Optum

# Optum Cancer Therapy Pathways Program

Effective Date: September 1, 2024

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# Overview

## Cancer Therapy Pathways Program

With the rapid approval of new therapies, along with the rising cost of cancer care, pathways serve a critical role in the delivery of high-quality and high-value cancer treatments while reducing an unwarranted variation in care.

The Optum Cancer Therapy Pathways Program aims to improve quality and value in cancer care by identifying anti-cancer regimens supported by evidence-based guidelines to help reduce total cost of care and improve outcomes.

The program's regimens are selected on the basis of clinical benefit (efficacy) and side-effect profile (toxicity). Among regimens with comparable efficacy and toxicity, additional consideration is given to the frequency of hospitalizations during therapy, duration of therapy, drug costs and total cost of care.

**NOTE: This list of regimens and the drugs with in them are still subject to the relevant payer plan language and policy; inclusion here is not a guarantee that they will be authorized or reimbursed by an individual payer.**

## Care decisions are between the physician and the patient.

The Cancer Therapy Pathways Program is not a substitute for the experience and judgment of a physician or other health care professional. Any clinician participating in the program must use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. Care decisions are between the physician and patient.

# B-Cell Lymphomas

## Diffuse Large B-Cell Lymphoma (include histological transformation and follicular grade 3 (high-grade))**

**1st Line of Therapy**

- Rituximab-CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone)
- Rituximab-mini-CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone)
- Rituximab-DA-EPOCH (Etoposide, Prednisone, Vincristine, Cyclophosphamide, Doxorubicin) (For Primary Mediastinal B-Cell Lymphoma (PMBCL) Only)

**2nd and Subsequent Lines of Therapy**

- Rituximab ± GDP (Gemcitabine, Dexamethasone, Cisplatin or Carboplatin)
- Rituximab ± ICE (Ifosfamide, Carboplatin, Etoposide)
- Rituximab ± DHAP (Dexamethasone, Cisplatin, Cytarabine)

## Diffuse Large B-Cell Lymphoma with translocations of MYC and BCL2 and/or BCL6 (double-/triple-hit lymphoma)**

- Rituximab-DA-EPOCH (Etoposide, Prednisone, Vincristine, Cyclophosphamide, Doxorubicin)

***Therapies that are administered at Centers of Excellence, including stem cell transplant or CAR T-cell therapy, are not included in pathways. Patients eligible for transplant or CAR T-cell therapy should be referred appropriately for evaluation.*

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## Follicular Lymphoma (Grade 1–2)**

### 1st Line of Therapy

- Bendamustine + Rituximab (BR)
- Rituximab (weekly for 4 doses)

### 2nd and Subsequent Lines of Therapy

- Bendamustine + Rituximab (BR)
- CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone) + Rituximab
- CVP (Cyclophosphamide, Vincristine, Prednisone) + Rituximab
- Rituximab
- Bendamustine + Obinutuzumab (rituximab refractory disease only)

*** Therapies that are administered at Centers of Excellence, including stem cell transplant or CAR T-cell therapy, are not included in pathways. Patients eligible for transplant or CAR T-cell therapy should be referred appropriately for evaluation.*

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## Mantle Cell Lymphoma**

### 1st Line of Therapy

- Nordic Regimen (Dose-Intensified Induction Immunochemotherapy with Rituximab + Cyclophosphamide, Vincristine, Doxorubicin, Prednisone [Maxi-CHOP]) Alternating with Rituximab + High-Dose Cytarabine
- Hyper-CVAD (Cyclophosphamide, Vincristine, Doxorubicin and Dexamethasone Alternating with High-Dose Methotrexate and Cytarabine) + Rituximab
- Bendamustine + Rituximab
- VR-CAP (Bortezomib, Rituximab, Cyclophosphamide, Doxorubicin and Prednisone)

### Maintenance After 1st Line of Therapy

- Rituximab

### 2nd Line of Therapy

- Bendamustine + Rituximab (BR)
- Acalabrutinib
- Ibrutinib
- Zanubrutinib

### 3rd and Subsequent Lines of Therapy

- Bendamustine + Rituximab (BR)
- Acalabrutinib
- Ibrutinib
- Zanubrutinib

*** Therapies that are administered at Centers of Excellence, including stem cell transplant or CAR T-cell therapy, are not included in pathways. Patients eligible for transplant or CAR T-cell therapy should be referred appropriately for evaluation.*

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## Marginal Zone Lymphoma**

**1st Line of Therapy**

- Antimicrobial therapy as indicated (e.g. H. Pylori eradication therapy (for Gastric MALT only))
- Bendamustine + Rituximab (BR)
- Rituximab (weekly for 4 doses)

**2nd and Subsequent Lines of Therapy (Non-Refractory Disease)**

- Bendamustine + Rituximab (BR)
- CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone) + Rituximab
- CVP (Cyclophosphamide, Vincristine, Prednisone) + Rituximab
- Rituximab
- Bendamustine + Obinutuzumab (rituximab refractory disease)

*** Therapies that are administered at Centers of Excellence, including stem cell transplant or CAR T-cell therapy, are not included in pathways. Patients eligible for transplant or CAR T-cell therapy should be referred appropriately for evaluation.*

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# Biliary Tract Cancers (Gallbladder, Intrahepatic and Extrahepatic Cholangiocarcinoma)

## Adjuvant Therapy

- Capecitabine

## Unresectable/Metastatic

### 1st Line of Therapy

- Gemcitabine + Cisplatin

### 2nd and Subsequent Lines of Therapy

- Fluorouracil/Leucovorin + Oxaliplatin (FOLFOX)
- Ivosidenib (in IDH1 Mutation Cholangiocarcinoma)

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# Bladder Cancer

## Non-Muscle Invasive, Neoadjuvant/Adjuvant

- Intravesical BCG (Bacillus Calmette-Guerin)
- Intravesical Gemcitabine

## Non-Muscle Invasive, Maintenance

- Intravesical BCG (Bacillus Calmette-Guerin)

## Muscle Invasive, Neoadjuvant/Adjuvant

- Gemcitabine + Cisplatin
- Nivolumab PD-L1 ≥ 1% (high-risk, adjuvant only)

## Radiosensitizing Chemotherapy for Organ-Preserving Chemoradiation

- Cisplatin + Fluorouracil (5FU)
- Gemcitabine

## Locally Advanced or Metastatic

**1st Line of Therapy**

- Gemcitabine + Cisplatin or Carboplatin

**Maintenance Post 1st Line of Therapy and No Progression**

- Avelumab

**2nd and Subsequent Lines of Therapy**

- Gemcitabine + Cisplatin or Carboplatin (if platinum-based therapy not used previously)
- Enfortumab Vedotin-ejfv (if not previously used)
- Erdafinitib (FGFR 3 mutations)

Any of the following

- Pembrolizumab (if IO not used previously)
- Nivolumab (if IO not used previously)
- Avelumab (if IO not used previously)

