Nivolumab + ipilimumab – Cemiplimab – Tremelimumab + durvalumab	– Capmatinib – Crizotinib – Tepotinib	– Selpercatinib – Cabozantinib – Pralsetinib	– Sotorasib – Adagrasib

IV. Renewal Criteria ^{Δ 1-3,5,6,15-17,50,51,53,57,62,65,68,69,70,72,73,75-77,82,85-87,95,101,103,109,112,15e}

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe infusion-related reactions, severe immune-mediated adverse reactions (e.g., pneumonitis, hepatitis, colitis, endocrinopathies, nephritis with renal dysfunction, dermatologic adverse reactions/rash, etc.), hepatotoxicity when used in combination with axitinib, complications of allogeneic hematopoietic stem cell transplantation (HSCT), etc.; **AND**

- For the following indications, patient has not exceeded a maximum of twenty-four (24) months of therapy:
 - Adrenal Gland Tumors
 - Biliary Tract Cancers
 - Bladder Cancer/Urothelial Carcinoma
 - Cervical Cancer
 - Classical Hodgkin Lymphoma (cHL)
 - CNS Cancer
 - Cutaneous Melanoma (in combination with ipilimumab or lenvatinib only)
 - Cutaneous Squamous Cell Carcinoma (cSCC)
 - Endometrial Carcinoma (Uterine Neoplasm)
 - Esophageal Cancer and Esophagogastric/Gastroesophageal Junction Cancer (first-line or subsequent therapy)
 - Gastric Cancer (first-line therapy)
 - Hepatocellular Carcinoma (HCC)
 - Merkel Cell Carcinoma (MCC)
 - MSI-H/dMMR Cancer
 - Non-Small Cell Lung Cancer (NSCLC) (first-line or subsequent therapy)
 - Primary Cutaneous Lymphomas
 - Primary Mediastinal Large B-Cell Lymphoma (PMBCL)
 - Renal Cell Carcinoma (RCC) (first-line or subsequent therapy)
 - Squamous Cell Carcinoma of the Head and Neck (SCCHN)
 - Thymic Carcinoma
 - Thyroid Carcinoma (Anaplastic Carcinoma)
 - Tumor Mutational Burden-High (TMB-H) Cancer
 - Triple Negative Breast Cancer (recurrent unresectable or metastatic disease)

Kaposi Sarcoma

- Coverage may NOT be renewed

NSCLC (adjuvant treatment)

- Patient has not exceeded a maximum of twelve (12) months of therapy

NSCLC (resectable disease)

- Patient has not exceeded a maximum of twelve (12) weeks of neoadjuvant therapy and thirty-nine (39) weeks of adjuvant therapy

NSCLC (continuous maintenance treatment)

- *Refer to Section III for criteria*

Renal Cell Carcinoma (adjuvant treatment)

- Patient has not exceeded a maximum of twelve (12) months of therapy

Triple Negative Breast Cancer (neoadjuvant treatment)

- Patient has not exceeded a maximum of twenty-four (24) weeks of therapy

Triple Negative Breast Cancer (adjuvant treatment)

- Patient has not exceeded a maximum of twenty-seven (27) weeks of therapy

Cutaneous Melanoma (subsequent treatment after prior anti-PD-1 immunotherapy or BRAF/MEK + anti-PD-1 immunotherapy) ‡

- *Refer to Section III for criteria*

Cutaneous Melanoma (neoadjuvant followed by adjuvant therapy)

- Patient has not exceeded a maximum of 8 weeks of neoadjuvant therapy (3 doses), followed by a maximum of 44 weeks (15 doses) of adjuvant therapy

Cutaneous Melanoma (adjuvant treatment, if no previous neoadjuvant pembrolizumab was used or re-induction therapy)

- Patient has not exceeded a maximum of twelve (12) months of therapy

Endometrial Carcinoma (continuous maintenance treatment)

- *Refer to Section III for criteria*

Cervical Cancer (continuous maintenance treatment)

- *Refer to Section III for criteria*

[^] Notes:

- Patients responding to therapy who relapse \geq 6 months after discontinuation due to duration (i.e., receipt of 24 months of therapy) are eligible to re-initiate PD-directed therapy.
- Patients previously presenting with aggressive disease who are exhibiting stable disease on treatment as their best response (or if therapy improved performance status) may be eligible for continued therapy beyond the 24-month limit without interruption or discontinuation.
- Patients who complete adjuvant therapy and progress \geq 6 months after discontinuation are eligible to re-initiate PD-directed therapy for metastatic disease.
- Patients whose tumors, upon re-biopsy, demonstrate a change in actionable mutation (e.g., MSS initial biopsy; MSI-H subsequent biopsy) may be eligible to re-initiate PD-directed therapy and will be evaluated on a case-by-case basis.

- Patients diagnosed with Renal Cell Carcinoma with clear cell histology who have received previous immuno-oncology therapy may be eligible for treatment with pembrolizumab as subsequent therapy and will be evaluated on a case-by-case basis.

V. Dosage/Administration ^Δ 1-6,8,12,13,15-17,22-48,50-57,62,65,68,70,72,73,75-77,82,83,85-87,91,92,95,101,103-106,109,112,15e

Indication	Dose
Biliary Tract Cancers, Bladder Cancer/Urothelial Carcinoma, Cervical, cSCC, Endometrial Carcinoma/ Uterine Neoplasms (excluding MSI-H/dMMR), HCC, Thyroid Carcinoma (Anaplastic) & SCCHN	200 mg intravenously every 3 weeks or 400 mg intravenously every 6 weeks up to a maximum of 24 months in patients without disease progression or unacceptable toxicity <i>*NMIBC treatment may continue up to a maximum of 24 months in patients without persistent or recurrent high-risk disease, disease progression, or unacceptable toxicity.</i>
Esophageal and Esophagogastric/ Gastroesophageal Junction Cancer	<u>First-line or subsequent therapy:</u> 200 mg intravenously every 3 weeks or 400 mg intravenously every 6 weeks up to a maximum of 24 months in patients without disease progression or unacceptable toxicity
Gastric Cancer	<u>First-line therapy:</u> 200 mg intravenously every 3 weeks or 400 mg intravenously every 6 weeks up to a maximum of 24 months in patients without disease progression or unacceptable toxicity
NSCLC	<u>First-line, subsequent, or continuation maintenance therapy:</u> 200 mg intravenously every 3 weeks or 400 mg intravenously every 6 weeks up to a maximum of 24 months in patients without disease progression or unacceptable toxicity <u>Adjuvant treatment of resected NSCLC:</u> 200 mg intravenously every 3 weeks or 400 mg intravenously every 6 weeks up to a maximum of 12 months in patients without disease recurrence or unacceptable toxicity <u>Neoadjuvant and adjuvant treatment of resectable NSCLC:</u> <ul style="list-style-type: none"> • Neoadjuvant therapy: 200 mg intravenously every 3 weeks or 400 mg intravenously every 6 weeks in combination with chemotherapy for 12 weeks or until disease progression that precludes definitive surgery or unacceptable toxicity • Adjuvant therapy: 200 mg intravenously every 3 weeks or 400 mg intravenously every 6 weeks as a single agent after surgery for 39 weeks or until disease recurrence or unacceptable toxicity

RCC	<p><u>First-line or subsequent therapy:</u> 200 mg intravenously every 3 weeks or 400 mg intravenously every 6 weeks up to a maximum of 24 months in patients without disease progression or unacceptable toxicity</p> <p><u>Adjuvant therapy:</u> 200 mg intravenously every 3 weeks or 400 mg intravenously every 6 weeks up to a maximum of 12 months in patients without disease recurrence or unacceptable toxicity</p>
TNBC	<p><u>Recurrent unresectable or metastatic disease:</u> 200 mg intravenously every 3 weeks or 400 mg intravenously every 6 weeks up to a maximum of 24 months in patients without disease progression or unacceptable toxicity</p> <p><u>Neoadjuvant therapy:</u> 200 mg intravenously every 3 weeks or 400 mg intravenously every 6 weeks up to a maximum of 24 weeks in patients without disease progression or unacceptable toxicity (up to 8 doses of 200 mg every 3 weeks or 4 doses of 400 mg every 6 weeks)</p> <p><u>Adjuvant therapy*:</u> 200 mg intravenously every 3 weeks or 400 mg intravenously every 6 weeks up to a maximum of 27 weeks in patients without disease recurrence or unacceptable toxicity (up to 9 doses of 200 mg every 3 weeks or 5 doses of 400 mg every 6 weeks)</p> <p><i>* Patients who experience disease progression or unacceptable toxicity related to KEYTRUDA with neoadjuvant treatment in combination with chemotherapy should not receive adjuvant single agent KEYTRUDA.</i></p>
Adrenal Gland Tumors & Thymic Carcinoma	200 mg intravenously every 3 weeks up to a maximum of 24 months in patients without disease progression or unacceptable toxicity
Cutaneous Melanoma	<p><u>Single-agent therapy (excluding neoadjuvant and adjuvant treatment or re-induction therapy):</u> 200 mg intravenously every 3 weeks or 400 mg intravenously every 6 weeks until disease progression or unacceptable toxicity</p> <p><u>In combination with ipilimumab or lenvatinib:</u> 200 mg intravenously every 3 weeks up to a maximum of 24 months in patients without disease progression or unacceptable toxicity</p> <p><u>Neoadjuvant and adjuvant treatment:</u></p> <ul style="list-style-type: none"> • 200 mg intravenously every 3 weeks for 3 doses in the neoadjuvant setting, followed by surgery and then adjuvant treatment (see below) • 200 mg intravenously every 3 weeks for 15 doses in the adjuvant setting in patients without disease progression or unacceptable toxicity <p><u>Adjuvant treatment (if no neoadjuvant pembrolizumab was used) or re-induction therapy:</u></p>

	<ul style="list-style-type: none"> • <u>Adults:</u> 200 mg intravenously every 3 weeks or 400 mg intravenously every 6 weeks up to a maximum of 12 months in patients without disease recurrence or unacceptable toxicity • <u>Pediatrics:</u> 2 mg/kg (up to 200 mg) intravenously every 3 weeks up to a maximum of 12 months in patients without disease recurrence or unacceptable toxicity
cHL, MCC, MSI-H/dMMR Cancer, PMBCL, & TMB-H Cancer	<p><u>Adults:</u> 200 mg intravenously every 3 weeks or 400 mg intravenously every 6 weeks up to a maximum of 24 months in patients without disease progression or unacceptable toxicity</p> <p><u>Pediatrics:</u> 2 mg/kg (up to 200 mg) intravenously every 3 weeks up to a maximum of 24 months in patients without disease progression or unacceptable toxicity</p>
CNS Cancer	<p><u>Adults:</u> 10 mg/kg intravenously every 2 weeks for up to 24 months in patients without disease progression or unacceptable toxicity</p> <p><u>Pediatrics:</u> 2 mg/kg (up to 200 mg) intravenously every 3 weeks for up to 24 months in patients without disease progression or unacceptable toxicity</p>
Primary Cutaneous Lymphomas	2 mg/kg intravenously every 3 weeks up to a maximum of 24 months in patients without disease progression or unacceptable toxicity
Soft Tissue Sarcoma	200 mg intravenously every 3 weeks
Ovarian, Fallopian Tube, and Primary Peritoneal Cancer	200 mg intravenously every 3 weeks until disease progression or unacceptable toxicity
Kaposi Sarcoma	200 mg intravenously every 3 weeks, up to a maximum of 6 months in patients without unacceptable toxicity

Dosing should be calculated using actual body weight and not flat dosing (as applicable) based on the following:

Weight ≤ 55 kg:

- Use 100 mg IV (2 mg/kg) every 21 days; **OR**
- Use 200 mg IV (4 mg/kg) every 42 days

Weight is ≤ 82.5 kg:

- Use 300 mg IV (4 mg/kg) every 42 days

Note: This information is not meant to replace clinical decision making when initiating or modifying medication therapy and should only be used as a guide. Patient-specific variables should be taken into account.

VI. Billing Code/Availability Information

HCPCS Code:

- J9271 – Injection, pembrolizumab, 1 mg; 1 billable unit = 1 mg

NDC:

- Keytruda 100 mg/4 mL single-dose vial: 00006-3026-xx

VII. References (STANDARD)

1. Keytruda [package insert]. Rahway, NJ; Merck & Co, Inc; June 2024. Accessed June 2024.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) pembrolizumab. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2024.
3. Alley EW, Lopez J, Santoro A, et al. Clinical safety and activity of pembrolizumab in patients with malignant pleural mesothelioma (KEYNOTE-028): preliminary results from a non-randomised, open-label, phase 1b trial. *Lancet Oncol.* 2017 May;18(5):623-630.
4. Ott PA, Bang YJ, Berton-Rigaud D, et al. Safety and Antitumor Activity of Pembrolizumab in Advanced Programmed Death Ligand 1-Positive Endometrial Cancer: Results From the KEYNOTE-028 Study. *J Clin Oncol.* 2017 Aug 1;35(22):2535-2541.
5. Ott PA, Piha-Paul SA, Munster P, et al. Safety and antitumor activity of the anti-PD-1 antibody pembrolizumab in patients with recurrent carcinoma of the anal canal. *Ann Oncol.* 2017 May 1;28(5):1036-1041. Doi: 10.1093/annonc/mdx029.
6. Zinzani PL, Ribrag V, Moskowitz CH, et al. Safety and tolerability of pembrolizumab in patients with relapsed/refractory primary mediastinal large B-cell lymphoma. *Blood.* 2017 Jul 20;130(3):267-270. Doi: 10.1182/blood-2016-12-758383. Epub 2017 May 10.
7. U.S. Food and Drug Administrations (FDA). Division of Drug Information. Health Alert. <https://www.fda.gov/drugs/drug-safety-and-availability/fda-alerts-health-care-professionals-and-oncology-clinical-investigators-about-efficacy-issue>. Accessed August 2018
8. Balar AV, Castellano D, O'Donnell PH, et al. First-line pembrolizumab in cisplatin-ineligible patients with locally advanced and unresectable or metastatic urothelial cancer (KEYNOTE-052): a multicenter, single-arm, phase 2 study. *Lancet Oncol* 2017; 18: 1483–92.
9. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Merkel Cell Carcinoma. Version 1.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®.

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10. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Bladder Cancer. Version 4.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2024.
11. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Non-Small Cell Lung Cancer. Version 6.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2024.
12. Ghorani E, Kaur B, Fisher RA, et al. Pembrolizumab is effective for drug-resistant gestational trophoblastic neoplasia. *Lancet*. 2017 Nov 25;390(10110):2343-2345.
13. Chung HC, Lopez-Martin JA, Kao S, et al. Phase 2 study of pembrolizumab in advanced small-cell lung cancer (SCLC): KEYNOTE-158. *J Clin Oncol* 2018;36: Abstract 8506
14. National Institutes of Health. Study of Pembrolizumab (MK-3475) Versus Placebo After Complete Resection of High-Risk Stage III Melanoma (MK-3475-054/KEYNOTE-054). Available at: <http://clinicaltrials.gov/show/NCT02362594>.
15. Khodadoust M, Rook AH, Porcu P, et al. Pembrolizumab in Relapsed and Refractory Mucocutaneous Mycosis Fungoides and Sézary Syndrome: A Multicenter Phase II Study. *J Clin Oncol*. 2020 Jan 1;38(1):20-28. Doi: 10.1200/JCO.19.01056. Epub 2019 Sep 18.
16. Giaccone, G, Kim C, Thompson J, et al. Pembrolizumab in patients with thymic carcinoma: a single-arm, single-centre, phase 2 study. *Lancet*. Volume 19, ISSUE 3, P347-355, March 01, 2018.
17. Cho J, Kim HS, Ku BM, et al. Pembrolizumab for Patients With Refractory or Relapsed Thymic Epithelial Tumor: An Open-Label Phase II Trial. *J Clin Oncol*. 2018 Jun 15;36(24):2673-2680. Doi: 10.1200/JCO.2017.77.3184. [Epub ahead of print]
18. Gupta S, Sonpavde G, Grivas P, et al. Defining “platinum-ineligible” patients with metastatic urothelial cancer (mUC). *J Clin Oncol*. 2019 Mar 1;37(7_suppl):451.
19. Fahrenbruch R, Kintzel P, Bott AM, et al. Dose Rounding of Biologic and Cytotoxic Anticancer Agents: A Position Statement of the Hematology/Oncology Pharmacy Association. *J Oncol Pract*. 2018 Mar;14(3):e130-e136.
20. Hematology/Oncology Pharmacy Association (2019). Intravenous Cancer Drug Waste Issue Brief. Retrieved from http://www.hoparx.org/images/hopa/advocacy/Issue-Briefs/Drug_Waste_2019.pdf

