OVERVIEW

Breast Cancer: Neoadjuvant/Adjuvant

Breast Cancer: Adjuvant (Residual Disease Post-Neoadjuvant Treatment)

Breast Cancer: Metastatic and Recurrent – Endocrine Therapy

Breast Cancer: Metastatic and Recurrent – Chemotherapy

Pancreatic Cancer: Neoadjuvant (Resectable/Borderline Resectable)

Pancreatic Cancer: Adjuvant (Resectable)

Pancreatic Cancer: Locally Advanced/Metastatic

Melanoma: Adjuvant (Resectable)

Melanoma: Adjuvant (Resectable) – (BRAF Mutated)

Melanoma: Metastatic/Unresectable (BRAF Mutated/Symptomatic)

Melanoma: Metastatic/Unresectable (BRAF Wild Type/Mutated/Unknown)

Colon/Rectal Cancer: Adjuvant

Colon/Rectal Cancer: Metastatic KRAS/NRAS: Unknown/Mutant

Colon Cancer/Rectal: Metastatic KRAS/NRAS: Wild Type

Hepatocellular Carcinoma: Unresectable, not a transplant candidate, metastatic disease, inoperable by PS or comorbidity

Biliary Tract Cancers (Gallbladder, intrahepatic and extrahepatic cholangiocarcinoma): Adjuvant Therapy

Biliary Tract Cancers (Gallbladder, intrahepatic and extrahepatic cholangiocarcinoma): Unresectable/Metastatic

Small Cell Lung Cancer: Limited Stage – Adjuvant or Primary Therapy

Small Cell Lung Cancer: Extensive Stage – Adjuvant or Primary Therapy

Small Cell Lung Cancer: Extensive Stage – Adjuvant or Primary Therapy – Maintenance

Small Cell Lung Cancer: Subsequent Therapy: Relapse ≤ 6 months

Small Cell Lung Cancer: Subsequent Therapy: Relapse > 6 months

Ovarian, Fallopian, and Primary Peritoneal Cancer: Neoadjuvant Therapy
Ovarian, Fallopian, and Primary Peritoneal Cancer: Adjuvant or Primary Therapy
Ovarian, Fallopian, and Primary Peritoneal Cancer: Maintenance therapy after Primary therapy
Ovarian, Fallopian, and Primary Peritoneal Cancer: Platinum – Sensitive recurrent disease
Ovarian, Fallopian, and Primary Peritoneal Cancer: Platinum – Resistant recurrent disease
Change Control
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. UnitedHealthcare’s 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.

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.
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)

HER2 POSITIVE:
- Doxorubicin + Cyclophosphamide → Paclitaxel weekly + Trastuzumab* (AC → TH)
- Docetaxel + Carboplatin + Trastuzumab* (TCH)
- Paclitaxel + Trastuzumab*

Breast Cancer: Adjuvant (Residual Disease Post-Neoadjuvant Treatment)

HER 2 NEGATIVE:
- Capecitabine

HER2 POSITIVE:
- Ado-trastuzumab emtansine (T-DM1)

Breast Cancer: Metastatic and Recurrent – Endocrine Therapy

HER2 NEGATIVE:
1st Line of Therapy
- Anastrozole
- Letrozole
- Exemestane
- Tamoxifen
- Fulvestrant
- Anastrozole + Palbociclib
- Letrozole + Palbociclib
- Exemestane + Palbociclib
- Anastrozole + Abemaciclib
- Letrozole + Abemaciclib
- Exemestane + Abemaciclib

HER2 NEGATIVE:
2nd + Subsequent Lines of Therapy
- Anastrozole
- Letrozole
- Exemestane
- Tamoxifen
- Fulvestrant
- Anastrozole + Palbociclib
- Letrozole + Palbociclib
- Exemestane + Palbociclib
• Anastrozole + Abemaciclib
• Letrozole + Abemaciclib
• Exemestane + Abemaciclib
• Fulvestrant + Palbociclib
• Fulvestrant + Abemaciclib

**HER2 POSITIVE:**
• Anastrozole + Trastuzumab*
• Letrozole + Trastuzumab*
• Exemestane + Trastuzumab*
• Anastrozole + Lapatinib
• Letrozole + Lapatinib
• Exemestane + Lapatinib

**Breast Cancer: Metastatic and Recurrent – Chemotherapy**

**HER2 NEGATIVE:**

1st + Subsequent Lines of Therapy
- Doxorubicin
- Paclitaxel
- Docetaxel
- Capecitabine
- Gemcitabine
- Vinorelbine
- Atezolizumab + Nab-Paclitaxel (in PD-L1+ mTNBC only)

**HER2 POSITIVE:**

1st + Subsequent Lines of Therapy
- Docetaxel + Trastuzumab* + Pertuzumab
- Paclitaxel + Trastuzumab* + Pertuzumab
- Ado-Trastuzumab Emtansine (T-DM1)
- Paclitaxel + Trastuzumab*
- Vinorelbine + Trastuzumab*
- Gemcitabine + Trastuzumab*
- Capecitabine + Trastuzumab*

* Kanjinti™ is the preferred product under UnitedHealthcare commercial and UnitedHealthcare Community plans (in most markets) and all products preferred under UnitedHealthcare Medicare plans.
References:


103. Tutt, A., Tovey, H., Cheang, M.C., et al. (May 2018). Carboplatin in BRCA1/2-Mutated and Triple-Negative Breast Cancer BRCAness Subgroups: The TNT Trial. Retrieved from ncbi.nlm.nih.gov/pmc/articles/PMC6372067.


