Keytruda Qlex™ (pembrolizumab and berahyaluronidase alfa-pmph) (Subcutaneous)

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I. Length of Authorization Δ 1-3,5,6,15-17,50,51,53,57,62,65,68,69,72,73,75-77,82,85-87,95,101,103,117,118,123,124

- Initial: Prior authorization validity will be provided initially for 6 months, unless otherwise specified.
  - Neoadjuvant therapy in TNBC: Prior authorization validity may be provided for up to a maximum of twenty-four (24) weeks of therapy.*
  - Neoadjuvant therapy of resectable Head and Neck Cancers: Prior authorization validity may be provided for up to a maximum of six (6) weeks of therapy.
  - Neoadjuvant therapy for resectable NSCLC: Prior authorization validity may be provided for up to a maximum of twelve (12) weeks of therapy
  - Neoadjuvant therapy for Cutaneous Melanoma: Prior authorization validity may be provided for up to a maximum of nine (9) weeks of therapy (3 doses).
- Renewal: Prior authorization validity may be renewed every 6 months thereafter, unless otherwise specified.
  - Biliary Tract Cancers**, Bladder Cancer/Urothelial Carcinoma (excluding adjuvant therapy), Cervical Cancer, Cutaneous Melanoma (in combination with lenvatinib OR trametinib and dabrafenib), cSCC, Endometrial Carcinoma (Uterine Neoplasms), Esophageal and Esophagogastric/Gastroesophageal Junction Cancer (first-line, induction, or subsequent therapy), Gastric Cancer (first-line therapy), HCC, MCC, MSI-H/dMMR Cancer**, NSCLC (first-line or subsequent therapy), RCC (first-line or subsequent therapy), Head and Neck Cancers (excluding use as neoadjuvant or adjuvant treatment), Thymic Carcinoma, Thyroid Carcinoma, TMB-H Cancer, TNBC (recurrent unresectable or metastatic disease), and Pleural Mesothelomia: Prior authorization validity may be renewed up to a maximum of twenty-four (24) months of therapy.*

- Neoadjuvant therapy for all the following: TNBC, resectable NSCLC, Biliary Tract Cancer (MSI-H/dMMR Gallbladder Cancer), and resectable Head and Neck Cancer: Prior authorization validity may not be renewed.
- Therapy for MSI-H/dMMR Esophageal, Esophagogastric/Gastroesophageal Junction, and Gastric Cancer: Prior authorization validity may be renewed for a maximum of 48 weeks (16 doses) of postoperative therapy after surgery.
- Adjuvant therapy of resected NSCLC, Bladder/Urothelial Cancer, RCC, Head and Neck Cancer, and Cutaneous Melanoma *(if no previous neoadjuvant pembrolizumab was used)*: Prior authorization validity may be renewed up to a maximum of twelve (12) months of therapy.*
- Adjuvant therapy (following neoadjuvant therapy) for resectable NSCLC: Prior authorization validity may be renewed for up to a maximum of thirty-nine (39) weeks of adjuvant therapy.*
- Adjuvant therapy for Cutaneous Melanoma (following neoadjuvant treatment): Prior authorization validity may be renewed 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 TNBC: Prior authorization validity may be renewed up to a maximum of twenty-seven (27) weeks of therapy.*

***Excluding post-operative therapy for MSI-H/dMMR Esophageal, Esophagogastric/Gastroesophageal Junction, & Gastric Cancer, and Neoadjuvant therapy for Biliary Tract Cancer (MSI-H/dMMR Gallbladder cancer)*

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**
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

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

- 790 billable units every 6 weeks

III. Initial Approval Criteria [1,2]

Prior authorization validity 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 unless otherwise specified [Δ] *(Note: Not applicable when used as switch-therapy from intravenous pembrolizumab)*; **AND**
- Therapy will not be used concomitantly with intravenous pembrolizumab; **AND**
- Therapy will not be used concurrently with intravenous chemotherapy agents *(not applicable when used for FDA approved combination therapy indicated with* **†***)*; **AND**
- Intravenous pembrolizumab must be used for patients weighing <55 kg; **AND**

Substitution/Switch-Therapy for Intravenous Pembrolizumab ‡ [2,4,5,8-12,15-17,22-29,31,32,35-46,51-53,54-58,62,63,65-70,72-77,80,83-95,98,100,101,103-115,124,125,128,129]

- Used as substitution for OR switch-therapy from intravenous pembrolizumab; **AND**
  - Patient has previously met criteria for use of intravenous pembrolizumab *[see Keytruda IV-E policy Document Number: IC-0523, as applicable]*; **AND**
    - Patient has been receiving treatment with intravenous pembrolizumab and has shown a beneficial disease response and absence of unacceptable toxicity while on therapy; **OR**
  - Patient currently meets criteria for use of intravenous pembrolizumab *[see Keytruda IV-E policy Document Number: IC-0523, as applicable]*; **AND**
- Patient has any of the following indications for treatment *(may not be all inclusive)*:
  - Urothelial Carcinoma (Bladder Cancer)
  - Triple-Negative Breast Cancer (TNBC)
  - Cervical Cancer
  - Esophageal Cancer and Esophagogastric/Gastroesophageal Junction Cancer
  - Head and Neck Cancers
  - Hepatocellular Carcinoma (HCC)
  - Renal Cell Carcinoma (RCC)
  - Cutaneous Melanoma
  - Merkel Cell Carcinoma (MCC) (≥ 12 years of age)

- Non-Small Cell Lung Cancer (NSCLC)
- Cutaneous Squamous Cell Carcinoma (cSCC)
- Thymic Carcinoma
- Thyroid Carcinoma
- Endometrial Carcinoma (Uterine Neoplasms)
- Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Cancer (≥ 12 years of age)
- Tumor Mutational Burden-High (TMB-H) Cancer (≥ 12 years of age)

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 locally advanced unresectable or metastatic disease; **AND**
- Used as primary treatment

Urothelial Carcinoma (Bladder Cancer) † [1,2,8,10,35-37,88,93,99,111,192e]

- Used in combination with enfortumab vedotin; **AND**
  - Used as first-line therapy; **AND**
  - Patient has locally advanced or metastatic urothelial carcinoma; **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 locally advanced or metastatic urothelial carcinoma**; AND**
    - Used for disease that progressed during or following platinum-containing chemotherapy*; **OR**
    - Used as first-line therapy in patients 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 in the metastatic setting for cisplatin-ineligible patients such as those with a GFR less than 60 mL/min.* ▪ *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 locally 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 disease; **AND**
  - Used as neoadjuvant/preoperative therapy in combination with carboplatin and docetaxel; **AND**
    - Use of pembrolizumab is restricted to patients with a contraindication or intolerance to a neoadjuvant/preoperative regimen including doxorubicin and/or cyclophosphamide; **OR**
  - Used as adjuvant therapy as a single agent* following use as neoadjuvant/preoperative therapy in combination with chemotherapy

**There are no data on sequencing or combining adjuvant pembrolizumab with capecitabine or olaparib in patients who meet criteria for treatment with one or more of these agents. However, their sequential/combined use may be considered given high-risk of recurrence in patients with residual disease*

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**
  - Disease is not amenable to curative treatment (i.e., surgery and/or radiation); **AND**
  - Used as first-line therapy

**FIGO 2014 Stage III-IVA disease is locally advanced cervical cancer involving the lower third of the vagina, with or without extension to pelvic sidewall, or hydronephrosis/non-functioning kidney, or spread to adjacent pelvic organs*