21. Bach PB, Conti RM, Muller RJ, et al. Overspending driven by oversized single dose vials of cancer drugs. *BMJ*. 2016 Feb 29;352:i788.
22. Schachter J, Ribas A, Long GV, et al. Pembrolizumab versus ipilimumab for advanced melanoma: final overall survival results of a multicentre, randomised, open-label phase 3 study (KEYNOTE-006). *Lancet*. 2017 Oct 21;390(10105):1853-1862. Doi: 10.1016/S0140-6736(17)31601-X. Epub 2017 Aug 16.
23. Ribas A, Puzanov I, Dummer R, et al. Pembrolizumab versus investigator-choice chemotherapy for ipilimumab-refractory melanoma (KEYNOTE-002): a randomised, controlled, phase 2 trial. *Lancet Oncol*. 2015 Aug;16(8):908-18. Doi: 10.1016/S1470-2045(15)00083-2. Epub 2015 Jun 23.
24. Eggermont AMM, Blank CU, Mandalá M, et al. Adjuvant Pembrolizumab versus Placebo in Resected Stage III Melanoma. *N Engl J Med*. 2018 May 10;378(19):1789-1801. Doi: 10.1056/NEJMoa1802357. Epub 2018 Apr 15.
25. Gandhi L, Rodríguez-Abreu D, Gadgeel S, et al. Pembrolizumab plus Chemotherapy in Metastatic Non-Small-Cell Lung Cancer. *N Engl J Med*. 2018 May 31;378(22):2078-2092. Doi: 10.1056/NEJMoa1801005. Epub 2018 Apr 16.
26. Paz-Ares L, Luft A, Vicente D, et al. Pembrolizumab plus Chemotherapy for Squamous Non-Small-Cell Lung Cancer. *N Engl J Med*. 2018 Nov 22;379(21):2040-2051. Doi: 10.1056/NEJMoa1810865. Epub 2018 Sep 25.
27. Mok TSK, Wu YL, Kudaba I, et al. Pembrolizumab versus chemotherapy for previously untreated, PD-L1-expressing, locally advanced or metastatic non-small-cell lung cancer (KEYNOTE-042): a randomised, open-label, controlled, phase 3 trial. *Lancet*. 2019 May 4;393(10183):1819-1830. Doi: 10.1016/S0140-6736(18)32409-7. Epub 2019 Apr 4.
28. Reck M, Rodríguez-Abreu D, Robinson AG, et al. Pembrolizumab versus Chemotherapy for PD-L1-Positive Non-Small-Cell Lung Cancer. *N Engl J Med*. 2016 Nov 10;375(19):1823-1833. Epub 2016 Oct 8.
29. Herbst RS, Baas P, Kim DW, et al. Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small-cell lung cancer (KEYNOTE-010): a randomised controlled trial. *Lancet*. 2016 Apr 9;387(10027):1540-1550. Doi: 10.1016/S0140-6736(15)01281-7. Epub 2015 Dec 19.
30. Ott PA, Elez E, Hirt S, et al. Pembrolizumab in Patients With Extensive-Stage Small-Cell Lung Cancer: Results From the Phase Ib KEYNOTE-028 Study. *J Clin Oncol*. 2017 Dec 1;35(34):3823-3829. Doi: 10.1200/JCO.2017.72.5069. Epub 2017 Aug 16.
31. Burtneß B, Harrington KJ, Greil R, et al. Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study. *Lancet*. 2019 Nov 23;394(10212):1915-1928. Doi: 10.1016/S0140-6736(19)32591-7. Epub 2019 Nov 1.
32. Chow LQM, Haddad R, Gupta S, et al. Antitumor Activity of Pembrolizumab in Biomarker-Unselected Patients With Recurrent and/or Metastatic Head and Neck Squamous Cell

- Carcinoma: Results From the Phase Ib KEYNOTE-012 Expansion Cohort. Antitumor Activity of Pembrolizumab in Biomarker-Unselected Patients With Recurrent and/or Metastatic Head and Neck Squamous Cell Carcinoma: Results From the Phase Ib KEYNOTE-012 Expansion Cohort.
33. Chen R, Zinzani PL, Fanale MA, et al. Phase II Study of the Efficacy and Safety of Pembrolizumab for Relapsed/Refractory Classic Hodgkin Lymphoma. *J Clin Oncol*. 2017 Jul 1;35(19):2125-2132. Doi: 10.1200/JCO.2016.72.1316. Epub 2017 Apr 25.
 34. Armand P, Rodig S, Melnichenko V, et al. Pembrolizumab in Relapsed or Refractory Primary Mediastinal Large B-Cell Lymphoma. *J Clin Oncol*. 2019 Dec 1;37(34):3291-3299. Doi: 10.1200/JCO.19.01389. Epub 2019 Oct 14.
 35. Powles T, Gschwend JE, Loriot Y, et al. Phase 3 KEYNOTE-361 trial: Pembrolizumab (pembro) with or without chemotherapy versus chemotherapy alone in advanced urothelial cancer. DOI: 10.1200/JCO.2017.35.15_suppl.TPS4590 *Journal of Clinical Oncology* 35, no. 15_suppl. Published online May 30, 2017.
 36. Bellmunt J, de Wit R, Vaughn DJ, et al. Pembrolizumab as Second-Line Therapy for Advanced Urothelial Carcinoma. *N Engl J Med*. 2017 Mar 16;376(11):1015-1026. Doi: 10.1056/NEJMoa1613683. Epub 2017 Feb 17.
 37. Balar AV, Kulkarni GS, Uchio, EM, et al. Keynote 057: Phase II trial of Pembrolizumab (pembro) for patients (pts) with high-risk (HR) nonmuscle invasive bladder cancer (NMIBC) unresponsive to bacillus calmette-guérin (BCG). DOI: 10.1200/JCO.2019.37.7_suppl.350 *Journal of Clinical Oncology* 37, no. 7_suppl (March 01, 2019) 350-350. Published online February 26, 2019.
 38. Le DT, Kim TW, Van Cutsem E, et al. Phase II Open-Label Study of Pembrolizumab in Treatment-Refractory, Microsatellite Instability-High/Mismatch Repair-Deficient Metastatic Colorectal Cancer: KEYNOTE-164. *J Clin Oncol*. 2020 Jan 1;38(1):11-19. Doi: 10.1200/JCO.19.02107. Epub 2019 Nov 14.
 39. Fuchs CS, Doi T, Jang RW, et al. Safety and Efficacy of Pembrolizumab Monotherapy in Patients With Previously Treated Advanced Gastric and Gastroesophageal Junction Cancer: Phase 2 Clinical KEYNOTE-059 Trial. *JAMA Oncol*. 2018 May 10;4(5):e180013. Doi: 10.1001/jamaoncol.2018.0013. Epub 2018 May 10.
 40. Kojima T, Muro K, Francois E, et al. Pembrolizumab versus chemotherapy as second-line therapy for advanced esophageal cancer: Phase III KEYNOTE-181 study. DOI: 10.1200/JCO.2019.37.4_suppl.2 *Journal of Clinical Oncology* 37, no. 4_suppl (February 01, 2019) 2-2. Published online January 29, 2019.
 41. Shah M, Kojima T, Hochhauser D, et al. Efficacy and Safety of Pembrolizumab for Heavily Pretreated Patients With Advanced, Metastatic Adenocarcinoma or Squamous Cell Carcinoma of the Esophagus: The Phase 2 KEYNOTE-180 Study. *JAMA Oncol* .550-546:(4)5;2019 . Doi:10.1001/jamaoncol.2018.5441.

42. Chung HC, Ros W, Delord JP, et al. Efficacy and Safety of Pembrolizumab in Previously Treated Advanced Cervical Cancer: Results From the Phase II KEYNOTE-158 Study. *J Clin Oncol*. 2019 Jun 10;37(17):1470-1478. Doi: 10.1200/JCO.18.01265. Epub 2019 Apr 3.
43. Zhu AX, Finn RS, Edeline J, et al. Pembrolizumab in patients with advanced hepatocellular carcinoma previously treated with sorafenib (KEYNOTE-224): a non-randomised, open-label phase 2 trial. *Lancet Oncol*. 2018 Jul;19(7):940-952. Doi: 10.1016/S1470-2045(18)30351-6. Epub 2018 Jun 3.
44. Nghiem P, Bhatia S, Lipson EJ, et al. Durable Tumor Regression and Overall Survival in Patients With Advanced Merkel Cell Carcinoma Receiving Pembrolizumab as First-Line Therapy. *J Clin Oncol*. 2019 Mar 20;37(9):693-702. Doi: 10.1200/JCO.18.01896. Epub 2019 Feb 6.
45. Rini BI, Plimack ER, Stus V, et al. Pembrolizumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2019 Mar 21;380(12):1116-1127. Doi: 10.1056/NEJMoa1816714. Epub 2019 Feb 16.
46. Makker V, Taylor MH, Aghajanian C, et al. Lenvatinib (LEN) and pembrolizumab (PEMBRO) in advanced endometrial cancer (EC). *Annals of Oncology*, Volume 30, Issue Supplement_5, October 2019, MDZ250.002, <https://doi.org/10.1093/annonc/mdz250.002>.
47. Goldberg SB, Gettinger SN, Mahajan A, et al. Pembrolizumab for patients with melanoma or non-small-cell lung cancer and untreated brain metastases: early analysis of a non-randomised, open-label, phase 2 trial. *Lancet Oncol*. 2016 Jul;17(7):976-983. Doi: 10.1016/S1470-2045(16)30053-5. Epub 2016 Jun 3.
48. Kwong YL, Chan TSY, Tan D, et al. PD1 blockade with pembrolizumab is highly effective in relapsed or refractory NK/T-cell lymphoma failing l-asparaginase. *Blood*. 2017 Apr 27;129(17):2437-2442. Doi: 10.1182/blood-2016-12-756841. Epub 2017 Feb 10.
49. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Central Nervous System Cancers. Version 1.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2024.
50. Kluger HM, Chiang V, Mahajan A, et al. Long-Term Survival of Patients With Melanoma With Active Brain Metastases Treated With Pembrolizumab on a Phase II Trial. *J Clin Oncol*. 2019 Jan 1;37(1):52-60. doi: 10.1200/JCO.18.00204. Epub 2018 Nov 8.
51. Marabelle A, Le DT, Ascierto PA, et al. Efficacy of Pembrolizumab in Patients With Noncolorectal High Microsatellite Instability/Mismatch Repair-Deficient Cancer: Results From the Phase II KEYNOTE-158 Study. *J Clin Oncol*. 2020 Jan 1;38(1):1-10. doi: 10.1200/JCO.19.02105. Epub 2019 Nov 4.
52. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Anal Carcinoma. Version 1.2024. National Comprehensive Cancer Network,

2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2024.
53. Kottschade LA, McWilliams RR, Markovic SN, et al. The Use of Pembrolizumab for the Treatment of Metastatic Uveal Melanoma. *Melanoma Res.* 2016 Jun;26(3):300-3. doi: 10.1097/CMR.0000000000000242.
54. Algazi AP, Tsai KK, Shoushtari AN, et al. Clinical Outcomes in Metastatic Uveal Melanoma Treated With PD-1 and PD-L1 Antibodies. *Cancer.* 2016 Nov 15;122(21):3344-3353. doi: 10.1002/cncr.30258.
55. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Gestational Trophoblastic Neoplasia. Version 1.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2024.
56. Burgess MA, Bolejack V, Van Tine BA, et al. Multicenter phase II study of pembrolizumab (P) in advanced soft tissue (STS) and bone sarcomas (BS): Final results of SARCO28 and biomarker analyses. *J Clin Oncol* 2017; 35, no. 15_suppl (May 20, 2017) 11008-11008.
57. Marabelle A, Fakih M, Lopez J, et al. Association of Tumor Mutational Burden with Outcomes in Patients with Select Advanced Solid Tumors Treated with Pembrolizumab in KEYNOTE-158. *Ann Oncol.* 2019;30(suppl_5):v475-v532. doi: 10.1093/annonc/mdz253.
58. Grob JJ, Gonzalez R, Basset-Seguin N, et al. Pembrolizumab Monotherapy for Recurrent or Metastatic Cutaneous Squamous Cell Carcinoma: A Single-Arm Phase II Trial (KEYNOTE-629). *J Clin Oncol.* 2020 Sep 1;38(25):2916-2925. doi: 10.1200/JCO.19.03054.
59. Andre T, Shiu KK, Kim TW, et al. Pembrolizumab versus chemotherapy for microsatellite instability-high/mismatch repair deficient metastatic colorectal cancer: The phase 3 KEYNOTE-177 Study. *J Clin Oncol.* 2020;38(18_suppl):LBA4-LBA4.
60. Georger B, Kang HJ, Yalon-Oren M, et al. Pembrolizumab in paediatric patients with advanced melanoma or a PD-L1-positive, advanced, relapsed, or refractory solid tumour or lymphoma (KEYNOTE-051): interim analysis of an open-label, single-arm, phase 1-2 trial. *Lancet Oncol.* 2020;21(1):121-133. doi:10.1016/S1470-2045(19)30671-0.
61. Pembrolizumab Improves Progression-Free Survival in Relapsed/Refractory Hodgkin Lymphoma. *Oncologist.* 2020;25 Suppl 1(Suppl 1):S18-S19. doi:10.1634/theoncologist.2020-0561.
62. Raj N, Zheng Y, Kelly V, et al. PD-1 Blockade in Advanced Adrenocortical Carcinoma. *J Clin Oncol.* 2020 Jan 1;38(1):71-80. doi: 10.1200/JCO.19.01586.

63. Naing A, Meric-Bernstam F, Stephen B, et al. Phase 2 study of pembrolizumab in patients with advanced rare cancers [published correction appears in *J Immunother Cancer*. 2020 Apr;8(1):]. *J Immunother Cancer*. 2020;8(1):e000347. doi:10.1136/jitc-2019-000347.
64. Cortes J, Cescon DW, Rugo HS, et al. KEYNOTE-355: Randomized, double-blind, phase III study of pembrolizumab + chemotherapy versus placebo + chemotherapy for previously untreated locally recurrent inoperable or metastatic triple-negative breast cancer. *Journal of Clinical Oncology* 38, no. 15_suppl(May 20, 2020)1000-1000.
65. Olson D, Luke JJ, Poklepovic AS, et al. Significant antitumor activity for low-dose ipilimumab (IPI) with pembrolizumab (PEMBRO) immediately following progression on PD1 Ab in melanoma (MEL) in a phase II trial. *J Clin Oncol* 2020;38(15_suppl): abstract 10004.
66. Kato K, Shah MA, Enzinger P, et al. KEYNOTE-590: Phase III study of first-line chemotherapy with or without pembrolizumab for advanced esophageal cancer. *Future Oncol*. 2019 Apr;15(10):1057-1066. doi: 10.2217/fon-2018-0609.
67. Chung HC, Bang YJ, S Fuchs C, et al. First-line pembrolizumab/placebo plus trastuzumab and chemotherapy in HER2-positive advanced gastric cancer: KEYNOTE-811. *Future Oncol*. 2021 Feb;17(5):491-501. doi: 10.2217/fon-2020-0737.
68. Carlino MS, Menzies AM, Atkinson V, et al. Long-term Follow-up of Standard-Dose Pembrolizumab Plus Reduced-Dose Ipilimumab in Patients with Advanced Melanoma: KEYNOTE-029 Part 1B. *Clin Cancer Res*. 2020 Oct 1;26(19):5086-5091. doi: 10.1158/1078-0432.CCR-20-0177.
69. Schmid P, Cortes J, Puztai L, et al. Pembrolizumab for Early Triple-Negative Breast Cancer. *N Engl J Med*. 2020 Feb 27;382(9):810-821. doi: 10.1056/NEJMoa1910549.
70. Colombo N, Dubot C, Lorusso D, et al. Pembrolizumab for Persistent, Recurrent, or Metastatic Cervical Cancer. *N Engl J Med*. 2021 Sep 18. doi: 10.1056/NEJMoa2112435.
71. Bellmunt, J. (2023). Treatment of metastatic urothelial cancer of the bladder and urinary tract. In Lerner SP, Shah S (Eds.), *UptoDate*. Last updated: December 19, 2023. Accessed January 17, 2024. Available from https://www.uptodate.com/contents/treatment-of-metastatic-urothelial-cancer-of-the-bladder-and-urinary-tract?search=cisplatin%20ineligible&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1.
72. Chung HC, Piha-Paul SA, Lopez-Martin J, et al. Pembrolizumab After Two or More Lines of Previous Therapy in Patients With Recurrent or Metastatic SCLC: Results From the KEYNOTE-028 and KEYNOTE-158 Studies. *J Thorac Oncol*. 2020 Apr;15(4):618-627. doi: 10.1016/j.jtho.2019.12.109. Epub 2019 Dec 20.
73. Ott PA, Elez E, Hirt S, et al. Pembrolizumab in Patients With Extensive-Stage Small-Cell Lung Cancer: Results From the Phase Ib KEYNOTE-028 Study. *J Clin Oncol*. 2017 Dec 1;35(34):3823-3829. doi: 10.1200/JCO.2017.72.5069. Epub 2017 Aug 16.

74. Motzer R, Alekseev B, Rha SY, et al; CLEAR Trial Investigators. Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma. *N Engl J Med*. 2021 Apr 8;384(14):1289-1300. doi: 10.1056/NEJMoa2035716.
75. McKay RR, Bossé D, Xie W, et al. The Clinical Activity of PD-1/PD-L1 Inhibitors in Metastatic Non-Clear Cell Renal Cell Carcinoma. *Cancer Immunol Res*. 2018 Jul;6(7):758-765. doi: 10.1158/2326-6066.CIR-17-0475.
76. McDermott DF, Lee JL, Ziobro M, et al. Open-Label, Single-Arm, Phase II Study of Pembrolizumab Monotherapy as First-Line Therapy in Patients With Advanced Non-Clear Cell Renal Cell Carcinoma. *J Clin Oncol*. 2021 Mar 20;39(9):1029-1039. doi: 10.1200/JCO.20.02365.
77. Habra MA, Stephen B, Campbell M, et al. Phase II clinical trial of pembrolizumab efficacy and safety in advanced adrenocortical carcinoma. *J Immunother Cancer*. 2019 Sep 18;7(1):253. doi: 10.1186/s40425-019-0722-x.
78. Choueiri TK, Tomczak P, Park SH, et al; KEYNOTE-564 Investigators. Adjuvant Pembrolizumab after Nephrectomy in Renal-Cell Carcinoma. *N Engl J Med*. 2021 Aug 19;385(8):683-694. doi: 10.1056/NEJMoa2106391.
79. Gupta S, Bellmunt J, Plimack ER, et al. Defining “platinum-ineligible” patients with metastatic urothelial cancer (mUC). *J Clin Oncol*. 2022 June 1;40(16_suppl):4577.
80. Makker V, Colombo N, Casado Herráez A, et al; Study 309-KEYNOTE-775 Investigators. Lenvatinib plus Pembrolizumab for Advanced Endometrial Cancer. *N Engl J Med*. 2022 Feb 3;386(5):437-448. doi: 10.1056/NEJMoa2108330. Epub 2022 Jan 19.
81. Cacciotti C, Choi J, Alexandrescu S, et al. Immune checkpoint inhibition for pediatric patients with recurrent/refractory CNS tumors: a single institution experience. *J Neurooncol*. 2020 Aug;149(1):113-122. doi: 10.1007/s11060-020-03578-6. Epub 2020 Jul 5. PMID: 32627129
82. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium[®]) Pediatric Aggressive Mature B-Cell Lymphomas. Version 1.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium[®] is a derivative work of the NCCN Guidelines[®]. NATIONAL COMPREHENSIVE CANCER NETWORK[®], NCCN[®], and NCCN GUIDELINES[®] are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2024.
83. Wilky BA, Trucco MM, Subhawong TK, et al. Axitinib plus pembrolizumab in patients with advanced sarcomas including alveolar soft-part sarcoma: a single-centre, single-arm, phase 2 trial. *Lancet Oncol*. 2019 Jun;20(6):837-848. doi: 10.1016/S1470-2045(19)30153-6.
84. O'Brien M, Paz-Ares L, Marreaud S, et al; EORTC-1416-LCG/ETOP 8-15 – PEARLS/KEYNOTE-091 Investigators. Pembrolizumab versus placebo as adjuvant therapy for completely resected stage IB-IIIa non-small-cell lung cancer (PEARLS/KEYNOTE-091): an interim analysis of a randomised, triple-blind, phase 3 trial. *Lancet Oncol*. 2022 Oct;23(10):1274-1286. doi: 10.1016/S1470-2045(22)00518-6.

85. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Kaposi Sarcoma. Version 1.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2024.
86. Delyon J, Biard L, Renaud M, et al. PD-1 blockade with pembrolizumab in classic or endemic Kaposi's sarcoma: a multicentre, single-arm, phase 2 study. *Lancet Oncol*. 2022 Apr;23(4):491-500. doi: 10.1016/S1470-2045(22)00097-3.
87. Arance AM, de la Cruz-Merino L, Petrella TM, et al. Lenvatinib (len) plus pembrolizumab (pembro) for patients (pts) with advanced melanoma and confirmed progression on a PD-1 or PD-L1 inhibitor: Updated findings of LEAP-004. *Journal of Clinical Oncology* 2021 39:15_suppl, 9504-9504.
88. Hoimes CJ, Petrylak DP, Flaig TW, et al. EV-103 study: A phase 1b dose-escalation and dose-expansion study of enfortumab vedotin in combination with immune checkpoint inhibitor (CPI) therapy for treatment of patients with locally advanced or metastatic urothelial cancer. *Journal of Clinical Oncology* 2018 36:6_suppl, TPS532-TPS532.
89. Groisberg R, Hong DS, Behrang A, et al. Characteristics and outcomes of patients with advanced sarcoma enrolled in early phase immunotherapy trials. *J Immunother Cancer*. 2017 Dec 19;5(1):100. doi: 10.1186/s40425-017-0301-y.
90. Florou V, Rosenberg AE, Wieder E, et al. Angiosarcoma patients treated with immune checkpoint inhibitors: a case series of seven patients from a single institution. *J Immunother Cancer*. 2019 Aug 8;7(1):213. doi: 10.1186/s40425-019-0689-7.
91. Eskander R, Sill M, Beffa L, et al. Pembrolizumab plus Chemotherapy in Advanced Endometrial Cancer. *N Engl J Med* 2023; 388:2159-2170 DOI: 10.1056/NEJMoa2302312.
92. Marabelle A, Cassier PA, Fakih M, et al. Pembrolizumab for previously treated advanced anal squamous cell carcinoma: results from the non-randomised, multicohort, multicentre, phase 2 KEYNOTE-158 study. *Lancet Gastroenterol Hepatol*. 2022 May;7(5):446-454. doi: 10.1016/S2468-1253(21)00382-4.
93. Hoimes CJ, Flaig TW, Milowsky MI, et al. Enfortumab Vedotin Plus Pembrolizumab in Previously Untreated Advanced Urothelial Cancer. *J Clin Oncol*. 2023 Jan 1;41(1):22-31. doi: 10.1200/JCO.22.01643.
94. Kelley RK, Ueno M, Yoo C, et al; KEYNOTE-966 Investigators. Pembrolizumab in combination with gemcitabine and cisplatin compared with gemcitabine and cisplatin alone for patients with advanced biliary tract cancer (KEYNOTE-966): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2023 Jun 3;401(10391):1853-1865.
95. Ludford K, Ho WJ, Thomas JV, et al. Neoadjuvant pembrolizumab in localized microsatellite instability high/deficient mismatch repair solid tumors. *J Clin Oncol* 2023;41:2181-2190.

96. Bryan LJ, Casulo C, Allen PB, et al. Pembrolizumab added to ifosfamide, carboplatin, and etoposide chemotherapy for relapsed or refractory classic Hodgkin lymphoma: A multi-institutional phase 2 investigator-initiated nonrandomized clinical trial. *JAMA Oncol* 2023;9:683-691.
97. Moskowitz AJ, Shah G, Schöder H, et al. Phase II trial of pembrolizumab plus gemcitabine, vinorelbine, and liposomal doxorubicin as second-line therapy for relapsed or refractory classical Hodgkin lymphoma. *J Clin Oncol* 2021;39:3109-3117
98. Rha SY, Oh DY, Yañez P, et al. Pembrolizumab plus chemotherapy versus placebo plus chemotherapy for HER2-negative advanced gastric cancer (KEYNOTE-859): a multicentre, randomised, double-blind, phase 3 trial. *Lancet*. 2023 Oct 21; 24(11):1181-1195.
99. Hoimes CJ, Petrylak DP, Flaig TW, et al. EV-103 study: A phase 1b dose-escalation and dose-expansion study of enfortumab vedotin in combination with immune checkpoint inhibitor (CPI) therapy for treatment of patients with locally advanced or metastatic urothelial cancer. *Journal of Clinical Oncology* 36, no. 6_suppl. DOI: 10.1200/JCO.2018.36.6_suppl.TPS532.
100. Lorusso D, Colombo N, Coleman RL, et al., ENGOT-cx11/KEYNOTE-A18: A phase III, randomized, double-blind study of pembrolizumab with chemoradiotherapy in patients with high-risk locally advanced cervical cancer. *JCO* 38, TPS6096-TPS6096(2020). DOI:10.1200/JCO.2020.38.15_suppl.TPS6096.
101. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Esophageal and Esophagogastric Junction Cancers. Version 3.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2024.
102. Metges JP, Kato K, Sun JM, et al. First-line pembrolizumab plus chemotherapy versus chemotherapy in advanced esophageal cancer: Longer-term efficacy, safety, and quality-of-life results from the phase 3 KEYNOTE-590 study. *JCO* 40, 241-241(2022). DOI:10.1200/JCO.2022.40.4_suppl.241.
103. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Gastric Cancer. Version 2.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2024.
104. Zsiros E, Lynam S, Attwood KM, et al. Efficacy and Safety of Pembrolizumab in Combination With Bevacizumab and Oral Metronomic Cyclophosphamide in the Treatment of Recurrent Ovarian

- Cancer: A Phase 2 Nonrandomized Clinical Trial. *JAMA Oncol.* 2021 Jan 1;7(1):78-85. doi: 10.1001/jamaoncol.2020.5945. PMID: 33211063; PMCID: PMC7677872.
105. Poblete S, Caulkins M, Loecher C, et al. Pembrolizumab in combination with bevacizumab and oral metronomic cyclophosphamide for recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer: Real-life clinical experience [abstract]. *Ann Oncol* 2022;33(Suppl): Abstract 569P. DOI:<https://doi.org/10.1016/j.annonc.2022.07.697>.
106. Sacco AG, Chen R, Worden FP, et al. Pembrolizumab plus cetuximab in patients with recurrent or metastatic head and neck squamous cell carcinoma: an open-label, multi-arm, non-randomised, multicentre, phase 2 trial. *Lancet Oncol.* 2021 Jun;22(6):883-892. doi: 10.1016/S1470-2045(21)00136-4. Epub 2021 May 11. PMID: 33989559.
107. Qin S, Chen Z, Fang W, et al. Pembrolizumab Versus Placebo as Second-Line Therapy in Patients From Asia With Advanced Hepatocellular Carcinoma: A Randomized, Double-Blind, Phase III Trial. *J Clin Oncol.* 2023 Mar 1;41(7):1434-1443. doi: 10.1200/JCO.22.00620. Epub 2022 Dec 1. PMID: 36455168; PMCID: PMC9995104.
108. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Thyroid Carcinoma. Version 2.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to [NCCN.org](https://www.nccn.org). Accessed June 2024.
109. Dierks C, et al. Phase II ATLEP trial: final results for lenvatinib/pembrolizumab in metastasized anaplastic and poorly differentiated thyroid carcinoma. *Ann Oncol* 2022;33(Suppl S7):S750-S757. doi:10.1016/annonc/annonc1077
110. Ludford K, Ho WJ, Thomas JV, et al. Neoadjuvant pembrolizumab in localized microsatellite instability high/deficient mismatch repair solid tumors. *J Clin Oncol* 2023;41:2181-2190.
111. Powles T, Valderrama B, Gupta S, et al. Enfortumab Vedotin and Pembrolizumab in Untreated Advanced Urothelial Cancer. *N Engl J Med* 2024;390:875-888
112. Patel SP, Othus M, Chen Y, et al. Neoadjuvant-adjuvant or adjuvant-only pembrolizumab in advanced melanoma. *N Engl J Med* 2023;388:813-823
113. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Small Bowel Adenocarcinoma. Version 3.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to [NCCN.org](https://www.nccn.org). Accessed June 2024.
114. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Rectal Cancer. Version 2.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL

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115. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Colon Cancer. Version 3.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2024.
116. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Invasive Breast Cancer. Version 2.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2024.

VIII. References (ENHANCED)

- 1e. Robert C, Schachter J, Long GV, et al. Pembrolizumab versus Ipilimumab in Advanced Melanoma. *N Engl J Med*. 2015 Jun 25;372(26):2521-32. doi: 10.1056/NEJMoa1503093.
- 2e. Robert C, Long GV, Brady B, et al. Nivolumab in previously untreated melanoma without BRAF mutation. *N Engl J Med*. 2015 Jan 22;372(4):320-30. doi: 10.1056/NEJMoa1412082.
- 3e. Ascierto PA, Long GV, Robert C, et al. Survival Outcomes in Patients With Previously Untreated BRAF Wild-Type Advanced Melanoma Treated With Nivolumab Therapy: Three-Year Follow-up of a Randomized Phase 3 Trial [published correction appears in *JAMA Oncol*. 2019 Feb 1;5(2):271]. *JAMA Oncol*. 2019;5(2):187–194. doi:10.1001/jamaoncol.2018.4514.
- 4e. Larkin J, Chiarion-Sileni V, Gonzalez R, et al. Combined Nivolumab and Ipilimumab or Monotherapy in Untreated Melanoma [published correction appears in *N Engl J Med*. 2018 Nov 29;379(22):2185]. *N Engl J Med*. 2015;373(1):23–34. doi:10.1056/NEJMoa1504030.
- 5e. Wolchok JD, Chiarion-Sileni V, Gonzalez R, et al. Overall Survival with Combined Nivolumab and Ipilimumab in Advanced Melanoma [published correction appears in *N Engl J Med*. 2018 Nov 29;379(22):2185]. *N Engl J Med*. 2017;377(14):1345–1356. doi:10.1056/NEJMoa1709684.
- 6e. Hamid O, Puzanov I, Dummer R, et al. Final analysis of a randomised trial comparing pembrolizumab versus investigator-choice chemotherapy for ipilimumab-refractory advanced melanoma. *Eur J Cancer*. 2017 Nov;86:37-45. doi: 10.1016/j.ejca.2017.07.022.
- 7e. Hodi FS, O'Day SJ, McDermott DF, et al. Improved survival with ipilimumab in patients with metastatic melanoma [published correction appears in *N Engl J Med*. 2010 Sep 23;363(13):1290]. *N Engl J Med*. 2010;363(8):711–723. doi:10.1056/NEJMoa1003466.

- 8e. Larkin J, Minor D, D'Angelo S, et al. Overall Survival in Patients With Advanced Melanoma Who Received Nivolumab Versus Investigator's Choice Chemotherapy in CheckMate 037: A Randomized, Controlled, Open-Label Phase III Trial. *J Clin Oncol*. 2018;36(4):383–390. doi:10.1200/JCO.2016.71.8023.
- 9e. Hersh EM, O'Day SJ, Ribas A, et al. A phase 2 clinical trial of nab-paclitaxel in previously treated and chemotherapy-naive patients with metastatic melanoma. *Cancer*. 2010 Jan 1;116(1):155–63.
- 10e. Kottschade LA, Suman VJ, Amatruda T 3rd, et al. A phase II trial of nab-paclitaxel (ABI-007) and carboplatin in patients with unresectable stage IV melanoma: a North Central Cancer Treatment Group Study, N057E(1). *Cancer*. 2011 Apr 15;117(8):1704–10.
- 11e. Agarwala SS, et al. Randomized phase III study of paclitaxel plus carboplatin with or without sorafenib as second-line treatment in patients with advanced melanoma. *Journal of Clinical Oncology* 2007 25:18_suppl, 8510-8510.
- 12e. Rao RD, et al. Combination of paclitaxel and carboplatin as second-line therapy for patients with metastatic melanoma. *Cancer*. 2006 Jan 15;106(2):375–82.
- 13e. Middleton MR, et al. Randomized phase III study of temozolomide versus dacarbazine in the treatment of patients with advanced metastatic malignant melanoma. *J Clin Oncol*. 2000 Jan;18(1):158–66.
- 14e. Einzig AI, et al. A phase II study of taxol in patients with malignant melanoma. *Invest New Drugs*. 1991 Feb;9(1):59–64.
- 15e. Robert C, Ribas A, Schachter J, et al. Pembrolizumab versus ipilimumab in advanced melanoma (KEYNOTE-006): post-hoc 5-year results from an open-label, multicentre, randomised, controlled, phase 3 study. *Lancet Oncol* 2019; 20:1239.
- 16e. Eggermont AM, Chiarion-Sileni V, Grob JJ, et al. Prolonged Survival in Stage III Melanoma with Ipilimumab Adjuvant Therapy [published correction appears in *N Engl J Med*. 2018 Nov 29;379(22):2185]. *N Engl J Med*. 2016;375(19):1845–1855. doi:10.1056/NEJMoa1611299.
- 17e. Weber J, Mandala M, Del Vecchio M, et al. Adjuvant Nivolumab versus Ipilimumab in Resected Stage III or IV Melanoma. *N Engl J Med*. 2017 Nov 9;377(19):1824–1835. doi: 10.1056/NEJMoa1709030.
- 18e. Piulats JM, De La Cruz-Merino L, Curiel Garcia MT, et al. Phase II multicenter, single arm, open label study of Nivolumab in combination with Ipilimumab in untreated patients with metastatic uveal melanoma. *Annals of Oncology* (2018) 29 (suppl_8): viii442-viii466. doi:10.1093/annonc/mdy289.
- 19e. Zimmer L, Vaubel J, Mohr P, et al. Phase II DeCOG-study of ipilimumab in pretreated and treatment-naïve patients with metastatic uveal melanoma. *PLoS One*. 2015;10(3):e0118564. Published 2015 Mar 11. doi:10.1371/journal.pone.0118564.
- 20e. Piulats Rodriguez JM, Ochoa de Olza M, Codes M, et al. Phase II study evaluating ipilimumab as a single agent in the first-line treatment of adult patients (Pts) with metastatic uveal melanoma (MUM): The GEM-1 trial. *J Clin Oncol* 2014; 32S:ASCO #9033.

- 21e. Luke JJ, Callahan MK, Postow MA, et al. Clinical activity of ipilimumab for metastatic uveal melanoma: a retrospective review of the Dana-Farber Cancer Institute, Massachusetts General Hospital, Memorial Sloan-Kettering Cancer Center, and University Hospital of Lausanne experience. *Cancer*. 2013;119(20):3687–3695. doi:10.1002/cncr.28282.
- 22e. Nghiem PT, Bhatia S, Lipson EJ, et al. PD-1 Blockade with Pembrolizumab in Advanced Merkel-Cell Carcinoma. *N Engl J Med*. 2016;374(26):2542–2552. doi:10.1056/NEJMoa1603702.
- 23e. D'Angelo SP, Russell J, Lebbé C, et al. Efficacy and Safety of First-line Avelumab Treatment in Patients With Stage IV Metastatic Merkel Cell Carcinoma: A Preplanned Interim Analysis of a Clinical Trial. *JAMA Oncol*. 2018;4(9):e180077. doi:10.1001/jamaoncol.2018.0077.
- 24e. Kaufman HL, Russell JS, Hamid O, et al. Updated efficacy of avelumab in patients with previously treated metastatic Merkel cell carcinoma after ≥ 1 year of follow-up: JAVELIN Merkel 200, a phase 2 clinical trial. *J Immunother Cancer*. 2018;6(1):7. Published 2018 Jan 19. doi:10.1186/s40425-017-0310-x.
- 25e. Topalian SL, Bhatia S, Hollebecque A, et al. Abstract CT074: Non-comparative, open-label, multiple cohort, phase 1/2 study to evaluate nivolumab (NIVO) in patients with virus-associated tumors (CheckMate 358): Efficacy and safety in Merkel cell carcinoma (MCC). *Cancer Res* 2017;77(13 Suppl):Abstract nr CT074.
- 26e. Planchard D, Smit EF, Groen HJM, et al. Dabrafenib plus trametinib in patients with previously untreated BRAFV600E-mutant metastatic non-small-cell lung cancer: an open-label, phase 2 trial. *Lancet Oncol*. 2017 Oct;18(10):1307-1316. doi: 10.1016/S1470-2045(17)30679-4.
- 27e. Planchard D, Kim TM, Mazieres J, et al. Dabrafenib in patients with BRAF(V600E)-positive advanced non-small-cell lung cancer: a single-arm, multicentre, open-label, phase 2 trial. *Lancet Oncol*. 2016 May;17(5):642-50. doi: 10.1016/S1470-2045(16)00077-2.
- 28e. Gautschi O, Milia J, Cabarro B, et al. Targeted Therapy for Patients with BRAF-Mutant Lung Cancer: Results from the European EURAF Cohort. *J Thorac Oncol*. 2015 Oct;10(10):1451-7. doi: 10.1097/JTO.0000000000000625.
- 29e. Drilon A, Laetsch TW, Kummar S, et al. Efficacy of Larotrectinib in TRK Fusion-Positive Cancers in Adults and Children. *N Engl J Med*. 2018;378(8):731–739. doi:10.1056/NEJMoa1714448.
- 30e. Doebele R, Paz-Ares L, Farago AF, et al. Entrectinib in NTRK-fusion positive (NTRK-FP) non-small cell lung cancer (NSCLC): Integrated analysis of patients enrolled in three trials (STARTRK-2, STARTRK-1 and ALKA-372-001)[abstract]. AACR Annual Meeting. Atlanta, GA:Abstract CT131.
- 31e. Carbone DP, Reck M, Paz-Ares L, et al. First-Line Nivolumab in Stage IV or Recurrent Non-Small-Cell Lung Cancer. *N Engl J Med*. 2017;376(25):2415–2426. doi:10.1056/NEJMoa1613493.
- 32e. Hellmann MD, Ciuleanu TE, Pluzanski A, et al. Nivolumab plus Ipilimumab in Lung Cancer with a High Tumor Mutational Burden. *N Engl J Med*. 2018 May 31;378(22):2093-2104. doi: 10.1056/NEJMoa1801946.
- 33e. Brahmer J, Reckamp KL, Baas P, et al. Nivolumab versus Docetaxel in Advanced Squamous-Cell Non-Small-Cell Lung Cancer. *N Engl J Med*. 2015;373(2):123–135. doi:10.1056/NEJMoa1504627.

