Cancer Care Quality Program

Treatment Pathways

EFFECTIVE: NOVEMBER 1, 2017
LAST REVIEWED AUGUST 29, 2017

UPDATES FOR 3rd QUARTER 2017

UPDATES TO EXISTING CANCER TREATMENT PATHWAYS

• Bladder Cancer (Urothelial)
  – Changed Neoadjuvant Therapy | Clinical Stage II, III, or Stage IV without evidence of metastases (cT2, cT3, cT4) to Neoadjuvant Therapy | Clinical Stage II, III, IV without evidence of metastases (cT2, cT3, cT4, M0)
  – Added ‘3 cycles’ to CMV: cisplatin, methotrexate, and vinblastine | Neoadjuvant Therapy | Clinical Stage II, III, IV without evidence of metastases (cT2, cT3, cT4, M0)
  – Removed ddMVAC: dose dense methotrexate, vinblastine, doxorubicin (Adryamycin), and cisplatin | Neoadjuvant Therapy | Clinical Stage II, III, IV without evidence of metastases (cT2, cT3, cT4, M0)
  – Added “4 cycles” to gemcitabine (Gemzar) and cisplatin | Neoadjuvant Therapy | Clinical Stage II, III, IV without evidence of metastases (cT2, cT3, cT4, M0)
  – Removed mitomycin C intravesical | Adjuvant Therapy | Stage I or II after TURBT* or following resection of recurrent or persistent disease
- Added “†” in the setting of recurrent/metastatic disease, a substitution of carbo for cisplatin will be considered a pathway option for gemcitabine (Gemzar) and cisplatin | Metastatic Disease | First line therapy (1st line)
- Added Metastatic Disease | Second line therapy (2nd line)
- Added gemcitabine (Gemzar) | Metastatic Disease | Second line therapy (2nd line)
- Added paclitaxel | Metastatic Disease | Second line therapy (2nd line)
- Added pembrolizumab (Keytruda) Metastatic Disease | Second line therapy (2nd line)

- Colorectal Cancer
  - Added “†” in the setting of recurrent/metastatic disease, a substitution of carbo for cisplatin will be considered a pathway option for gemcitabine (Gemzar) and cisplatin | Metastatic Disease | First line therapy (1st line)
- Added Metastatic Disease | Second line therapy (2nd line)
- Added gemcitabine (Gemzar) | Metastatic Disease | Second line therapy (2nd line)
- Added paclitaxel | Metastatic Disease | Second line therapy (2nd line)
- Added pembrolizumab (Keytruda) Metastatic Disease | Second line therapy (2nd line)

• Colorectal Cancer
  - Removed FLOX: fluorouracil (5-FU), leucovorin, and oxaliplatin | Adjuvant Therapy*
  - Added FOLFOX: fluorouracil (5-FU), leucovorin, and oxaliplatin | Adjuvant Therapy*
  - Removed Modified FOLFOX-6: fluorouracil (5-FU), leucovorin, and oxaliplatin | Adjuvant Therapy*
  - Added clarification for FOLFIRI "+bevacizumab" | Metastatic disease | RAS Wild Type (WT) or Mutant (MT) † | First or second lines of therapy (1st line or 2nd line)
  - Added FOLFOX: fluorouracil (5-FU), leucovorin, and oxaliplatin | Metastatic disease | RAS Wild Type (WT) or Mutant (MT) † | First or second lines of therapy (1st line or 2nd line)
  - Added clarification for FOLFOXIRI "+bevacizumab" | Metastatic disease | RAS Wild Type (WT) or Mutant (MT) † | First or second lines of therapy (1st line or 2nd line)
  - Removed Modified FOLFOX-6: fluorouracil (5-FU), leucovorin, and oxaliplatin | Metastatic disease | RAS Wild Type (WT) or Mutant (MT) † | First or second lines of therapy (1st line or 2nd line)
  - Removed Modified FOLFOX-6: fluorouracil (5-FU), leucovorin, and oxaliplatin with bevacizumab (Avastin) | Metastatic disease | RAS Wild Type (WT) or Mutant (MT) † | First or second lines of therapy (1st line or 2nd line)
  - Changed Metastatic disease | RAS WT | Second lines of therapy (2nd line) to Metastatic disease | RAS wild type (WT) | First or Second lines of therapy (1st or 2nd line)
  - Added clarification for FOLFIRI "+ panitumumab" | Metastatic disease | RAS wild type (WT) | First or Second lines of therapy (1st or 2nd line)
  - Removed FOLFOX-6: fluorouracil (5-FU) leucovorin, and oxaliplatin with panitumumab (Vectibix) | Metastatic disease | RAS wild type (WT) | First or Second lines of therapy (1st or 2nd line)
  - Added FOLFOX + panitumumab: fluorouracil (5-FU), leucovorin, and oxaliplatin with panitumumab (Vectibix) | Metastatic disease | RAS wild type (WT) | First or Second lines of therapy (1st line or 2nd line)
  - Removed Metastatic disease | RAS WT or MT | Third and subsequent lines of therapy (3rd line +)
  - Removed Trifluridine + tipiracil (Lonsurf) | Metastatic disease | RAS WT or MT | First and subsequent lines of therapy (3rd line +)
  - Added FOLFOX: fluorouracil (5-FU), leucovorin, and oxaliplatin with panitumumab (Vectibix) | Metastatic disease | RAS wild type (WT) | First or Second lines of therapy (1st line or 2nd line)
  - Added Metastatic disease | MSI-H or dMMR | Second line therapy (2nd line)
  - Added pembrolizumab (Keytruda) | Metastatic disease | MSI-H or dMMR | Second line therapy (2nd line)
  - Added clarification metastatic disease | RAS “wild type” (WT) | Third and subsequent lines of therapy (3rd line +)
  - Removed irinotecan (Camptosar) and panitumumab (Vectibix)

• NHL: Chronic Lymphocytic Leukemia (CLL) / Small Lymphocytic Lymphoma (SLL)
  - Changed First Line Therapy (1st line) | Without 17p Deletion or Unspecified to First Line Therapy (1st line) | Without 17p Deletion
  - Added BR: bendamustine (Bendeka, Treanda) and rituximab (Rituxan) | First Line Therapy (1st line) | Without 17p Deletion
  - Changed Second and subsequent line therapy (2nd line +) | Without 17p Deletion or Unspecified to Second and subsequent line therapy (2nd line +)
  - Removed FCR: fludarabine (Fludara), cyclophosphamide, and rituximab (Rituxan) | Second and subsequent line therapy (2nd line +)
  - Added Metastatic disease | MSI-H or dMMR | Second line therapy (2nd line)
  - Added pembrolizumab (Keytruda) | Metastatic disease | MSI-H or dMMR | Second line therapy (2nd line)
  - Added clarification metastatic disease | RAS “wild type” (WT) | Third and subsequent lines of therapy (3rd line +)
  - Removed irinotecan (Camptosar) and panitumumab (Vectibix)
  - Added footnotes: indications to initiate treatment may include (not limited to):
    - NHL: Mantle Cell Lymphoma
      - Changed First line of therapy (1st line) | Ineligible for transplant (not ASCT candidate) to First line of therapy (1st line) | Not ASCT Candidate
      - Removed FCMM: fludarabine (Fludara), cyclophosphamide, mitoxantrone (Nevantrone), and rituximab (Rituxan)
      - Removed **+” from lenalidomide (Revlimid) | Second and subsequent lines of therapy (2nd line +)
      - Removed Footer: * following two prior therapies including bortezomib
  - Ovarian Cancer
    - Removed carboplatin and paclitaxel | Adjuvant or Primary Therapy | Stage II, III, IV
    - Added note “Stage III only” for IV paclitaxel and intraperitoneal (IP) cisplatin + IP paclitaxel | Adjuvant or Primary Therapy | Stage II, III, IV
    - Added carboplatin | Recurrent Disease | First or subsequent line of therapy (1st Line +) platinum-sensitive†
    - Removed cisplatin and gemcitabine (Gemzar) | First or subsequent line of therapy (1st Line +) platinum-sensitive†
    - Added tamoxifen | Recurrent Disease | Second or subsequent line of therapy (2nd line +) | Platinum resistant
    - Updated footnote
CONTENTS