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# Breast Cancer

## Neoadjuvant/Adjuvant

**HER2 Negative:**

- Doxorubicin + Cyclophosphamide (dose dense) → Paclitaxel weekly (ddAC → weekly T)
- Doxorubicin + Cyclophosphamide (dose dense) → Paclitaxel every 2 weeks (ddAC → q2w T)
- Docetaxel + Cyclophosphamide (TC)
- Olaparib (for BRCA 1/2 mutation positive; adjuvant therapy only)

**HER2 Positive:**

- Doxorubicin + Cyclophosphamide → Paclitaxel weekly + Trastuzumab (AC → TH)
- Docetaxel + Carboplatin + Trastuzumab (TCH)
- Paclitaxel + Trastuzumab

## Adjuvant (Residual Disease Post-Neoadjuvant Treatment)

**Triple negative breast cancer (TNBC):**

- Capecitabine

**HER2 Positive (to completion of 1 yr of HER2 therapy):**

- Ado-trastuzumab Emtansine (T-DM1)
- Trastuzumab

## Adjuvant (No Residual Disease Post-Neoadjuvant Treatment)

**HER2 Positive:**

- Trastuzumab to completion 1 yr of HER2 therapy

## Metastatic and Recurrent — Endocrine Therapy

**HER2 Negative: 1st Line of Therapy**

- Fulvestrant + Anastrozole
- Fulvestrant + Letrozole
- Anastrozole + Palbociclib
- Letrozole + Palbociclib
- Exemestane + Palbociclib
- Anastrozole + Abemaciclib

- Letrozole + Abemaciclib
- Exemestane + Abemaciclib
- Anastrozole + Ribociclib
- Letrozole + Ribociclib
- Exemestane + Ribociclib

**HER2 Negative: 1st + Subsequent Lines of Therapy**

- Anastrozole
- Letrozole
- Exemestane
- Tamoxifen
- Fulvestrant

**HER2 Negative: 2nd + Subsequent Lines of Therapy**

- Anastrozole
- Letrozole
- Exemestane
- Tamoxifen
- Fulvestrant
- Fulvestrant + Palbociclib
- Fulvestrant + Abemaciclib
- Fulvestrant + Ribociclib

**HER2 positive: 1st + Subsequent Lines of Therapy**

- Anastrozole + Trastuzumab
- Letrozole + Trastuzumab
- Exemestane + Trastuzumab
- Anastrozole + Lapatinib
- Letrozole + Lapatinib
- Exemestane + Lapatinib

## Metastatic and Recurrent — Chemotherapy

**HER2 Negative: 1st + Subsequent Lines of Therapy**

- Doxorubicin
- Paclitaxel
- Docetaxel

- Capecitabine
- Gemcitabine
- Vinorelbine
- Olaparib or talzoparib (Germline BRCA 1/2 Mutation Positive)
- Fam-trastuzumab deruxtecan--nxki (For patients with tumors that are HER2 IHC 1+ or 2+ and ISH negative, who have received at least 1 prior line of chemotherapy for metastatic disease and, if tumor is HR+, are refractory to endocrine therapy.)

**HER2 Negative: 3rd + Subsequent Lines of Therapy**

- Sacituzumab Govitecan-hziy (For patients who are hormone positive, HER 2 negative)

**HER2 Negative, Triple Negative Breast Cancer (TNBC): 1st Line and Subsequent Lines of Therapy**

- Cisplatin or Carboplatin (PD-L1 CPS < 10 and germline BRCA 1/2 mutation)
- Pembrolizumab + Paclitaxel (CPS ≥ 10)
- Pembrolizumab + Gemcitabine + Carboplatin (CPS ≥ 10)
- Sacituzumab Govitecan-hziy (after 2 prior therapies for metastatic disease)

**HER2 Positive: 1st Line of Therapy**

- Docetaxel + Trastuzumab + Pertuzumab
- Paclitaxel + Trastuzumab + Pertuzumab

**HER2 Positive: 2nd Line of Therapy**

- Ado-Trastuzumab Emtansine (T-DM1)
- Fam-trastuzumab deruxtecan-nxki
- Tucatinib + trastuzumab + capecitabine (In patients with CNS involvement)

**HER2 Positive: 3rd + Subsequent Lines of therapy**

- Tucatinib + trastuzumab + capecitabine
- Ado-Trastuzumab Emtansine (T-DM1)

**HER2 Positive: 4th + Subsequent Lines of therapy**

- Paclitaxel + Trastuzumab
- Vinorelbine + Trastuzumab
- Gemcitabine + Trastuzumab
- Capecitabine + Trastuzumab

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# Colon/Rectal Cancer

## Adjuvant

- Fluorouracil + Leucovorin + Oxaliplatin (FOLFOX)
- Capecitabine + Oxaliplatin (CAPEOX)
- Fluorouracil (5-FU)/Leucovorin

## Metastatic — pMMR/ MSS

**RAS/BRAF Wild Type or Mutant**

**1st and 2nd Lines of Therapy**

- Fluorouracil + Leucovorin + Oxaliplatin (FOLFOX) +/- Bevacizumab
- Fluorouracil + Leucovorin + Irinotecan (FOLFIRI) +/- Bevacizumab
- Fluorouracil + Leucovorin +/- Bevacizumab
- Capecitabine

**RAS/BRAF Wild Type -Left-sided Tumor Only**

**1st and 2nd Lines of Therapy**

- Fluorouracil + Leucovorin + Oxaliplatin (FOLFOX) + Cetuximab
- Fluorouracil + Leucovorin + Irinotecan (FOLFIRI) + Cetuximab
- Fluorouracil + Leucovorin + Oxaliplatin (FOLFOX) + Panitumumab
- Fluorouracil + Leucovorin + Irinotecan (FOLFIRI) + Panitumumab

## Metastatic — dMMR/ MSI-H

**RAS/BRAF Wild Type or Mutant**

**1st Line of Therapy**

- Pembrolizumab

**2nd and Subsequent Lines of Therapy**

- FOLFOX +/- Bevacizumab
- FOLFIRI +/- Bevacizumab
- 5-FU + Leucovorin +/- Bevacizumab
- Capecitabine

**RAS/BRAF Wild Type - ~~Left-sided Tumor Only~~**

**2nd and Subsequent Lines of Therapy**

- FOLFOX + Cetuximab*
- FOLFIRI + Cetuximab*
- FOLFOX + Panitumumab*
- FOLFIRI + Panitumumab*

* If no prior progression on KRAS/NRAS/BRAF WT therapy

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# Chronic Lymphocytic Leukemia (CLL)/ Small Lymphocytic Lymphoma (SLL)

**1st line of therapy**

- Ibrutinib
- Acalabrutinib
- Zanubrutinib
- Venetoclax + Obinutuzumab
- Bendamustine + Rituximab (without del(17p)/TP53 mutation)

**2nd and Subsequent lines of therapy**

- Ibrutinib
- Acalabrutinib
- Zanubrutinib
- Venetoclax + Rituximab
- Bendamustine + Rituximab (without del(17p)/TP53 mutation)

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# Chronic Myeloid Leukemia

## Chronic Phase

### 1st Line Therapy (all risk categories)

- Imatinib

### 2nd Line and Subsequent Therapy

- Dasatinib
- Imatinib
- Nilotinib

(either one, two, or all)