- 34e. Borghaei H, Paz-Ares L, Horn L, et al. Nivolumab versus Docetaxel in Advanced Nonsquamous Non-Small-Cell Lung Cancer. *N Engl J Med*. 2015;373(17):1627–1639. doi:10.1056/NEJMoa1507643.
- 35e. Barlesi F, Park K, Ciardiello F, et al. Primary analysis from OAK, a randomized phase III study comparing atezolizumab with docetaxel in 2L/3L NSCLC. *Ann of Oncol* 2016 Oct;27(suppl_6):LBA44_PR.
- 36e. Vermorken JB, Mesia R, Rivera F, et al. Platinum-Based Chemotherapy plus Cetuximab in Head and Neck Cancer. *N Engl J Med* 2008; 359:1116-1127.
- 37e. Mok TS, Wu Y-L, Ahn M-J, et al. Osimertinib or Platinum-Pemetrexed in EGFR T790M-Positive Lung Cancer. *N Engl J Med*. 2017;376(7):629–640. doi:10.1056/NEJMoa1612674.
- 38e. Solomon BJ, Besse B, Bauer TM, et al. Lorlatinib in patients with ALK-positive non-small-cell lung cancer: results from a global phase 2 study [published correction appears in *Lancet Oncol*. 2019 Jan;20(1):e10]. *Lancet Oncol*. 2018;19(12):1654–1667. doi:10.1016/S1470-2045(18)30649-1.
- 39e. Ou SH, Ahn JS, De Petris L, et al. Alectinib in Crizotinib-Refractory ALK-Rearranged Non-Small-Cell Lung Cancer: A Phase II Global Study. *J Clin Oncol*. 2016;34(7):661–668. doi:10.1200/jco.2015.63.9443.
- 40e. Huber RM, Hansen KH, Paz-Ares Rodríguez L, et al. Brigatinib in Crizotinib-Refractory ALK+ NSCLC: 2-Year Follow-up on Systemic and Intracranial Outcomes in the Phase 2 ALTA Trial. *J Thorac Oncol*. 2020;15(3):404–415. doi:10.1016/j.jtho.2019.11.004.
- 41e. Shaw AT, Kim TM, Crinò L, et al. Ceritinib versus chemotherapy in patients with ALK-rearranged non-small-cell lung cancer previously given chemotherapy and crizotinib (ASCEND-5): a randomised, controlled, open-label, phase 3 trial. *Lancet Oncol*. 2017;18(7):874–886. doi:10.1016/S1470-2045(17)30339-X.
- 42e. Cohen EEW, Soulières D, Le Tourneau C, et al. Pembrolizumab versus methotrexate, docetaxel, or cetuximab for recurrent or metastatic head-and-neck squamous cell carcinoma (KEYNOTE-040): a randomised, open-label, phase 3 study. *Lancet*. 2019 Jan 12;393(10167):156-167.
- 43e. Cohen EE, Harrington KJ, Le Tourneau C, et al. LBA45_PR - Pembrolizumab (pembro) vs standard of care (SOC) for recurrent or metastatic head and neck squamous cell carcinoma (R/M HNSCC): Phase 3 KEYNOTE-040. *Ann Oncol*. 2017;28(suppl_5):605-649. doi:10.1093/annonc/mdx440.
- 44e. Ferris RL, Blumenschein G Jr, Fayette J, et al. Nivolumab for Recurrent Squamous-Cell Carcinoma of the Head and Neck. *N Engl J Med*. 2016;375(19):1856–1867. doi:10.1056/NEJMoa1602252.
- 45e. Chen R, Zinzani PL, Lee HJ, et al. Pembrolizumab in relapsed or refractory Hodgkin lymphoma: 2-year follow-up of KEYNOTE-087. *Blood*. 2019;134(14):1144–1153. doi:10.1182/blood.2019000324.

- 46e. Armand P, Shipp MA, Ribrag V, et al. Programmed Death-1 Blockade With Pembrolizumab in Patients With Classical Hodgkin Lymphoma After Brentuximab Vedotin Failure. *J Clin Oncol*. 2016;34(31):3733–3739. doi:10.1200/JCO.2016.67.3467.
- 47e. Younes A, Santoro A, Shipp M, et al. Nivolumab for classical Hodgkin's lymphoma after failure of both autologous stem-cell transplantation and brentuximab vedotin: a multicentre, multicohort, single-arm phase 2 trial. *Lancet Oncol*. 2016;17(9):1283–1294. doi:10.1016/S1470-2045(16)30167-X.
- 48e. Moskowitz AJ, Hamlin PA Jr, Perales MA, et al. Phase II study of bendamustine in relapsed and refractory Hodgkin lymphoma. *J Clin Oncol*. 2013;31(4):456–460. doi:10.1200/JCO.2012.45.3308.
- 49e. Gopal AK, Press OW, Shustov AR, et al. Efficacy and safety of gemcitabine, carboplatin, dexamethasone, and rituximab in patients with relapsed/refractory lymphoma: a prospective multi-center phase II study by the Puget Sound Oncology Consortium. *Leuk Lymphoma*. 2010;51(8):1523–1529. doi:10.3109/10428194.2010.491137.
- 50e. Rodriguez MA, Cabanillas FC, Hagemester FB, et al. A phase II trial of mesna/ifosfamide, mitoxantrone and etoposide for refractory lymphomas. *Ann Oncol*. 1995 Jul;6(6):609-11.
- 51e. Colwill R, Crump M, Couture F, et al. Mini-BEAM as salvage therapy for relapsed or refractory Hodgkin's disease before intensive therapy and autologous bone marrow transplantation. *J Clin Oncol*. 1995 Feb;13(2):396-402.
- 52e. Martín A, Fernández-Jiménez MC, et al. Long-term follow-up in patients treated with Mini-BEAM as salvage therapy for relapsed or refractory Hodgkin's disease. *Br J Haematol*. 2001 Apr;113(1):161-71.
- 53e. Armand P, Engert A, Younes A, et al. Nivolumab for Relapsed/Refractory Classic Hodgkin Lymphoma After Failure of Autologous Hematopoietic Cell Transplantation: Extended Follow-Up of the Multicohort Single-Arm Phase II CheckMate 205 Trial [published correction appears in *J Clin Oncol*. 2018 Sep 10;36(26):2748]. *J Clin Oncol*. 2018;36(14):1428–1439. doi:10.1200/JCO.2017.76.0793.
- 54e. Balar AV, Galsky MD, Rosenberg JE, et al. Atezolizumab as first-line treatment in cisplatin-ineligible patients with locally advanced and metastatic urothelial carcinoma: a single-arm, multicentre, phase 2 trial [published correction appears in *Lancet*. 2017 Aug 26;390(10097):848]. *Lancet*. 2017;389(10064):67–76. doi:10.1016/S0140-6736(16)32455-2.
- 55e. De Santis M, Bellmunt J, Mead G, et al. Randomized phase II/III trial assessing gemcitabine/carboplatin and methotrexate/carboplatin/vinblastine in patients with advanced urothelial cancer who are unfit for cisplatin-based chemotherapy: EORTC study 30986. *J Clin Oncol*. 2012;30(2):191–199. doi:10.1200/JCO.2011.37.3571.
- 56e. Apolo AB, Infante JR, Balmanoukian A, et al. Avelumab, an Anti-Programmed Death-Ligand 1 Antibody, In Patients With Refractory Metastatic Urothelial Carcinoma: Results From a

- Multicenter, Phase Ib Study. *J Clin Oncol*. 2017;35(19):2117–2124. doi:10.1200/JCO.2016.71.6795.
- 57e. Patel MR, Ellerton J, Infante JR, et al. Avelumab in metastatic urothelial carcinoma after platinum failure (JAVELIN Solid Tumor): pooled results from two expansion cohorts of an open-label, phase 1 trial. *Lancet Oncol*. 2018 Jan;19(1):51-64.
- 58e. Rosenberg JE, Hoffman-Censits J, Powles T, et al. Atezolizumab in patients with locally advanced and metastatic urothelial carcinoma who have progressed following treatment with platinum-based chemotherapy: a single-arm, multicentre, phase 2 trial. *Lancet*. 2016;387(10031):1909–1920. doi:10.1016/S0140-6736(16)00561-4.
- 59e. Powles T, Durán I, van der Heijden MS, et al. Atezolizumab versus chemotherapy in patients with platinum-treated locally advanced or metastatic urothelial carcinoma (IMvigor211): a multicentre, open-label, phase 3 randomised controlled trial. *Lancet*. 2018 Feb 24;391(10122):748-757. doi: 10.1016/S0140-6736(17)33297-X.
- 60e. Sharma P, Retz M, Siefker-Radtke A, et al. Nivolumab in metastatic urothelial carcinoma after platinum therapy (CheckMate 275): a multicentre, single-arm, phase 2 trial. *Lancet Oncol*. 2017 Mar;18(3):312-322. doi: 10.1016/S1470-2045(17)30065-7.
- 61e. Massard C, Gordon MS, Sharma S, et al. Safety and Efficacy of Durvalumab (MEDI4736), an Anti-Programmed Cell Death Ligand-1 Immune Checkpoint Inhibitor, in Patients With Advanced Urothelial Bladder Cancer. *J Clin Oncol*. 2016;34(26):3119–3125. doi:10.1200/JCO.2016.67.9761.
- 62e. Siefker-Radtke AO, Necchi A, Park SH, et al. First results from the primary analysis population of the phase 2 study of erdafitinib (ERDA; JNJ-42756493) in patients (pts) with metastatic or unresectable urothelial carcinoma (mUC) and FGFR alterations (FGFRalt). *J Clin Oncol* 2018;36(15_suppl):4503.
- 63e. Overman MJ, McDermott R, Leach JL, et al. Nivolumab in patients with metastatic DNA mismatch repair-deficient or microsatellite instability-high colorectal cancer (CheckMate 142): an open-label, multicentre, phase 2 study [published correction appears in *Lancet Oncol*. 2017 Sep;18(9):e510]. *Lancet Oncol*. 2017;18(9):1182–1191. doi:10.1016/S1470-2045(17)30422-9.
- 64e. Lenz HJ, Lonardi S, Zagonel V, et al. Nivolumab (NIVO) + low-dose ipilimumab (IPI) as first-line (1L) therapy in microsatellite instability-high/DNA mismatch repair deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC): Clinical update [abstract]. *Journal of Clinical Oncology* 2019;37:3521-3521.
- 65e. Le DT, Uram JN, Wang H, et al. PD-1 Blockade in Tumors with Mismatch-Repair Deficiency. *N Engl J Med*. 2015;372(26):2509–2520. doi:10.1056/NEJMoa1500596.
- 66e. Tawbi HA, Burgess M, Bolejack V, et al. Pembrolizumab in advanced soft-tissue sarcoma and bone sarcoma (SARC028): a multicentre, two-cohort, single-arm, open-label, phase 2 trial. *Lancet Oncol*. 2017 Nov;18(11):1493-1501. doi: 10.1016/S1470-2045(17)30624-1.
- 67e. Le DT, Durham JN, Smith KN, et al. Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade. *Science*. 2017;357(6349):409–413. doi:10.1126/science.aan6733.

- 68e. Adra N, Einhorn LH, Althouse SK, et al. Phase II trial of pembrolizumab in patients with platinum refractory germ-cell tumors: a Hoosier Cancer Research Network Study GU14-206. *Ann Oncol*. 2018 Jan 1;29(1):209-214. doi: 10.1093/annonc/mdx680.
- 69e. Shields LBE, Gordinier ME. Pembrolizumab in Recurrent Squamous Cell Carcinoma of the Vulva: Case Report and Review of the Literature. *Gynecol Obstet Invest*. 2019;84(1):94-98. doi: 10.1159/000491090.
- 70e. Gbolahan OB, Porter RF, Salter JT, et al. A Phase II Study of Pemetrexed in Patients with Recurrent Thymoma and Thymic Carcinoma. *J Thorac Oncol*. 2018 Dec;13(12):1940-1948.
- 71e. Palmieri G, Buonerba C, Ottaviano M, et al. Capecitabine plus gemcitabine in thymic epithelial tumors: final analysis of a Phase II trial. *Future Oncol*. 2014 Nov;10(14):2141-7.
- 72e. Thomas A, Rajan A, Berman A, et al. Sunitinib in patients with chemotherapy-refractory thymoma and thymic carcinoma: an open-label phase 2 trial [published correction appears in *Lancet Oncol*. 2015 Mar;16(3):e105]. *Lancet Oncol*. 2015;16(2):177-186. doi:10.1016/S1470-2045(14)71181-7.
- 73e. Zucali PA, De Pas T, Palmieri G, et al. Phase II Study of Everolimus in Patients With Thymoma and Thymic Carcinoma Previously Treated With Cisplatin-Based Chemotherapy. *J Clin Oncol*. 2018 Feb 1;36(4):342-349.
- 74e. Loehrer PJ Sr, Wang W, Johnson DH, et al. Octreotide alone or with prednisone in patients with advanced thymoma and thymic carcinoma: an Eastern Cooperative Oncology Group Phase II Trial. *J Clin Oncol*. 2004 Jan 15;22(2):293-9.
- 75e. Umemura S, Segawa Y, Fujiwara K, et al. A case of recurrent metastatic thymoma showing a marked response to paclitaxel monotherapy. *Jpn J Clin Oncol*. 2002 Jul;32(7):262-5.
- 76e. Alley EW, Lopez J, Santoro A, et al. Long-Term Overall Survival for Patients with Malignant Pleural Mesothelioma on Pembrolizumab Enrolled in KEYNOTE-028. *J Thorac Oncol*. 2017 Jan;12(1):S294.
- 77e. Metaxas Y, Rivalland G, Mauti LA, et al. Pembrolizumab as Palliative Immunotherapy in Malignant Pleural Mesothelioma. *J Thorac Oncol*. 2018 Nov;13(11):1784-1791.
- 78e. Jassem J, Ramlau R, Santoro A, et al, "Phase III Trial of Pemetrexed Plus Best Supportive Care Compared With Best Supportive Care in Previously Treated Patients With Advanced Malignant Pleural Mesothelioma," *J Clin Oncol*, 2008, 26(10):1698-704. [PubMed 18375898]
- 79e. Zucali PA, Simonelli M, Michetti G, et al. Second-line chemotherapy in malignant pleural mesothelioma: results of a retrospective multicenter survey. *Lung Cancer*. 2012 Mar;75(3):360-7.
- 80e. Scherpereel A, Mazieres J, Greillier L, et al. Nivolumab or nivolumab plus ipilimumab in patients with relapsed malignant pleural mesothelioma (IFCT-1501 MAPS2): a multicentre, open-label, randomised, non-comparative, phase 2 trial. *Lancet Oncol*. 2019 Feb;20(2):239-253.