^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 has locally advanced unresectable or metastatic disease; **AND**
  - Used as first-line therapy and tumor expresses PD-L1 (CPS ≥ 1) as determined by an FDA-approved or CLIA compliant test❖; **AND**
    - Patient has HER2-positive adenocarcinoma; **AND**
      - Used in combination with trastuzumab AND fluorouracil or capecitabine AND oxaliplatin or cisplatin; **OR**
    - Patient has HER2-negative adenocarcinoma; **AND**
      - Used in combination with oxaliplatin or cisplatin AND either fluorouracil or capecitabine; **OR**
    - Patient has squamous cell carcinoma; **AND**
      - Used in combination with oxaliplatin or cisplatin AND either fluorouracil or capecitabine; **OR**
  - Used as subsequent therapy; **AND**
    - Used as a single agent; **AND**
    - Patient has squamous cell carcinoma; **AND**
    - Tumor expresses PD-L1 (CPS ≥ 10) as determined by an FDA-approved or CLIA compliant test❖**; AND**
    - Patients with HER2-positive disease must have previously received HER2-directed therapy (e.g., trastuzumab, etc.), unless contraindicated

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

- Patient has locally advanced unresectable or metastatic disease; **AND**
- Tumor expresses PD-L1 (CPS ≥ 1) as determined by an FDA-approved or CLIA compliant test❖**; AND**
- Used as first-line therapy; **AND**
  - Patient has HER2-positive adenocarcinoma; **AND**
    - Used in combination with trastuzumab AND fluorouracil or capecitabine AND oxaliplatin or cisplatin; **OR**
  - Patient has HER2-negative adenocarcinoma; **AND**
    - Used in combination with oxaliplatin or cisplatin AND either fluorouracil or capecitabine

Head and Neck Cancers † [1,2,31,32,106,125,129,42e,188e]

- Patient has unresectable, recurrent, or metastatic squamous cell carcinoma; **AND**
- Patient has NON-nasopharyngeal cancer; **AND**
  - Used in combination with carboplatin or cisplatin AND fluorouracil; **AND**
    - Used as first line therapy; **OR**
  - Used as a single agent; **AND**
    - Tumor expresses PD-L1 (CPS ≥1) as determined by an FDA-approved or CLIA-compliant test❖; **AND**
      - ➢ Used as first-line therapy †; **OR**
      - ➢ Used as subsequent therapy for disease that has progressed on or after platinum-containing chemotherapy

Hepatocellular Carcinoma (HCC) † Φ [1,2,43,107]

- Used as a single agent; **AND**
- Patient does not have Child-Turcotte-Pugh (CTP) Class C liver disease; **AND**
- Disease is secondary to hepatitis B; **AND**
- Patient has received prior systemic therapy other than a PD-1/PD-L1- containing regimen

Renal Cell Carcinoma (RCC) † [1,2,45,74-76,281e,289e,290e]

- Patient has clear cell histology; **AND**
  - Used in combination with axitinib; **AND**
    - Used as first-line therapy for advanced disease; **AND**

        - Use of pembrolizumab will be restricted to patients with a contraindication or intolerance to pembrolizumab/lenvatinib; **OR**
    - Used in combination with lenvatinib; **AND**
        - Used as first-line therapy for advanced disease; **OR**
    - Used as a single agent; **AND**
        - Used as adjuvant therapy; **AND**
            - Patient has intermediate-high or high risk of recurrence following nephrectomy; **OR**
            - Patient has undergone nephrectomy and resection of metastatic lesions; **OR**
- Patient has non-clear cell histology; **AND**
    - Used in combination with lenvatinib; **AND**
    - Used as first line therapy for advanced disease

Pleural Mesothelioma (PM) † [1,2]

- Used in combination with pemetrexed and AND either cisplatin or carboplatin; **AND**
- Used as first line therapy for unresectable advanced or metastatic disease

Cutaneous Melanoma † Φ [1,2,22-24,65,68,87,112,15e]

- Used as a single agent for unresectable or metastatic* disease; **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) † Φ [1,2,9,44,22e]

- Patient is at least 12 years of age; **AND**
- Used as a single agent; **AND**
- Used as first-line therapy**; AND**
- Used for one of the following:
    - Patient has recurrent locally advanced disease; **AND**
        - Both curative surgery and curative radiation therapy are not feasible; **OR**
    - Patient has M1 disseminated disease; **AND**

- Use of pembrolizumab will be restricted to patients with a contraindication or intolerance to retifanlimab

Non-Small Cell Lung Cancer (NSCLC) † [1,2,11,25-29,84,120e,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; **AND**

PD-L1 expression ≥50%:

- Use of pembrolizumab will be restricted to patients with a contraindication or intolerance to cemiplimab; **OR**

- Used as neoadjuvant therapy; **AND**
  - Patient has resectable 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 ≥4 cm), II, or IIIA disease; **OR**
- Used for metastatic disease; **AND**
  - Used as first-line therapy; **AND**
    - Used in combination with pemetrexed AND either carboplatin or cisplatin for non-squamous cell histology with no EGFR or ALK genomic tumor aberrations; **AND**
      - ➢ Use of pembrolizumab will be restricted to patients with a contraindication or intolerance to cemiplimab/pemetrexed/(carboplatin or cisplatin); **OR**
    - Used in combination with carboplatin AND either paclitaxel or albumin-bound paclitaxel for squamous cell histology; **AND**
      - ➢ Use of pembrolizumab will be restricted to patients with a contraindication or intolerance to cemiplimab/paclitaxel/(carboplatin or cisplatin); **OR**
    - Used as a single agent; **AND**

- Used in patients with tumors expressing PD-L1 (TPS ≥1%) as determined by an FDA-approved or CLIA compliant test❖; **AND**
- Patient has no EGFR or ALK genomic tumor aberrations; **AND**

PD-L1 expression ≥50%:

- Use of pembrolizumab will be restricted to patients with a contraindication or intolerance to cemiplimab; **OR**

- Used as subsequent therapy as a single agent; **AND**
  - Used in patients with tumors expressing PD-L1 (TPS ≥1%) as determined by an FDA-approved or CLIA compliant test❖; **AND**
  - Patient has disease progression on or after platinum-containing chemotherapy *(Note: Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations§)*

§ Genomic Aberration/Mutational Driver Targeted Therapies: Refer to guidelines for appropriate use.

Cutaneous Squamous Cell Carcinoma (cSCC) †[1,2,58,125e]

- Used as a single agent; **AND**
- Patient has locally advanced or metastatic disease that is not curable by surgery or radiation; **AND**
- Use of pembrolizumab will be restricted to patients with a contraindication or intolerance to cemiplimab

Endometrial Carcinoma (Uterine Neoplasms) † [1,2,46,80,91,255e]

- Used in combination with lenvatinib; **AND**
  - Disease is mismatch repair proficient (pMMR) or NOT microsatellite instability-high (MSI-H) as determined by an FDA-approved or CLIA-compliant test❖; **AND**
  - Used as subsequent therapy for advanced disease; **AND**
  - Patient has disease progression following prior platinum-based therapy in any setting and are not candidates for curative surgery or radiation; **OR**
- Used in combination with carboplatin and paclitaxel, followed by single agent maintenance therapy; **AND**
  - Used for primary advanced disease (*excluding use in patients with carcinosarcoma*); **AND**
    - Patient has Stage III or IV disease♦; **AND**

Patients with dMMR tumors ONLY:

▪ Use of pembrolizumab will be restricted to patients with a contraindication or intolerance to durvalumab/carboplatin/paclitaxel; **OR**

  - Used for recurrent disease (*excluding use in patients with carcinosarcoma*); **AND**
    - Used as first-line therapy; **AND**

<u>Patients with dMMR tumors ONLY:</u> ▪ Use of pembrolizumab will be restricted to patients with a contraindication or intolerance to durvalumab/carboplatin/paclitaxel; **OR**

- Used as a single agent as maintenance therapy following treatment with pembrolizumab in combination with carboplatin and paclitaxel

♦*Note: For patients not meeting the eligibility criteria for NRG-GY018, carboplatin/paclitaxel + pembrolizumab should be considered for stage III-IV dMMR tumors.*

Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Cancer † ‡ [1,2,4,38,51,110,113-115]

- Patient has microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), as determined by an FDA-approved or CLIA compliant test❖; **AND**
- Used as a single agent; **AND**
  - Patient has unresectable or metastatic solid tumors; **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, unless contraindicated; **OR**
      - Patient has no satisfactory alternative treatment options; **AND**
    - Patient is at least 12 years of age; **OR**
  - Used as initial therapy for unresectable or metastatic colorectal cancer

Tumor Mutational Burden-High (TMB-H) Cancer † [1,2]

- Patient is at least 12 years of age; **AND**
- Patient has tumor mutational burden-high (TMB-H) [≥ 10 mutations/megabase (mut/Mb)] disease, 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 has unresectable or metastatic solid tumors; **AND**
- Used for disease progression following prior treatment and patient has no satisfactory alternative treatment options

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.*	

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.

Enhanced Oncology Value (EOV) Program – Redacted indications
Uses not listed above have inadequate data to support efficacy and are excluded from prior authorization validity. Other treatment options including, but are not limited to, the following may be appropriate: radiation therapy, surgery, traditional chemotherapy (e.g., platinum, taxane), compassionate use/expanded access programs, clinical trials, supportive care, integrative and complementary therapies.

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

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

IV. Renewal Criteria [Δ 1-3,5,6,15-17,50,51,53,57,62,65,68,69,70,72,73,75-77,82,85-87,95,101,103,109,112,117-124]

Prior authorization validity can be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Duration of authorization has not been exceeded *(refer to Section I)*; **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: immune-mediated adverse reactions (e.g., pneumonitis, hepatitis, colitis, endocrinopathies, nephritis/renal dysfunction, rash/dermatitis [including Stevens-Johnson syndrome (SJS), drug rash with eosinophilia and systemic symptoms (DRESS), and toxic epidermal necrolysis (TEN)], myocarditis, pericarditis, vasculitis, solid organ transplant rejection, etc.), severe infusion-related reactions, complications of allogeneic hematopoietic stem cell transplantation (HSCT), etc.

Δ Notes:

- Patients responding to therapy who relapse ≥ 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 ≥ 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.

V. Dosage/Administration Δ 1-6,8,12,13,15-17,22-48,50-57,62,65,68,70,72,73,75-77,82,83,85-87,91,92,95,101,103-106,109,112,117-124,126-129,15e

Indication	Dose
Bladder Cancer/Urothelial Carcinoma	**Adjuvant treatment:** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks for up to a maximum of 12 months of therapy in patients without disease progression or unacceptable toxicity **Single agent:** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks until disease progression or unacceptable toxicity for up to 24 months **Locally Advanced or Metastatic disease: †** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks with enfortumab vedotin until disease progression or unacceptable toxicity for up to 24 months
Head and Neck Cancers	**Neoadjuvant therapy for resectable disease:** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks up to a maximum of 6 weeks in patients without disease progression or unacceptable toxicity

	Adjuvant treatment for resectable disease *(single agent)*: 395 mg/4,800 units every 3 weeks or 790 mg/9,600 every 6 weeks up to a maximum of 12 months in patients without disease progression or unacceptable toxicity **First-line therapy: †** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks with carboplatin or cisplatin AND fluorouracil, until disease progression or unacceptable toxicity for up to 24 months **All other treatment settings:** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 every 6 weeks until disease progression or unacceptable toxicity for up to 24 months
Cervical Cancer	**Single agent:** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks until disease progression or unacceptable toxicity for up to 24 months **All other treatment settings: †** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks with chemoradiotherapy or chemotherapy with or without bevacizumab, until disease progression or unacceptable toxicity for up to 24 months
Biliary Tract Cancers	**Neoadjuvant as a single agent *(MSI-H/dMMR Gallbladder Cancer only)*:** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks up to a maximum of 6 months in patients without disease progression or unacceptable toxicity **Unresectable or Metastatic disease: †** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks with gemcitabine and cisplatin until disease progression or unacceptable toxicity for up to 24 months
Endometrial Carcinoma/Uterine Neoplasms	**Primary advanced or recurrent disease: †** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks with carboplatin and paclitaxel followed by single agent maintenance, until disease progression or unacceptable toxicity for up to 24 months **First-line or subsequent therapy with lenvatinib:** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks until disease progression or unacceptable toxicity for up to 24 months **Single agent:** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks until disease progression or unacceptable toxicity for up to 24 months

Esophageal and Esophagogastric/ Gastroesophageal Junction Cancer	**First-line therapy:** † 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks with fluoropyrimidine- and platinum-containing chemotherapy and trastuzumab for HER2 positive disease, until disease progression or unacceptable toxicity for up to 24 months **Single agent *(Induction OR Subsequent therapy for squamous cell carcinoma)*:** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks until disease progression or unacceptable toxicity for up to 24 months **Neoadjuvant therapy as a single agent *(MSI-H/dMMR disease ONLY)*:** 395 mg/4,800 units every 3 weeks for at least 12 weeks, followed by surgery and then post-operative therapy *(See below)* **Post-operative therapy as a single agent *(MSI-H/dMMR disease ONLY)*:** 395 mg/4,800 units every 3 weeks for 48 weeks (16 cycles)
Gastric Cancer	**First-line therapy *(HER2 positive/negative adenocarcinoma)*:** † 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks with fluoropyrimidine- and platinum-containing chemotherapy and trastuzumab for HER2 positive disease, until disease progression or unacceptable toxicity for up to 24 months **Neoadjuvant therapy as a single agent *(MSI-H/dMMR disease ONLY)*:** 395 mg/4,800 units every 3 weeks for at least 12 weeks, followed by surgery and then post-operative therapy *(See below)* **Post-operative therapy as a single agent *(MSI-H/dMMR disease ONLY)*:** 395 mg/4,800 units every 3 weeks for 48 weeks (16 cycles)

NSCLC	**Neoadjuvant and adjuvant treatment of resectable NSCLC: †** • Neoadjuvant therapy: 395 mg/4,800 units every 3 weeks or 790 mg/9,600 every 6 weeks in combination with chemotherapy for 12 weeks or until disease progression that precludes definitive surgery or unacceptable toxicity • Adjuvant therapy: 395 mg/4,800 units every 3 weeks or 790 mg/9,600 every 6 weeks as a single agent after surgery for 39 weeks or until disease recurrence or unacceptable toxicity **Adjuvant treatment of resected NSCLC:** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 every 6 weeks up to a maximum of 12 months in patients without disease recurrence or unacceptable toxicity **First-line therapy *(metastatic squamous or nonsquamous disease)*: †** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks with histology based chemotherapy, until disease progression or unacceptable toxicity for up to 24 months **All other settings as a single agent:** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks until disease progression or unacceptable toxicity for up to 24 months
RCC	**First-line therapy:** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks with chemotherapy until disease progression or unacceptable toxicity for up to 24 months **Adjuvant therapy:** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks up to a maximum of 12 months in patients without disease recurrence or unacceptable toxicity
TNBC	**Recurrent unresectable or metastatic disease: †** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks with chemotherapy until disease progression or unacceptable toxicity for up to 24 months **Neoadjuvant therapy: †** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks up to a maximum of 24 weeks in patients without disease progression or unacceptable toxicity (up to 8 doses of 395 mg/4,800 units every 3 weeks or 4 doses of 790 mg/9,600 every 6 weeks) **Adjuvant therapy*:**