- Ponatinib (T313I mutation only)
- Asciminib (third and subsequent)


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# Esophageal Cancer

## Perioperative

- Capecitabine + Oxaliplatin
- Fluorouracil +/- Leucovorin, Cisplatin
- Fluorouracil +/- Leucovorin, Oxaliplatin
- Fluorouracil +Leucovorin + Oxaliplatin + Docetaxel (FLOT)

## Preoperative or Definitive Chemoradiotherapy

- Capecitabine + Cisplatin + RT
- Capecitabine + Oxaliplatin + RT
- Carboplatin + Paclitaxel + RT
- Fluorouracil +/- Leucovorin + Cisplatin + RT
- Fluorouracil +/- Leucovorin + Oxaliplatin + RT

## Recurrent or Metastatic Disease

**HER2 Positive (HER2+) Disease: 1st Line of Therapy**

- Capecitabine + Cisplatin + Trastuzumab
- Capecitabine + Oxaliplatin + Trastuzumab
- Fluorouracil +/- Leucovorin + Oxaliplatin + Trastuzumab
- Fluorouracil +/- Leucovorin + Cisplatin + Trastuzumab

**HER2 Negative (HER2-) or Unknown Disease: 1$^{st}$ Line of Therapy**

- Capecitabine + Cisplatin
- Capecitabine + Oxaliplatin
- Capecitabine + Cisplatin + Nivolumab (Squamous Cell CPS ≥ 1)
- Capecitabine + Oxaliplatin + Nivolumab (Adenocarcinoma CPS ≥ 5 or Squamous Cell CPS ≥ 1)
- Fluorouracil +/- Leucovorin + Oxaliplatin
- Fluorouracil +/- Leucovorin + Cisplatin
- Fluorouracil +/- Leucovorin + Oxaliplatin + Nivolumab (Adenocarcinoma CPS ≥ 5 or Squamous Cell CPS ≥ 1)
- Fluorouracil +/- Leucovorin + Cisplatin + Nivolumab (Squamous Cell CPS ≥ 1)
- Capecitabine + Oxaliplatin + Pembrolizumab (CPS ≥ 10)
- Fluorouracil ± Leucovorin + Cisplatin+ Pembrolizumab (CPS ≥ 10)
- Fluorouracil ± Leucovorin + Oxaliplatin + Pembrolizumab (CPS ≥ 10)

- Capecitabine + Cisplatin + Pembrolizumab (CPS ≥ 10)

**HER2- and HER2+ Disease: 2nd + Subsequent Lines of Therapy**

- Docetaxel
- Irinotecan
- Paclitaxel
- Paclitaxel + Ramucirumab (for adenocarcinoma)
- Fam-trastuzumab deruxtecan (HER2+ Disease and adenocarcinoma only)

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# Gastric Cancer

## Perioperative

- Capecitabine + Oxaliplatin
- Fluorouracil +/- Leucovorin + Cisplatin
- Fluorouracil +/-Leucovorin + Oxaliplatin
- Fluorouracil + Leucovorin + Oxaliplatin + Docetaxel (FLOT)

## Postoperative Chemoradiotherapy

- Capecitabine + RT
- Fluorouracil + RT

## Postoperative Chemotherapy

- Capecitabine
- Capecitabine + Oxaliplatin
- Fluorouracil

## Recurrent or Metastatic Disease

**HER2 Positive (HER2+) Disease: 1st Line of Therapy**

- Fluorouracil +/- Leucovorin + Cisplatin + Trastuzumab
- Fluorouracil +/- Leucovorin + Oxaliplatin + Trastuzumab
- Capecitabine + Cisplatin + Trastuzumab
- Capecitabine + Oxaliplatin + Trastuzumab

**HER2 Negative (HER2-) or Unknown Disease:*: 1st Line of Therapy***

- Capecitabine + Oxaliplatin
- Capecitabine + Oxaliplatin + Nivolumab (CPS ≥ 5)
- Capecitabine + Oxaliplatin + Pembrolizumab (CPS ≥ 10)
- Capecitabine + Cisplatin
- Capecitabine + Cisplatin + Pembrolizumab (CPS ≥ 10)
- Fluorouracil +/- Leucovorin + Cisplatin
- Fluorouracil +/- Leucovorin + Cisplatin + Pembrolizumab (CPS ≥ 10)
- Fluorouracil +/- Leucovorin, Oxaliplatin
- Fluorouracil +/- Leucovorin, Oxaliplatin, Nivolumab, (CPS ≥ 5)
- Fluorouracil +/- Leucovorin + Oxaliplatin + Pembrolizumab (CPS ≥ 10

**HER2- and HER2+ Disease: 2nd and Subsequent Lines of Therapy**

- Docetaxel
- Irinotecan
- Paclitaxel
- Paclitaxel + Ramucirumab
- Fam-trastuzumab deruxtecan (HER2+ disease only)

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# Head and Neck Cancer

## Primary Definitive Therapy

**Non-Nasopharyngeal**

- Cisplatin + Concurrent Radiation Therapy

**Nasopharyngeal**

- Cisplatin + Concurrent Radiation Therapy
- Cisplatin + Gemcitabine

## Adjuvant Therapy

**Non-Nasopharyngeal**

- Cisplatin + Concurrent Radiation Therapy

**Nasopharyngeal**

- Cisplatin + Fluorouracil (5FU)
- Carboplatin + Fluorouracil (5FU)

## Recurrent/Metastatic/Unresectable

**Non-Nasopharyngeal: 1st Line of Therapy**

- Cisplatin or Carboplatin + Fluorouracil (5FU) + Cetuximab
- Cisplatin + Fluorouracil (5FU)
- Cisplatin or Carboplatin + Docetaxel
- Cisplatin or Carboplatin + Paclitaxel
- Cisplatin or Carboplatin + Fluorouracil (5FU) + Pembrolizumab (CPS ≥ 1 only)
- Carboplatin + Paclitaxel + Pembrolizumab (CPS ≥ 1 only)
- Pembrolizumab (CPS ≥ 1 only)

**Non-Nasopharyngeal: 2nd and Subsequent Lines of Therapy**

- Cisplatin or Carboplatin + Fluorouracil (5FU) + Cetuximab
- Cisplatin + Fluorouracil (5FU)
- Cisplatin or Carboplatin + Docetaxel
- Cisplatin or Carboplatin + Paclitaxel

  Either or Both:
- Nivolumab (if IO not used previously)

- Pembrolizumab (if IO not used previously)

**Nasopharyngeal: 1st Line of Therapy**

- Cisplatin + Gemcitabine

  Either One, Both or All:

- Toripalimab + Cisplatin + Gemcitabine
- Pembrolizumab + Cisplatin + Gemcitabine
- Nivolumab + Cisplatin + Gemcitabine

