Medical Oncology Program

Cancer Treatment Pathways

EFFECTIVE FEBRUARY 5, 2018
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AIM Medical Oncology Program

The goal of the AIM Oncology program is to help provide access to quality and affordable cancer care. A key component of the program is AIM Cancer Treatment Pathways.

AIM 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. AIM Pathways are intended to support the use of quality cancer care.

The Cancer Care Quality Program may consider dosage and drug schedules (i.e. the interval between doses) in selection of a Pathway regimen.

Selecting a Pathway depends upon a number of factors – the type of cancer, the stage of disease, and the biomarkers or specific genetic profile of the cancer. Within each cancer type, separate Pathways are usually available for early stage and advanced cancer, sub-types of cancer (e.g. HER2 positive) and different lines of therapy.

Pathways are not available for every medical condition, but are intended to be applicable for individuals with the most common cancer types. 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 option available for every specific situation. The treating oncologist will determine if, in his/her medical opinion, an AIM 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 choice.

It is important to note that, for some health plans, we will review requested services in accordance with client medical policies and clinical guidelines. If a request is received from a provider that is not an AIM Pathway regimen, it may be reviewed and may be authorized if it is determined to be medically necessary pursuant to medical policies and clinical guidelines.

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Effective February 5, 2018
### Bladder Cancer (Urothelial) Pathways

<table>
<thead>
<tr>
<th>Neoadjuvant Therapy</th>
<th>Clinical Stage II, III, or IV Without Evidence of Metastases (cT2, cT3, cT4a, cT4b, M0)</th>
</tr>
</thead>
</table>
| **CMV:** cisplatin, methotrexate, and vinblastine 3 cycles⁴,⁵  
  Gemcitabine (Gemzar) and cisplatin 4 cycles²  |

<table>
<thead>
<tr>
<th>Adjuvant Therapy</th>
<th>Stage I or II After TURBT* or Following Resection of Recurrent or Persistent Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BCG:</strong> bacillus calmette-guerin, intravesical²⁰,²⁴</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>First Line of Therapy (1st Line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gemcitabine (Gemzar)⁶,¹⁷,¹⁸</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>Second Line of Therapy (2nd Line)</th>
</tr>
</thead>
</table>
| Gemcitabine (Gemzar)⁹  
  Paclitaxel¹⁴  
  Pembrolizumab (Keytruda)³⁷  |

* 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

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Effective February 5, 2018
BLADDER CANCER (UROTHELIAL) REFERENCES

NCCN Clinical Practice Guidelines: Bladder Cancer V5.201


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# Breast Cancer Pathways: Neoadjuvant

## Neoadjuvant Therapy | HER2 Negative

<table>
<thead>
<tr>
<th>Pathway</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AC ⇒ weekly T</td>
<td>doxorubicin (Adriamycin) and cyclophosphamide (every 3 weeks) followed by weekly paclitaxel&lt;sup&gt;8,33,42,60&lt;/sup&gt;</td>
</tr>
<tr>
<td>ddAC ⇒ weekly T</td>
<td>dose dense doxorubicin (Adriamycin) and cyclophosphamide followed by weekly paclitaxel&lt;sup&gt;8,11,12,39&lt;/sup&gt;</td>
</tr>
<tr>
<td>TC</td>
<td>docetaxel (Taxotere) and cyclophosphamide&lt;sup&gt;10,43&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

## Neoadjuvant Therapy | HER2 Positive

<table>
<thead>
<tr>
<th>Pathway</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AC ⇒ TH</td>
<td>doxorubicin (Adriamycin) and cyclophosphamide followed by paclitaxel and trastuzumab (Herceptin)&lt;sup&gt;1,14,23,24,26&lt;/sup&gt;</td>
</tr>
<tr>
<td>TCH</td>
<td>docetaxel (Taxotere), carboplatin, and trastuzumab (Herceptin)&lt;sup&gt;25,49&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