	395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks up to a maximum of 27 weeks in patients without disease recurrence or unacceptable toxicity (up to 9 doses of 395 mg/4,800 units every 3 weeks or 5 doses of 790 mg/9,600 units every 6 weeks) ** 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.*
Cutaneous Melanoma	**Single-agent therapy *(excluding neoadjuvant and adjuvant treatment)*:** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks until disease progression or unacceptable toxicity **In combination with lenvatinib OR trametinib and dabrafenib:** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks until disease progression or unacceptable toxicity for up to 24 months **Neoadjuvant and adjuvant treatment:** • 395 mg/4,800 units every 3 weeks for 3 doses in the neoadjuvant setting, followed by surgery and then adjuvant treatment (see below) • 395 mg/4,800 units every 3 weeks for 15 doses in the adjuvant setting in patients without disease progression or unacceptable toxicity **Adjuvant treatment (*if no neoadjuvant pembrolizumab was used*):** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks up to a maximum of 12 months in patients without disease recurrence or unacceptable toxicity
Pleural Mesothelioma	**First-line therapy: †** 395 mg/4,800 units every 3 weeks or 790 mg/9,600 units every 6 weeks with pemetrexed and platinum chemotherapy until disease progression or unacceptable toxicity for up to 24 months
All other indications	395 mg/4,800 units every 3 weeks or 790 mg/9,600 every 6 weeks until disease progression or unacceptable toxicity for up to 24 months

VI. Billing Code/Availability Information

HCPCS Code:

- J9277 – Injection, pembrolizumab, 1 mg and berahyaluronidase alfa-pmph; 1 billable unit = 1 mg *(Effective 04/01/2026)*
- J9999 – Not otherwise classified, antineoplastic drugs *(Discontinue use on 04/01/2026)*

NDC(s):

- Keytruda Qlex single-dose vial providing 395 mg pembrolizumab and 4,000 units berahyaluronidase alfa per 2.4 mL (165 mg/2,000 units per mL): 00006-3083-xx
- Keytruda Qlex single-dose vial providing 790 mg pembrolizumab and 9,600 units berahyaluronidase alfa per 2.4 mL (165 mg/2,000 units per mL): 00006-5083-xx

VII. References (STANDARD)

1. Keytruda Qlex [package insert]. Rahway, NJ; Merck & Co., Inc.; September 2025. Accessed November 2025.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) pembrolizumab. National Comprehensive Cancer Network, 2025. 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 November 2025.
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 1.2026. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE

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10. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Bladder Cancer. Version 1.2025. National Comprehensive Cancer Network, 2025. 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 November 2025.
11. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Non-Small Cell Lung Cancer. Version 8.2025. National Comprehensive Cancer Network, 2025. 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 November 2025.
12. Ghorani E, Kaur B, Fisher RA, et al. Pembrolizumab is effective for drug-resistant gestational trophoblastic neoplasia. Lancet. 2017 Nov 25;390(10110):2343-2345.7
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 85067
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 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:JCO2017773184. 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, Mandala 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, Hiret 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. 2019;5(4):546-550. 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 2.2025. National Comprehensive Cancer Network, 2025. 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 October 2025.
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 4.2025. National Comprehensive Cancer Network, 2025. 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 October 2025.
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 3.2025. National Comprehensive Cancer Network, 2025. 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 October 2025.
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 SARC028 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. Geoerger 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)30671-0.0

61. Pembrolizumab Improves Progression-Free Survival in Relapsed/Refractory Hodgkin Lymphoma. Oncologist. 2020;25 Suppl 1(Suppl 1):S18-S19. doi:10.1634/theoncologist.2020-0561.0
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 Oncology38, 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, Pusztai 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., Valderrama BP (2025). Treatment of metastatic urothelial cancer of the bladder and urinary tract. In Lerner SP, Shah S (Eds.), UptoDate. Last updated: Sep 02, 2025. Accessed September 10, 2025. Available from https://www.uptodate.com/contents/treatment-of-metastatic-urothelial-cancer-of-the-bladder-and-urinary-tract
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, Hiret 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 2.2025. National Comprehensive Cancer Network, 2025. 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 October 2025.
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 2.2026. National Comprehensive Cancer Network, 2025. 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 October 2025.
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 4.2025. National Comprehensive Cancer Network, 2025. 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 November 2025.
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 3.2025. National Comprehensive Cancer Network, 2025. 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 November 2025.

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.A
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.A
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 1.2025. National Comprehensive Cancer Network, 2025. 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 November 2025.
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 4.2025. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®.

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114. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Rectal Cancer. Version 4.2025. National Comprehensive Cancer Network, 2025. 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 November 2025.
115. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Colon Cancer. Version 5.2025. National Comprehensive Cancer Network, 2025. 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 November 2025.
116. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Breast Cancer. Version 5.2025. National Comprehensive Cancer Network, 2025. 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 November 2025.
117. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pembrolizumab: Biliary Tract Cancers, BIL12. National Comprehensive Cancer Network, 2025. 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 Guidelines, go online to NCCN.org. Accessed June 2025.
118. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pembrolizumab: Biliary Tract Cancers, BIL33. National Comprehensive Cancer Network, 2025. 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 Guidelines, go online to NCCN.org. Accessed June 2025.
119. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pembrolizumab: Melanoma: Cutaneous, MEL39. National Comprehensive Cancer Network, 2025. 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 Guidelines, go online to NCCN.org. Accessed June 2025.

120. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pembrolizumab: Thymomas and Thymic Carcinomas, THYM19. National Comprehensive Cancer Network, 2025. 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 Guidelines, go online to NCCN.org. Accessed June 2025.
121. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pembrolizumab: Vulvar Cancer, VUL12. National Comprehensive Cancer Network, 2025. 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 Guidelines, go online to NCCN.org. Accessed June 2025.
122. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pembrolizumab: Adrenal Gland Tumors, AGT9. National Comprehensive Cancer Network, 2025. 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 Guidelines, go online to NCCN.org. Accessed June 2025.
123. Armand P, Murawski N, Molin D, et al. Pembrolizumab in relapsed or refractory Richter syndrome. Br J Haematol 2020;190:e117-e120.
124. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Penile Cancer. Version 2.2025. National Comprehensive Cancer Network, 2025. 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 October 2025.
125. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Head and Neck Cancers. Version 5.2025. National Comprehensive Cancer Network, 2025. 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 November 2025.
126. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pembrolizumab: Penile Cancer, PEN19. National Comprehensive Cancer Network, 2025. 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 Guidelines, go online to NCCN.org. Accessed June 2025.

127. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pembrolizumab: Penile Cancer, PEN20. National Comprehensive Cancer Network, 2025. 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 Guidelines, go online to NCCN.org. Accessed June 2025.
128. Apolo AB, Ballman KV, Sonpavde G, et al. Adjuvant Pembrolizumab versus Observation in Muscle-Invasive Urothelial Carcinoma. N Engl J Med. 2025;392(1):45-55
129. French JD, Haugen BR, Worden FP, et al. Combination targeted therapy with pembrolizumab and lenvatinib in progressive, radioiodine-refractory differentiated thyroid cancers. Clin Cancer Res 2024;30:3757-3767.
130. National Institutes of Health. Study of Pembrolizumab Given Prior to Surgery and in Combination With Radiotherapy Given Post-surgery for Advanced Head and Neck Squamous Cell Carcinoma (MK-3475-689). Available at: https://clinicaltrials.gov/study/NCT03765918.
131. Keytruda [package insert]. Rahway, NJ; Merck & Co., Inc.; August 2025. Accessed November 2025.

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. 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, Cabarrou 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, Hagemeister 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. Geoerger 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, Csőszi 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

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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, er 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. Garmezy 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. Rao S, Anandappa G, Capdevila J, et al. A phase II study of retifanlimab (INCMGA00012) in patients with squamous carcinoma of the anal canal who have progressed following platinum-based

chemotherapy (POD1UM-202). ESMO Open. 2022 Aug;7(4):100529. doi: 10.1016/j.esmoop.2022.100529. Epub 2022 Jul 8. PMID: 35816951; PMCID: PMC9463376.

210e. Bouffet E, Larouche V, Campbell BB, et al. Immune Checkpoint Inhibition for Hypermutant Glioblastoma Multiforme Resulting From Germline Biallelic Mismatch Repair Deficiency. J Clin Oncol. 2016 Jul 1;34(19):2206-11.

211e. You B, Bolze P, Lotz J, et al. Avelumab in Patients With Gestational Trophoblastic Tumors With Resistance to Single-Agent Chemotherapy: Cohort A of the TROPHIMMUN Phase II Trial. J Clin Oncol. 2020;38(27):3129-3137. DOI: 10.1200/JCO.20.00803

212e. Chu Q, Perrone F, Tu W, et al. Pembrolizumab plus chemotherapy versus chemotherapy in untreated advanced pleural mesothelioma in Canada, Italy, and France: a phase 3, open-label, randomised controlled trial. Lancet. 2023 Dec 16;402(10419):2295-2306. Doi: 10.1016/S1040-6736(23)01613-6. Epub 2023 Nov 3

213e. Lemma GL, Lee JW, Aisner SC, et al. Phase II study of carboplatin and paclitaxel in advanced thymoma and thymic carcinoma. J Clin Oncol 2011;29:2060-2065.

214e. Shapira-Frommer R, Mileshkin L, Manzyuk L, et al. Efficacy and safety of pembrolizumab for patients with previously treated advanced vulvar squamous cell carcinoma: Results from the phase 2 KEYNOTE158 study. Gynecol Oncol 2022;166:211-218.

215e. Baas P, Scherpereel A, Nowak AK, et al. First-line nivolumab plus ipilimumab in unresectable malignant pleural mesothelioma (CheckMate 743): a multicentre, randomised, open-label, phase 3 trial [published correction appears in Lancet. 2021 Feb 20;397(10275):670. doi: 10.1016/S0140-6736(21)00369-X]. *Lancet*. 2021;397(10272):375-386. doi:10.1016/S0140-6736(20)32714-8.

216e. Zalcman G, Mazieres J, Margery J, et al. Bevacizumab for newly diagnosed pleural mesothelioma in the Mesothelioma Avastin Cisplatin Pemetrexed Study (MAPS): a randomised, controlled, open-label, phase 3 trial [published correction appears in Lancet. 2016 Apr 2;387(10026):e24. doi: 10.1016/S0140-6736(16)30084-8]. *Lancet*. 2016;387(10026):1405-1414. doi:10.1016/S0140-6736(15)01238-6

217e. Migden MR, Khushalani NI, Chang ALS, et al. Cemiplimab in locally advanced cutaneous squamous cell carcinoma: results from an open-label, phase 2, single-arm trial. The Lancet Oncology. 2020;21(2):294-305. doi:https://doi.org/10.1016/s1470-2045(19)30728-4

218e. Li J, Xu Y, Zang A, et al. Tislelizumab in previously treated, locally advanced unresectable/metastatic microsatellite instability-high/mismatch repair-deficient solid tumors. PubMed. 2024;36(3):257-269. doi:https://doi.org/10.21147/j.issn.1000-9604.2024.03.03

219e. Chen Y, Wang Y, Zhang H, et al. Short-course radiotherapy combined with chemotherapy and PD-1 inhibitor in low-lying early rectal cancer: study protocol for a single-arm, multicentre, prospective, phase II trial (TORCH-E). BMJ Open. 2023;13(10):e076048-e076048. doi:https://doi.org/10.1136/bmjopen-2023-076048

220e. André T, Berton D, Curigliano G, et al. Antitumor Activity and Safety of Dostarlimab Monotherapy in Patients With Mismatch Repair Deficient Solid Tumors: A Nonrandomized Controlled Trial. JAMA network open. 2023;6(11):e2341165. doi:https://doi.org/10.1001/jamanetworkopen.2023.41165

221e. Lakhani N, Cosman R, Banerji U, et al. A first-in-human phase I study of the PD-1 inhibitor, retifanlimab (INCMGA00012), in patients with advanced solid tumors (POD1UM-101). ESMO Open. 2024;9(4):102254-102254. doi:https://doi.org/10.1016/j.esmoop.2024.102254

222e. Xia F, Wang Y, Wang H, et al. Randomized Phase II Trial of Immunotherapy-Based Total Neoadjuvant Therapy for Proficient Mismatch Repair or Microsatellite Stable Locally Advanced Rectal Cancer (TORCH). J Clin Oncol. 2024 Oct;42(28):3308-3318. doi: 10.1200/JCO.23.02261.

223e. Li J, Xu Y, Zang, A et al. Tislelizumab in previously treated, locally advanced unresectable/metastatic microsatellite instability-high/mismatch repair-deficient solid tumors. Chin J Cancer Res. 2024 Jun 30;36(3):257-269. doi: 10.21147/j.issn.1000-9604.2024.03.03

224e. Ding W, LaPlant BR, Call TG, et al. Pembrolizumab in patients with CLL and Richter transformation or with relapsed CLL. Blood. 2017;129(26):3419-3427. doi:https://doi.org/10.1182/blood-2017-02-765685

225e. Jain N, Jayastu Senapati, Beenu Thakral, et al. A phase 2 study of nivolumab combined with ibrutinib in patients with diffuse large B-cell Richter transformation of CLL. Blood Advances. 2023;7(10):1958-1966. doi:https://doi.org/10.1182/bloodadvances.2022008790

226e. Othman Al-Sawaf, Ligtvoet R, Robrecht S, et al. Tislelizumab plus zanubrutinib for Richter transformation: the phase 2 RT1 trial. Nature Medicine. Published online December 9, 2023. doi:https://doi.org/10.1038/s41591-023-02722-9

227e. Mato AR, Woyach JA, Brown JR, et al. Pirtobrutinib after a Covalent BTK Inhibitor in Chronic Lymphocytic Leukemia. N Engl J Med. 2023 Jul 6;389(1):33-44. doi: 10.1056/NEJMoa2300696.