Cancer Care Quality Program 4
Bladder Cancer (Urothelial) Pathways 5
Breast Cancer Pathways: Neoadjuvant 6
Breast Cancer Pathways: Adjuvant 7
Breast Cancer Pathways: Advanced/Metastatic Disease 8
Breast Cancer Pathways: Endocrine Therapy for Recurrent or Metastatic Disease 9
Chronic Myelogenous Leukemia (CML) Pathways 10
Colorectal Cancer Pathways 11
Gastric, Esophageal, and Gastroesophageal Junction Cancer (Adenocarcinoma) Pathways 12
Head and Neck Cancer Pathways 13
Hodgkin’s Lymphoma Pathways 14
Kidney Cancer Pathways 15
Lung Cancer: Non-Small Cell Pathways 16
Lung Cancer: Small Cell Lung Cancer Pathways 18
Melanoma Pathways 19
Myeloma Pathways 20
NHL: Chronic Lymphocytic Leukemia (CLL) / Small Lymphocytic Lymphoma (SLL) Pathways 21
NHL: Diffuse Large B-Cell Lymphoma Pathways 22
NHL: Follicular Lymphoma and Marginal Zone Lymphoma Pathways 23
NHL: Mantle Cell Lymphoma Pathways 24
Ovarian Cancer Pathways 25
Pancreatic Cancer (Adenocarcinoma) Pathways 26
Prostate Cancer (Adenocarcinoma) Pathways 27
Testicular (Germ Cell Tumors) Cancer Pathways 29
Uterine (Endometrial) Cancer Pathways 30
bladder Cancer References 31
breast Cancer (Adjuvant) Pathways References 33
breast Cancer (Neoadjuvant) Pathways References 36
breast Cancer Pathways References: Metastatic 40
Breast Cancer Pathways References: Endocrine Therapy for Recurrent or Metastatic Disease 45
Chronic Myelogenous Leukemia (CML) Pathways References 48
Colorectal Cancer Pathways References 51
Gastric and Esophageal Adenocarcinoma Pathway References 56
Head and Neck Pathway References 59
Hodgkin’s Lymphoma Pathways References 61
Kidney Cancer Pathways References 63
Lung Cancer: Non-Small Cell Lung Cancer Pathways References 65
Lung Cancer: Small Cell Lung Cancer Pathways References 70
Melanoma Pathways References 72
Myeloma Pathways References 75
NHL: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Pathways References 80
NHL: Diffuse Large B-Cell Lymphoma Pathways References 83
NHL: Follicular Lymphoma and Marginal Zone Lymphoma Pathways References 86
NHL: Mantle Cell lymphoma Pathways References 89
Ovarian Cancer Pathways References 91
Pancreatic Cancer Pathways References 94
Prostate Cancer (Adenocarcinoma) Pathways References 96
Testicular Cancer (Germ Cell) Pathways References 99
Uterine Cancer Pathways References 101
Cancer Care Quality Program

The goal of the Cancer Care Quality Program is to help provide access to quality and affordable cancer care. A key component of the Cancer Care Quality Program is Cancer Treatment Pathways (“Pathways”).

The Pathways are developed using a rigorous process of evidence-based medicine. Pathways differ from clinical practice guidelines in that the objective of a Pathway is to identify a subset of regimens supported by clinical evidence and practice guidelines with the goal of further reducing unwarranted variation in care and cost. Pathways are selected based on: clinical benefit (efficacy), safety/side effects (especially those leading to hospitalizations & impacting quality of life), strength of national guideline recommendations, and cost of regimens. The Pathways developed for this Program are intended to support quality cancer care.

Pathways are not available for every medical condition but are intended to be applicable for 80%-90% of individuals with the most common types of cancer. Selecting the best cancer treatment depends upon a number of factors – the type of cancer, the stage, the biomarkers or specific genetic profile of the cancer, and unique aspects of each individual's medical condition. Given the complexity of cancer and all of the unique individual circumstances, it would not be possible to have a Pathway for every specific situation. The treating oncologist will determine if, in his/her medical opinion, a Pathway treatment regimen is the best option for a patient or whether, given his or her unique circumstances, another treatment regimen will be a better treatment for him or her.

It is important to note that we will review requested services in accordance with our medical policies and clinical guidelines. When a request is received from a provider that requires medical necessity review, whether it is a Pathway or non-pathway regimen it may be authorized if it is determined to be medically necessary pursuant to our medical policies and clinical guidelines.

Feedback to enhance the Cancer Care Quality Program, Pathways, and/or questions can be emailed to cancer.quality@anthem.com. Requests for the evidence summaries reviewed to develop individual Pathways can also be sent to the same email address.
Bladder Cancer (Urothelial) Pathways

Neoadjuvant Therapy | Clinical Stage II, III, or IV without evidence of metastases (cT2, cT3, cT4a, cT4b, M0)

**CMV:** cisplatin, methotrexate, and vinblastine 3 cycles

**ddMVAC:** dose dense methotrexate, vinblastine, doxorubicin (Adriamycin), and cisplatin1,3,16,19 No Longer Effective 11/1/2017

Gemcitabine (Gemzar) and cisplatin 4 cycles2

**Adjuvant Therapy | Stage I or II after TURBT* or following resection of recurrent or persistent disease**

**BCG:** bacillus calmette-guerin, intravesical20-24

Mitomycin C intravesical20-24 No Longer Effective 11/1/2017

**Metastatic Disease | First line therapy (1st line)**

Gemcitabine (Gemzar) and cisplatin†6,17,18

**Metastatic Disease | Second line therapy (2nd line) (Added Effective 11/1/2017)**

Gemcitabine (Gemzar)9 (Added Effective 11/1/2017)

Paclitaxel14 (Added Effective 11/1/2017)

Pembrolizumab (Keytruda)37 (Added Effective 11/1/2017)

---

*TURBT: Transurethral Resection of Bladder Tumor

†In the setting of recurrent/metastatic disease, a substitution of carboplatin for cisplatin will be considered a Pathway option
Breast Cancer Pathways: Neoadjuvant

<table>
<thead>
<tr>
<th>Neoadjuvant Therapy</th>
<th>HER2 Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AC</strong> → <strong>weekly T</strong>: doxorubicin (Adriamycin) and cyclophosphamide (every 3 weeks) followed by weekly paclitaxel</td>
<td>8, 9, 23, 54</td>
</tr>
<tr>
<td><strong>ddAC</strong> → <strong>weekly T</strong>: dose dense doxorubicin (Adriamycin) and cyclophosphamide followed by weekly paclitaxel</td>
<td>13, 23, 33-34</td>
</tr>
<tr>
<td><strong>TC</strong>: docetaxel (Taxotere) and cyclophosphamide</td>
<td>10, 20</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Neoadjuvant Therapy</th>
<th>HER2 Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AC</strong>→<strong>TH</strong>: doxorubicin (Adriamycin) and cyclophosphamide followed by paclitaxel and trastuzumab (Herceptin)</td>
<td>25, 38, 40, 45, 48, 50</td>
</tr>
<tr>
<td><strong>TCH</strong>: docetaxel (Taxotere), carboplatin, and trastuzumab (Herceptin)</td>
<td>40, 50</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Neoadjuvant Therapy</th>
<th>HER2 Positive</th>
<th>Hormone receptor (ER/PR) negative</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TCH+P</strong>: docetaxel (Taxotere), carboplatin, trastuzumab (Herceptin), and pertuzumab (Perjeta)</td>
<td>41, 42, 56-57</td>
<td></td>
</tr>
</tbody>
</table>
Breast Cancer Pathways: Adjuvant

**Adjuvant Therapy | HER2 Negative**

**AC weekly T:** doxorubicin (Adriamycin) and cyclophosphamide (every 3 weeks) followed by weekly paclitaxel\(^1\text{-}^3\)

**ddAC weekly T:** dose dense doxorubicin (Adriamycin) and cyclophosphamide followed by weekly paclitaxel\(^5\text{-}^7\)