## Neoadjuvant Therapy | HER2 Positive | Hormone Receptor (ER/PR) Negative

<table>
<thead>
<tr>
<th>Pathway</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCH+P</td>
<td>docetaxel (Taxotere), carboplatin, trastuzumab (Herceptin), and pertuzumab (Perjeta)&lt;sup&gt;50,51,54,55,57&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

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BREAST CANCER NEOADJUVANT REFERENCES


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


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Breast Cancer Pathways: Adjuvant

**Adjuvant Therapy | HER2 Negative**

**AC → weekly T**: doxorubicin (Adriamycin) and cyclophosphamide (every 3 weeks) followed by weekly paclitaxel\(^8\), \(^9\), \(^11\), \(^33\)

**ddAC → weekly T**: dose dense doxorubicin (Adriamycin) and cyclophosphamide followed by weekly paclitaxel\(^8\), \(^9\), \(^11\), \(^12\), \(^60\)

**TC**: docetaxel (Taxotere) and cyclophosphamide\(^10\), \(^19\)

**Adjuvant Therapy | HER2 Positive**

**AC → TH**: doxorubicin (Adriamycin) and cyclophosphamide followed by paclitaxel and trastuzumab (Herceptin)\(^23\), \(^26\)

**TCH**: docetaxel (Taxotere), carboplatin, and trastuzumab (Herceptin)\(^25\), \(^26\)

**TH**: paclitaxel and trastuzumab (Herceptin)\(^34\)  *(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

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BREAST CANCER ADJUVANT REFERENCES


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Coverage criteria. Health plan medical policy/clinical guidelines should be consulted to determine whether proposed services will be covered.

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


51. 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 2 randomised trial. Lancet Oncol 17.6 (2016): 791-800. PMID: 27179402

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Effective February 5, 2018
# Breast Cancer Pathways: Advanced/Metastatic Disease

## Metastatic Disease | HER2 Negative | First and Subsequent Lines of Therapy (1st Line+)

- Capecitabine (Xeloda)\(^4,24-26,28,60,65\)
- Doxorubicin (Adriamycin)\(^4,5,9,65\)
- Gemcitabine (Gemzar)\(^14,60\)
- Paclitaxel\(^18-20,65\)
- Vinorelbine (Navelbine)\(^15-17,65\)

## Metastatic Disease | HER2 Positive | First Line of Therapy (1st Line)

- Capecitabine (Xeloda) and trastuzumab (Herceptin)\(^40-43\)
- Gemcitabine (Gemzar) and trastuzumab (Herceptin)\(^44,45\)
- Paclitaxel and trastuzumab (Herceptin)\(^35,36\)
- Pertuzumab (Perjeta), trastuzumab (Herceptin), and docetaxel (Taxotere)\(^32,33,35\)
- Pertuzumab (Perjeta), trastuzumab (Herceptin), and paclitaxel\(^34\)
- Vinorelbine (Navelbine) and trastuzumab (Herceptin)\(^46,47\)

## Metastatic Disease | HER2 Positive | Second and Subsequent Lines of Therapy (2nd Line+)

- Ado-trastuzumab emtansine (Kadcyla)\(^59,61,62\)
- Capecitabine (Xeloda) and lapatinib (Tykerb)\(^51,52\)
- Capecitabine (Xeloda) and trastuzumab (Herceptin)\(^40-43\)
- Gemcitabine (Gemzar) and trastuzumab (Herceptin)\(^44,45\)
- Paclitaxel and trastuzumab (Herceptin)\(^35,36\)
- Pertuzumab (Perjeta), trastuzumab (Herceptin), and docetaxel (Taxotere)\(^32,33,35,82\)
- Pertuzumab (Perjeta), trastuzumab (Herceptin), and paclitaxel\(^34\)
- Trastuzumab (Herceptin) and lapatinib (Tykerb)\(^49,50\)
- Trastuzumab (Herceptin) monotherapy\(^37,48\)
- Vinorelbine (Navelbine) and trastuzumab (Herceptin)\(^46,47\)