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# Hepatocellular Carcinoma

## Unresectable, Not a Transplant Candidate, Metastatic Disease, Inoperable by PS or Comorbidity

### 1st Line of Therapy

- Atezolizumab + Bevacizumab*
- Durvalumab +/- Tremelimumab

### 2nd and Subsequent Lines of Therapy

- Regorafenib
- Cabozantinib
- Sorafenib
- Lenvatinib

**For patients that have not received treatment with a checkpoint inhibitor.*

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# Hodgkin Lymphoma (HL)

### 1st Line of Therapy

- Doxorubicin + Bleomycin + Vinblastine + Dacarbazine (ABVD)
- Doxorubicin + Vinblastine + Dacarbazine (AVD)
- Escalated bleomycin + etoposide + doxorubicin + cyclophosphamide + vincristine + procarbazine + prednisone (escBEACOPP)

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# Kidney Cancer

## Relapsed or Metastatic (Clear Cell)

### Adjuvant

- Pembrolizumab

### 1st Line of Therapy (all risk levels)

- Axitinib + Avelumab
- Axitinib + Pembrolizumab
- Cabozantinib + Nivolumab
- Lenvatinib + Pembrolizumab
- Nivolumab + Ipilimumab

### 2nd and Subsequent lines of therapy

- Axitinib
- Cabozantinib
- Pazopanib
- Sunitinib
- Tivozanib (who received ≥ 2 prior systemic therapies)
- Nivolumab (if immune checkpoint inhibitor not received previously)

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# Non-Small Cell Lung Cancer

## Neoadjuvant/Adjuvant

**Nonsquamous**

- Nivolumab + Carboplatin or Cisplatin + Paclitaxel (Neoadjuvant only)
- Nivolumab + Carboplatin or Cisplatin + Pemetrexed (Neoadjuvant only)
- Cisplatin + Vinorelbine
- Cisplatin or Carboplatin + Pemetrexed ± Concurrent Radiation Therapy (RT)
- Carboplatin + Paclitaxel ± Concurrent Radiation Therapy (RT)
- Cisplatin + Etoposide + Concurrent Radiation Therapy (RT)
- Osimertinib (in completely resected stage IB – IIIA EGFR (exon 19del, L858R) directly following completion of adjuvant chemotherapy or are ineligible to receive platinum-based chemotherapy)

**Squamous**

- Nivolumab + Carboplatin or Cisplatin + Paclitaxel (Neoadjuvant only)
- Nivolumab + Carboplatin or Cisplatin + Gemcitabine (Neoadjuvant only)
- Cisplatin + Vinorelbine
- Carboplatin + Paclitaxel ± Concurrent Radiation Therapy (RT)
- Cisplatin + Etoposide + Concurrent Radiation Therapy (RT)
- Osimertinib (in completely resected stage IB — IIIA EGFR (exon 19del, L858R) directly following completion of adjuvant chemotherapy or are ineligible to receive platinum-based chemotherapy)

**Consolidation after chemoradiation, Stage III Unresectable, No Progression, and PS 0–1**

- Durvalumab

## Advanced/Metastatic: EGFR exon 19 deletion, L858R, S768I, L861Q, and/or G719X Mutation Positive

**1st and Subsequent Lines of Therapy**

- Dacomitinib
- Osimertinib

## Advanced/Metastatic: ALK Rearrangement Positive

**1st and Subsequent Lines of Therapy**

- Alectinib
- Brigatinib

- Lorlatinib

## Advanced/Metastatic (EGFR, ALK, RET Wild Type)

**Nonsquamous: 1st Line of Therapy**

- Pembrolizumab Single Agent (PD-L1 ≥ 50% only)
- Atezolizumab (PD-L1 ≥ 50% only)
- Cemiplimab-rwlc (PD-L1 ≥ 50% only)
- Carboplatin/Cisplatin + Pemetrexed + Pembrolizumab (regardless of PD-L1)
- Carboplatin/Cisplatin + Pemetrexed + Cemiplimab-rwlc, (regardless of PD-L1)
- Carboplatin/Cisplatin + Paclitaxel + Cemiplimab-rwlc (regardless of PD-L1)
- Carboplatin/Cisplatin + Pemetrexed (IO Ineligible)
- Carboplatin/Cisplatin + Paclitaxel (IO Ineligible)

**Nonsquamous: Maintenance**

- Cemiplimab-rwlc +/- Pemetrexed
- Pemetrexed
- Pembrolizumab +/- Pemetrexed

**Nonsquamous: 2nd and Subsequent Lines of Therapy**

- Docetaxel
- Pemetrexed
- Gemcitabine

**Squamous: 1st Line of Therapy**

- Pembrolizumab Single Agent (PD-L1 ≥ 50% only)
- Atezolizumab (PD-L1 ≥ 50% only)
- Cemiplimab-rwlc (PD-L1 ≥ 50% only)
- Carboplatin + Paclitaxel + Pembrolizumab (regardless of PD-L1)
- Carboplatin/Cisplatin + Paclitaxel + Cemiplimab-rwlc (regardless of PD-L1)
- Carboplatin/Cisplatin + Paclitaxel (IO Ineligible)
- Carboplatin/Cisplatin + Gemcitabine (IO Ineligible)

**Squamous: Maintenance**

- Cemiplimab-rwlc
- Pembrolizumab

### Squamous: 2nd and Subsequent Lines of Therapy

- Docetaxel
- Gemcitabine

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# Melanoma

## Neoadjuvant (Resectable), Stage III

- Nivolumab 240mg + Ipilimumab 80mg x 2 cycles

## Adjuvant (Resectable), Stage III

- Nivolumab
- Pembrolizumab

## Adjuvant (Resectable) — (BRAF Mutated)

- Dabrafenib + Trametinib
- Nivolumab
- Pembrolizumab

## Metastatic/Unresectable (BRAF Mutated/Symptomatic)

**1st and Subsequent Lines of Therapy**

Either one, two or all BRAF/MEK inhibitor combinations

- Dabrafenib + Trametinib
- Encorafenib + Binimetinib
- Vemurafenib + Cobimetinib

## Metastatic/Unresectable (BRAF Wild-Type/Mutated/Unknown)

**1st and Subsequent Lines of Therapy**

- Nivolumab (3mg/kg) + Ipilimumab (1mg/kg)

- Nivolumab*
- Pembrolizumab*

Either one or both immunotherapies

**For patients that have not received treatment with a checkpoint inhibitor, had a history of progression on a checkpoint inhibitor < 3 months after treatment discontinuation.*

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# Multiple Myeloma: Primary Therapy**

## Transplant Eligible and Ineligible

- Bortezomib + Lenalidomide + Dexamethasone (VRD)
- Bortezomib + Cyclophosphamide + Dexamethasone (CyBorD or VCD)
- Bortezomib, Daratumumab, Lenalidomide, Dexamethasone (D+VRd) – transplant eligible only

## Maintenance Therapy**

**Transplant Eligible or Ineligible**

- Lenalidomide
- Bortezomib

## Relapsed or Refractory**

**1st Relapse**

- Daratumumab + Lenalidomide + Dexamethasone (DRD)
- Daratumumab + Bortezomib + Dexamethasone (DVD)
- Bortezomib + Lenalidomide + Dexamethasone (VRD)
- Bortezomib + Cyclophosphamide + Dexamethasone (CyBorD or VCD)