**TC:** docetaxel (Taxotere) and cyclophosphamide\(^3,^4\)

**Adjuvant Therapy | HER2 Positive**

**AC-TH:** doxorubicin (Adriamycin) and cyclophosphamide followed by paclitaxel and trastuzumab (Herceptin)\(^7,^10\text{-}^12\)

**TCH:** docetaxel (Taxotere), carboplatin, and trastuzumab (Herceptin)\(^11\)

**TH:** paclitaxel and trastuzumab (Herceptin)\(^9\text{-}^3\) (Pathway for stage I HER2 Positive breast cancer only)

*Adjuvant chemotherapy pathways do NOT apply to individuals with Hormone-Receptor positive, lymph node negative, OncotypeDX™ LOW risk score*
# Breast Cancer Pathways: Advanced/Metastatic Disease

## Metastatic disease | HER2 Negative | First and subsequent lines of therapy (1st line +)

- Capecitabine (Xeloda)\(^{13,27-30}\)
- Doxorubicin (Adriamycin)\(^{13-18}\)
- Gemcitabine (Gemzar)\(^{20}\)
- Paclitaxel\(^{13,16, 24-26}\)
- Vinorelbine (Navelbine)\(^{21-23}\)

## Metastatic disease | HER2 Positive | First line of therapy (1st line)

- Capecitabine (Xeloda) and trastuzumab (Herceptin)\(^{13,36-39}\)
- Gemcitabine (Gemzar) and Trastuzumab (Herceptin)\(^{40,41}\)
- Paclitaxel and trastuzumab (Herceptin)
- Pertuzumab (Perjeta), trastuzumab (Herceptin), and docetaxel (Taxotere)\(^{12,33-35}\)
- Pertuzumab (Perjeta), trastuzumab (Herceptin), and paclitaxel\(^{34}\)
- Vinorelbine (Navelbine) and trastuzumab (Herceptin)\(^{36,42,43}\)

## Metastatic disease | HER2 Positive | Second and subsequent lines of therapy (2nd line +)

- Ado-trastuzumab emtansine (Kadcyla)\(^{50}\)
- Capecitabine (Xeloda) and lapatinib (Tykerb)\(^{44,45}\)
- Capecitabine (Xeloda) and trastuzumab (Herceptin)\(^{20,36-39}\)
- Gemcitabine (Gemzar) and trastuzumab (Herceptin)\(^{40,42}\)
- Paclitaxel and trastuzumab (Herceptin)
- Pertuzumab (Perjeta), trastuzumab (Herceptin), and docetaxel (Taxotere)
- Pertuzumab (Perjeta), trastuzumab (Herceptin), and paclitaxel
- Trastuzumab (Herceptin) and lapatinib (Tykerb)\(^{48}\)
- Trastuzumab (Herceptin) monotherapy\(^{25,46,47}\)
- Vinorelbine (Navelbine) and trastuzumab (Herceptin)\(^{32,43}\)
Breast Cancer Pathways: Endocrine Therapy for Recurrent or Metastatic Disease

**First line therapy (1st line) | Recurrent or Metastatic Disease | Hormone receptor positive**

- Anastrozole (Arimidex)*1,6,7,10,11,22,33
- Fulvestrant, (Faslodex) high dose*5,7,22,26,33,42
- Letrozole (Femara)*3,12-14,38
- Letrozole (Femara) and palbociclib (Ibrance)*40
- Tamoxifen*12,26

**Second and subsequent lines of therapy (2nd line +) | Recurrent or Metastatic Disease | Hormone receptor positive**

- Anastrozole (Arimidex)*1,6,7,10,11,22,33
- Exemestane (Aromasin)*4,20,21,39
- Fulvestrant (Faslodex) high dose*
- Fulvestrant (Faslodex) and palbociclib (Ibrance)*40
- Letrozole (Femara)*3,12-14,38
- Tamoxifen†12,26

**First and subsequent lines of therapy (1st line +) | Recurrent or Metastatic Disease | Hormone receptor positive | HER2 positive**

- Anastrozole (Arimidex) and trastuzumab (Herceptin)*46
- Letrozole (Femara) and trastuzumab (Herceptin)*49

* With ovarian suppression for premenopausal individuals. Ovarian suppression utilizes LHRH agonists given as monthly injections. 3-month depot dosing does not reliably suppress estrogen levels.

† Tamoxifen is considered Pathway for premenopausal individuals with or without ovarian suppression.
# Chronic Myelogenous Leukemia (CML) Pathways

## First Line Therapy (1st line)

- **Dasatinib** (Sprycel) for intermediate or high risk disease
- **Imatinib** (Gleevec)
- **Nilotinib** (Tasigna) for intermediate or high risk disease

## Second Line Therapy (2nd line)  
**Following treatment failure, suboptimal response†, or intolerance to first line therapy**

- **Bosutinib** (Bosulif)
- **Dasatinib** (Sprycel)
- **Nilotinib** (Tasigna)
- **Ponatinib‡** (Iclusig)

## Third line of therapy (3rd line)

- **Ponatinib** (Iclusig)

---

* For patients with intermediate or high risk disease based on Sokal or Hasford Score:
  - **Sokal**: Intermediate Risk=0.8-1.2; High Risk>1.2
  - **Hasford**: Intermediate Risk=781-1480; High Risk>1480

† Defined as lack of complete hematologic response or BCR-ABL1 transcripts > 10% (IS) or lack of partial cytogenetic response on bone marrow cytogenetics.

‡ Pathway option for second line therapy only after failure, suboptimal response, or intolerance of a second generation TKI has been used in the first line setting, or T315I mutation has been identified.
Colorectal Cancer Pathways

**Adjuvant Therapy**

Capecitabine (Xeloda)\(^{52,69}\)

**FLOX**: fluorouracil (5-FU), leucovorin, and oxaliplatin\(^{5,8,49,69}\) No Longer Effective 11/1/2017

**FOLFOX**: fluorouracil (5-FU), leucovorin, and oxaliplatin \(^{7,8,50,51,60,69}\) (Added Effective 11/1/2017)

**FULV**: fluorouracil (5FU) and leucovorin\(^{1,4,7,49,52,69}\) No Longer Effective 11/1/2017

**Modified FOLFOX-6**: fluorouracil (5-FU), leucovorin, and oxaliplatin\(^{7,8,51,60,69}\) No Longer Effective 11/1/2017

**Metastatic disease | RAS Wild Type (WT) or Mutant (MT) † | First or second lines of therapy (1st or 2nd line)**

Capecitabine (Xeloda)\(^{27}\)

**FOLFIRI**: fluorouracil (5FU), leucovorin, and irinotecan (Camptosar)\(^{18,23,30,32,34}\)

**FOLFIRI** + bevacizumab; fluorouracil (5FU), leucovorin, and irinotecan (Camptosar) with bevacizumab (Avastin)\(^{21,23,31,36,44,45,58}\)

**FOLFOX**: fluorouracil (5FU), leucovorin, and oxaliplatin \(^{24,26,28,30,34}\) (Added Effective 11/1/2017)

**FOLFOX** + bevacizumab; fluorouracil (5FU), leucovorin, oxaliplatin, with bevacizumab (Avastin)\(^{25,26,28,33,44,45,70}\) (Added Effective 11/1/2017)

**FOLFOXIRI** + bevacizumab; fluorouracil (5FU), leucovorin, oxaliplatin, irinotecan (Camptosar), and bevacizumab (Avastin)\(^{25,26,28,33,44,45,70}\)

**FULV**: fluorouracil (5FU) and leucovorin\(^{22,27,35}\)

**FULV**: fluorouracil (5FU) and leucovorin with bevacizumab (Avastin)\(^{22,27,35}\)

**Modified FOLFOX-6**: fluorouracil (5FU), leucovorin, and oxaliplatin\(^{24,26,28,30,34}\) No Longer Effective 11/1/2017

**Modified FOLFOX-6**: fluorouracil (5FU), leucovorin, and oxaliplatin with bevacizumab (Avastin)\(^{25,26,28,33,44,45,70}\) No Longer Effective 11/1/2017