- 81e. Scherpereel A, Mazieres J, Greillier L, et al. Second or 3rd line nivolumab (Nivo) versus nivo plus ipilimumab (Ipi) in malignant pleural mesothelioma (MPM) patients: Updated results of the IFCT-1501 MAPS2 randomized phase 2 trial. *Ann Oncol*. 2017 Sept;28(5):mdx440.074.
- 82e. Disselhorst MJ, Quispel-Janssen J, Lalezari F, et al. Ipilimumab and nivolumab in the treatment of recurrent malignant pleural mesothelioma (INITIATE): results of a prospective, single-arm, phase 2 trial. *Lancet Respir Med*. 2019 Mar;7(3):260-270.
- 83e. Quispel-Janssen J, van der Noort V, de Vries JF, et al. Programmed Death 1 Blockade With Nivolumab in Patients With Recurrent Malignant Pleural Mesothelioma. *J Thorac Oncol*. 2018 Oct;13(10):1569-1576.
- 84e. Popat S, Curioni-Fontecedro A, Polydoropoulou V, et al. A multicentre randomized phase III trial comparing pembrolizumab (P) versus single-agent chemotherapy (CT) for advanced pretreated malignant pleural mesothelioma (MPM): Results from the European Thoracic Oncology Platform (ETOP 9-15) PROMISE-meso trial. *Ann Oncol* 2019; 30S: ESMO #LBA91_PR.
- 85e. Tawbi HA, Forsyth PA, Hodi S, et al. Efficacy and safety of the combination of nivolumab (NIVO) plus ipilimumab (IPI) in patients with symptomatic melanoma brain metastases (CheckMate 204). *J Clin Oncol* 2019; 37S.
- 86e. Long GV, Atkinson V, Lo S, et al. Combination nivolumab and ipilimumab or nivolumab alone in melanoma brain metastases: a multicentre randomised phase 2 study. *Lancet Oncol* 2018; 19:672.
- 87e. Margolin K, Ernstoff MS, Hamid O, et al. Ipilimumab in patients with melanoma and brain metastases: an open-label, phase 2 trial. *Lancet Oncol*. 2012 May;13(5):459-65. doi: 10.1016/S1470-2045(12)70090-6.
- 88e. Morris VK, Salem ME, Nimeiri H, et al. Nivolumab for previously treated unresectable metastatic anal cancer (NCI9673): a multicentre, single-arm, phase 2 study. *Lancet Oncol*. 2017;18(4):446–453. doi:10.1016/S1470-2045(17)30104-3.
- 89e. Chung HC, Piha-Paul SA, Lopez-Martin J, et al. Pembrolizumab After Two or More Lines of Previous Therapy in Patients With Recurrent or Metastatic SCLC: Results From the KEYNOTE-028 and KEYNOTE-158 Studies. *J Thorac Oncol*. 2020;15(4):618–627. doi:10.1016/j.jtho.2019.12.109.
- 90e. Antonia SJ, López-Martin JA, Bendell J, et al. Nivolumab alone and nivolumab plus ipilimumab in recurrent small-cell lung cancer (CheckMate 032): a multicentre, open-label, phase 1/2 trial. *Lancet Oncol*. 2016 Jul;17(7):883-895. doi: 10.1016/S1470-2045(16)30098-5.
- 91e. Reck M, Vicente D, Ciuleanu T, et al. LBA5: Efficacy and safety of nivolumab (nivo) monotherapy versus chemotherapy (chemo) in recurrent small cell lung cancer (SCLC): Results from CheckMate 331 [abstract]. *Ann Oncol* 2018;29:43.
- 92e. von Pawel J, Schiller JH, Shepherd FA, et al. Topotecan versus cyclophosphamide, doxorubicin, and vincristine for the treatment of recurrent small-cell lung cancer. *J Clin Oncol*. 1999 Feb;17(2):658-67.

- 93e. O'Brien ME, Ciuleanu TE, Tsekov H, et al. Phase III trial comparing supportive care alone with supportive care with oral topotecan in patients with relapsed small-cell lung cancer. *J Clin Oncol*. 2006 Dec 1;24(34):5441-7.
- 94e. Yamamoto N, Tsurutani J, Yoshimura N, et al. Phase II study of weekly paclitaxel for relapsed and refractory small cell lung cancer. *Anticancer Res*. 2006 Jan-Feb;26(1B):777-81.
- 95e. Smit EF, Fokkema E, Biesma B, Groen HJ, Snoek W, Postmus PE. A phase II study of paclitaxel in heavily pretreated patients with small-cell lung cancer. *Br J Cancer*. 1998;77(2):347-351. doi:10.1038/bjc.1998.54.
- 96e. Smyth JF, Smith IE, Sessa C, et al. Activity of docetaxel (Taxotere) in small cell lung cancer. The Early Clinical Trials Group of the EORTC. *Eur J Cancer*. 1994;30A(8):1058-60.
- 97e. Masuda N, Fukuoka M, Kusunoki Y, et al. CPT-11: a new derivative of camptothecin for the treatment of refractory or relapsed small-cell lung cancer. *J Clin Oncol*. 1992 Aug;10(8):1225-9.
- 98e. Pietanza MC, Kadota K, Huberman K, et al. Phase II trial of temozolomide in patients with relapsed sensitive or refractory small cell lung cancer, with assessment of methylguanine-DNA methyltransferase as a potential biomarker. *Clin Cancer Res*. 2012 Feb 15;18(4):1138-45. doi: 10.1158/1078-0432.CCR-11-2059.
- 99e. El-Khoueiry AB, Sangro B, Yau T, et al. Nivolumab in patients with advanced hepatocellular carcinoma (CheckMate 040): an open-label, non-comparative, phase 1/2 dose escalation and expansion trial. *Lancet*. 2017 Jun 24;389(10088):2492-2502. doi: 10.1016/S0140-6736(17)31046-2.
- 100e. Crocenzi TS, El-Khoueiry AB, Yau T, et al. Nivolumab (nivo) in sorafenib (sor)-naive and -experienced pts with advanced hepatocellular carcinoma (HCC): CheckMate 040 study. *J Clin Oncol* 35, 2017 (suppl; abstr 4013).
- 101e. Qin S, Bai Y, Lim HY, et al. Randomized, multicenter, open-label study of oxaliplatin plus fluorouracil/leucovorin versus doxorubicin as palliative chemotherapy in patients with advanced hepatocellular carcinoma from Asia. *J Clin Oncol*. 2013 Oct 1;31(28):3501-8. doi: 10.1200/JCO.2012.44.5643.
- 102e. Bruix J, Qin S, Merle P, et al. Regorafenib for patients with hepatocellular carcinoma who progressed on sorafenib treatment (RESORCE): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2017 Jan 7;389(10064):56-66.
- 103e. Abou-Alfa GK, Meyer T, Cheng AL, et al. Cabozantinib in Patients with Advanced and Progressing Hepatocellular Carcinoma. *N Engl J Med*. 2018 Jul 5;379(1):54-63.
- 104e. Zhu AX, Park JO, Ryoo BY, et al. Ramucirumab versus placebo as second-line treatment in patients with advanced hepatocellular carcinoma following first-line therapy with sorafenib (REACH): a randomised, double-blind, multicentre, phase 3 trial. *Lancet Oncol*. 2015 Jul;16(7):859-70.

- 105e. Zhu AX, Kang YK, Yen CJ, et al. Ramucirumab after sorafenib in patients with advanced hepatocellular carcinoma and increased α -fetoprotein concentrations (REACH-2): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol*. 2019 Feb;20(2):282-296.
- 106e. Pulini S, Rupoli S, Goteri G, et al. Pegylated liposomal doxorubicin in the treatment of primary cutaneous T-cell lymphomas. *Haematologica*. 2007;92(5):686–689. doi:10.3324/haematol.10879.
- 107e. Dummer R, Quaglino P, Becker JC, et al. Prospective international multicenter phase II trial of intravenous pegylated liposomal doxorubicin monochemotherapy in patients with stage IIB, IVA, or IVB advanced mycosis fungoides: final results from EORTC 21012. *J Clin Oncol*. 2012;30(33):4091–4097.
- 108e. Duvic M, Talpur R, Wen S, Kurzrock R, David CL, Apisarnthanarax N. Phase II evaluation of gemcitabine monotherapy for cutaneous T-cell lymphoma. *Clin Lymphoma Myeloma*. 2006;7(1):51–58. doi:10.3816/CLM.2006.n.039.
- 109e. Sternberg CN, Davis ID, Mardiak J, et al. Pazopanib in locally advanced or metastatic renal cell carcinoma: results of a randomized phase III trial. *J Clin Oncol*. 2010 Feb 20;28(6):1061-8.
- 110e. Sternberg CN, Hawkins RE, Wagstaff J, et al. A randomised, double-blind phase III study of pazopanib in patients with advanced and/or metastatic renal cell carcinoma: final overall survival results and safety update. *Eur J Cancer*. 2013 Apr;49(6):1287-96.
- 111e. Motzer RJ, Hutson TE, Tomczak P, et al. Sunitinib versus interferon alfa in metastatic renal-cell carcinoma. *N Engl J Med*. 2007 Jan 11;356(2):115-24.
- 112e. Motzer RJ, Tannir NM, McDermott DF, et al. Nivolumab plus Ipilimumab versus Sunitinib in Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2018;378(14):1277–1290.
- 113e. Choueiri TK, Halabi S, Sanford BL, et al. Cabozantinib Versus Sunitinib As Initial Targeted Therapy for Patients With Metastatic Renal Cell Carcinoma of Poor or Intermediate Risk: The Alliance A031203 CABOSUN Trial. *J Clin Oncol*. 2016;35(6):591–597.
- 114e. Lorusso D, Ferrandina G, Colombo N, et al. Randomized phase II trial of carboplatin-paclitaxel (CP) compared to carboplatin-paclitaxel-bevacizumab (CP-B) in advanced (stage III-IV) or recurrent endometrial cancer: The MITO END-2 trial. *Journal of Clinical Oncology* 2015 33:15_suppl, 5502-5502.
- 115e. Aghajanian C, Sill MW, Darcy KM, et al. Phase II trial of bevacizumab in recurrent or persistent endometrial cancer: a Gynecologic Oncology Group study. *J Clin Oncol*. 2011;29(16):2259–2265.
- 116e. Lincoln S, Blessing JA, Lee RB, Rocereto TF. Activity of paclitaxel as second-line chemotherapy in endometrial carcinoma: a Gynecologic Oncology Group study. *Gynecol Oncol*. 2003;88(3):277–281. doi:10.1016/s0090-8258(02)00068-9.
- 117e. Muggia FM, Blessing JA, Sorosky J, Reid GC. Phase II trial of the pegylated liposomal doxorubicin in previously treated metastatic endometrial cancer: a Gynecologic Oncology Group study. *J Clin Oncol*. 2002;20(9):2360–2364. doi:10.1200/JCO.2002.08.171.

- 118e. Oza AM, Elit L, Tsao MS, et al. Phase II study of temsirolimus in women with recurrent or metastatic endometrial cancer: a trial of the NCIC Clinical Trials Group. *J Clin Oncol.* 2011;29(24):3278–3285. doi:10.1200/JCO.2010.34.1578.
- 119e. Eckstein M, Cimadamore A, Hartmann A, et al. PD-L1 assessment in urothelial carcinoma: a practical approach. *Ann Transl Med.* 2019;7(22):690. doi:10.21037/atm.2019.10.24.
- 120e. Rittmeyer A, Barlesi F, Waterkamp D, et al. Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a phase 3, open-label, multicentre randomised controlled trial [published correction appears in *Lancet.* 2017 Apr 8;389(10077):e5]. *Lancet.* 2017;389(10066):255-265. doi:10.1016/S0140-6736(16)32517-X.
- 121e. Duvic M, Hymes K, Heald P, et al. Bexarotene is effective and safe for treatment of refractory advanced-stage cutaneous T-cell lymphoma: multinational phase II-III trial results. *J Clin Oncol.* 2001;19(9):2456-2471. doi:10.1200/JCO.2001.19.9.2456
- 122e. Groisberg R, Hong DS, Behrang A, et al. Characteristics and outcomes of patients with advanced sarcoma enrolled in early phase immunotherapy trials. *J Immunother Cancer.* 2017;5(1):100. Published 2017 Dec 19. doi:10.1186/s40425-017-0301-y.
- 123e. Maki RG, Wathen JK, Patel SR, et al. Randomized phase II study of gemcitabine and docetaxel compared with gemcitabine alone in patients with metastatic soft tissue sarcomas: results of sarcoma alliance for research through collaboration study 002 [corrected] [published correction appears in *J Clin Oncol.* 2007 Aug 20;25(24):3790]. *J Clin Oncol.* 2007;25(19):2755-2763. doi:10.1200/JCO.2006.10.4117.
- 124e. Judson I, Verweij J, Gelderblom H, et al. Doxorubicin alone versus intensified doxorubicin plus ifosfamide for first-line treatment of advanced or metastatic soft-tissue sarcoma: a randomised controlled phase 3 trial. *Lancet Oncol.* 2014;15(4):415-423. doi:10.1016/S1470-2045(14)70063-4.
- 125e. Migden MR, Rischin D, Schmults CD, et al. PD-1 Blockade with Cemiplimab in Advanced Cutaneous Squamous-Cell Carcinoma. *N Engl J Med.* 2018;379(4):341-351. doi:10.1056/NEJMoa1805131.
- 126e. Georger B, Kang HJ, Yalon-Oren M, et al. Pembrolizumab in paediatric patients with advanced melanoma or a PD-L1-positive, advanced, relapsed, or refractory solid tumour or lymphoma (KEYNOTE-051): interim analysis of an open-label, single-arm, phase 1-2 trial. *Lancet Oncol.* 2020 Jan;21(1):121-133. doi: 10.1016/S1470-2045(19)30671-0.
- 127e. Haak HR, Hermans J, van de Velde CJ, Lentjes EG, Goslings BM, Fleuren GJ, Krans HM. Optimal treatment of adrenocortical carcinoma with mitotane: results in a consecutive series of 96 patients. *Br J Cancer.* 1994 May;69(5):947-51. doi: 10.1038/bjc.1994.183.
- 128e. Berruti A, Terzolo M, Sperone P, et al. Etoposide, doxorubicin and cisplatin plus mitotane in the treatment of advanced adrenocortical carcinoma: a large prospective phase II trial. *Endocr Relat Cancer.* 2005 Sep;12(3):657-66. doi: 10.1677/erc.1.01025.

- 129e. Fassnacht M, Terzolo M, Allolio B, et al. FIRM-ACT Study Group. Combination chemotherapy in advanced adrenocortical carcinoma. *N Engl J Med*. 2012 Jun 7;366(23):2189-97. doi: 10.1056/NEJMoa1200966.
- 130e. Schmid P, Adams S, Rugo HS, et al. Atezolizumab and Nab-Paclitaxel in Advanced Triple-Negative Breast Cancer. *N Engl J Med*. 2018 Nov 29;379(22):2108-2121. doi: 10.1056/NEJMoa1809615.
- 131e. Moehler M, Shitara K, Garrido M, et al. Nivolumab (nivo) plus chemotherapy (chemo) versus chemo as first-line (1L) treatment for advanced gastric cancer/gastroesophageal junction cancer (GC/GEJC)/esophageal adenocarcinoma (EAC): First results of the CheckMate 649 study. [abstract]. Presented at the Oral Presentation presented at the ESMO 2020 Annual Meeting; September 19-21, 2020; Virtual Meeting.
- 132e. Kato K, Sun JM, Shah M.A., et al. Pembrolizumab plus chemotherapy versus chemotherapy as first-line therapy in patients with advanced esophageal cancer: The phase 3 KEYNOTE-590 study. [abstract]. Presented at the Oral Presentation presented at the ESMO 2020 Annual Meeting; September 19-21, 2020; Virtual Meeting.
- 133e. Sezer A, Kilickap S, Gümüş M, et al. Cemiplimab monotherapy for first-line treatment of advanced non-small-cell lung cancer with PD-L1 of at least 50%: a multicentre, open-label, global, phase 3, randomised, controlled trial. *Lancet*. 2021 Feb 13;397(10274):592-604.
- 134e. Powles T, Park SH, Voog E, et al. Maintenance avelumab + best supportive care (BSC) versus BSC alone after platinum-based first-line (1L) chemotherapy in advanced urothelial carcinoma (UC): JAVELIN Bladder 100 phase III interim analysis. *J Clin Oncol*. 2020;38(18_suppl):LBA1-LBA1.
- 135e. Graff JN, Alumkal JJ, Drake CG, et al. Early evidence of anti-PD-1 activity in enzalutamide-resistant prostate cancer. *Oncotarget*. 2016;7(33):52810-52817. doi:10.18632/oncotarget.10547.
- 136e. Spigel DR, De Marinis F, Giaccone G, et al. IMpower110: Interim overall survival (OS) analysis of a phase III study of atezolizumab (atezo) vs platinum-based chemotherapy (chemo) as first-line (1L) treatment (tx) in PD-L1–selected NSCLC [abstract]. *Ann Oncol* 2019;30(suppl_5):Abstract 6256.
- 137e. Kato K, Cho BC, Takahashi M, et al. Nivolumab versus chemotherapy in patients with advanced esophageal squamous cell carcinoma refractory or intolerant to previous chemotherapy (ATTRACTION-3): a multicentre, randomised, open-label, phase 3 trial. *Lancet Oncol*. 2019;20(11):1506-1517. doi:10.1016/S1470-2045(19)30626-6.
- 138e. Wolf J, Seto T, Han JY, et al. Capmatinib in MET Exon 14-Mutated or MET-Amplified Non-Small-Cell Lung Cancer. *N Engl J Med*. 2020 Sep 3;383(10):944-957. doi: 10.1056/NEJMoa2002787.
- 139e. Paik PK, Felip E, Veillon R, et al. Tepotinib in Non-Small-Cell Lung Cancer with MET Exon 14 Skipping Mutations. *N Engl J Med*. 2020 Sep 3;383(10):931-943. doi: 10.1056/NEJMoa2004407.