**2nd Relapse**

- Daratumumab + Lenalidomide + Dexamethasone (DRD)
- Daratumumab + Bortezomib + Dexamethasone (DVD)
- Elotuzumab + Pomalidomide + Dexamethasone (EPD)
- Carfilzomib + Lenalidomide + Dexamethasone (KRD)
- Pomalidomide + Bortezomib + Dexamethasone (PVD)
- Bortezomib + Lenalidomide + Dexamethasone (VRD)
- Bortezomib + Cyclophosphamide + Dexamethasone (CyBorD or VCD)

  Either or Both:

- Isatuximab-irfc + Pomalidomide + Dexamethasone (Isa-PD)
- Daratumumab + Pomalidomide + Dexamethasone (DPd)

*** Therapies that are administered at Centers of Excellence, including stem cell transplant or CAR T-cell therapy, are not included in pathways. Patients eligible for transplant or CAR T-cell therapy should be referred appropriately for evaluation.*

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# Ovarian, Fallopian and Primary Peritoneal Cancer

## Neoadjuvant Therapy

- Carboplatin + Paclitaxel**

## Adjuvant or Primary Therapy

- Carboplatin + Paclitaxel**

## Maintenance Therapy After Primary Therapy

- Olaparib (Germline/Somatic BRCA Mutation Only)
- Niraparib
- Rucaparib

## Platinum – Sensitive Recurrent Disease

**1st + Subsequent Lines of Therapy**

- Carboplatin + Gemcitabine
- Carboplatin + Liposomal Doxorubicin
- Carboplatin + Paclitaxel

## Maintenance Therapy After Platinum — Sensitive

- Olaparib
- Niraparib

## Platinum — Resistant Recurrent Disease

**1st and Subsequent Lines of Therapy**

- Gemcitabine
- Liposomal Doxorubicin
- Liposomal Doxorubicin + Bevacizumab
- Paclitaxel (weekly)
- Paclitaxel (weekly) + Bevacizumab
- Tamoxifen
- Mirvetuximab soravtansine-gynx (FRα expressing tumors, ≥ 75% positive tumor cells)

***Only intravenous carboplatin + paclitaxel are pathway regimens.*

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# Pancreatic Cancer (Adenocarcinoma)

## Neoadjuvant (Resectable/Borderline Resectable)

- Fluorouracil/Leucovorin + Oxaliplatin + Irinotecan (FOLFIRINOX/mFOLFIRINOX)
- Gemcitabine + Albumin-Bound Paclitaxel (G-nP)

## Adjuvant (Resectable)

- Fluorouracil/Leucovorin + Oxaliplatin + Irinotecan (mFOLFIRINOX)
- Gemcitabine + Capecitabine
- Gemcitabine

## Locally Advanced/Metastatic

**1st Line of Therapy**

- Fluorouracil/Leucovorin + Oxaliplatin + Irinotecan (FOLFIRINOX/mFOLFIRINOX)
- Gemcitabine + Albumin-Bound Paclitaxel (G-nP)
- Gemcitabine

**Maintenance, Metastatic**

- Fluorouracil/Leucovorin
- Capecitabine

**2nd and Subsequent Lines of Therapy**

- Gemcitabine + Albumin-Bound Paclitaxel (G-nP)
- Gemcitabine
- Fluorouracil +/- Leucovorin
- Fluorouracil/Leucovorin + Oxaliplatin (OFF)
- Fluorouracil/Leucovorin + Oxaliplatin (FOLFOX)
- Fluorouracil/Leucovorin + Irinotecan (FOLFIRI)
- Fluorouracil/Leucovorin + Oxaliplatin + Irinotecan (FOLFIRINOX/mFOLFIRINOX)

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# Prostate Cancer

## Androgen Deprivation Therapy (ADT)

- Goserelin
- Leuprolide (HCPCS: J9217: Eligard, Lupron Depot)
- Triptorelin

## Castration Sensitive

**Neoadjuvant, Adjuvant in lieu of local therapy**

- ADT

**Recurrent or Metastatic**

- ADT
- Abiraterone (Zytiga®), Prednisone + ADT
- Abiraterone (Zytiga®), Prednisone + Docetaxel + ADT

## Castration Resistant

**Recurrent or Metastatic**

- Abiraterone (Zytiga®), Prednisone + ADT
- Docetaxel + ADT
- Olaparib + Abiraterone (Zytiga®), Prednisone + ADT (BRCA 1/2, no prior novel hormone)
- Cabazitaxel + ADT (after prior docetaxel therapy)
- Enzalutamide + ADT (after prior abiraterone therapy)

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# Small Cell Lung Cancer

## Limited Stage – Primary Therapy

- Carboplatin + Etoposide
- Cisplatin + Etoposide

## Extensive Stage – Primary Therapy

- Carboplatin + Etoposide + Atezolizumab
- Carboplatin + Etoposide + Durvalumab
- Cisplatin + Etoposide + Durvalumab
- Carboplatin + Etoposide
- Cisplatin + Etoposide

## Extensive Stage – Maintenance after Primary Therapy

- Atezolizumab
- Durvalumab

## Subsequent Therapy: Relapse ≤ 6 months

- Topotecan (IV)
- Paclitaxel
- Irinotecan

## Subsequent Therapy: Relapse > 6 months

- Carboplatin + Etoposide
- Cisplatin + Etoposide
- Topotecan (IV)
- Irinotecan

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# Uterine Carcinoma (Endometrial)

## Adjuvant

- Carboplatin + Paclitaxel
- Dostarlimab + Carboplatin + Paclitaxel (stage III-IV tumors, dMMR/MSI-H only)

## Metastatic or Recurrent

### 1st Line of Therapy

- Carboplatin + Paclitaxel
- Carboplatin + Paclitaxel + Trastuzumab (for stage III/IV or recurrent HER2-positive uterine serous carcinoma only)
- Dostarlimab + Carboplatin + Paclitaxel (stage III-IV tumors, dMMR/MSI-H only)*
- Lenvatinib + Pembrolizumab (pMMR only, after prior platinum-based therapy including neoadjuvant and adjuvant)*

### 2nd and Subsequent Lines of Therapy

- Lenvatinib + Pembrolizumab (pMMR only)*
- Docetaxel
- Paclitaxel
- Doxorubicin
- Liposomal Doxorubicin