**Metastatic disease | RAS wild type (WT) | First or second lines of therapy (1st or 2nd line)** (Added Effective 11/1/2017)

FOLFIRI + panitumumab; fluorouracil (5FU), leucovorin, and irinotecan (Camptosar) with panitumumab (Vectibix)\(^{11,62}\)

FOLFOX: fluorouracil (5FU), leucovorin, and oxaliplatin with panitumumab (Vectibix)\(^{12,53,59}\) No Longer Effective 11/1/2017

FOLFOX + panitumumab: fluorouracil (5-FU), leucovorin, and oxaliplatin with panitumumab (Vectibix)\(^{11,53,59}\) (Added Effective 11/1/2017)

Irinotecan (Camptosar) and panitumumab (Vectibix)\(^{47}\)

**Metastatic disease | RAS WT or MT ‡ | Third and subsequent lines of therapy (3rd line +)** No Longer Effective 11/1/2017

Trifluridine + tipiracil (Lonsurf)\(^{85}\) No Longer Effective 11/1/2017

**Metastatic disease | MSI-H or dMMR | Second line therapy (2nd line)** (Added Effective 11/1/2017)

Pembrolizumab (Keytruda)\(^{91}\) (Added Effective 11/1/2017)

**Metastatic disease | RAS wild type (WT) | Third and subsequent lines of therapy (3rd line +)**

Irinotecan (Camptosar) and panitumumab (Vectibix)\(^{47}\) No Longer Effective 11/1/2017

Panitumumab (Vectibix) monotherapy\(^{13,56,61}\)

* Adjuvant Pathways do not apply to stage II MSI-H (microsatellite instability-high) disease.
† Exon 2 KRAS, non-exon 2 KRAS, and NRAS mutations; testing recommended for all patients with metastatic disease.
‡ Limit to one line of therapy
Gastric, Esophageal, and Gastroesophageal Junction Cancer (Adenocarcinoma) Pathways

**Primary therapy | Resectable and unresectable disease**

Cisplatin and fluorouracil (5FU)\(^3,4\)

Fluorouracil (5FU) and cisplatin with concurrent radiation therapy (RT)\(^3,5\)

Paclitaxel and carboplatin with concurrent RT\(^5\)

**Post-operative treatment**

Fluorouracil (5FU) and leucovorin with concurrent RT\(^3,8\)

**Recurrent/metastatic or locally advanced/inoperable disease | HER2 Negative | First line of therapy (1\(^{st}\) line)**

Cisplatin and fluorouracil (5FU)\(^1,9,2,2,26\)

Fluorouracil (5FU) and irinotecan (Camptosar)\(^2,5,26\)

**FLO/FOLFOX**: fluorouracil (5FU), leucovorin, and oxaliplatin\(^2,7\)

**FLP**: fluorouracil (5FU), leucovorin, and cisplatin\(^2,7\)

**Recurrent/metastatic or locally advanced/inoperable disease | HER2 Positive | First line of therapy (1\(^{st}\) line)**

Cisplatin, fluorouracil (5FU), and trastuzumab (Herceptin)\(^1,5\)

**Recurrent/metastatic or locally advanced/inoperable disease | Second line of therapy (2\(^{nd}\) line)**

Irinotecan (Camptosar)\(^2,4,29\)

Paclitaxel\(^3,3\)
Head and Neck Cancer Pathways

Hypopharynx and larynx: candidate for local therapy (M0) | Primary systemic therapy & concurrent radiation therapy (RT)
High dose cisplatin* with concurrent RT

Hypopharynx and larynx: candidate for local therapy (M0) | Post-operative systemic therapy & concurrent radiation therapy (RT)
High dose cisplatin* with concurrent RT

Lip, oral cavity, oropharynx, ethmoid sinus, maxillary sinus, occult primary: candidate for local therapy (M0) | Primary systemic therapy & concurrent radiation therapy (RT)
High dose cisplatin* with concurrent RT

Lip, oral cavity, oropharynx, ethmoid sinus, maxillary sinus, occult primary: candidate for local therapy (M0) | Post-operative systemic therapy & concurrent radiation therapy (RT)
High dose cisplatin* with concurrent RT

Nasopharynx: candidate for local therapy (M0) | Primary systemic therapy & concurrent radiation therapy (RT) followed by adjuvant therapy
High dose cisplatin* with concurrent RT following by cisplatin and fluorouracil (5FU)

Nasopharynx | Metastatic and recurrent disease | First Line and subsequent lines of therapy | Performance Status 0,1,2
Cisplatin† and fluorouracil (5FU)
Cisplatin† and gemcitabine (Gemzar)
Cisplatin† and paclitaxel
Cisplatin OR carboplatin (single agent)
Gemcitabine (Gemzar)
Methotrexate
Paclitaxel

Non-Nasopharyngeal (Squamous cell) | Metastatic and recurrent disease | First Line | Performance Status 0,1,2
Carboplatin, fluorouracil (5FU), and cetuximab (Erbitux)
Cisplatin, fluorouracil (5FU), and cetuximab (Erbitux)

Non-nasopharyngeal (Squamous cell) | Metastatic and recurrent disease | Second Line and Subsequent lines of therapy | Performance Status 0,1,2
Fluorouracil (5FU)
Methotrexate
Nivolumab (Opdivo)
Paclitaxel

* “High dose cisplatin” refers to dosing to achieve total dose of 200-300 mg/m2 of cisplatin over the course of the radiotherapy. There are several different appropriate cisplatin schedules that may be used.
† Substitution of carboplatin for cisplatin, and vice-versa, is acceptable for metastatic disease
Hodgkin’s Lymphoma Pathways

Classical Hodgkin | Early or Late Stage | with or without Radiation Therapy (RT)

**ABVD**: doxorubicin (Adriamycin), bleomycin, vinblastine, and dacarbazine (DTIC)\(^1\text{-}^3,30,32\)
Kidney Cancer Pathways

**Metastatic | First line therapy (1\textsuperscript{st} line) | Clear Cell and Non-clear Cell**

- Pazopanib (Votrient)\textsuperscript{4-7}
- Sunitinib (Sutent)\textsuperscript{1-3}
- Temsirolimus (Torisel)\textsuperscript{12}

**Metastatic | Second line therapy (2\textsuperscript{nd} line) | Clear Cell**

- Axitinib (Inlyta)\textsuperscript{22}
- Cabozantinib (Cabometyx)\textsuperscript{28,30,31}
- Nivolumab (Opdivo)\textsuperscript{29,30,32}
- Sorafenib (Nexavar)\textsuperscript{22,24}
# Lung Cancer: Non-Small Cell Pathways

## Adjuvant Therapy

- Cisplatin and vinorelbine (Navelbine)\(^{53,54}\)
- Gemcitabine (Gemzar) and cisplatin
- Paclitaxel and carboplatin\(^{52}\)

## Primary Therapy for Locally Advanced / Unresectable | Stage III

- Paclitaxel (every 3 weeks) and carboplatin with XRT\(^{92}\)

## Metastatic disease | ALK Positive or ROS1 Positive | First line (1st line)

- Crizotinib (Xalkori)\(^{1,58}\)

## Metastatic disease | EGFR Positive | First line (1st line)

- Afatinib (Gilotrif)\(^{6}\)
- Erlotinib (Tarceva)\(^{41,42,73,87}\)

## Metastatic disease | Non-squamous | ECOG PS: 0, 1, 2 | First line (1st line)

- Carboplatin* and paclitaxel\(^{7,16,54}\)
- Cisplatin* and gemcitabine (Gemzar)\(^{8,11,13,22-25}\)
- Cisplatin* and pemetrexed (Alimta)\(^{17,18}\)
- Paclitaxel, carboplatin, and bevacizumab (Avastin)\(^{13,14,30,31}\)

## Metastatic disease | Squamous | ECOG PS: 0, 1, 2 | First line (1st line)

- Carboplatin* and paclitaxel\(^{7-16}\)
- Cisplatin* and gemcitabine (Gemzar)\(^{8,11,13,17,23,75}\)

## Metastatic disease | PD-L1 Positive | First line (1st line)

- Pembrolizumab (Keytruda)\(^{102}\)

## Metastatic disease | Non-squamous | ECOG PS: 0, 1, 2 | Maintenance

- Continuation bevacizumab (Avastin)\(^{36-38}\)
- Continuation pemetrexed (Alimta)\(^{39}\)
- Switch pemetrexed (Alimta)\(^{41}\)

* Administered at a dose of 2 mg/kg (up to a maximum of 200 mg).