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BREAST CANCER ADVANCED/METASTATIC REFERENCES


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2005/11/19. PMID: 16293863


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efficacy and safety of pertuzumab given in combination with trastuzumab plus an aromatase inhibitor in first-line patients with HER2-positive and
hormone receptor-positive metastatic or locally advanced breast cancer. San Antonio Breast Cancer Symposium 2016. Abstract S3-04

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Breast Cancer Pathways: Endocrine Therapy for Recurrent or Metastatic Disease

<table>
<thead>
<tr>
<th>Recurrent or Metastatic Disease</th>
<th>Hormone Receptor Positive</th>
<th>First Line of Therapy (1st Line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastrozole (Arimidex)*1,6,7,10,11,22,33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fulvestrant, (Faslodex) high dose*5,7,22,26,33,42</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Letrozole (Femara)*3,12-14,38</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Letrozole (Femara) and palbociclib (Ibrance)*40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tamoxifen†12,26</td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Recurrent or Metastatic Disease</th>
<th>Hormone Receptor Positive</th>
<th>Second and Subsequent Lines of Therapy (2nd Line+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastrozole (Arimidex)*1,6,7,10,11,22,33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exemestane (Aromasin)*4,20,21,39</td>
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<tr>
<td>Fulvestrant (Faslodex) high dose*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fulvestrant (Faslodex) and palbociclib (Ibrance)*40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Letrozole (Femara)*3,12-14,38</td>
<td></td>
<td></td>
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<tr>
<td>Tamoxifen†12,26</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Recurrent or Metastatic Disease</th>
<th>Hormone Receptor Positive</th>
<th>HER2 Positive</th>
<th>First and Subsequent Lines of Therapy (1st Line+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastrozole (Arimidex) and trastuzumab (Herceptin)*46</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Letrozole (Femara) and trastuzumab (Herceptin)*49</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*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.
BREAST CANCER ENDOCRINE THERAPY FOR RECURRENT OR METASTATIC DISEASE REFERENCES


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35. Ellis MJ, Prahland 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

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44. 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


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Effective February 5, 2018
Chronic Myelogenous Leukemia (CML) Pathways

**First Line of Therapy (1st Line)**
- Dasatinib* (Sprycel) for intermediate or high risk disease
  \(^{1,2,30,39}\)
- Imatinib (Gleevec) \(^{1-4,6,8,30,33-35}\)
- Nilotinib* (Tasigna) for intermediate or high risk disease
  \(^{6,8,31,32}\)

**Second Line of Therapy (2nd Line) | Following Treatment Failure, Suboptimal Response†, or Intolerance to 1st Line**
- Bosutinib (Bosulif) \(^{23,33}\)
- Dasatinib (Sprycel) \(^{1,2,9,10,12,36}\)
- Nilotinib (Tasigna) \(^{16,17,18,31,32}\)
- Ponatinib‡ (Iclusig) \(^{26}\)

**Third Line of Therapy (3rd Line)**
- Ponatinib (Iclusig) \(^{26}\)

*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.

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Effective February 5, 2018
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CHRONIC MYELOGENOUS LEUKEMIA (CML) REFERENCES

NCCN Clinical Practice Guidelines: Chronic Myelogenous Leukemia V2.2017


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Effective February 5, 2018
# Colorectal Cancer Pathways

## Adjuvant Therapy*

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capecitabine (Xeloda)</td>
<td>52,69</td>
</tr>
</tbody>
</table>

### FOLFOX:
fluorouracil (5-FU), leucovorin, and oxaliplatin 7,8,50,51,60,69.

### FULV:
fluorouracil (5FU) and leucovorin 1,4,7,49,52,69.

## 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

### FOLFOX + bevacizumab:
fluorouracil (5FU), leucovorin, oxaliplatin, with bevacizumab (Avastin) 25,26,28,33,44,45,70

### FOLFOXIRI + bevacizumab:
fluorouracil (5FU), leucovorin, oxaliplatin, and irinotecan (Camptosar) with 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) 22,35