**For patients that have not received treatment with a checkpoint inhibitor.*


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# Change control

| Date | Changes |
|---|---|
| **July 1, 2020** | Added change control<br>New pathways — Small Cell Lung Cancer and Hepatobiliary Cancer<br>Updates to existing pathways<br>• **Melanoma Pathways:**<br>– Removed “Stages IIIB and IIIC” from Adjuvant<br>• **Colon Pathways:**<br>– Updated name to “Colon/Rectal” to reflect pathways for rectal cancer<br>– Removed FOLFOX/FOLFIRI + Cetuximab regimen from Colon Cancer: Metastatic KRAS/NRAS: Wild Type – 1st and 2nd Lines of Therapy |
| **Aug. 1, 2020** | New pathways — Ovarian Cancer |
| **Oct. 1, 2020** | New pathways — Non-Small-Cell Lung Cancer<br>Updates to existing pathways<br>• **Breast Pathways:**<br>– Added capecitabine + lapatinib to pathways for HER2 POSITIVE: 1st + Subsequent Lines of Therapy<br>• **Pancreatic Pathways:**<br>– Added fluorouracil/leucovorin to Locally Advanced/Metastatic: 2nd + Subsequent Lines of Therapy<br>• **Colon/Rectal Pathways:**<br>– Added capecitabine + oxaliplatin (CAPEOX) to pathways for Adjuvant<br>– Added new category of pathways for Metastatic: MSI/dMMR: 1st + Subsequent Lines of Therapy |
| **Nov. 1, 2020** | New pathways — Head and Neck Cancer<br>Updates to existing pathways<br>• **Melanoma Pathways:**<br>– Removed Nivolumab single agent from Adjuvant and Metastatic/Unresectable |

| Date | Changes |
|---|---|
| **Jan. 1, 2021** | New pathways — Multiple Myeloma |
| **March 1, 2021** | New pathways — Diffuse Large B-Cell Lymphoma<br>Updates to existing pathways<br>• **Hepatocellular carcinoma:**<br>– Added Atezolizumab + Bevacizumab regimen to pathways as 1st Line of Therapy and 2nd + Subsequent Lines of Therapy<br>– Added Sorafenib or Lenvatinib to 2nd + Subsequent Lines of Therapy<br>• **Biliary tract cancers:**<br>– Added FOLFOX, Pemigatinib (in FGFR2 mutation cholangiocarcinoma), and Ivosidenib (in IDH1 mutation cholangiocarcinoma) to pathways as 2nd + subsequent lines of therapy |
| **May 1, 2021** | New pathways — Follicular Lymphoma and Marginal Zone Lymphoma |
| **June 1, 2021** | New pathways — Mantle Cell Lymphoma<br>Updates to existing pathways<br>• **Follicular Lymphoma and Marginal Zone Lymphoma**<br>– Added pathway options for refractory disease |
| **July 1, 2021** | Updates to existing pathways<br>• **Mantle Cell Lymphoma**<br>– Added pathway option for maintenance after first line of therapy<br>• **Lung Cancer** |
| **Sept. 1, 2021** | Updates to existing pathways<br>• **Ovarian Cancer**<br>– Added carboplatin to pathways as Primary/Adjuvant Therapy<br>• **Head and Neck Cancer**<br>– Added “Cisplatin/Carboplatin + 5FU + Cetuximab, followed by Cetuximab Maintenance (Extreme regimen),” “Cisplatin/Carboplatin + Docetaxel/Paclitaxel,” and “Cisplatin + 5FU” regimens to pathways as non-nasopharyngeal: recurrent/metastatic unresectable: 2nd + subsequent line of therapy |
| **Oct. 1, 2021** | New pathways — Bladder Cancer |

| Date | Changes |
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| **Dec. 1, 2021** | Updates to existing pathways<br>• **Breast Pathways:**<br>– Added olaparib (for BRCA 1/2 mutation positive) to pathways for Neoadjuvant/Adjuvant – HER2 Negative<br>– Added trastuzumab to pathways for Adjuvant (residual disease post-neoadjuvant therapy) – HER2 Positive<br>– Removed atezolizumab + nab-paclitaxel (in PD-L1 Positive and metastatic TNBC) from pathways<br>• **Pancreatic Pathways:**<br>– Added FOLFIRINOX/mFOLFIRINOX to pathways for locally advanced or metastatic — 2nd + Subsequent Lines of Therapy<br>• **Colon/Rectal Pathways:**<br>– Added fluorouracil + leucovorin ± bevacizumab to pathways for metastatic disease<br>• **Melanoma**<br>– Added pembrolizumab to pathways for Adjuvant (Resectable): BRAF Mutated |
| **March 1, 2022** | Updates to existing pathways<br>• **Breast Pathways:**<br>– Added pembrolizumab + paclitaxel (mTNBC and PD-L1 expression threshold for positivity combined positive score ≥ 10) to pathways<br>– Added pembrolizumab + gemcitabine + carboplatin (mTNBC and PD-L1 expression threshold for positivity combined positive score ≥ 10) to pathways<br>– Added sacituzumab govitecan-hziy (mTNBC and after 2 prior therapies for metastatic disease) to pathways<br>– Added fam-trastuzumab deruxtecan-nxki to pathways for 2nd + Subsequent Lines of Therapy in HER2 Positive metastatic disease<br>• **Multiple Myeloma**<br>– Removed Bortezomib + Thalidomide + Dexamethasone (VTD) from relapsed or refractory disease<br>– Removed Carfilzomib + Pomalidomide + Dexamethasone (KPD) from relapsed or refractory disease: 2nd Line of Therapy<br>• **Lymphoma, Diffuse Large B-Cell**<br>– Added rituximab-mini-CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone) to pathways for 1st Line of Therapy<br>• **Lymphoma, Follicular**<br>– Removed 3rd + Subsequent Lines of Therapy (refractory disease) category and changed “2nd Line of Therapy (refractory disease)’ to ‘2nd + Subsequent Lines of Therapy (refractory disease)”<br>– Removed Duvelisib, Idelalisib, Umbralisib from pathways<br>• **Lymphoma, Marginal Zone**<br>– Removed 3rd + Subsequent Lines of Therapy (refractory disease) category and changed “2nd Line of Therapy (refractory disease)’ to ‘2nd + Subsequent Lines of Therapy (refractory disease)”<br>– Removed Duvelisib, Idelalisib, Umbralisib from pathways |