† In the setting of recurrent/metastatic NSCLC, a substitution of carboplatin for cisplatin (or vice-versa) will be considered a Pathway option.
Lung Cancer: Non-Small Cell Pathways (Continued)

<table>
<thead>
<tr>
<th>Metastatic disease</th>
<th>ALK Positive or EGFR Positive</th>
<th>ECOG PS: 0, 1, 2</th>
<th>Second line (2nd line) after targeted 1st line therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Carbothristin* and paclitaxel</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cisplatin* and gemcitabine (Gemzar)*3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cisplatin* and pemetrexed (Alimta)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic disease</th>
<th>EGFR T790M mutation</th>
<th>Second line (2nd line) after targeted 1st line therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Osimertinib (Tagrisso)*186,90</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic disease</th>
<th>Non-squamous</th>
<th>ECOG PS: 0, 1, 2</th>
<th>Second line (2nd line)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Docetaxel (Taxotere)*43-47,55</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nivolumab (Opdivo)*72</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pemetrexed (Alimta)*31,32</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic disease</th>
<th>Squamous</th>
<th>ECOG PS: 0, 1, 2</th>
<th>Second line (2nd line)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nivolumab (Opdivo)*59,61</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* In the setting of recurrent/metastatic NSCLC, a substitution of carboplatin for cisplatin (or vice-versa) will be considered a Pathway option

† For patients with EGFR T790M mutation
## Lung Cancer: Small Cell Lung Cancer Pathways

### Limited Stage | Primary, Adjuvant, or First Line Therapy (1st line)

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin and etoposide (Toposar) ± XRT³</td>
</tr>
<tr>
<td>Cisplatin and etoposide (Toposar) ± XRT¹²</td>
</tr>
</tbody>
</table>

### Extensive Stage | First line of therapy (1st line)

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin and etoposide (Toposar)⁹</td>
</tr>
</tbody>
</table>

### Second and subsequent lines of therapy (2nd line +) | Relapse greater than 6 months

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin and etoposide (Toposar)⁹</td>
</tr>
</tbody>
</table>
# Melanoma Pathways

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>First and subsequent lines of therapy (1st line +)</th>
<th>Any BRAF status</th>
<th>ECOG PS: 0,1,2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembrolizumab (Keytruda)*</td>
<td></td>
<td>35,45,55,56</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>First line of therapy (1st line)</th>
<th>BRAF mutated †</th>
<th>Symptomatic disease</th>
<th>ECOG PS: 0,1,2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vemurafenib (Zelboraf) and cobimetinib (Cotellic)</td>
<td></td>
<td>26,40-42</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>Second and subsequent lines of therapy (2nd line +)</th>
<th>BRAF mutated †</th>
<th>ECOG PS: 0, 1, 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vemurafenib (Zelboraf) and cobimetinib (Cotellic)</td>
<td></td>
<td>26,40-42</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>Second and subsequent lines of therapy (2nd line +)</th>
<th>Any BRAF status</th>
<th>ECOG PS: 0, 1, 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipilimumab (Yervoy)</td>
<td></td>
<td>1,14,15,35,36</td>
<td></td>
</tr>
</tbody>
</table>

* Administered at a dose of 2 mg/kg (up to a maximum of 200 mg).

† BRAF mutations include V600E and V600K mutations.
**Myeloma Pathways**

### Primary/First line of therapy (1st line) | Transplant candidates

**VRD/VDR**: bortezomib (Velcade), lenalidomide (Revlimid), and dexamethasone\(^{88}\)

### Primary/First Line of therapy (1st line) | Ineligible for transplant

**CyBorD or VDC**: bortezomib (Velcade), cyclophosphamide, and dexamethasone

**R-dex**: lenalidomide (Revlimid) and low-dose dexamethasone\(^{11,34,35}\)

**VRD/VDR**: bortezomib (Velcade), lenalidomide (Revlimid), and dexamethasone

**VD**: bortezomib (Velcade) and dexamethasone\(^{1,3,24,85}\)

### Maintenance therapy | Post-transplant

Lenalidomide (Revlimid)

### Relapsed Disease | Second and subsequent lines of therapy (2nd line +)

**CRd or KRd**: carfilzomib (Kyprolis), lenalidomide (Revlimid), and dexamethasone\(^{82}\)

**DRD**: daratumumab (Darzalex), lenalidomide (Revlimid), and dexamethasone\(^{100}\)

**DVD**: daratumumab (Darzalex), bortezomib (Velcade), and dexamethasone\(^{103}\)

### Relapsed Disease | Third and subsequent lines of therapy (3rd line +)

**Daratumumab (Darzalex)\(^{95}\)**

**Elotuzumab (Empliciti), lenalidomide (Revlimid), and dexamethasone\(^{97}\)**
NHL: Chronic Lymphocytic Leukemia (CLL) / Small Lymphocytic Lymphoma (SLL) Pathways

First Line of Therapy (1st line) | With 17p Deletion
Ibrutinib (Imbruvica)\textsuperscript{28,37,46,47}

First Line of Therapy (1st line) | Without 17p Deletion
BR: bendamustine (Bendeka, Treanda) and rituximab (Rituxan)\textsuperscript{13,14,15,39,51} (Added Effective 11/1/2017)
FCR: fludarabine (Fludara), cyclophosphamide, and rituximab (Rituxan)\textsuperscript{1-2,39,51}
Ibrutinib (Imbruvica)\textsuperscript{28,37,46,47}
Obinutuzumab (Gazyva) and chlorambucil (Leukeran)\textsuperscript{16}

Second and subsequent lines of therapy (2nd line +) | With 17p Deletion
Ibrutinib (Imbruvica)\textsuperscript{28,37,41,46,47}
Idelalisib (Zydelig)\textsuperscript{43}
Idelalisib (Zydelig) and rituximab (Rituxan)\textsuperscript{38}

Second and subsequent lines of therapy (2nd line +) | Without 17p Deletion
BR: bendamustine (Bendeka, Treanda) and rituximab (Rituxan)\textsuperscript{13,14,15,42}
FCR: fludarabine (Fludara), cyclophosphamide, and rituximab (Rituxan)\textsuperscript{1-2} No Longer Effective 11/1/2017
Ibrutinib (Imbruvica)\textsuperscript{28,37,41,46,47}
Idelalisib (Zydelig)\textsuperscript{43}
Idelalisib (Zydelig) and rituximab (Rituxan)\textsuperscript{38}

Indications to initiate treatment may include (not limited to):
1. WBC elevation above 200-300 x 10\textsuperscript{9}
2. Signs of leukostasis
3. Lymphocyte doubling time of less than 6 months
4. In low or intermediate risk disease:
   a. Significant disease-related symptoms such as severe fatigue, weight loss, night sweats, otherwise unexplained fever
   b. Signs of end-organ damage
   c. Significant or progressive bulky disease, such as massive splenomegaly (≥6 cm below the costal margin) or massive lymphadenopathy (≥10 cm in longest diameter)
   d. Clinically significant progressive or symptomatic anemia or thrombocytopenia
      i. Not caused by autoimmune etiology, unless poor response to conventional immunosuppressive therapy
5. High risk disease, particularly with progressive cytopenias
# NHL: Diffuse Large B-Cell Lymphoma Pathways

## First line of therapy (1st line)

**R-CHOP (21):** cyclophosphamide, doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, and rituximab (Rituxan)

## First line of therapy (1st line) | Contraindication to anthracycline

**R-CEOP:** cyclophosphamide, etoposide (Toposar), vincristine (Vincasar), prednisone, and rituximab (Rituxan)

## Second and subsequent line of therapy (2nd line +) | Transplant candidates

**R-GDP:** gemcitabine (Gemzar), dexamethasone, cisplatin, and rituximab (Rituxan) OR gemcitabine (Gemzar), dexamethasone, carboplatin, and rituximab (Rituxan)