Pancreatic Cancer: Neoadjuvant (Resectable/Borderline Resectable)

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

Pancreatic Cancer: Adjuvant (Resectable)

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

Pancreatic Cancer: Locally Advanced/Metastatic

1st Line of Therapy

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

2nd + Subsequent Lines of Therapy

- Gemcitabine + Albumin-bound Paclitaxel (G-nP)
- Gemcitabine
- Fluorouracil/Leucovorin + Oxaliplatin (OFF)
- Fluorouracil/Leucovorin + Oxaliplatin (FOLFOX)
- Fluorouracil/Leucovorin + Irinotecan (FOLFIRI)
References:


Melanoma: Adjuvant (Resectable)

- Pembrolizumab
- Nivolumab

Melanoma: Adjuvant (Resectable) – (BRAF Mutated)

- Dabrafenib + Trametinib

Melanoma: Metastatic/Unresectable (BRAF Mutated/Symptomatic)

- Vemurafenib + Cobimetinib

Melanoma: Metastatic/Unresectable (BRAF Wild Type/Mutated/Unknown)

1st + Subsequent Lines of Therapy

- Pembrolizumab
- Nivolumab
- Nivolumab + Ipilimumab
References:


Colon/Rectal Cancer: Adjuvant

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

Colon/Rectal Cancer: Metastatic KRAS/NRAS: Unknown/Mutant

1st and 2nd Lines of Therapy

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

Colon Cancer/Rectal: Metastatic KRAS/NRAS: Wild Type

1st and 2nd Lines of Therapy

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

* Mvasi™ is the preferred product under UnitedHealthcare commercial and UnitedHealthcare Community Plans (in most markets) and all products preferred under UnitedHealthcare Medicare plans.
References:


Hepatocellular Carcinoma: Unresectable, not a transplant candidate, metastatic disease, inoperable by PS or comorbidity

1st Line of Therapy
- Sorafenib
- Lenvatinib

2nd + Subsequent Lines of Therapy
- Regorafenib
- Cabozantinib

Biliary Tract Cancers (Gallbladder, intrahepatic and extrahepatic cholangiocarcinoma): Adjuvant Therapy
- Capecitabine

Biliary Tract Cancers (Gallbladder, intrahepatic and extrahepatic cholangiocarcinoma): Unresectable/Metastatic

1st Line of Therapy
- Gemcitabine + Cisplatin
References:


Small Cell Lung Cancer: Limited Stage – Adjuvant or Primary Therapy

- Carboplatin + Etoposide
- Cisplatin + Etoposide

Small Cell Lung Cancer: Extensive Stage – Adjuvant or Primary Therapy

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

Small Cell Lung Cancer: Extensive Stage – Adjuvant or Primary Therapy – Maintenance

- Atezolizumab
- Durvalumab

Small Cell Lung Cancer: Subsequent Therapy: Relapse ≤ 6 months

- Topotecan IV
- Paclitaxel
- Irinotecan

Small Cell Lung Cancer: Subsequent Therapy: Relapse > 6 months

- Carboplatin + Etoposide
- Cisplatin + Etoposide
References:


Ovarian, Fallopian and Primary Peritoneal Cancer: Neoadjuvant Therapy

- Carboplatin + Paclitaxel**

Ovarian, Fallopian and Primary Peritoneal Cancer: Adjuvant or Primary Therapy

- Carboplatin + Paclitaxel**

Ovarian, Fallopian and Primary Peritoneal Cancer: Maintenance Therapy After Primary Therapy

- Olaparib (germline/somatic BRCA mutation only)
- Niraparib

Ovarian, Fallopian and Primary Peritoneal Cancer: Platinum – Sensitive Recurrent Disease

1st + Subsequent Lines of Therapy

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

Maintenance Therapy

- Olaparib
- Niraparib

Ovarian, Fallopian and Primary Peritoneal Cancer: Platinum – Resistant Recurrent Disease

1st + Subsequent Lines of Therapy

- Gemcitabine
- Liposomal Doxorubicin
- Liposomal Doxorubicin + Bevacizumab*
- Paclitaxel (weekly)
- Paclitaxel (weekly) + Bevacizumab*
- Tamoxifen

**Only intravenous carboplatin + paclitaxel are pathway regimens

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References:


74. Jin, W. Roles of TrkC Signaling in the Regulation of Tumorigenicity and Metastasis of Cancer. Cancers 2020, 12, 147.


UnitedHealthcare

77. Diaz L, Marabelle A, et al. Efficacy of Pembrolizumab in Phase 2 KEYNOTE-164 and KEYNOTE-158 Studies of Microsatellite Instability High Cancers Presented at the European Society for Medical Oncology Congress; Madrid, Spain; 8-12 September 2017. Poster 386P.


110. Jin, W. Roles of TrkC Signaling in the Regulation of Tumorigenicity and Metastasis of Cancer. Cancers 2020, 12, 147.


## Change Control

<table>
<thead>
<tr>
<th>Date</th>
<th>Changes</th>
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| July 1, 2020 | Added change control  
New Pathways – Small Cell Lung Cancer and Hepatobiliary Cancer  
Updates to existing pathways –  
  • Melanoma Pathways:  
    o Removed “Stages IIIB and IIIC” from Adjuvant  
  • Colon Pathways:  
    o Updated name to “Colon/Rectal” to reflect pathways for rectal cancer  
    o 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                                           |