| Date | Changes |
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| **April 1, 2022** | Updates to existing pathways<br>• Multiple Myeloma<br>– Removed Panobinostat + Bortezomib + Dexamethasone from relapsed or refractory disease<br>• Small Cell Lung Cancer<br>– Added topotecan, paclitaxel, and irinotecan to pathways for subsequent line(s), relapse > 6 months<br>• Non-Small Cell Lung Cancer<br>– Removed pathways for advanced/metastatic, ROS1 rearrangement, MET Exon 14 skipping, BRAF V600E, RET rearrangement, and NTRK gene fusion |
| **May 1, 2022** | Updates to existing pathways<br>• Hepatobiliary Tract Cancers<br>– Removed pemigatinib (for FGFR2 mutated cholangiocarcinoma)<br>• Head and Neck Cancer<br>– No change to current pathway |
| **July 1, 2022** | New Pathways — Hodgkin Lymphoma and Kidney Cancer |
| **Aug. 1, 2022** | New Pathways — Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) |
| **Sept. 1, 2022** | New Pathways — Uterine (Endometrial) Cancer |
| **Nov. 1, 2022** | Updates to existing pathways<br>• Breast Cancer<br>– Added Ribociclib + anastrozole/letrozole/exemestane to Metastatic and Recurrent – Endocrine therapy, HER2 negative, first line<br>– Added Ribociclib + fulvestrant to Metastatic and Recurrent – Endocrine therapy, HER2 negative, 2nd and subsequent lines of therapy<br>– Added Fam-trastuzumab deruxtecan-nxki to HER2 IHC 1+ or 2+/ISH negative metastatic or recurrent disease: 2nd + subsequent lines of therapy<br>– Removed Talazoparib (Germline BRCA 1/2 Mutation Positive) from Metastatic and Recurrent – Chemotherapy, HER2 NEGATIVE: 1st and subsequent lines of therapy<br>• Bladder Cancer<br>– Removed Cisplatin + Methotrexate + Vinblastine (CMV) from Neoadjuvant/Adjuvant<br>• Colon Cancer<br>– Added Fluorouracil + Leucovorin + Oxaliplatin (FOLFOX) + Cetuximab and Fluorouracil + Leucovorin + Irinotecan (FOLFIRI) + Cetuximab to Metastatic KRAS/NRAS: Wild Type: 1st and 2nd line of therapy and MSI-H/dMMR: 1st + subsequent lines of therapy for left-sided colon cancer<br>• Melanoma<br>– Added Nivolumab single agent to Adjuvant and Metastatic/ Unresectable<br>– Added Dabrafenib + Trametinib to metastatic/ unresectable (BRAF mutated/ symptomatic) |
| **Feb. 1, 2023** | New Pathways — **Chronic Myeloid Leukemia (CML), Esophageal and Esophagogastric Cancers, Gastric Cancer, and Prostate Cancer** |

| Date | Changes |
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| **May 1, 2023** | Update to existing pathways<br>• **Non-Small Cell Lung Cancer**<br>– Added Carboplatin/Cisplatin + Pemetrexed/Paclitaxel + Cemiplimab-rwlc (PD-L1: < 1%, 1 – 49%, and ≥ 50%) to Advanced/Metastatic – Nonsquamous (EGFR, ALK, RET WT) – 1st line of therapy<br>– Added Carboplatin + Paclitaxel + Cemiplimab-rwlc (PD-L1: < 1%, 1 – 49%, and ≥ 50%) to Advanced/Metastatic – Squamous (EGFR, ALK, RET WT) – 1st line of therapy<br>– Added Cemiplimab-rwlc ± Pemetrexed to Advanced/Metastatic – Nonsquamous (EGFR, ALK, RET WT) – Maintenance<br>– Added Cemiplimab-rwlc to Advanced/Metastatic – Squamous (EGFR, ALK, RET WT) – Maintenance<br>• **Ovarian**<br>– Rucaparib – added to maintenance therapy following primary therapy (voted upon by committee 8/2022, NCCN went live with it V1.2023, December 22, 2022 – published in CGP tool on 5.12.2023) |
| **June 1, 2023** | Updates to existing pathway<br>• **Breast Cancer**<br>– Added Cisplatin/Carboplatin to Metastatic and Recurrent – Chemotherapy, HER2 negative, 1st line and subsequent lines of therapy, TNBC |
| **June 23, 2023** | Updates to existing pathways<br>• **Hepatobiliary split into two cancers, Hepatocellular and Biliary Tract Cancers** |
| **Aug. 1, 2023** | Update to existing pathway<br>• **Melanoma**<br>– Removed Nivolumab (1mg/kg) + Ipilimumab (3mg/kg); kept Nivolumab (3mg/kg) + Ipilimumab (1mg/kg) as pathway |
| **Sept. 1, 2023** | Update to existing pathways<br>• **Ovarian Cancer**<br>– Carboplatin single-agent is removed from adjuvant/primary therapy as it has been removed from NCCN guidelines.<br>• **Uterine/Endometrial Cancer**<br>– Add dostarlimab + carboplatin/paclitaxel to primary/ adjuvant in dMMR/MSI-H patients.<br>– Add dostarlimab + carboplatin/paclitaxel to first-line therapy for recurrent disease in dMMR/MSI-H patients and if prior ICI therapy was not received.<br>– Add pembrolizumab + lenvatinib to first line recurrent therapy in pMMR patients for patients who had not received prior ICI therapy.<br>– Pembrolizumab + lenvatinib is 2nd line in pMMR patients, added the variable, for patients who had not received prior ICI therapy.<br>– Remove nivolumab, avelumab, and dostarlimab from 2nd line pathways in patients that dMMR/MSI-H and pembrolizumab in TMB-H (≥10 mutations/mega-base) or dMMR/MSI-H tumors.<br>– Move the following therapies to 2nd line recurrent: Docetaxel (2B), doxorubicin, liposomal doxorubicin, and paclitaxel. |

| Date | Changes |
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| **Oct. 1, 2023** | Update to existing pathways<br>• **Bladder Cancer**<br>– Add nivolumab to adjuvant therapy in muscle invasive bladder cancer in patients who are high-risk and PD-L1 ≥ 1%.<br>– Carboplatin single-agent is removed from adjuvant/primary therapy as it has been removed from NCCN guidelines.<br>• **Colorectal Cancer**<br>– Changed pembrolizumab to the only first-line agent in patients who are dMMR/MSI-H.<br>– The following regimens were moved to second and subsequent lines of therapy in patients who are dMMR/MSI-H:<br>– FOLFOX ± Bevacizumab<br>– 5-FU + Leucovorin ± Bevacizumab<br>– Capecitabine<br>– FOLFIRI ± Bevacizumab<br>– FOLFOX + Cetuximab*<br>– FOLFIRI + Cetuximab*<br>– FOLFOX + Panitumumab*<br>– FOLFIRI + Panitumumab*<br>– * KRAS/NRAS/BRAF WT and left-sided tumor only |
| **Dec. 1, 2023** | Update to existing pathways<br>• **Bladder Cancer**<br>– Add BCG maintenance for NMIBC<br>• **Esophageal, Esophagogastric Cancer**<br>– Addition of the following regimens in first-line recurrent or metastatic disease, HER2 negative or unknown disease<br>– Capecitabine + Oxaliplatin + Pembrolizumab (CPS ≥ 10)<br>– Fluorouracil ± Leucovorin + Cisplatin+ Pembrolizumab (CPS ≥ 10)<br>– Fluorouracil ± Leucovorin + Oxaliplatin + Pembrolizumab (CPS ≥ 10)<br>– Capecitabine + Cisplatin + Pembrolizumab (CPS ≥ 10)<br>– Inclusion of “Unknown” to HER2 negative disease<br>• **Multiple Myeloma**<br>– Removal bortezomib + thalidomide + dexamethasone (VTD) due to removal from NCCN<br>• **Breast Cancer**<br>– The following regimens for HER2 positive moved to 4th line and subsequent due to NCCN updates:<br>– Capecitabine + Lapatinib<br>– Paclitaxel + Trastuzumab<br>– Vinorelbine + Trastuzumab<br>– Gemcitabine + Trastuzumab<br>– Capecitabine + Trastuzumab |