**R-ICE:** ifosfamide (Ifex), carboplatin, etoposide (Toposar), and rituximab (Rituxan)

## Second and subsequent line of therapy (2nd line +) | Non-Transplant candidates

**BR:** bendamustine (Bendeka, Treanda) and rituximab (Rituxan)

**R-GDP:** gemcitabine (Gemzar), dexamethasone, cisplatin, and rituximab (Rituxan) OR gemcitabine (Gemzar), dexamethasone, carboplatin, and rituximab (Rituxan)

**R-GemOx:** gemcitabine (Gemzar), oxaliplatin, and rituximab (Rituxan)

Rituximab (Rituxan) monotherapy reserved for frail patients or elderly patients
**NHL: Follicular Lymphoma and Marginal Zone Lymphoma Pathways**

---

**Gastric MALT (Mucosa-associated Lymphoid Tissue) Lymphoma: Stage IE or IIE, *H. pylori* positive**

Antibiotic therapy for *H. pylori* eradication\(^{33,34}\)

---

**Splenenic Marginal Zone Lymphoma † OR Gastric MALT Lymphoma: First line of therapy (1st line)**

- Rituximab (Rituxan) monotherapy\(^{27-29}\)

---

**Follicular (Grade I-IIIA) Lymphoma and other Marginal Zone Lymphomas | First line of therapy (1st line)**

- **BR:** bendamustine (Bendeka, Treanda) and rituximab (Rituxan)\(^5,6\)
- **R-CHOP (21):** cyclophosphamide, doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, and rituximab (Rituxan)\(^1,3,5\)
- **R-CVP:** cyclophosphamide, vincristine (Vincasar), prednisone, and rituximab (Rituxan)\(^1,4\)
- Rituximab (Rituxan) monotherapy\(^7,17\)

---

**Follicular (Grade I-IIIA) Lymphoma and other Marginal Zone Lymphomas | First line of therapy (1st line) | Additional options for the elderly or infirm**

- Chlorambucil (Leukeran)\(^10\)
- Chlorambucil (Leukeran) and rituximab (Rituxan)\(^10,11\)
- Cyclophosphamide\(^11-13\)
- Cyclophosphamide and rituximab (Rituxan)

---

**Follicular Lymphoma (Grade III) | First Line Therapy (1st line)**

- **R-CHOP (21):** cyclophosphamide, doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, and rituximab (Rituxan)\(^1,3,5\)
- **R-CEOP:** cyclophosphamide, etoposide (Toposar), vincristine (Vincasar), prednisone, and rituximab (Rituxan)\(^35-37\)

---

* Gastric MALT with translocation 11;18 (t11;18) (q21;q21) predicts a lower response rate to anti-*H.pylori* treatment. Radiation therapy or other local intervention may be indicated.

† Splenectomy is also a recommended option for Splenic Marginal Zone Lymphoma (NCCN 2A).
# NHL: Mantle Cell Lymphoma Pathways

## First line of therapy (1st line) | ASCT Candidates

**Alternating R-CHOP/R-DHAP:** cyclophosphamide, doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, rituximab (Rituxan), alternating with dexamethasone, cisplatin, cytarabine (Ara-C), and rituximab (Rituxan)\(^4,5,28,30,31\)

**Nordic Regimen:** dose-intensified rituximab (Rituxan), cyclophosphamide, vincristine (Vincasar), doxorubicin (Adriamycin), prednisone, alternating with rituximab (Rituxan), and high-dose cytarabine (Ara-C)\(^3\)

## First line of therapy (1st line) | Not ASCT Candidates

**BR:** bendamustine (Bendeka, Treanda) and rituximab (Rituxan)\(^9,10\)

## Second and subsequent lines of therapy (2nd line +)

**BR:** bendamustine (Bendeka, Treanda) and rituximab (Rituxan)

**Bortezomib (Velcade)**\(^{17}\)

**FCMR:** fludarabine (Fludara), cyclophosphamide, mitoxantrone (Novantrone), and rituximab (Rituxan)\(^{13}\) *No Longer Effective 11/1/2017*

**Ibrutinib (Imbruvica)**\(^{19,20}\)

**Lenalidomide (Revlimid)**\(^{20,23}\)
Ovarian Cancer Pathways

**Adjuvant Therapy | Stage IA/B (Grade 2 or 3) or IC (Grade 1-3)**

Carboplatin and dose dense (weekly) paclitaxel
Carboplatin and paclitaxel

**Adjuvant or Primary Therapy | Stage II, III, IV**

Carboplatin* and paclitaxel
Carboplatin and dose dense (weekly) paclitaxel
Intravenous (IV) paclitaxel and Intraperitoneal (IP) cisplatin and IP paclitaxel (Stage III only)

**Recurrent Disease | First and subsequent line of therapy (1st line +) | Platinum-sensitive***

Carboplatin (Added Effective 11/1/2017)
Carboplatin and gemcitabine (Gemzar)
Carboplatin and paclitaxel
Carboplatin and weekly paclitaxel
Cisplatin and gemcitabine (Gemzar) No Longer Effective 11/1/2017

**Recurrent Disease | Maintenance Therapy | Platinum-sensitive** (Added Effective 11/1/2017)

Niraparib (Zejula) (Added Effective 11/1/2017)

**Recurrent Disease | Second or subsequent lines of therapy (2nd line +) | Platinum resistant**

Bevacizumab (Avastin) monotherapy
Docetaxel (Taxotere)
Gemcitabine (Gemzar)
Liposomal doxorubicin (Doxil or Lipodox)
Paclitaxel (weekly)
Paclitaxel and bevacizumab (Avastin)
Tamoxifen (Added Effective 11/1/2017)
Topotecan (Hycamtin)
Topotecan (Hycamtin) and bevacizumab (Avastin)
Vinorelbine (Navelbine)

* Platinum sensitive disease is defined as recurrence of greater than 6 months after prior platinum-based therapy
### Pancreatic Cancer (Adenocarcinoma) Pathways

#### Adjuvant Therapy

- Capecitabine (Xeloda) and gemcitabine (Gemzar)\(^{36, 40}\)
- **FULV**: fluorouracil (5FU) and leucovorin\(^{4,6,9}\)
- Gemcitabine (Gemzar)\(^{1,3-7}\)

#### Locally Advanced/Unresectable and Metastatic Disease | First Line Therapy (1\(^{st}\) line) | ECOG PS: 0, 1, 2

- **FOLFIRINOX**: fluorouracil (5FU), leucovorin, irinotecan (Camptosar), and oxaliplatin\(^{5,21}\)
- Gemcitabine (Gemzar)\(^{6,15,21}\)
- Gemcitabine (Gemzar) and nab-paclitaxel (Abraxane)\(^{5,15,33}\)

#### Locally Advanced/Unresectable and Metastatic Disease | Second line of therapy (2\(^{nd}\) line) | ECOG PS: 0,1,2

- **OFF**: fluorouracil (5FU), leucovorin, and oxaliplatin\(^{32}\)
- Gemcitabine (Gemzar) monotherapy\(^{21}\)
Prostate Cancer (Adenocarcinoma) Pathways

**Adjuvant Therapy | Post-prostatectomy | Lymph node positive (LN+)**

- Goserelin (Zoladex)$^{1,2}$
- Leuprolide (Eligard/Lupron)$^{1,2}$
- Triptorelin (Trelstar)$^{1,2}$

**Intermediate risk | Primary treatment with radiotherapy (RT)**

- Goserelin* (Zoladex)$^{3,5}$
- Leuprolide* (Eligard/Lupron)$^{3,5}$
- Triptorelin* (Trelstar)$^{3,5}$

**High Risk (T3a or Gleason 8-10), Very High Risk (T3b-T4), and Locally Advanced Prostate Cancer (LN+) | Primary treatment with radiotherapy**

- Goserelin* (Zoladex)$^{4}$
- Histrelin* (Vantas)$^{4}$
- Leuprolide* (Eligard/Lupron)$^{4}$
- Triptorelin* (Trelstar)$^{4}$

**Recurrent and Metastatic disease | Hormone Sensitive**

- Docetaxel (Taxotere) (every 3 weeks) with Androgen Deprivation Therapy (ADT)$^{†19}$
- Goserelin (Zoladex)$^{**6}$
- Histrelin (Vantas)$^{**6}$
- Leuprolide (Eligard/Lupron)$^{**6}$
- Triptorelin (Trelstar)$^{**6}$

---

*May be coadministered with bicalutamide (Casodex) or flutamide (Eulexin) for up to 30 days in patients who are at risk of developing symptoms associated with testosterone flare.