- 140e. Oaknin A, Tinker AV, Gilbert L, et al. Clinical Activity and Safety of the Anti-Programmed Death 1 Monoclonal Antibody Dostarlimab for Patients With Recurrent or Advanced Mismatch Repair-Deficient Endometrial Cancer: A Nonrandomized Phase 1 Clinical Trial. *JAMA Oncol.* 2020 Oct 1. doi: 10.1001/jamaoncol.2020.4515. [Epub ahead of print]
- 141e. Motzer R, Alekseev B, Rha SY, et al. Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma. *N Engl J Med.* 2021 Apr 8;384(14):1289-1300. doi: 10.1056/NEJMoa2035716.
- 142e. Choueiri TK, Powles T, Burotto M, et al. 696O_PR Nivolumab + cabozantinib vs sunitinib in first-line treatment for advanced renal cell carcinoma: First results from the randomized phase III CheckMate 9ER trial. Volume 31, SUPPLEMENT 4, S1159, September 01, 2020.
- 143e. Younes A, Gopal AK, Smith SE, et al. Results of a pivotal phase II study of brentuximab vedotin for patients with relapsed or refractory Hodgkin's lymphoma. *J Clin Oncol.* 2012;30(18):2183-2189. doi:10.1200/JCO.2011.38.0410.
- 144e. Gopal AK, Chen R, Smith SE, et al. Durable remissions in a pivotal phase 2 study of brentuximab vedotin in relapsed or refractory Hodgkin lymphoma. *Blood.* 2015;125(8):1236-1243. doi:10.1182/blood-2014-08-595801.
- 145e. Chen RW, Palmer J, Martin, et al. Results of a Phase II Trial of Brentuximab Vedotin As First Line Salvage Therapy in Relapsed/Refractory HL Prior to AHCT [abstract]. *Blood* 2014;124:Abstract 501.
- 146e. Zinzani PL, Ribrag V, Moskowitz CH, et al. Safety and tolerability of pembrolizumab in patients with relapsed/refractory primary mediastinal large B-cell lymphoma. *Blood.* 2017;130(3):267-270. doi:10.1182/blood-2016-12-758383.
- 147e. Powles T, Park SH, Voog E, et al. Maintenance avelumab + best supportive care (BSC) versus BSC alone after platinum-based first-line (1L) chemotherapy in advanced urothelial carcinoma (UC): JAVELIN Bladder 100 phase III interim analysis. *J Clin Oncol.* 2020;38(18_suppl):LBA1-LBA1.
- 148e. McDermott DF, Lee JL, Ziobro M, et al. Open-Label, Single-Arm, Phase II Study of Pembrolizumab Monotherapy as First-Line Therapy in Patients With Advanced Non-Clear Cell Renal Cell Carcinoma. *J Clin Oncol.* 2021 Mar 20;39(9):1029-1039. doi: 10.1200/JCO.20.02365.
- 149e. Koshkin VS, Barata PC, Zhang T, et al. Clinical activity of nivolumab in patients with non-clear cell renal cell carcinoma. *J Immunother Cancer.* 2018;6(1):9. Published 2018 Jan 29. doi:10.1186/s40425-018-0319-9.
- 150e. Armstrong AJ, Halabi S, Eisen T, et al. Everolimus versus sunitinib for patients with metastatic non-clear cell renal cell carcinoma (ASPEN): a multicentre, open-label, randomised phase 2 trial. *Lancet Oncol.* 2016;17(3):378-388. doi:10.1016/S1470-2045(15)00515-X.
- 151e. Campbell MT, Bilen MA, Shah AY, et al. Cabozantinib for the treatment of patients with metastatic non-clear cell renal cell carcinoma: A retrospective analysis. *Eur J Cancer.* 2018 Nov;104:188-194. doi: 10.1016/j.ejca.2018.08.014.

- 152e. Hughes BG, Munoz-Couselo E, Mortier L, et al. Phase 2 study of pembrolizumab (pembro) for locally advanced (LA) or recurrent/metastatic (R/M) cutaneous squamous cell carcinoma (cSCC): KEYNOTE-629. Presented at: AACR Annual Meeting; April 10-15, 2021; Virtual. Abstract CT006.
- 153e. Rudin CM, Awad MM, Navarro A, et al. Pembrolizumab or Placebo Plus Etoposide and Platinum as First-Line Therapy for Extensive-Stage Small-Cell Lung Cancer: Randomized, Double-Blind, Phase III KEYNOTE-604 Study. *J Clin Oncol.* 2020;38(21):2369-2379. Doi:10.1200/JCO.20.00793.
- 154e. Powles T, Csósz T, Özgüroğlu M, et al. Pembrolizumab alone or combined with chemotherapy versus chemotherapy as first-line therapy for advanced urothelial carcinoma (KEYNOTE-361): a randomised, open-label, phase 3 trial. *Lancet Oncol.* 2021 Jul;22(7):931-945. doi: 10.1016/S1470-2045(21)00152-2.
- 155e. Moskowitz AJ, Shah G, Schöder H, et al. Phase II Trial of Pembrolizumab Plus Gemcitabine, Vinorelbine, and Liposomal Doxorubicin as Second-Line Therapy for Relapsed or Refractory Classical Hodgkin Lymphoma. *J Clin Oncol* 2021;39:3109-3117.
- 156e. Bartlett NL, Niedzwiecki D, Johnson JL, et al. Gemcitabine, vinorelbine, and pegylated liposomal doxorubicin (GVD), a salvage regimen in relapsed Hodgkin's lymphoma: CALGB 59804. *Ann Oncol.* 2007 Jun;18(6):1071-9. doi: 10.1093/annonc/mdm090.
- 157e. Moskowitz CH, Bertino JR, Glassman JR, et al. Ifosfamide, carboplatin, and etoposide: a highly effective cytoreduction and peripheral-blood progenitor-cell mobilization regimen for transplant-eligible patients with non-Hodgkin's lymphoma. *J Clin Oncol.* 1999 Dec;17(12):3776-85. doi: 10.1200/JCO.1999.17.12.3776.
- 158e. Pires da Silva I, Ahmed T, Reijers ILM, et al. Ipilimumab alone or ipilimumab plus anti-PD-1 therapy in patients with metastatic melanoma resistant to anti-PD-(L)1 monotherapy: a multicentre, retrospective, cohort study. *Lancet Oncol.* 2021 Jun;22(6):836-847. doi: 10.1016/S1470-2045(21)00097-8.
- 159e. Gauvain C, Vauléon E, Chouaid C, et al. Intracerebral efficacy and tolerance of nivolumab in non-small-cell lung cancer patients with brain metastases. *Lung Cancer.* 2018 Feb;116:62-66. doi: 10.1016/j.lungcan.2017.12.008. Epub 2017 Dec 14. Erratum in: *Lung Cancer.* 2019 Oct;136:159.
- 160e. Goldman JW, Crino L, Vokes EE, et al. Nivolumab (nivo) in Patients (pts) With Advanced (adv) NSCLC and Central Nervous System (CNS) Metastases (mets). *J Thorac Oncol* 2016;11:S238-S239.
- 161e. Naumann RW, Hollebecque A, Meyer T, et al. Safety and Efficacy of Nivolumab Monotherapy in Recurrent or Metastatic Cervical, Vaginal, or Vulvar Carcinoma: Results From the Phase I/II CheckMate 358 Trial. *J Clin Oncol.* 2019 Nov 1;37(31):2825-2834.
- 162e. O'Malley DM, Bariani GM, Cassier PA, et al. Pembrolizumab in Patients With Microsatellite Instability-High Advanced Endometrial Cancer: Results From the KEYNOTE-158 Study. *J Clin Oncol.* 2022 Mar 1;40(7):752-761. doi: 10.1200/JCO.21.01874. Epub 2022 Jan 6.

- 163e. Tawbi HA, Schadendorf D, Lipson EJ, et al. Relatlimab and Nivolumab versus Nivolumab in Untreated Advanced Melanoma. *N Engl J Med*. 2022 Jan 6;386(1):24-34. doi: 10.1056/NEJMoa2109970.
- 164e. Wilky BA, Trucco MM, Subhawong TK, et al. Axitinib plus pembrolizumab in patients with advanced sarcomas including alveolar soft-part sarcoma: a single-centre, single-arm, phase 2 trial. *Lancet Oncol*. 2019 Jun;20(6):837-848. doi: 10.1016/S1470-2045(19)30153-6. Epub 2019 May 8.
- 165e. Stacchiotti S, Negri T, Zaffaroni N, et al. Sunitinib in advanced alveolar soft part sarcoma: evidence of a direct antitumor effect. *Ann Oncol*. 2011 Jul;22(7):1682-1690. doi: 10.1093/annonc/mdq644. Epub 2011 Jan 17.
- 166e. Stacchiotti S, Mir O, Le Cesne A, et al. Activity of Pazopanib and Trabectedin in Advanced Alveolar Soft Part Sarcoma. *Oncologist*. 2018 Jan;23(1):62-70. doi: 10.1634/theoncologist.2017-0161. Epub 2017 Jul 28.
- 167e. Doki Y, Ajani JA, Kato K, et al. Nivolumab Combination Therapy in Advanced Esophageal Squamous-Cell Carcinoma. *N Engl J Med*. 2022 Feb 3;386(5):449-462. doi: 10.1056/NEJMoa2111380.
- 168e. Foss F, Horwitz SM, Coiffier B, et al. Pralatrexate is an effective treatment for relapsed or refractory transformed mycosis fungoides: a subgroup efficacy analysis from the PROPEL study. *Clin Lymphoma Myeloma Leuk*. 2012 Aug;12(4):238-43.
- 169e. Luke JJ, Rutkowski P, Queirolo P, et al. Pembrolizumab versus placebo as adjuvant therapy in completely resected stage IIB or IIC melanoma (KEYNOTE-716): a randomised, double-blind, phase 3 trial. *Lancet*. 2022 Apr 30;399(10336):1718-1729.
- 170e. Josting A, Rudolph C, Reiser M, et al. Time-intensified dexamethasone/cisplatin/cytarabine: an effective salvage therapy with low toxicity in patients with relapsed and refractory Hodgkin's disease. *Ann Oncol*. 2002 Oct;13(10):1628-35.
- 171e. Felip E, Altorki N, Zhou C, et al. Adjuvant atezolizumab after adjuvant chemotherapy in resected stage IB-IIIa non-small-cell lung cancer (IMpower010): a randomised, multicentre, open-label, phase 3 trial. *Lancet*. 2021 Oct 9;398(10308):1344-1357. doi: 10.1016/S0140-6736(21)02098-5. Epub 2021 Sep 20.
- 172e. Zer A, Icht O, Yosef L, et al. Phase II single-arm study of nivolumab and ipilimumab (Nivo/Ipi) in previously treated classical Kaposi sarcoma (cKS). *Ann Oncol*. 2022 Jul;33(7):720-727. doi: 10.1016/j.annonc.2022.03.012.
- 173e. Sun JM, Shen L, Shah MA, et al. Pembrolizumab plus chemotherapy versus chemotherapy alone for first-line treatment of advanced oesophageal cancer (KEYNOTE-590): a randomised, placebo-controlled, phase 3 study. *Lancet*. 2021 Aug 28;398(10302):759-771. doi: 10.1016/S0140-6736(21)01234-4.
- 174e. Ascierto PA, Lipson EJ, Dummer R, et al. Nivolumab and Relatlimab in Patients With Advanced Melanoma That Had Progressed on Anti-Programmed Death-1/Programmed Death Ligand 1

- Therapy: Results From the Phase I/IIa RELATIVITY-020 Trial. *J Clin Oncol*. 2023 Feb 13;JCO2202072. doi: 10.1200/JCO.22.02072.
- 175e. Rossi E, Pagliara MM, Orteschi D, et al. Pembrolizumab as first-line treatment for metastatic uveal melanoma. *Cancer Immunol Immunother*. 2019 Jul;68(7):1179-1185. doi: 10.1007/s00262-019-02352-6. Epub 2019 Jun 7. PMID: 31175402; PMCID: PMC6584707.
- 176e. Gadgeel S, Dziubek K, Nagasaka M, et al. Pembrolizumab in Combination With Platinum-Based Chemotherapy in Recurrent EGFR/ALK-Positive Non-Small Cell Lung Cancer (NSCLC). 2021 Oct;16(suppl_S863).
- 177e. Hoimes CJ, Flaig TW, Milowsky MI, et al. Enfortumab Vedotin Plus Pembrolizumab in Previously Untreated Advanced Urothelial Cancer. *J Clin Oncol*. 2023 Jan 1;41(1):22-31. doi: 10.1200/JCO.22.01643.
- 178e. Florou V, Rosenberg AE, Wieder E, et al. Angiosarcoma patients treated with immune checkpoint inhibitors: a case series of seven patients from a single institution. *J Immunother Cancer*. 2019 Aug 8;7(1):213. doi: 10.1186/s40425-019-0689-7. Erratum in: *J Immunother Cancer*. 2019 Nov 6;7(1):285.
- 179e. Marabelle A, Cassier PA, Fakih M, et al. Pembrolizumab for previously treated advanced anal squamous cell carcinoma: results from the non-randomised, multicohort, multicentre, phase 2 KEYNOTE-158 study. *Lancet Gastroenterol Hepatol*. 2022 May;7(5):446-454.
- 180e. Coleman RL, Lorusso D, Gennigens C, et al; innovaTV 204/GOG-3023/ENGOT-cx6 Collaborators. Efficacy and safety of tisotumab vedotin in previously treated recurrent or metastatic cervical cancer (innovaTV 204/GOG-3023/ENGOT-cx6): a multicentre, open-label, single-arm, phase 2 study. *Lancet Oncol*. 2021 May;22(5):609-619.
- 181e. Kim SJ, Hyeon J, Cho I, Ko YH, Kim WS. Comparison of Efficacy of Pembrolizumab between Epstein-Barr Virus–Positive and –Negative Relapsed or Refractory Non-Hodgkin Lymphomas. *Cancer Res Treat*. 2019 Apr;51(2):611-622.
- 182e. Li X, Cheng Y, Zhang M, et al. Activity of pembrolizumab in relapsed/refractory NK/T-cell lymphoma. *J Hematol Oncol*. 2018 Jan 31;11(1):15.
- 183e. Mirza M, Chase D, Slomovitz B, et al. Dostarlimab for Primary Advanced or Recurrent Endometrial Cancer. March 27, 2023. doi: 10.1056/NEJMoa2216334.
- 184e. Wakelee H, Liberman M, Kato T, et al. Perioperative Pembrolizumab for Early-Stage Non-Small-Cell Lung Cancer. *N Engl J Med*. 2023 Aug 10;389(6):491-503. doi: 10.1056/NEJMoa2302983. Epub 2023 Jun 3. PMID: 37272513.
- 185e. Forde PM, Spicer J, Lu S, et al (2021). Nivolumab (NIVO) + platinum-doublet chemotherapy (chemo) vs chemo as neoadjuvant treatment (tx) for resectable (1B-IIIa) non-small cell lung cancer NSCLC in the phase 3 CheckMate 816 trial. American Association for Cancer Research Annual Meeting 2021. Abstract CT003.
- 186e. Shitara K, Van Cutsem E, Bang YJ, et al. Efficacy and Safety of Pembrolizumab or Pembrolizumab Plus Chemotherapy vs Chemotherapy Alone for Patients With First-line,

Advanced Gastric Cancer: The KEYNOTE-062 Phase 3 Randomized Clinical Trial. *JAMA Oncol* 2020;6:1571-1580

- 187e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium[®]) Biliary Tract Cancers. Version 2.2024. National Comprehensive Cancer Network, 2024. The NCCN Compendium[®] is a derivative work of the NCCN Guidelines[®]. NATIONAL COMPREHENSIVE CANCER NETWORK[®], NCCN[®], and NCCN GUIDELINES[®] are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2024.
- 188e. Sacco AG, Chen R, Worden FP, et al Pembrolizumab plus cetuximab in patients with recurrent or metastatic head and neck squamous cell carcinoma: an open-label, multi-arm, non-randomised, multicentre, phase 2 trial. *Lancet Oncol* 2021;22:883-892.
- 189e. Sato J, Satouchi M, Itoh S, et al. Lenvatinib in patients with advanced or metastatic thymic carcinoma (REMORA): a multicentre, phase 2 trial. *Lancet Oncol* 2020; 21:843-850
- 190e. André T, Tougeron D, Piessen G, et al. Neoadjuvant Nivolumab Plus Ipilimumab and Adjuvant Nivolumab in Localized Deficient Mismatch Repair/Microsatellite Instability-High Gastric or Esophagogastric Junction Adenocarcinoma: The GERCOR NEONIPIGA Phase II Study. *J Clin Oncol*. 2023 Jan 10;41(2):255-265.
- 191e. Pietrantonio F, Raimondi A, Lonardi S, et al. INFINITY: A multicentre, single-arm, multi-cohort, phase II trial of tremelimumab and durvalumab as neoadjuvant treatment of patients with microsatellite instability-high (MSI) resectable gastric or gastroesophageal junction adenocarcinoma (GAC/ GEJAC). *Journal of Clinical Oncology* 2023;41:358-358
- 192e. Powles TB, Valderrama B, Gupta S, et al. LBA6 EV-302/KEYNOTE-A39: Open-label, randomized phase III study of enfortumab vedotin in combination with pembrolizumab (EV +P) vs chemotherapy in previously untreated locally advanced metastatic urothelial carcinoma (la/mUC). *Annals of Oncology*, Volume 34, Issue Supplement_2, October 2023, MDZ250.002, <https://doi.org/10.1016/j.annonc.2023.10.106>.
- 193e. van der Heijden MS, Sonpavde G, Powles T, et al. Nivolumab plus Gemcitabine-Cisplatin in Advanced Urothelial Carcinoma. *N Engl J Med*. 2023 Nov 9;389(19):1778-1789.
- 194e. Dzienis M, Cundom J, Fuentes CS, et al. Pembrolizumab + carboplatin + paclitaxel as first-line therapy in recurrent/metastatic head and neck squamous cell carcinoma: Phase 4 KEYNOTE-B10 study. presented at european society for medical oncology (ESMO) congress; September 9-13, 2022; Paris, France.
- 195e. Grignani G, Rutkowski P, Lebbé C. A Phase 2 Study of Retifanlimab in Patients With Advanced or Metastatic Merkel Cell Carcinoma (POD1UM-201) Presented at the Society for Immunotherapy of Cancer's 36th Annual Meeting Washington, DC • November 10–14, 2021 [Epub ahead of print].