| Date | Changes |
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| **March 1, 2024** | Update to existing pathways<br>• **Prostate Cancer**<br>– Addition of the following regimen in castrate resistant metastatic recurrent prostate cancer with no prior novel hormone therapy, without and with prior docetaxel<br>– Olaparib + Abiraterone (BRCA 1/2)<br>• **Non-Small Cell Lung Cancer**<br>– Addition of the following regimens in Neoadjuvant / Adjuvant therapy<br>– Carboplatin + Pemetrexed +/- XRT<br>– Nivolumab + Carboplatin or Cisplatin + Paclitaxel (Neoadjuvant only)<br>– Nivolumab + Carboplatin or Cisplatin + Pemetrexed (Neoadjuvant only, Nonsquamous only)<br>– Nivolumab + Carboplatin or Cisplatin + Gemcitabine (Neoadjuvant only, Squamous only)<br>– Addition of the following regimens to Advanced/ Metastatic First-Line in “IO Ineligible”<br>– Carboplatin or Cisplatin + Paclitaxel<br>– Carboplatin or Cisplatin + Pemetrexed (Nonsquamous only)<br>– Carboplatin + Cisplatin + Gemcitabine (Squamous only)<br>– Addition of the following regimens to Advanced/ Metastatic Second-Line<br>– Gemcitabine |
| **April 1, 2024** | Update to existing pathways<br>• **Chronic Myeloid Leukemia**<br>– Removal of dasatinib and nilotinib from first-line therapy<br>– Addition of dasatinib, nilotinib, and imatinib to second-line and subsequent therapy<br>– Removal of Omacetaxine from second-line and subsequent therapy<br>– Limit the use of ponatinib to T315I mutation only<br>– Addition of asciminib to third-line and subsequent<br>• **Gastric Cancer (reviewed 10/2023)**<br>– Addition of the following regimens in first-line recurrent or metastatic disease, HER2 negative or unknown disease<br>– Capecitabine + Oxaliplatin + Pembrolizumab (CPS ≥ 10)<br>– Fluorouracil ± Leucovorin + Oxaliplatin + Pembrolizumab (CPS ≥ 10)<br>– Fluorouracil ± Leucovorin + Cisplatin+ Pembrolizumab (CPS ≥ 10)<br>– Capecitabine + Cisplatin + Pembrolizumab (CPS ≥ 10)<br>– Inclusion of “Unknown” to HER2 negative disease |

| Date | Changes |
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| **May 1, 2024** | Update to existing pathways<br>• **Multiple Myeloma**<br>– Addition of the following regimen to Primary Therapy, Transplant Eligible<br>– Daratumumab + Bortezomib + Lenalidomide + Dexamethasone (DVRd)<br>– Addition of the following regimen to Relapsed/ Refractory, second relapse<br>– Daratumumab + Pomalidomide + Dexamethasone (DPd)<br>• **Pancreatic Cancer**<br>– Addition of the following regimens to maintenance therapy for metastatic disease<br>– Fluorouracil + Leucovorin<br>– Capecitabine<br>• **Hepatocellular**<br>– Addition of the following regimen to first-line therapy<br>– Durvalumab<br>– Removal of the following regimens to first-line therapy<br>– Lenvatinib<br>– Sorafenib<br>• **Biliary Tract Cancers**<br>– Removal of the following regimen<br>– Durvalumab + Cisplatin + Gemcitabine |
| **June 1, 2024** | Update to existing pathways<br>• **Head and Neck**<br>– Addition of the following regimen to Non-Nasopharyngeal recurrent, metastatic, unresectable 1st line of therapy<br>– Carboplatin + Paclitaxel + Pembrolizumab (CPS ≥ 1)<br>– Addition of the following regimens to Nasopharyngeal recurrent, metastatic, unresectable 1st line of therapy<br>– Cisplatin + Gemcitabine + Toripalimab<br>– Cisplatin + Gemcitabine + Pembrolizumab<br>– Cisplatin + Gemcitabine + Nivolumab<br>• **Follicular Lymphoma**<br>– Addition of the following regimen to first-line therapy<br>– Rituximab (weekly for 4 doses)<br>• **Mantle Cell Lymphoma**<br>– Removal of the following regimen to first-line therapy (due to NCCN removal)<br>– Alternating RCHOP/RDHAP (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, Prednisone)/(Rituximab, Dexamethasone, Cytarabine, Cisplatin)<br>– Removal of the following regimen third-line and subsequent therapy (due to NCCN removal)<br>– Lenalidomide<br>• **Marginal Zone Lymphoma**<br>– Removal of the following regimen to first-line therapy<br>– Chlorambucil +/- Rituximab |

| Date | Changes |
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| **July 1, 2024** | • **Kidney Cancer**<br>– Addition of the following regimen to adjuvant therapy<br>– Pembrolizumab<br>– Addition of the following regimen to relapsed or metastatic 1st line of therapy<br>– Nivolumab + Ipilimumab |
| **August 1, 2024** | • **Breast Cancer**<br>– Addition of the following regimen to metastatic, HER 2 negative breast cancer<br>– Fulvestrant + Letrozole<br>– Addition of the following regimen to metastatic, HER 2 negative, hormone positive breast cancer in 3rd and subsequent lines of therapy<br>– Sacituzumab Govitecan-hziy<br>– Addition of the following regimen to metastatic, HER 2 positive in 2nd line for patients with CNS involvement<br>– Tucatinib + Trastuzumab + Capecitabine<br>– Addition of the following regimen to metastatic, HER 2 positive in 3rd and subsequent lines of therapy<br>– Tucatinib + Trastuzumab + Capecitabine<br>– Removal of the following regimen to metastatic, HER 2 positive in 4th and subsequent lines of therapy<br>– Lapatinib + Capecitabine |
| **September 1, 2024** | • **Uterine / Endometrial Cancer – No changes**<br>• **Ovarian Cancer**<br>– Addition of the following regimen to recurrent disease platinum resistant or platinum-refractory<br>– Mirvetuximab soravtansine-gynx (FRα expressing tumors, ≥75% positive tumor cells<br>• **Bladder Cancer**<br>– Changed enfortumab vedotin to locally advanced or metastatic 2nd line and subsequent from 3rd line and subsequent<br>– Addition of the following regimen to locally advanced or metastatic 2nd line and subsequent<br>– Erdaftinib in FGFR 3 mutations |
| **Addition pending NCCN addition** | • **Prostate Cancer (1/2024)**<br>– Addition of the following regimen in castrate resistant metastatic recurrent prostate cancer with no prior novel hormone therapy, without and with prior docetaxel<br>– Olaparib + Abiraterone + ADT (HRRm)<br>• **Non-Small Cell Lung Cancer (1/2024)**<br>– Addition of the following regimen to Advanced/ Metastatic First-Line<br>– Atezolizumab + Carboplatin or Cisplatin + Paclitaxel (Nonsquamous only)<br>– Addition of the following regimen to Advanced/ Metastatic Maintenance (when above is adopted)<br>– Atezolizumab (Nonsquamous)<br>• **Melanoma (6/2024)**<br>– Addition of the following regimen in stage III melanoma, neoadjuvant<br>– Nivolumab + Ipilimumab x 2 cycles |