**ADT: histrelin (Vantas), goserelin (Zoladex), leuprolide (Eligard/Lupron), triptorelin (Trelstar)**
Prostate Cancer (Adenocarcinoma) Pathways
(Continued)

Recurrent and Metastatic Disease | Hormone Resistant | First and subsequent lines of therapy (1st line+)

- Abiraterone (Zytiga) with continued ADT**8,12,26,27
- Degarelix (Firmagon) with bicalutamide (Casodex)7
- Docetaxel** (Taxotere) (every 3 weeks) with continued ADT**9,10,19
- Goserelin (Zoladex) with bicalutamide (Casodex)6,7
- Leuprolide (Eligard/Lupron) with bicalutamide (Casodex)6,7
- Triptorelin (Trelstar) with bicalutamide (Casodex)6,7

Recurrent and Metastatic Disease | Hormone Resistant | Second and subsequent lines of therapy (2nd line+)

- Cabazitaxel (Jevtana) with ADT **11
- Docetaxel (Taxotere) rechallenge with ADT**21,22
- Enzalutamide (Xtandi)** with ADT16
- Continued ADT** with supportive care ± dexamethasone13,14,15,16,24

*May be coadministered with bicalutamide (Casodex) or flutamide (Eulexin) for up to 30 days in patients who are at risk of developing symptoms associated with testosterone flare.

**ADT: histrelin (Vantas), goserelin (Zoladex), leuprolide (Eligard/Lupron), triptorelin (Trelstar)
# Testicular (Germ Cell Tumors) Cancer Pathways

<table>
<thead>
<tr>
<th>Stage</th>
<th>Therapy Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Seminoma</strong></td>
<td>**Stage II-III A</td>
</tr>
<tr>
<td><strong>BEP</strong></td>
<td>bleomycin, etoposide (Toposar), and cisplatin$^5$</td>
</tr>
<tr>
<td><strong>EP</strong></td>
<td>etoposide (Toposar) and cisplatin$^4$</td>
</tr>
<tr>
<td><strong>Seminoma</strong></td>
<td>**Stage IIIB-C</td>
</tr>
<tr>
<td><strong>BEP</strong></td>
<td>bleomycin, etoposide (Toposar), and cisplatin$^{5,6}$</td>
</tr>
<tr>
<td><strong>Nonseminoma</strong></td>
<td>**Stage II-III A</td>
</tr>
<tr>
<td><strong>BEP</strong></td>
<td>bleomycin, etoposide (Toposar), and cisplatin$^{5,6}$</td>
</tr>
<tr>
<td><strong>EP</strong></td>
<td>etoposide (Toposar) and cisplatin$^4$</td>
</tr>
<tr>
<td><strong>Nonseminoma</strong></td>
<td>**Stage IIIB-C</td>
</tr>
<tr>
<td><strong>BEP</strong></td>
<td>bleomycin, etoposide (Toposar), and cisplatin$^{5,6}$</td>
</tr>
<tr>
<td><strong>Nonseminoma</strong></td>
<td><strong>Adjuvant Therapy after RPLND</strong></td>
</tr>
<tr>
<td><strong>EP</strong></td>
<td>etoposide (Toposar) and cisplatin$^{8,9,26}$</td>
</tr>
</tbody>
</table>

$^*$RPLND: Retroperitoneal Lymph Node Dissection
## Uterine (Endometrial) Cancer Pathways

<table>
<thead>
<tr>
<th>Therapy Type</th>
<th>Therapeutic Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>**Adjuvant Therapy</td>
<td>Stage III-IV or High Risk Histologies**</td>
</tr>
<tr>
<td></td>
<td>Carboplatin and paclitaxel⁵,⁶</td>
</tr>
<tr>
<td>**Recurrent / Metastatic</td>
<td>First and Subsequent Lines of Therapy (1st line +)**</td>
</tr>
<tr>
<td></td>
<td>Carboplatin and paclitaxel⁵,2⁷-2⁹</td>
</tr>
<tr>
<td></td>
<td>Cisplatin and doxorubicin (Adriamycin)²⁴,²⁵</td>
</tr>
</tbody>
</table>
BLADDER CANCER REFERENCES


Piccart-Gebhart M, Holmes AP, Baselga J, et al. First results from the phase III ALTTO trial (BIG 2-06; NCCTG [Alliance] N063D) comparing one year of anti-HER2 therapy with lapatinib alone (L), trastuzumab alone (T), their sequence (T->L), or their combination (T+L) in the adjuvant treatment of HER2-positive early breast cancer (EBC). J Clin Oncol. 2014; 32(18 Supp); LBA4.


Briefing Book: Perjeta (pertuzumab) prepared for Oncology Drugs Advisory Committee Meeting. San Francisco: Genentech, Inc. August 9, 2013.

FDA Briefing Document for sBLA 125409/51, Pertuzumab (PERJETA®). Oncologic Drugs Advisory Committee Meeting, September 12, 2013.


Gianni, Luca, et al. 5-year analysis of neoadjuvant pertuzumab and trastuzumab in patients with locally advanced, inflammatory, or early-stage HER2-positive breast cancer (NeoSphere): a multicentre, open-label, phase 3 trial. The Lancet Oncology 17.6 (2016): 791-800. PMID: 27179402

Schneeweiss A. Pertuzumab and trastuzumab plus standard neoadjuvant anthracycline-containing and anthracycline free chemotherapy regimens in patients with HER2-positive early breast cancer: Efficacy analysis of a phase II cardiac safety study (TRYPHAENA). SABCS 2016


BREAST CANCER (NEOADJUVANT) PATHWAYS REFERENCES


15. Martin M, Villar A, GEICAM Group (Spanish Breast Cancer Research Group), Spain, et al. Doxorubicin in combination with fluorouracil and cyclophosphamide (i.e. FAC regimen, day 1, 21) versus methotrexate in combination with fluorouracil and cyclophosphamide (i.e. CMF regimen, day 1, 21) as adjuvant chemotherapy for operable breast cancer: a study by the GEICAM group. Ann Oncol. 2003 Jun;14(6):833-842.


53 Briefing Book: Perjeta (pertuzumab) prepared for Oncology Drugs Advisory Committee Meeting. San Francisco: Genentech, Inc. August 9, 2013.

54 FDA Briefing Document for sBLA 125409/51, Pertuzumab (PERJETA®). Oncologic Drugs Advisory Committee Meeting, September 12, 2013.