## Metastatic Disease | RAS Wild Type (WT) | First or Second Lines of Therapy (1st or 2nd Line)

### FOLFIRI + panitumumab:
fluorouracil (5FU), leucovorin, and irinotecan (Camptosar) with panitumumab (Vectibix) ‡11,62

### FOLFOX + panitumumab:
fluorouracil (5-FU), leucovorin, and oxaliplatin with panitumumab (Vectibix) ‡12,53,59

Irinotecan (Camptosar) and panitumumab (Vectibix) ‡47

## Metastatic Disease | MSI-H or dMMR | Second Line of Therapy (2nd Line)

Pembrolizumab (Keytruda) 91

## Metastatic Disease | RAS Wild Type (WT) | Third or Subsequent Lines of Therapy (3rd Line+)

Panitumumab (Vectibix) monotherapy ‡13,61,56

*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

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Effective February 5, 2018
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coverage criteria. Health plan medical policy/clinical guidelines should be consulted to determine whether proposed services will be covered.

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# Gastric, Esophageal, and Gastroesophageal Junction Cancer (Adenocarcinoma) Pathways

## Primary Therapy | Resectable and Unresectable Disease

- Cisplatin and fluorouracil (5FU)<sup>3,4</sup>
- Fluorouracil (5FU) and cisplatin with concurrent radiation therapy (RT)<sup>3,6</sup>
- Paclitaxel and carboplatin with concurrent RT<sup>5</sup>

## Post-Operative Treatment

- Fluorouracil (5FU) and leucovorin with concurrent RT<sup>3,8</sup>

## Recurrent/Metastatic or Locally Advanced/Inoperable Disease | HER2 Negative | First Line of Therapy (1st Line)

- Cisplatin and fluorouracil (5FU)<sup>13,18,21,26</sup>
- Fluorouracil (5FU) and irinotecan (Camptosar)<sup>25,26</sup>
- **FLO/FOLFOX**: fluorouracil (5FU), leucovorin, and oxaliplatin<sup>27</sup>
- **FLP**: fluorouracil (5FU), leucovorin, and cisplatin<sup>27</sup>

## Recurrent/Metastatic or Locally Advanced/Inoperable Disease | HER2 Positive | First Line of Therapy (1st Line)

- Cisplatin, fluorouracil (5FU), and trastuzumab (Herceptin)<sup>13</sup>

## Recurrent/Metastatic or Locally Advanced/Inoperable Disease | Second Line of Therapy (2nd Line)

- Irinotecan (Camptosar)<sup>24,29</sup>
- Paclitaxel<sup>33</sup>

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Effective February 5, 2018
GASTRIC, ESOPHAGEAL, AND GASTROESOPHAGEAL JUNCTION (ADENOCARCINOMA) CANCERS


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# Head and Neck Cancer Pathways

## Non-Nasopharyngeal (Squamous Cell Carcinoma) | Candidate for Local Therapy (M0) | Primary Systemic Therapy or Post-Operative Systemic Therapy

- High dose cisplatin* with concurrent RT\(^3,10,37\)

## Non-Nasopharyngeal (Squamous Cell Carcinoma) | Metastatic and Recurrent Disease | First Line of Therapy (1st line)

- Carboplatin, fluorouracil (5FU), and cetuximab (Erbitux)\(^{14}\)
- Cisplatin, fluorouracil (5FU), and cetuximab (Erbitux)\(^{14}\)

## Non-Nasopharyngeal (Squamous Cell Carcinoma) | Metastatic and Recurrent Disease | Second and Subsequent Lines of Therapy (2nd line+)

- Nivolumab (Opdivo)\(^{35}\)
- Paclitaxel\(^{23}\)

## Nasopharynx | Candidate for Local Therapy (M0) | Primary Systemic Therapy with Concurrent RT Followed by Adjuvant Therapy – No Longer Effective 2/5/2018 – Revision Below

- High dose cisplatin* with concurrent RT, followed by adjuvant cisplatin and fluorouracil (5FU) – No Longer Effective 2/5/2018
- High dose cisplatin* with concurrent RT\(^{13,37}\) – Added Effective 2/5/2018