228e. Armand P, Murawski N, Molin D, et al. Pembrolizumab in relapsed or refractory Richter syndrome. British Journal of Haematology. 2020;190(2). doi:https://doi.org/10.1111/bjh.16762

229e. Maluf FC, Trindade K, Almeida Preto DD et al. A phase II trial of pembrolizumab plus platinum-based chemotherapy as first-line systemic therapy in advanced penile cancer: HERCULES (LACOG 0218) trial. J Clin Oncol. 2024;42(16_suppl):5009. doi.org/10.1200/JCO.2024.42

230e. Pagliaro LC, Williams DL, Daliani D, et al. Neoadjuvant paclitaxel, ifosfamide, and cisplatin chemotherapy for metastatic penile cancer: a phase II study. J Clin Oncol. 2010 Aug 20;28(24):3851-7. doi: 10.1200/JCO.2010.29.5477. Epub 2010 Jul 12.

231e. Lorenzo GD, Buonerba C, Federico P, et al. Cisplatin and 5-fluorouracil in inoperable, stage IV squamous cell carcinoma of the penis. BJU Int. 2012 Dec;110(11 Pt B):E661-6. doi: 10.1111/j.1464-410X.2012.11453.x. Epub 2012 Sep 10.

232e. Janne PA, Wozniak AJ, Belani CP. Open-Label Study of Pemetrexed Alone or in Combination with Cisplatin for the Treatment of Patients with Peritoneal Mesothelioma: Outcomes of an Expanded Access Program. Clin Lung Cancer. 2005 July;(7)1:40-46

233e. Vogelzang NJ, Rusthoven JJ, Symanowski J, et al. Phase III study of pemetrexed in combination with cisplatin versus cisplatin alone in patients with malignant pleural mesothelioma. J Clin Oncol. 2003 Jul 15;21(14):2636-44. doi: 10.1200/JCO.2003.11.136.

234e. Krug LM, Pass HI, Rusch VW, et al. Multicenter phase II trial of neoadjuvant pemetrexed plus cisplatin followed by extrapleural pneumonectomy and radiation for malignant pleural mesothelioma. J Clin Oncol. 2009 Jun 20;27(18):3007-13. doi: 10.1200/JCO.2008.20.3943.

235e. Thieke C, Nicolay N, Sterzing F, et al. Long-term results in malignant pleural mesothelioma treated with neoadjuvant chemotherapy, extrapleural pneumonectomy and intensity-modulated radiotherapy. Radiat Oncol. 2015 Dec 30:10:267. doi: 10.1186/s13014-015-0575-5.

236e. Polizzotto MN, Uldrick TS, Wyvill KM, et al. Pomalidomide for Symptomatic Kaposi's Sarcoma in People With and Without HIV Infection: A Phase I/II Study. J Clin Oncol. 2016 Dec;34(34):4125-4131

237e. Taylor MH, Lee CH, Makker V, et al. Phase IB/II Trial of Lenvatinib Plus Pembrolizumab in Patients With Advanced Renal Cell Carcinoma, Endometrial Cancer, and Other Selected Advanced Solid Tumors. J Clin Oncol. 2020 Apr 10;38(11):1154-1163. doi: 10.1200/JCO.19.01598.

238e. Bennani NN, Pederson LD, Atherton P, et al. A Phase II Study of Nivolumab in Patients with Relapsed or Refractory Peripheral T-Cell Lymphoma. Blood. 2019;134(S1):467

239e. Lesokhin AM, Ansell SM, Armand P, et al. Nivolumab in Patients With Relapsed or Refractory Hematologic Malignancy: Preliminary Results of a Phase Ib Study. J Clin Oncol. 2016 Aug 10;34(23):2698-704. doi: 10.1200/JCO.2015.65.9789.

240e. Kim SJ, Lim JQ, Laurensia Y, et al. Avelumab for the treatment of relapsed or refractory extranodal NK/T-cell lymphoma: an open-label phase 2 study. Blood. 2020 Dec 10;136(24):2754-2763. doi: 10.1182/blood.2020007247

241e. Penel N, Bui BN, Bay JO, et al. Phase II trial of weekly paclitaxel for unresectable angiosarcoma: the ANGIOTAX Study. J Clin Oncol. 2008 Nov 10;26(32):5269-74. doi: 10.1200/JCO.2008.17.3146

242e. Antman K, Crowly J, Balcerzak SP, et al. An intergroup phase III randomized study of doxorubicin and dacarbazine with or without ifosfamide and mesna in advanced soft tissue and bone sarcomas. J Clin Oncol. 1993 Jul;11(7):1276-85. doi: 10.1200/JCO.1993.11.7.1276

243e. 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]. J Clin Oncol. 2007 Jul 1;25(19):2755-63. doi: 10.1200/JCO.2006.10.4117.

244e. Van der Graaf, Blay JY, Chawla SP, et al. Pazopanib for metastatic soft-tissue sarcoma (PALETTE): a randomised, double-blind, placebo-controlled phase 3 trial. Lancet. 2012 May 19;379(9829):1879-86. doi: 10.1016/S0140-6736(12)60651-5.

245e. Schoffski P, Ray-Coquard IL, Cioffi A, et al. Activity of eribulin mesylate in patients with soft-tissue sarcoma: a phase 2 study in four independent histological subtypes. Lancel Oncol. 2011 Oct;12(11):1045-52. doi: 10.1016/S1470-2045(11)70230-3.

246e. 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. Journal for ImmunoTherapy of Cancer. 2019;7(1). doi:https://doi.org/10.1186/s40425-019-0689-7

247e. 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. Journal of Clinical Oncology. 2007;25(19):2755-2763. doi:https://doi.org/10.1200/jco.2006.10.4117

248e. Samuels BL, Chawla SP, Patel S, et al. Clinical outcomes and safety with trabectedin therapy in patients with advanced soft tissue sarcomas following failure of prior chemotherapy: results of a worldwide expanded access program study. Annals of Oncology. 2013;24(6):1703-1709. doi:https://doi.org/10.1093/annonc/mds659

249e. García-Del-Muro X, López-Pousa A, Maurel J, et al. Randomized phase II study comparing gemcitabine plus dacarbazine versus dacarbazine alone in patients with previously treated soft tissue sarcoma: a Spanish Group for Research on Sarcomas study. Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology. 2011;29(18):2528-2533. doi:https://doi.org/10.1200/JCO.2010.33.6107

250e. 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. doi: 10.1200/JCO.2006.06.5821.

251e. Eckardt JR, von Pawel J, Pujol JL, et al. Phase III study of oral compared with intravenous topotecan as second-line therapy in small-cell lung cancer. J Clin Oncol. 2007 May 20;25(15):2086-92. doi: 10.1200/JCO.2006.08.3998.

252e. Edelman MJ, Dvorkin M, Laktionov K, et al. Randomized phase 3 study of the anti-disialoganglioside antibody dinutuximab and irinotecan vs irinotecan or topotecan for second-line treatment of small cell lung cancer. Lung Cancer. 2022 Apr:166:135-142. doi: 10.1016/j.lungcan.2022.03.003.

253e. Duvic M, Tetzlaff MT, Gangar P, et al. Results of a Phase II Trial of Brentuximab Vedotin for CD30+ Cutaneous T-Cell Lymphoma and Lymphomatoid Papulosis. J Clin Oncol. 2015 Nov 10;33(32):3759-65. doi: 10.1200/JCO.2014.60.3787.