63 Gianni L, Pienkowski T, Im YH, et al. 5-year analysis of neoadjuvant pertuzumab and trastuzumab in patients with locally advanced, inflammatory, or early-stage HER2-positive breast cancer (NeoSphere): a multicentre, open-label, phase 2 randomised trial. The Lancet Oncology. 2016;17(6):791-800. Epub 2016/05/18. PMID: 27179402


BREAST CANCER PATHWAYS REFERENCES: METASTATIC


BREAST CANCER PATHWAYS REFERENCES: ENDOCRINE THERAPY FOR RECURRENT OR METASTATIC DISEASE


Elis MJ, Phrahlan M, Green NL, Mari E, Robertson JFR. Abstract OT3-2-09: FALCON: A randomised, double-blind, multicentre, phase III study comparing fulvestrant 500 mg with anastrozole 1 mg for postmenopausal women with hormone receptor-positive locally advanced or metastatic breast cancer who have not previously been treated with any hormonal therapy. Cancer Res. 2013 Dec 15;73:OT3-2-09. http://cancerres.aacrjournals.org/content/73/24_Supplement/OT3-2-09


Cristofanilli M, Bondarenko I, Ro, J, et al. [P41301] PALOMA3: Phase 3 trial of fulvestrant with or without palbociclib in pre and postmenopausal women with hormone receptor positive, HER2negative metastatic breast cancer that progressed on prior endocrine therapy—confirmed efficacy and safety. San Antonio Breast Cancer Symposium. December 11, 2015. Abstract P4-13-01


Kornblum NS MJ, Klein P et al. . PrECOG 0102: A randomized, double-blind, phase II trial of fulvestrant plus everolimus or placebo in post-menopausal women with hormone receptor (HR)-positive, HER2-negative metastatic breast cancer (MBC) resistant to aromatase inhibitor (AI) therapy. San Antonio Breast Cancer Symposium; San Antonio TX2016. SABCS Abstract S1-02


CHRONIC MYELOGENOUS LEUKEMIA (CML) PATHWAYS

REFERENCES


Cortes, Jorge E., et al. ‘Final study results of the phase 3 dasatinib versus imatinib in newly diagnosed chronic myeloid leukemia in chronic phase (CML-CP) trial (DASISION, CA180-056)’ Blood 124.21 (2014): 152-152. PMID: 27217448


COLORECTAL CANCER PATHWAYS REFERENCES


Gruenberger T, Bridgewater JA, Chau I, et al. Randomized, phase II study of bevacizumab with mFOLFOX6 or FOLFOXIRI in patients with initially unresectable liver metastases from colorectal cancer: resectability and safety in OLIVIA. J Clin Oncol. 2013;31(15s):A3619 Abstract 3619


Venoek AP, Niedzwiecki D, Lenz H, et al. CALGB/SWOG 80405: Phase III trial of irinotecan/5-FU/leucovorin (FOLFIRO) or oxaliplatin/5-FU/leucovorin (mFOLFOX6) with bevacizumab (BV) or cetuximab (CET) for patients (pts) with KRAS wild-type (wt) untreated metastatic adenocarcinoma of the colon or rectum (MCRC). J Clin Oncol. 32:5s, 2014 (suppl; abstr LBA3).


REFERENCES


37 Park SH, Sohn TS, Lee J, et al. Phase III trial to compare adjuvant chemotherapy with capecitabine and cisplatin versus concurrent chemoradiotherapy in gastric cancer: final report of the adjuvant chemoradiotherapy in stomach tumors trial, including survival and subset analyses. J Clin Oncol. 2015; Jan 5. PMID: 25559811


HEAD AND NECK PATHWAY REFERENCES


HODGKIN’S LYMPHOMA PATHWAYS REFERENCES


KIDNEY CANCER PATHWAYS REFERENCES


LUNG CANCER: NON-SMALL CELL LUNG CANCER PATHWAYS

REFERENCES


3. Erlotinib FDA label


14. FDA review documents


59 Opdivo Package Insert, BMS


Yoshioka H, Mitsudomi T, Morita S, et al.; West Japan Oncology Group. Final overall survival results of WJTOG 3405, a randomized phase 3 trial comparing gefitinib (G) with cisplatin plus docetaxel (CD) as the first-line treatment for patients with non-small cell lung cancer (NSCLC) harboring mutations of the epidermal growth factor receptor (EGFR). J Clin Oncol. 2014 May 20;32(15 suppl):8117. 8117


Perol M, Cuirneau TE, Arrieta O, et al. REVEL: A randomized, double-blind, phase III study of docetaxel (DOC) and ramucirumab (RAM; IMC-1121B) v DOC and placebo (PL) in the second-line treatment of stage IV non-small cell lung cancer (NSCLC) following disease progression after one prior platinum-based therapy. J Clin Oncol. 2014 May 20;32(15 suppl):LBA8006. LBA8006


LUNG CANCER: SMALL CELL LUNG CANCER PATHWAYS

REFERENCES


MELANOMA PATHWAYS REFERENCES


Experiencing Progression With Single-Agent BRAF Inhibitor.

[References]


Ascierto PA, McArthur GA, Dréno B, et. al. Cobimetinib combined with vemurafenib in advanced BRAF(V600)-mutant melanoma (coBRIM): updated efficacy results from a randomised, double-blind, phase 3 trial. Lancet Oncol. 2016 Sep;17(9):1248-60. PMID: 27480103


MYELOMA PATHWAYS REFERENCES


Richardson PG, Siegel DS, Vij R, et al. Randomized open-label phase 1/2 study of pomalidomide (POM) alone or in combination with low-dose dexamethasone (LoDex) in patients with relapsed and refractory multiple myeloma who have received prior treatment that includes lenalidoide (LEN) and bortezomib (BORT): Phase 2 results. [Abstract 634]. Blood. 2011. Accessed. Abstract 634


85 Straka C, Vogel M, Muller J, et al. Results from two phase III studies of bortezomib (BTZ) consolidation vs observation (OBS) post-transplant in patients (pts) with newly diagnosed multiple myeloma (NDMM). J Clin Oncol. 33, 2015 (suppl; abstr 8511). Abstract 8511

86 Dimopoulos MA, Moreau P, Palumbo A, et al. Carfilzomib and dexamethasone (Kd) vs bortezomib and dexamethasone (Vd) in patients (pts) with relapsed multiple myeloma (RMM): Results from the phase III study ENDEAVOR. J Clin Oncol 33, 2015 (suppl; abstr 8509). Abstract 8509


93 San-Miguel, Hungria V TM, Yoon S-S, et al. 3026 Final Analysis of Overall Survival from the Phase 3 Panorama 1 Trial of Panobinostat Plus Bortezomib and Dexamethasone Versus Placebo Plus Bortezomib and Dexamethasone in Patients with Relapsed or Relapsed and Refractory Multiple Myeloma. ASH. December 6, 2015. Abstract 3026


96 Moreau P, Masszi T, Grzasko N, et al. Ixazomib, an Investigational Oral Proteasome Inhibitor (PI), in Combination with Lenalidomide and Dexamethasone (IRd), Significantly Extends Progression-Free Survival (PFS) for Patients (Pts) with Relapsed and/or Refractory Multiple Myeloma (RRMM): The Phase 3 Tourmaline-MM1 Study (NCT01564537). ASH. December 7, 2015. Abstract 727

NHL: CHRONIC LYMPHOCYTIC LEUKEMIA/SMALL LYMPHOCYTIC LYMPHOMA PATHWAYS REFERENCES


NHL: DIFFUSE LARGE B-CELL LYMPHOMA PATHWAYS REFERENCES


Hodgkin’s lymphoma.

1289. PMID: 12181253


Lambertenghi Deliliers G, Butti C, Baldini L, et al. A cooperative study of epirubicin with cyclophosphamide, vincristine and prednisone (CEOP) in non-


Crump M, Baetz T, Couban S, et al. Gemcitabine, dexamethasone, and cisplatin in patients with recurrent or refractory aggressive histology B-cell non-


Lambertenghi Deliliers G, Butti C, Baldini L, et al. A cooperative study of epirubicin with cyclophosphamide, vincristine and prednisone (CEOP) in non-


NHL: FOLLICULAR LYMPHOMA AND MARGINAL ZONE LYMPHOMA PATHWAYS REFERENCES


NHL: MANTLE CELL LYMPHOMA PATHWAYS REFERENCES


Ovarian Cancer Pathways References


PANCREATIC CANCER PATHWAYS REFERENCES


37. De Bono J, Hardy-Bessard A, Kim C, et al. Phase III non-inferiority study of cabazitaxel (C) 20 mg/m2 (C20) versus 25 mg/m2 (C25) in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) previously treated with docetaxel (D). American Society of Clinical Oncology Annual Meeting; Chicago IL: American Society of Clinical Oncology; 2016 Abstract 5008


TESTICULAR CANCER (GERM CELL) PATHWAYS REFERENCES


24 Miller JC, Einhorn LH. Phase II study of daily oral etoposide in refractory germ cell tumors. Semin Oncol. 1990 Feb;17(1 Suppl 2):36-9. PMID: 2154858


UTERINE CANCER PATHWAYS REFERENCES