## Nasopharynx | Metastatic and Recurrent Disease | First and Subsequent Lines of Therapy (1st Line+)

- Carboplatin\(^{21}\)
- Cisplatin\(^{20,22}\)
- Cisplatin\(^1\) and gemcitabine (Gemzar)\(^{29,39}\)
- Cisplatin\(^1\) and paclitaxel\(^{18,22,29}\)
- Fluorouracil (5FU)\(^{22}\)
- Gemcitabine (Gemzar)\(^{31}\)
- Gemcitabine (Gemzar) and vinorelbine (Navelbine)\(^{30}\)
- Methotrexate\(^{24,26}\)
- Paclitaxel\(^{23}\)

*High dose cisplatin refers to dosing to achieve total dose of 200-300 mg/m\(^2\) 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

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Effective February 5, 2018
HEAD AND NECK CANCER REFERENCES

NCCN Clinical Practice Guidelines: Head and Neck Cancers V2.2017


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Effective February 5, 2018

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Effective February 5, 2018
# Hodgkin Lymphoma Pathways

## Classical Hodgkin Lymphoma | Early Stage (Stage I-IIA, Favorable and Unfavorable Risk)

**ABVD**: doxorubicin (Adriamycin), bleomycin, vinblastine, and dacarbazine (DTIC) ± ISRT*1-5,30,35,36

## Classical Hodgkin Lymphoma | Advanced Stage (Stage IIB, III, and IV)

**ABVD**: doxorubicin (Adriamycin), bleomycin, vinblastine, and dacarbazine (DTIC) ± ISRT*7-10,32

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*ISRT – Involved Site Radiation Therapy

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Effective February 5, 2018
HODGKIN LYMPHOMA REFERENCES

NCCN Clinical Practice Guidelines: Hodgkin Lymphoma V1.2017


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Effective February 5, 2018
# Kidney Cancer (Renal Cell Carcinoma) Pathways

## Metastatic Disease | First Line of Therapy (1st Line)

- High dose intravenous (IV) interleukin-2 (IL2, Proleukin)\textsuperscript{17,18} (clear cell only)
- Pazopanib (Votrient)\textsuperscript{4,5,7}
- Sunitinib (Sutent)\textsuperscript{1-3,37}  \textbf{Added Effective 2/5/2018}

## Metastatic Disease | First Line of Therapy (1st Line) | Poor Prognosis* or Non-Clear Cell Histology

- Temsirolimus (Torisel)\textsuperscript{12,23}

## Metastatic Disease | Second or Subsequent Lines of Therapy (2nd Line+) | Clear Cell Carcinoma

- Nivolumab (Opdivo)\textsuperscript{29,30,32}

*Poor prognosis patients have 3 or more of the following predictors of short survival:
- LDH greater than 1.5 x normal
- Hemoglobin less than normal (anemia)
- Corrected serum calcium (Ca) greater than 10 ng/dL
- Less than 1 year from diagnosis to the start of systemic therapy
- Karnofsky performance status \( \leq 70 \) (Unable to carry on normal activity or do active work, but able to perform self-care)
- 2 or more sites of organ metastases

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Effective February 5, 2018
KIDNEY CANCER (RENAL CELL CARCINOMA) REFERENCES

NCCN Practice Guideline: Kidney Cancer V1.2018


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Lung Cancer: Non-Small Cell Lung Cancer (NSCLC) Pathways

| Primary Therapy for Locally Advanced, Unresectable | Stage III | – No longer Effective 2/5/2018 - Revision Below |
| Neoadjuvant/Preoperative/Induction Therapy or Adjuvant/Definitive Therapy | – Revision Added Effective 2/5/2018 |
| --- | --- | --- |
| Cisplatin and etoposide (Toposar) with concurrent XRT |
| Paclitaxel and carboplatin with concurrent XRT |