254e. Patel SP, Othus M, Chae YK, et al. A Phase II Basket Trial of Dual Anti–CTLA-4 and Anti–PD-1 Blockade in Rare Tumors (DART SWOG 1609 Cohort 47) in Patients with Gestational Trophoblastic Neoplasia. Clinical Cancer Research. 2023;30(1):33-38. doi:https://doi.org/10.1158/1078-0432.ccr-23-2293

255e. Westin SN, Moore KN, Hye Sook Chon, et al. Durvalumab Plus Carboplatin/Paclitaxel Followed by Maintenance Durvalumab With or Without Olaparib as First-Line Treatment for Advanced Endometrial Cancer: The Phase III DUO-E Trial. *Journal of Clinical Oncology*. Published online October 21, 2023. doi:https://doi.org/10.1200/jco.23.02132.

256e. Sharma P, Stecklein SR, Yoder R, et al. Clinical and Biomarker Findings of Neoadjuvant Pembrolizumab and Carboplatin Plus Docetaxel in Triple-Negative Breast Cancer: NeoPACT Phase 2 Clinical Trial. JAMA Oncol. 2024 Feb 1;10(2):227-235. doi: 10.1001/jamaoncol.2023.5033.

257e. Early Breast Cancer Trialists' Collaborative Group (EBCTCG); Peto R, Davies C, Godwin J, et al. Comparisons between different polychemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100,000 women in 123 randomised trials. Lancet. 2012 Feb 4;379(9814):432-44. doi: 10.1016/S0140-6736(11)61625-5. Epub 2011 Dec 5.

258e. Vergote I, Van Nieuwenhuysen E, O'Cearbhaill RE, et al. Tisotumab Vedotin in Combination With Carboplatin, Pembrolizumab, or Bevacizumab in Recurrent or Metastatic Cervical Cancer: Results From the innovaTV 205/GOG-3024/ENGOT-cx8 Study. J Clin Oncol. 2023 Dec 20;41(36):5536-5549. doi: 10.1200/JCO.23.00720. Epub 2023 Aug 31.

259e. Qiu MZ, Oh DY, Kato K, et al. Tislelizumab plus chemotherapy versus placebo plus chemotherapy as first line treatment for advanced gastric or gastro-oesophageal junction adenocarcinoma: RATIONALE-305 randomised, double blind, phase 3 trial. BMJ. 2024 May 28;385:e078876.

260e. Liu Y, Wang C, Li X, Dong L, et al. Improved clinical outcome in a randomized phase II study of anti-PD-1 camrelizumab plus decitabine in relapsed/refractory Hodgkin lymphoma. J Immunother Cancer. 2021 Apr;9(4):e002347. doi: 10.1136/jitc-2021-002347.

261e. Wang C, Liu Y, Dong L, et al. Efficacy of Decitabine plus Anti-PD-1 Camrelizumab in Patients with Hodgkin Lymphoma Who Progressed or Relapsed after PD-1 Blockade Monotherapy. Clin Cancer Res. 2021 May 15;27(10):2782-2791. doi: 10.1158/1078-0432.CCR-21-0133. Epub 2021 Mar 5.

262e. Mei M, Chen L, Godfrey J, et al. Pembrolizumab plus vorinostat induces responses in patients with Hodgkin lymphoma refractory to prior PD-1 blockade. Blood. 2023 Oct 19;142(16):1359-1370. doi: 10.1182/blood.2023020485.

263e. Albiges L, Gurney H, Atduev V, et al. Pembrolizumab plus lenvatinib as first-line therapy for advanced non-clear-cell renal cell carcinoma (KEYNOTE-B61): a single-arm, multicentre, phase 2 trial. Lancet Oncol. 2023 Aug;24(8):881-891. doi: 10.1016/S1470-2045(23)00276-0. Epub 2023 Jul 11.

264e. Xu J, Kato K, Raymond E, et al. Tislelizumab plus chemotherapy versus placebo plus chemotherapy as first-line treatment for advanced or metastatic oesophageal squamous cell carcinoma (RATIONALE-306): a global, randomised, placebo-controlled, phase 3 study. Lancet Oncol. 2023 May;24(5):483-495. doi: 10.1016/S1470-2045(23)00108-0. Epub 2023 Apr 17. Erratum in: Lancet Oncol. 2024 Mar;25(3):e102.

265e. Wang Y, LaPlant BR, Parikh SA, et al. Efficacy of pembrolizumab monotherapy and in combination with BCR inhibitors for Richter transformation of chronic lymphocytic leukemia (CLL). J Clin Oncol. 2024 May 29;42(16_suppl):7050.

266e. Gutzmer R, Stroyakovskiy D, Gogas H, et al. Atezolizumab, vemurafenib, and cobimetinib as first-line treatment for unresectable advanced BRAFV600 mutation-positive melanoma (IMspire150):

primary analysis of the randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2020 Jun 13;395(10240):1835-1844.

267e. Ascierto PA, Stroyakovskiy D, Gogas H, et al. Overall survival with first-line atezolizumab in combination with vemurafenib and cobimetinib in BRAFV600 mutation-positive advanced melanoma (IMspire150): second interim analysis of a multicentre, randomised, phase 3 study. Lancet Oncol. 2023 Jan;24(1):33-44.

268e. Rousseau B, Bieche I, Pasmant E, et al. PD-1 Blockade in Solid Tumors with Defects in Polymerase Epsilon. Cancer Discov. 2022 Jun 2;12(6):1435-1448.

269e. von der Maase H, Hansen SW, Roberts JT, et al. Gemcitabine and cisplatin versus methotrexate, vinblastine, doxorubicin, and cisplatin in advanced or metastatic bladder cancer: results of a large, randomized, multinational, multicenter, phase III study. J Clin Oncol. 2000 Sep;18(17):3068-77.

270e. Sternberg CN, de Mulder PH, Schornagel JH, et al; European Organization for Research and Treatment of Cancer Genitourinary Tract Cancer Cooperative Group. Randomized phase III trial of high-dose-intensity methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC) chemotherapy and recombinant human granulocyte colony-stimulating factor versus classic MVAC in advanced urothelial tract tumors: European Organization for Research and Treatment of Cancer Protocol no. 30924. J Clin Oncol. 2001 May 15;19(10):2638-46.

271e. Grossman HB, Natale RB, Tangen CM, et al. Neoadjuvant chemotherapy plus cystectomy compared with cystectomy alone for locally advanced bladder cancer. N Engl J Med. 2003 Aug 28;349(9):859-66.

272e. Duan H, Shao C, Pan M, et al. Neoadjuvant Pembrolizumab and Chemotherapy in Resectable Esophageal Cancer: An Open-Label, Single-Arm Study (PEN-ICE). Front Immunol. 2022 Jun 2;13:849984.

273e. Uppaluri R, Haddad RI, Tao Y, et al; KEYNOTE-689 Investigators. Neoadjuvant and Adjuvant Pembrolizumab in Locally Advanced Head and Neck Cancer. N Engl J Med. 2025 Jul 3;393(1):37-50.

274e. French JD, Haugen BR, Worden FP, et al. Combination Targeted Therapy with Pembrolizumab and Lenvatinib in Progressive, Radioiodine-Refractory Differentiated Thyroid Cancers. Clin Cancer Res. 2024 Sep 3;30(17):3757-3767.

275e. Brose MS, Robinson B, Sherman SI, et al. Cabozantinib for radioiodine-refractory differentiated thyroid cancer (COSMIC-311): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol. 2021 Aug;22(8):1126-1138.

276e. Lee KK, Morris JC 3rd, Kumar A, et al. Pemetrexed-carboplatin salvage therapy in advanced thyroid cancers. Head Neck. 2025 Mar;47(3):813-821.