- 196e. Gogishvili M, Melkadze T, Makharadze T, et al. Cemiplimab plus chemotherapy versus chemotherapy alone in non-small cell lung cancer: a randomized, controlled, double-blind phase 3 trial. *Nat Med*. 2022 Nov;28(11):2374-2380.
- 197e. Markman M, Blessing J, Rubin SC, et al. Phase II trial of weekly paclitaxel (80 mg/m²) in platinum and paclitaxel-resistant ovarian and primary peritoneal cancers: a Gynecologic Oncology Group study. *Gynecol Oncol*. 2006 Jun;101(3):436-40.
- 198e. Gordon AN, Fleagle JT, Guthrie D, et al. Recurrent epithelial ovarian carcinoma: a randomized phase III study of pegylated liposomal doxorubicin versus topotecan. *J Clin Oncol*. 2001 Jul 15;19(14):3312-22.
- 199e. Naqash AR, O'Sullivan Coyne GH, Moore N, et al. Phase II study of atezolizumab in advanced alveolar soft part sarcoma (ASPS). *Journal of Clinical Oncology* 2021 39:15_suppl, 11519-11519.
- 200e. Zinzani PL, Thieblemont C, Melnichenko V, et al. Pembrolizumab in relapsed or refractory primary mediastinal large B-cell lymphoma: final analysis of KEYNOTE-170. *Blood*. 2023;142(2):141-145. doi:10.1182/blood.2022019340.
- 201e. Dinney CP, Greenberg RE, Steinberg GD. Intravesical valrubicin in patients with bladder carcinoma in situ and contraindication to or failure after bacillus Calmette-Guérin. *Urol Oncol*. 2013;31(8):1635-1642. doi:10.1016/j.urolonc.2012.04.010
- 202e. Tewari KS, Monk BJ, Vergote I, et al. Survival with Cemiplimab in Recurrent Cervical Cancer. *N Engl J Med* 2022;386:544-555.
- 203e. Head L, Kiseljak-Vassiliades K, Clark TJ, et al. Response to Immunotherapy in Combination With Mitotane in Patients With Metastatic Adrenocortical Cancer. *J Endocr Soc*. 2019;3(12):2295-2304. Published 2019 Oct 11. doi:10.1210/js.2019-00305.
- 204e. Pujade-Lauraine E, Hilpert F, Weber B, et al. Bevacizumab combined with chemotherapy for platinum-resistant recurrent ovarian cancer: The AURELIA open-label randomized phase III trial [published correction appears in *J Clin Oncol*. 2014 Dec 10;32(35):4025]. *J Clin Oncol*. 2014;32(13):1302-1308. doi:10.1200/JCO.2013.51.4489.
- 205e. Cannistra SA, Matulonis UA, Penson RT, et al. Phase II study of bevacizumab in patients with platinum-resistant ovarian cancer or peritoneal serous cancer [published correction appears in *J Clin Oncol*. 2008 Apr 1;26(10):1773]. *J Clin Oncol*. 2007;25(33):5180-5186. doi:10.1200/JCO.2007.12.0782.
- 206e. Ain KB, Egorin MJ, DeSimone PA. Treatment of anaplastic thyroid carcinoma with paclitaxel: phase 2 trial using ninety-six-hour infusion. Collaborative Anaplastic Thyroid Cancer Health Intervention Trials (CATCHIT) Group. *Thyroid*. 2000;10(7):587-594. doi:10.1089/thy.2000.10.587.
- 207e. Shimaoka K, Schoenfeld DA, DeWys WD, Creech RH, DeConti R. A randomized trial of doxorubicin versus doxorubicin plus cisplatin in patients with advanced thyroid carcinoma. *Cancer*. 1985;56(9):2155-2160. doi:10.1002/1097-0142(19851101)56:9<2155::aid-cncr2820560903>3.0.co;2-e.

208e. Garmez B, Gheeya J, Lin HY, et al. Clinical and Molecular Characterization of POLE Mutations as Predictive Biomarkers of Response to Immune Checkpoint Inhibitors in Advanced Cancers. JCO Precis Oncol. 2022;6:e2100267. doi:10.1200/PO.21.00267.

209e. Prime Therapeutics Management. Keytruda Clinical Literature Review Analysis. Last updated June 2024. Accessed June 2024.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C00.0	Malignant neoplasm of external upper lip
C00.1	Malignant neoplasm of external lower lip
C00.2	Malignant neoplasm of external lip, unspecified
C00.3	Malignant neoplasm of upper lip, inner aspect
C00.4	Malignant neoplasm of lower lip, inner aspect
C00.5	Malignant neoplasm of lip, unspecified, inner aspect
C00.6	Malignant neoplasm of commissure of lip, unspecified
C00.8	Malignant neoplasm of overlapping sites of lip
C00.9	Malignant neoplasm of lip, unspecified
C01	Malignant neoplasm of base of tongue
C02.0	Malignant neoplasm of dorsal surface of tongue
C02.1	Malignant neoplasm of border of tongue
C02.2	Malignant neoplasm of ventral surface of tongue
C02.3	Malignant neoplasm of anterior two-thirds of tongue, part unspecified
C02.4	Malignant neoplasm of lingual tonsil
C02.8	Malignant neoplasm of overlapping sites of tongue
C02.9	Malignant neoplasm of tongue, unspecified
C03.0	Malignant neoplasm of upper gum
C03.1	Malignant neoplasm of lower gum
C03.9	Malignant neoplasm of gum, unspecified
C04.0	Malignant neoplasm of anterior floor of mouth
C04.1	Malignant neoplasm of lateral floor of mouth
C04.8	Malignant neoplasm of overlapping sites of floor of mouth
C04.9	Malignant neoplasm of floor of mouth, unspecified
C05.0	Malignant neoplasm of hard palate
C05.1	Malignant neoplasm of soft palate
C05.8	Malignant neoplasm of overlapping sites of palate
C05.9	Malignant neoplasm of palate, unspecified
C06.0	Malignant neoplasm of cheek mucosa

ICD-10	ICD-10 Description
C06.2	Malignant neoplasm of retromolar area
C06.80	Malignant neoplasm of overlapping sites of unspecified parts of mouth
C06.89	Malignant neoplasm of overlapping sites of other parts of mouth
C06.9	Malignant neoplasm of mouth, unspecified
C07	Malignant neoplasm of parotid gland
C08.0	Malignant neoplasm of submandibular gland
C08.1	Malignant neoplasm of sublingual gland
C08.9	Malignant neoplasm of major salivary gland, unspecified
C09.0	Malignant neoplasm of tonsillar fossa
C09.1	Malignant neoplasm of tonsillar pillar (anterior) (posterior)
C09.8	Malignant neoplasm of overlapping sites of tonsil
C09.9	Malignant neoplasm of tonsil, unspecified
C10.0	Malignant neoplasm of vallecula
C10.1	Malignant neoplasm of anterior surface of epiglottis
C10.2	Malignant neoplasm of lateral wall of oropharynx
C10.3	Malignant neoplasm of posterior wall of oropharynx
C10.4	Malignant neoplasm of branchial cleft
C10.8	Malignant neoplasm of overlapping sites of oropharynx
C10.9	Malignant neoplasm of oropharynx, unspecified
C12	Malignant neoplasm of pyriform sinus
C13.0	Malignant neoplasm of postcricoid region
C13.1	Malignant neoplasm of aryepiglottic fold, hypopharyngeal aspect
C13.2	Malignant neoplasm of posterior wall of hypopharynx
C13.8	Malignant neoplasm of overlapping sites of hypopharynx
C13.9	Malignant neoplasm of hypopharynx, unspecified
C14.0	Malignant neoplasm of pharynx, unspecified
C14.2	Malignant neoplasm of Waldeyer's ring
C14.8	Malignant neoplasm of overlapping sites of lip, oral cavity and pharynx
C15.3	Malignant neoplasm of upper third of esophagus
C15.4	Malignant neoplasm of middle third of esophagus
C15.5	Malignant neoplasm of lower third of esophagus
C15.8	Malignant neoplasm of overlapping sites of esophagus
C15.9	Malignant neoplasm of esophagus, unspecified
C16.0	Malignant neoplasm of cardia
C16.1	Malignant neoplasm of fundus of stomach
C16.2	Malignant neoplasm of body of stomach

ICD-10	ICD-10 Description
C16.3	Malignant neoplasm of pyloric antrum
C16.4	Malignant neoplasm of pylorus
C16.5	Malignant neoplasm of lesser curvature of stomach, unspecified
C16.6	Malignant neoplasm of greater curvature of stomach, unspecified
C16.8	Malignant neoplasm of overlapping sites of stomach
C16.9	Malignant neoplasm of stomach, unspecified
C17.0	Malignant neoplasm of duodenum
C17.1	Malignant neoplasm of jejunum
C17.2	Malignant neoplasm of ileum
C17.3	Meckel's diverticulum, malignant
C17.8	Malignant neoplasm of overlapping sites of small intestine
C17.9	Malignant neoplasm of small intestine, unspecified
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of colon
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C22.0	Liver cell carcinoma
C22.1	Intrahepatic bile duct carcinoma
C22.8	Malignant neoplasm of liver, primary, unspecified as to type
C22.9	Malignant neoplasm of liver, not specified as primary or secondary
C23	Malignant neoplasm of gallbladder
C24.0	Malignant neoplasm of extrahepatic bile duct
C24.1	Malignant neoplasm of ampulla of Vater
C24.8	Malignant neoplasm of overlapping sites of biliary tract
C24.9	Malignant neoplasm of biliary tract, unspecified
C25.0	Malignant neoplasm of head of pancreas
C25.1	Malignant neoplasm of body of the pancreas

ICD-10	ICD-10 Description
C25.2	Malignant neoplasm of tail of pancreas
C25.3	Malignant neoplasm of pancreatic duct
C25.7	Malignant neoplasm of other parts of pancreas
C25.8	Malignant neoplasm of overlapping sites of pancreas
C25.9	Malignant neoplasm of pancreas, unspecified
C31.0	Malignant neoplasm of maxillary sinus
C31.1	Malignant neoplasm of ethmoidal sinus
C32.0	Malignant neoplasm of glottis
C32.1	Malignant neoplasm of supraglottis
C32.2	Malignant neoplasm of subglottis
C32.3	Malignant neoplasm of laryngeal cartilage
C32.8	Malignant neoplasm of overlapping sites of larynx
C32.9	Malignant neoplasm of larynx, unspecified
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus and lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C37	Malignant neoplasm of thymus
C40.00	Malignant neoplasm of scapula and long bones of unspecified upper limb
C40.01	Malignant neoplasm of scapula and long bones of right upper limb
C40.02	Malignant neoplasm of scapula and long bones of left upper limb
C40.10	Malignant neoplasm of short bones of unspecified upper limb
C40.11	Malignant neoplasm of short bones of right upper limb

ICD-10	ICD-10 Description
C40.12	Malignant neoplasm of short bones of left upper limb
C40.20	Malignant neoplasm of long bones of unspecified lower limb
C40.21	Malignant neoplasm of long bones of right lower limb
C40.22	Malignant neoplasm of long bones of left lower limb
C40.30	Malignant neoplasm of short bones of unspecified lower limb
C40.31	Malignant neoplasm of short bones of right lower limb
C40.32	Malignant neoplasm of short bones of left lower limb
C40.80	Malignant neoplasm of overlapping sites of bone and articular cartilage of unspecified limb
C40.81	Malignant neoplasm of overlapping sites of bone and articular cartilage of right limb
C40.82	Malignant neoplasm of overlapping sites of bone and articular cartilage of left limb
C40.90	Malignant neoplasm of unspecified bones and articular cartilage of unspecified limb
C40.91	Malignant neoplasm of unspecified bones and articular cartilage of right limb
C40.92	Malignant neoplasm of unspecified bones and articular cartilage of left limb
C41.0	Malignant neoplasm of bones of skull and face
C41.1	Malignant neoplasm of mandible
C41.2	Malignant neoplasm of vertebral column
C41.3	Malignant neoplasm of ribs, sternum and clavicle
C41.4	Malignant neoplasm of pelvic bones, sacrum and coccyx
C41.9	Malignant neoplasm of bone and articular cartilage, unspecified
C43.0	Malignant melanoma of lip
C43.111	Malignant melanoma of right upper eyelid, including canthus
C43.112	Malignant melanoma of right lower eyelid, including canthus
C43.121	Malignant melanoma of left upper eyelid, including canthus
C43.122	Malignant melanoma of left lower eyelid, including canthus
C43.20	Malignant melanoma of unspecified ear and external auricular canal
C43.21	Malignant melanoma of right ear and external auricular canal
C43.22	Malignant melanoma of left ear and external auricular canal
C43.30	Malignant melanoma of unspecified part of face
C43.31	Malignant melanoma of nose
C43.39	Malignant melanoma of other parts of face
C43.4	Malignant melanoma of scalp and neck
C43.51	Malignant melanoma of anal skin
C43.52	Malignant melanoma of skin of breast
C43.59	Malignant melanoma of other part of trunk
C43.60	Malignant melanoma of unspecified upper limb, including shoulder
C43.61	Malignant melanoma of right upper limb, including shoulder

ICD-10	ICD-10 Description
C43.62	Malignant melanoma of left upper limb, including shoulder
C43.70	Malignant melanoma of unspecified lower limb, including hip
C43.71	Malignant melanoma of right lower limb, including hip
C43.72	Malignant melanoma of left lower limb, including hip
C43.8	Malignant melanoma of overlapping sites of skin
C43.9	Malignant melanoma of skin, unspecified
C44.00	Unspecified malignant neoplasm of skin of lip
C44.02	Squamous cell carcinoma of skin of lip
C44.09	Other specified malignant neoplasm of skin of lip
C44.121	Squamous cell carcinoma of skin of unspecified eyelid, including canthus
C44.1221	Squamous cell carcinoma of skin of right upper eyelid, including canthus
C44.1222	Squamous cell carcinoma of skin of right lower eyelid, including canthus
C44.1291	Squamous cell carcinoma of skin of left upper eyelid, including canthus
C44.1292	Squamous cell carcinoma of skin of left lower eyelid, including canthus
C44.221	Squamous cell carcinoma of skin of unspecified ear and external auricular canal
C44.222	Squamous cell carcinoma of skin of right ear and external auricular canal
C44.229	Squamous cell carcinoma of skin of left ear and external auricular canal
C44.320	Squamous cell carcinoma of skin of unspecified parts of face
C44.321	Squamous cell carcinoma of skin of nose
C44.329	Squamous cell carcinoma of skin of other parts of face
C44.42	Squamous cell carcinoma of skin of scalp and neck
C44.520	Squamous cell carcinoma of anal skin
C44.521	Squamous cell carcinoma of skin of breast
C44.529	Squamous cell carcinoma of skin of other part of trunk
C44.621	Squamous cell carcinoma of skin of unspecified upper limb, including shoulder
C44.622	Squamous cell carcinoma of skin of right upper limb, including shoulder
C44.629	Squamous cell carcinoma of skin of left upper limb, including shoulder
C44.721	Squamous cell carcinoma of skin of unspecified lower limb, including hip
C44.722	Squamous cell carcinoma of skin of right lower limb, including hip
C44.729	Squamous cell carcinoma of skin of left lower limb, including hip
C44.82	Squamous cell carcinoma of overlapping sites of skin
C44.92	Squamous cell carcinoma of skin, unspecified
C46.0	Kaposi's sarcoma of skin
C46.1	Kaposi's sarcoma of soft tissue
C46.2	Kaposi's sarcoma of palate
C46.3	Kaposi's sarcoma of lymph nodes

ICD-10	ICD-10 Description
C46.4	Kaposi's sarcoma of gastrointestinal sites
C46.50	Kaposi's sarcoma of unspecified lung
C46.51	Kaposi's sarcoma of right lung
C46.52	Kaposi's sarcoma of left lung
C46.7	Kaposi's sarcoma of other sites
C46.9	Kaposi's sarcoma, unspecified
C48.0	Malignant neoplasm of retroperitoneum
C48.1	Malignant neoplasm of specified parts of peritoneum
C48.2	Malignant neoplasm of peritoneum, unspecified
C48.8	Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C49.0	Malignant neoplasm of connective and soft tissue of head, face and neck
C49.10	Malignant neoplasm of connective and soft tissue of unspecified upper limb, including shoulder
C49.11	Malignant neoplasm of connective and soft tissue of right upper limb, including shoulder
C49.12	Malignant neoplasm of connective and soft tissue of left upper limb, including shoulder
C49.20	Malignant neoplasm of connective and soft tissue of unspecified lower limb, including hip
C49.21	Malignant neoplasm of connective and soft tissue of right lower limb, including hip
C49.22	Malignant neoplasm of connective and soft tissue of left lower limb, including hip
C49.3	Malignant neoplasm of connective and soft tissue of thorax
C49.4	Malignant neoplasm of connective and soft tissue of abdomen
C49.5	Malignant neoplasm of connective and soft tissue of pelvis
C49.6	Malignant neoplasm of connective and soft tissue of trunk, unspecified
C49.8	Malignant neoplasm of overlapping sites of connective and soft tissue
C49.9	Malignant neoplasm of connective and soft tissue, unspecified
C4A.0	Merkel cell carcinoma of lip
C4A.10	Merkel cell carcinoma of eyelid, including canthus
C4A.111	Merkel cell carcinoma of right upper eyelid, including canthus
C4A.112	Merkel cell carcinoma of right lower eyelid, including canthus
C4A.121	Merkel cell carcinoma of left upper eyelid, including canthus
C4A.122	Merkel cell carcinoma of left lower eyelid, including canthus
C4A.20	Merkel cell carcinoma of unspecified ear and external auricular canal
C4A.21	Merkel cell carcinoma of right ear and external auricular canal
C4A.22	Merkel cell carcinoma of left ear and external auricular canal
C4A.30	Merkel cell carcinoma of unspecified part of face
C4A.31	Merkel cell carcinoma of nose
C4A.39	Merkel cell carcinoma of other parts of face
C4A.4	Merkel cell carcinoma of scalp and neck