**Adjuvant Therapy**

- Carboplatin and paclitaxel
- Cisplatin and gemcitabine (Gemzar)
- Cisplatin and vinorelbine (Navelbine)

**Metastatic Disease | Squamous | PD-L1 Expression <50% | First Line of Therapy (1st Line) | ECOG PS = 0–2**

- Carboplatin and paclitaxel
- Cisplatin and gemcitabine (Gemzar)

**Metastatic Disease | Non-Squamous | First Line of Therapy (1st Line) | ECOG PS = 0–2**

- Carboplatin and paclitaxel
- Carboplatin, paclitaxel, and bevacizumab (Avastin)
- Cisplatin and gemcitabine (Gemzar)
- Cisplatin and pemetrexed (Alimta)

**Metastatic Disease | Non-Squamous | Maintenance | ECOG PS = 0–2**

- Continuation bevacizumab (Avastin)
- Continuation pemetrexed (Alimta)
- Switch pemetrexed (Alimta)

**Metastatic Disease | Second or Subsequent Lines of Therapy (2nd Line+) | ECOG PS = 0–2**

- Atezolizumab (Tecentriq)
- Nivolumab (Opdivo)
- Pemetrexed (Alimta) (Non-Squamous histology/pathology)

*PD-L1 current assay level ≥ %50
†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.

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Effective February 5, 2018
## Lung Cancer: Non-Small Cell Lung Cancer (NSCLC) Pathways (continued)

### Metastatic Disease | ALK Positive | First Line of Therapy (1st Line)
- Alectinib (Alecensa)\(^{108}\)

### Metastatic Disease | EGFR Positive | First Line of Therapy (1st Line)
- Erlotinib (Tarceva)\(^{2-5,73}\) – **No Longer Effective 2/5/2018**
- Osimertinib (Tagrisso)\(^{114}\) – **Added Effective 2/5/2018**

### Metastatic Disease | ALK and EGFR Negative | PD-L1 Expression High (>50%) | First Line of Therapy (1st Line) | ECOG PS = 0–2
- **Revision Below**

### Metastatic Disease | ALK and EGFR Negative | PD-L1 Positive* | First Line of Therapy (1st Line) | ECOG PS = 0–2
- Pembrolizumab\(†\) (Keytruda)\(^{102}\)

### Metastatic Disease | ALK or EGFR Positive | Second or Subsequent Lines of Therapy (2nd Line+)
- Carboplatin‡ and paclitaxel\(^7,16,54\)
- Cisplatin‡ and gemcitabine (Gemzar)\(^8,11,13,22,25\)
- Cisplatin‡ and pemetrexed (Alimta)\(^17,18\)

### Metastatic Disease | EGFR Positive | ECOG PS = 3, 4
- Erlotinib (Tarceva)\(^42,48,50,51\)

### Metastatic Disease | EGFR T790M Mutation | Second Line (2nd Line) After Targeted 1st Line Therapy – **No longer effective 2/5/2018**
- Osimertinib (Tagrisso)\(^86,114\) – **No Longer Effective 2/5/2018**

*PD-L1 current assay level ≥ 50%
†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.
REFERENCES

NCCN Clinical Practice Guidelines: Non-Small Cell Lung Cancer V3.2017

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References

14. FDA review documents

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Lung Cancer: Small Cell Lung Cancer Pathways

<table>
<thead>
<tr>
<th>Limited Stage</th>
<th>Primary, Adjuvant, or First Line of Therapy (1st Line)</th>
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<tbody>
<tr>
<td></td>
<td>Carboplatin and etoposide (Toposar) ± XRT(^3)</td>
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<tr>
<td></td>
<td>Cisplatin and etoposide (Toposar) ± XRT(^{1,2})</td>
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<th>Extensive Stage</th>
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<tr>
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<tr>
<th>Second and Subsequent Lines of Therapy (2nd Line+)</th>
<th>Relapse Greater than Six (6) Months</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Carboplatin and etoposide (Toposar)(^9)</td>
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</table>