277e. Johnston PB, Inwards DJ, Colgan JP, et al. A Phase II trial of the oral mTOR inhibitor everolimus in relapsed Hodgkin lymphoma. Am J Hematol. 2010 May;85(5):320-4.

278e. Budde LE, Wu D, Martin DBet al. Bendamustine with rituximab, etoposide and carboplatin (T(R)EC) in relapsed or refractory aggressive lymphoma: a prospective multicentre phase 1/2 clinical trial. Br J Haematol. 2018 Nov;183(4):601-607.

279e. Gutierrez A, Rodriguez J, Martinez-Serra J, et al. Gemcitabine and oxaliplatinum: an effective regimen in patients with refractory and relapsing Hodgkin lymphoma. Onco Targets Ther. 2014 Nov 13;7:2093-100.

280e. Choueiri TK, Escudier B, Powles T, et al; METEOR Investigators. Cabozantinib versus Everolimus in Advanced Renal-Cell Carcinoma. N Engl J Med. 2015 Nov 5;373(19):1814-23.

281e. Motzer RJ, Escudier B, McDermott DF, et al; CheckMate 025 Investigators. Nivolumab versus Everolimus in Advanced Renal-Cell Carcinoma. N Engl J Med. 2015 Nov 5;373(19):1803-13.

282e. Bijelic L, Stuart OA, Sugarbaker P. Adjuvant bidirectional chemotherapy with intraperitoneal pemetrexed combined with intravenous Cisplatin for diffuse malignant peritoneal mesothelioma. Gastroenterol Res Pract. 2012;2012:890450.

283e. McCaffrey JP, Hilton S, Dutta R, et al. Phase II trial of docetaxel in patients with advanced or metastatic transitional-cell carcinoma. 1997;15(5):1853-1857. doi:https://doi.org/10.1200/jco.1997.15.5.185

284e. Boorjian SA, Alemozaffar M, Konety BR, et al. Intravesical nadofaragene firadenovec gene therapy for BCG-unresponsive non-muscle-invasive bladder cancer: a single-arm, open-label, repeat-dose clinical trial. The Lancet Oncology. 2021;22(1):107-117. doi:https://doi.org/10.1016/S1470-2045(20)30540-4

285e. Chamie K, Chang SS, Kramolowsky E, et al. IL-15 Superagonist NAI in BCG-Unresponsive Non–Muscle-Invasive Bladder Cancer. NEJM Evidence. 2023;2(1). doi:https://doi.org/10.1056/evidoa2200167

286e. Mai H, Chen Q, Chen D, et al. Toripalimab Plus Chemotherapy for Recurrent or Metastatic Nasopharyngeal Carcinoma. JAMA. 2023;330(20):1961-1961. doi:https://doi.org/10.1001/jama.2023.20181

287e. Zhang L, Huang Y, Hong S, et al. Gemcitabine plus cisplatin versus fluorouracil plus cisplatin in recurrent or metastatic nasopharyngeal carcinoma: a multicentre, randomised, open-label, phase 3 trial. The Lancet. 2016;388(10054):1883-1892. doi:https://doi.org/10.1016/s0140-6736(16)31388-5

288e. Lurain K, Ramaswami R, Ekwede I, et al. Cancer Immunotherapy Trials Network 12: Pembrolizumab in HIV-Associated Kaposi Sarcoma. Journal of Clinical Oncology. Published online October 2, 2024. doi:https://doi.org/10.1200/jco.24.00640

289e. Lee CH, Yogesh Shah A, Rao A, et al. Final database lock results of the phase 2 cohort of lenvatinib + pembrolizumab for progressive disease after a PD-1/PD-L1-containing therapy in metastatic clear cell renal cell carcinoma. The Oncologist. 2023;28(Supplement_1):S3-S4. doi:https://doi.org/10.1093/oncolo/oyad216.006

290e. Choueiri TK, Escudier B, Powles T, et al. Cabozantinib versus Everolimus in Advanced Renal-Cell Carcinoma. New England Journal of Medicine. 2015;373(19):1814-1823. doi:https://doi.org/10.1056/nejmoa1510016

291e. Tedeschi A, Frustaci AM, Condoluci A, et al. Atezolizumab, venetoclax, and obinutuzumab combination in Richter transformation diffuse large B-cell lymphoma (MOLTO): a multicentre, single-arm, phase 2 trial. The Lancet Oncology. 2024;25(10):1298-1309. doi:https://doi.org/10.1016/s1470-2045(24)00396-6

292e. Prime Therapeutics Management. Keytruda IV/SQ Clinical Literature Review Analysis. Last updated November 2025. Accessed November 2025.

Appendix A – Non-Quantitative Treatment Limitations (NQTL) Factor Checklist

Non-quantitative treatment limitations (NQTLs) refer to the methods, guidelines, standards of evidence, or other conditions that can restrict how long or to what extent benefits are provided under a health plan. These may include things like utilization review or prior authorization. The utilization management NQTL applies comparably, and not more stringently, to mental health/substance use disorder (MH/SUD) Medical Benefit Prescription Drugs and medical/surgical (M/S) Medical Benefit Prescription Drugs. The table below lists the factors that were considered in designing and applying prior authorization to this drug/drug group, and a summary of the conclusions that Prime's assessment led to for each.

Factor	Conclusion
Indication	Yes: Consider for PA
Safety and efficacy	No: PA not a priority
Potential for misuse/abuse	No: PA not a priority
Cost of drug	Yes: Consider for PA

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

ICD-10	ICD-10 Description
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
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

ICD-10	ICD-10 Description
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
C11.0	Malignant neoplasm of superior wall of nasopharynx
C11.1	Malignant neoplasm of posterior wall of nasopharynx
C11.2	Malignant neoplasm of lateral wall of nasopharynx
C11.3	Malignant neoplasm of anterior wall of nasopharynx
C11.8	Malignant neoplasm of overlapping sites of nasopharynx
C11.9	Malignant neoplasm of nasopharynx, 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
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

ICD-10	ICD-10 Description
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
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
C25.2	Malignant neoplasm of tail of pancreas
C25.3	Malignant neoplasm of pancreatic duct

ICD-10	ICD-10 Description
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
C30.0	Malignant neoplasm of nasal cavity
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

ICD-10	ICD-10 Description
C40.10	Malignant neoplasm of short bones of unspecified upper limb
C40.11	Malignant neoplasm of short bones of right upper limb
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

ICD-10	ICD-10 Description
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
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

ICD-10	ICD-10 Description
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
C45.0	Mesothelioma of pleura
C45.2	Mesothelioma of pericardium
C45.7	Mesothelioma of other sites
C45.9	Mesothelioma, unspecified
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
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
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

ICD-10	ICD-10 Description
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
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

ICD-10	ICD-10 Description
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
C53.0	Malignant neoplasm of endocervix
C53.1	Malignant neoplasm of exocervix
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

ICD-10	ICD-10 Description
C55	Malignant neoplasm of uterus, part unspecified
C61	Malignant neoplasm of prostate
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
C73	Malignant neoplasm of thyroid gland
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
C79.89	Secondary malignant neoplasm of other specified sites

ICD-10	ICD-10 Description
C7B.1	Secondary Merkel cell carcinoma
C80.0	Disseminated malignant neoplasm, unspecified
C80.1	Malignant (primary) neoplasm, unspecified
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
Z85.51	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
Z85.821	Personal history of Merkel cell carcinoma
Z85.830	Personal history of malignant neoplasm of bone
Z85.850	Personal history of malignant neoplasm of thyroid

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