ICD-10	ICD-10 Description
C4A.51	Merkel cell carcinoma of anal skin
C4A.52	Merkel cell carcinoma of skin of breast
C4A.59	Merkel cell carcinoma of other part of trunk
C4A.60	Merkel cell carcinoma of unspecified upper limb, including shoulder
C4A.61	Merkel cell carcinoma of right upper limb, including shoulder
C4A.62	Merkel cell carcinoma of left upper limb, including shoulder
C4A.70	Merkel cell carcinoma of unspecified lower limb, including hip
C4A.71	Merkel cell carcinoma of right lower limb, including hip
C4A.72	Merkel cell carcinoma of left lower limb, including hip
C4A.8	Merkel cell carcinoma of overlapping sites
C4A.9	Merkel cell carcinoma, unspecified
C50.011	Malignant neoplasm of nipple and areola, right female breast
C50.012	Malignant neoplasm of nipple and areola, left female breast
C50.019	Malignant neoplasm of nipple and areola, unspecified female breast
C50.021	Malignant neoplasm of nipple and areola, right male breast
C50.022	Malignant neoplasm of nipple and areola, left male breast
C50.029	Malignant neoplasm of nipple and areola, unspecified male breast
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast
C50.119	Malignant neoplasm of central portion of unspecified female breast
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.129	Malignant neoplasm of central portion of unspecified male breast
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
C50.212	Malignant neoplasm of upper-inner quadrant of left female breast
C50.219	Malignant neoplasm of upper-inner quadrant of unspecified female breast
C50.221	Malignant neoplasm of upper-inner quadrant of right male breast
C50.222	Malignant neoplasm of upper-inner quadrant of left male breast
C50.229	Malignant neoplasm of upper-inner quadrant of unspecified male breast
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
C50.319	Malignant neoplasm of lower-inner quadrant of unspecified female breast
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast
C50.322	Malignant neoplasm of lower-inner quadrant of left male breast
C50.329	Malignant neoplasm of lower-inner quadrant of unspecified male breast
C50.411	Malignant neoplasm of upper-outer quadrant of right female breast

ICD-10	ICD-10 Description
C50.412	Malignant neoplasm of upper-outer quadrant of left female breast
C50.419	Malignant neoplasm of upper-outer quadrant of unspecified female breast
C50.421	Malignant neoplasm of upper-outer quadrant of right male breast
C50.422	Malignant neoplasm of upper-outer quadrant of left male breast
C50.429	Malignant neoplasm of upper-outer quadrant of unspecified male breast
C50.511	Malignant neoplasm of lower-outer quadrant of right female breast
C50.512	Malignant neoplasm of lower-outer quadrant of left female breast
C50.519	Malignant neoplasm of lower-outer quadrant of unspecified female breast
C50.521	Malignant neoplasm of lower-outer quadrant of right male breast
C50.522	Malignant neoplasm of lower-outer quadrant of left male breast
C50.529	Malignant neoplasm of lower-outer quadrant of unspecified male breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.619	Malignant neoplasm of axillary tail of unspecified female breast
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.629	Malignant neoplasm of axillary tail of unspecified male breast
C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.819	Malignant neoplasm of overlapping sites of unspecified female breast
C50.821	Malignant neoplasm of overlapping sites of right male breast
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.829	Malignant neoplasm of overlapping sites of unspecified male breast
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.919	Malignant neoplasm of unspecified site of unspecified female breast
C50.921	Malignant neoplasm of unspecified site of right male breast
C50.922	Malignant neoplasm of unspecified site of left male breast
C50.929	Malignant neoplasm of unspecified site of unspecified male breast
C51.0	Malignant neoplasm of labium majus
C51.1	Malignant neoplasm of labium minus
C51.2	Malignant neoplasm of clitoris
C51.8	Malignant neoplasm of overlapping sites of vulva
C51.9	Malignant neoplasm of vulva, unspecified
C53.0	Malignant neoplasm of endocervix
C53.1	Malignant neoplasm of exocervix

ICD-10	ICD-10 Description
C53.8	Malignant neoplasm of overlapping sites of cervix uteri
C53.9	Malignant neoplasm of cervix uteri, unspecified
C54.0	Malignant neoplasm of isthmus uteri
C54.1	Malignant neoplasm of endometrium
C54.2	Malignant neoplasm of myometrium
C54.3	Malignant neoplasm of fundus uteri
C54.8	Malignant neoplasm of overlapping sites of corpus uteri
C54.9	Malignant neoplasm of corpus uteri, unspecified
C55	Malignant neoplasm of uterus, part unspecified
C56.1	Malignant neoplasm of right ovary
C56.2	Malignant neoplasm of left ovary
C56.3	Malignant neoplasm of bilateral ovaries
C56.9	Malignant neoplasm of unspecified ovary
C57.00	Malignant neoplasm of unspecified fallopian tube
C57.01	Malignant neoplasm of right fallopian tube
C57.02	Malignant neoplasm of left fallopian tube
C57.10	Malignant neoplasm of unspecified broad ligament
C57.11	Malignant neoplasm of right broad ligament
C57.12	Malignant neoplasm of left broad ligament
C57.20	Malignant neoplasm of unspecified round ligament
C57.21	Malignant neoplasm of right round ligament
C57.22	Malignant neoplasm of left round ligament
C57.3	Malignant neoplasm of parametrium
C57.4	Malignant neoplasm of uterine adnexa, unspecified
C57.7	Malignant neoplasm of other specified female genital organs
C57.8	Malignant neoplasm of overlapping sites of female genital organs
C57.9	Malignant neoplasm of female genital organ, unspecified
C60.0	Malignant neoplasm of prepuce
C60.1	Malignant neoplasm of glans penis
C60.2	Malignant neoplasm of body of penis
C60.8	Malignant neoplasm of overlapping sites of penis
C60.9	Malignant neoplasm of penis, unspecified
C61	Malignant neoplasm of prostate
C62.00	Malignant neoplasm of unspecified undescended testis
C62.01	Malignant neoplasm of undescended right testis
C62.02	Malignant neoplasm of undescended left testis

ICD-10	ICD-10 Description
C62.10	Malignant neoplasm of unspecified descended testis
C62.11	Malignant neoplasm of descended right testis
C62.12	Malignant neoplasm of descended left testis
C62.90	Malignant neoplasm of unspecified testis, unspecified whether descended or undescended
C62.91	Malignant neoplasm of right testis, unspecified whether descended or undescended
C62.92	Malignant neoplasm of left testis, unspecified whether descended or undescended
C63.7	Malignant neoplasm of other specified male genital organs
C63.8	Malignant neoplasm of overlapping sites of male genital organs
C64.1	Malignant neoplasm of right kidney, except renal pelvis
C64.2	Malignant neoplasm of left kidney, except renal pelvis
C64.9	Malignant neoplasm of unspecified kidney, except renal pelvis
C65.1	Malignant neoplasm of right renal pelvis
C65.2	Malignant neoplasm of left renal pelvis
C65.9	Malignant neoplasm of unspecified renal pelvis
C66.1	Malignant neoplasm of right ureter
C66.2	Malignant neoplasm of left ureter
C66.9	Malignant neoplasm of unspecified ureter
C67.0	Malignant neoplasm of trigone of bladder
C67.1	Malignant neoplasm of dome of bladder
C67.2	Malignant neoplasm of lateral wall of bladder
C67.3	Malignant neoplasm of anterior wall of bladder
C67.4	Malignant neoplasm of posterior wall of bladder
C67.5	Malignant neoplasm of bladder neck
C67.6	Malignant neoplasm of ureteric orifice
C67.7	Malignant neoplasm of urachus
C67.8	Malignant neoplasm of overlapping sites of bladder
C67.9	Malignant neoplasm of bladder, unspecified
C68.0	Malignant neoplasm of urethra
C72.0	Malignant neoplasm of spinal cord
C72.1	Malignant neoplasm of cauda equina
C74.00	Malignant neoplasm of cortex of unspecified adrenal gland
C74.01	Malignant neoplasm of cortex of right adrenal gland
C74.02	Malignant neoplasm of cortex of left adrenal gland
C74.90	Malignant neoplasm of unspecified part of unspecified adrenal gland
C74.91	Malignant neoplasm of unspecified part of right adrenal gland
C74.92	Malignant neoplasm of unspecified part of left adrenal gland

ICD-10	ICD-10 Description
C76.0	Malignant neoplasm of head, face and neck
C77.0	Secondary and unspecified malignant neoplasm of lymph nodes of head, face and neck
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
C79.31	Secondary malignant neoplasm of brain
C7A.1	Malignant poorly differentiated neuroendocrine tumors
C7A.8	Other malignant neuroendocrine tumors
C7B.00	Secondary carcinoid tumors unspecified site
C7B.01	Secondary carcinoid tumors of distant lymph nodes
C7B.02	Secondary carcinoid tumors of liver
C7B.03	Secondary carcinoid tumors of bone
C7B.04	Secondary carcinoid tumors of peritoneum
C7B.1	Secondary Merkel cell carcinoma
C7B.8	Other secondary neuroendocrine tumors
C80.0	Disseminated malignant neoplasm, unspecified
C80.1	Malignant (primary) neoplasm, unspecified
C81.10	Nodular sclerosis Hodgkin lymphoma, unspecified site
C81.11	Nodular sclerosis Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.12	Nodular sclerosis Hodgkin lymphoma, intrathoracic lymph nodes
C81.13	Nodular sclerosis Hodgkin lymphoma, intra-abdominal lymph nodes
C81.14	Nodular sclerosis Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.15	Nodular sclerosis Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.16	Nodular sclerosis Hodgkin lymphoma, intrapelvic lymph nodes
C81.17	Nodular sclerosis Hodgkin lymphoma, spleen
C81.18	Nodular sclerosis Hodgkin lymphoma, lymph nodes of multiple sites
C81.19	Nodular sclerosis Hodgkin lymphoma, extranodal and solid organ sites
C81.20	Mixed cellularity Hodgkin lymphoma, unspecified site
C81.21	Mixed cellularity Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.22	Mixed cellularity Hodgkin lymphoma, intrathoracic lymph nodes
C81.23	Mixed cellularity Hodgkin lymphoma, intra-abdominal lymph nodes
C81.24	Mixed cellularity Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.25	Mixed cellularity Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.26	Mixed cellularity Hodgkin lymphoma, intrapelvic lymph nodes

ICD-10	ICD-10 Description
C81.27	Mixed cellularity Hodgkin lymphoma, spleen
C81.28	Mixed cellularity Hodgkin lymphoma, lymph nodes of multiple sites
C81.29	Mixed cellularity Hodgkin lymphoma, extranodal and solid organ sites
C81.30	Lymphocyte depleted Hodgkin lymphoma, unspecified site
C81.31	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.32	Lymphocyte depleted Hodgkin lymphoma, intrathoracic lymph nodes
C81.33	Lymphocyte depleted Hodgkin lymphoma, intra-abdominal lymph nodes
C81.34	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.35	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.36	Lymphocyte depleted Hodgkin lymphoma, intrapelvic lymph nodes
C81.37	Lymphocyte depleted Hodgkin lymphoma, spleen
C81.38	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of multiple sites
C81.39	Lymphocyte depleted Hodgkin lymphoma, extranodal and solid organ sites
C81.40	Lymphocyte-rich Hodgkin lymphoma, unspecified site
C81.41	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.42	Lymphocyte-rich Hodgkin lymphoma, intrathoracic lymph nodes
C81.43	Lymphocyte-rich Hodgkin lymphoma, intra-abdominal lymph nodes
C81.44	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.45	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.46	Lymphocyte-rich Hodgkin lymphoma, intrapelvic lymph nodes
C81.47	Lymphocyte-rich Hodgkin lymphoma, spleen
C81.48	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of multiple sites
C81.49	Lymphocyte-rich Hodgkin lymphoma, extranodal and solid organ sites
C81.70	Other Hodgkin lymphoma unspecified site
C81.71	Other Hodgkin lymphoma lymph nodes of head, face, and neck
C81.72	Other Hodgkin lymphoma intrathoracic lymph nodes
C81.73	Other Hodgkin lymphoma intra-abdominal lymph nodes
C81.74	Other Hodgkin lymphoma lymph nodes of axilla and upper limb
C81.75	Other Hodgkin lymphoma lymph nodes of inguinal region and lower limb
C81.76	Other Hodgkin lymphoma intrapelvic lymph nodes
C81.77	Other Hodgkin lymphoma spleen
C81.78	Other Hodgkin lymphoma lymph nodes of multiple sites
C81.79	Other Hodgkin lymphoma extranodal and solid organ sites
C81.90	Hodgkin lymphoma, unspecified, unspecified site
C81.91	Hodgkin lymphoma, unspecified, lymph nodes of head, face, and neck
C81.92	Hodgkin lymphoma, unspecified, intrathoracic lymph nodes

ICD-10	ICD-10 Description
C81.93	Hodgkin lymphoma, unspecified, intra-abdominal lymph nodes
C81.94	Hodgkin lymphoma, unspecified, lymph nodes of axilla and upper limb
C81.95	Hodgkin lymphoma, unspecified, lymph nodes of inguinal region and lower limb
C81.96	Hodgkin lymphoma, unspecified, intrapelvic lymph nodes
C81.97	Hodgkin lymphoma, unspecified, spleen
C81.98	Hodgkin lymphoma, unspecified, lymph nodes of multiple sites
C81.99	Hodgkin lymphoma, unspecified, extranodal and solid organ sites
C83.90	Non-follicular (diffuse) lymphoma, unspecified, unspecified site
C83.91	Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of head, face, and neck
C83.92	Non-follicular (diffuse) lymphoma, unspecified, intrathoracic lymph nodes
C83.93	Non-follicular (diffuse) lymphoma, unspecified, intra-abdominal lymph nodes
C83.94	Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of axilla and upper limb
C83.95	Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of inguinal region and lower limb
C83.96	Non-follicular (diffuse) lymphoma, unspecified, intrapelvic lymph nodes
C83.97	Non-follicular (diffuse) lymphoma, unspecified, spleen
C83.98	Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of multiple sites
C83.99	Non-follicular (diffuse) lymphoma, unspecified, extranodal and solid organ sites
C84.00	Mycosis fungoides, unspecified site
C84.01	Mycosis fungoides, lymph nodes of head, face, and neck
C84.02	Mycosis fungoides, intrathoracic lymph nodes
C84.03	Mycosis fungoides, intra-abdominal lymph nodes
C84.04	Mycosis fungoides, lymph nodes of axilla and upper limb
C84.05	Mycosis fungoides, lymph nodes of inguinal region and lower limb
C84.06	Mycosis fungoides, intrapelvic lymph nodes
C84.07	Mycosis fungoides, spleen
C84.08	Mycosis fungoides, lymph nodes of multiple sites
C84.09	Mycosis fungoides, extranodal and solid organ sites
C84.10	Sézary disease, unspecified site
C84.11	Sézary disease, lymph nodes of head, face, and neck
C84.12	Sézary disease, intrathoracic lymph nodes
C84.13	Sézary disease, intra-abdominal lymph nodes
C84.14	Sézary disease, lymph nodes of axilla and upper limb
C84.15	Sézary disease, lymph nodes of inguinal region and lower limb
C84.16	Sézary disease, intrapelvic lymph nodes
C84.17	Sézary disease, spleen
C84.18	Sézary disease, lymph nodes of multiple sites

ICD-10	ICD-10 Description
C84.19	Sézary disease, extranodal and solid organ sites
C85.20	Mediastinal (thymic) large B-cell lymphoma, unspecified site
C85.21	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of head, face and neck
C85.22	Mediastinal (thymic) large B-cell lymphoma, intrathoracic lymph nodes
C85.23	Mediastinal (thymic) large B-cell lymphoma, intra-abdominal lymph nodes
C85.24	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of axilla and upper limb
C85.25	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C85.26	Mediastinal (thymic) large B-cell lymphoma, intrapelvic lymph nodes
C85.27	Mediastinal (thymic) large B-cell lymphoma, spleen
C85.28	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of multiple sites
C85.29	Mediastinal (thymic) large B-cell lymphoma, extranodal and solid organ sites
D09.0	Carcinoma in situ of bladder
D15.0	Benign neoplasm of other and unspecified intrathoracic organs
D37.01	Neoplasm of uncertain behavior of lip
D37.02	Neoplasm of uncertain behavior of tongue
D37.05	Neoplasm of uncertain behavior of pharynx
D37.09	Neoplasm of uncertain behavior of other specified sites of the oral cavity
D37.1	Neoplasm of uncertain behavior of stomach
D37.8	Neoplasm of uncertain behavior of other specified digestive organs
D37.9	Neoplasm of uncertain behavior of digestive organ, unspecified
D38.0	Neoplasm of uncertain behavior of larynx
D38.4	Neoplasm of uncertain behavior of thymus
D38.5	Neoplasm of uncertain behavior of other respiratory organs
D38.6	Neoplasm of uncertain behavior of respiratory organ, unspecified
Z85.00	Personal history of malignant neoplasm of unspecified digestive organ
Z85.01	Personal history of malignant neoplasm of esophagus
Z85.028	Personal history of other malignant neoplasm of stomach
Z85.068	Personal history of other malignant neoplasm of small intestine
Z85.07	Personal history of malignant neoplasm of pancreas
Z85.09	Personal history of malignant neoplasm of other digestive organs
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.238	Personal history of other malignant neoplasm of thymus
Z85.3	Personal history of malignant neoplasm of breast
Z85.42	Personal history of malignant neoplasm of other parts of uterus
Z85.46	Personal history of malignant neoplasm of prostate
Z85.47	Personal history of malignant neoplasm of testis

ICD-10	ICD-10 Description
Z85.51	Personal history of malignant neoplasm of bladder
Z85.528	Personal history of other malignant neoplasm of kidney
Z85.59	Personal history of malignant neoplasm of other urinary tract organ
Z85.71	Personal history of Hodgkin Lymphoma
Z85.820	Personal history of malignant melanoma of skin
Z85.830	Personal history of malignant neoplasm of bone
Z85.831	Personal history of malignant neoplasm of soft tissue
Z85.850	Personal history of malignant neoplasm of thyroid
Z85.858	Personal history of malignant neoplasm of other endocrine glands

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