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LUNG CANCER: SMALL CELL LUNG CANCER REFERENCES


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Effective February 5, 2018
## Melanoma Pathways: Metastatic Melanoma

### Stage III B/IIIC (Resected) | Adjuvant Therapy – Added Effective 2/5/2018

| Nivolumab (Opdivo) | Added Effective 2/5/2018 |

### Metastatic Disease | First and Subsequent Lines of Therapy (1st Line+) | Any BRAF Status | ECOG PS: 0, 1, 2

| Pembrolizumab* (Keytruda) |

### Metastatic Disease | First Line of Therapy (1st Line) | BRAF Mutated† | Symptomatic Disease | ECOG PS: 0, 1, 2

| Vemurafenib (Zelboraf) and cobimetinib (Cotellic) |

### Metastatic Disease | Second and Subsequent Lines of Therapy (2nd Line+) | BRAF Mutated† | ECOG PS: 0, 1, 2

| Vemurafenib (Zelboraf) and cobimetinib (Cotellic) |

### Metastatic Disease | Second and Subsequent Lines of Therapy (2nd Line+) | Any BRAF Status | ECOG PS: 0, 1, 2

| Ipilimumab (Yervoy) |

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

†BRAF mutations include V600E and V600K mutations.

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MELANOMA: METASTATIC MELANOMA REFERENCES

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Myeloma Pathways: Multiple Myeloma

**Primary/First Line of Therapy (1st Line) | Transplant Candidates**

**VRD/VDR**: bortezomib (Velcade), lenalidomide (Revlimid), and dexamethasone\(^{10,12,79}\)

**Primary/First Line of Therapy (1st Line) | Non-Transplant Candidates**

**CyBorD or VDC**: bortezomib (Velcade), cyclophosphamide, and dexamethasone\(^{9,10,84}\)

**R-dex**: lenalidomide (Revlimid) and low-dose dexamethasone\(^{10,11,13,73}\)

**VRD/VDR**: bortezomib (Velcade), lenalidomide (Revlimid), and dexamethasone\(^{10,12,79}\)

**VD**: bortezomib (Velcade) and dexamethasone\(^{1,3,12,24,89}\)

**Maintenance Therapy | Post-Transplant**

Lenalidomide (Revlimid)\(^{26,27,83,92}\)

**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\(^{97}\)

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42. Anderson KC, Jagannath S, Jakubowiak A, et al. Phase II study of lenalidomide (Len), bortezomib (Bz), and dexamethasone (Dex) in patients (pts) with relapsed or refractory multiple myeloma (MM). J Clin Oncol. 2008; 26(15S):A8545 Abstract 8545


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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


104. Pawlyn CD, FE; Kaiser, MF; et al. Primary IMiD Refractory Myeloma; Results from 3894 Patients Treated in the Phase III Myeloma XI Study. Blood; San Diego CA2016. ASH Abstract 1144


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NHL: Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Pathways

First Line of Therapy (1st Line) | With 17p Deletion
Ibrutinib (Imbruvica)\textsuperscript{28,37,41,46,47}

First Line of Therapy (1st Line) | Without 17p Deletion

\textbf{BR}: bendamustine (Bendeka, Treanda) and rituximab (Rituxan)\textsuperscript{13,14,15,39,51}

\textbf{FCR}: fludarabine (Fludara), cyclophosphamide, and rituximab (Rituxan)\textsuperscript{1,2,39,51}

Ibrutinib (Imbruvica)\textsuperscript{29,37,46,47}

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

\textbf{BR}: bendamustine (Bendeka, Treanda) and rituximab (Rituxan)\textsuperscript{13,14,15,42}

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):

- WBC elevation above 200-300 x 10\textsuperscript{9}
- Signs of leukostasis
- Lymphocyte doubling time of less than 6 months
- In low or intermediate risk disease:
  - Significant disease-related symptoms such as severe fatigue, weight loss, night sweats, otherwise unexplained fever
  - Signs of end-organ damage
  - Significant or progressive bulky disease, such as massive splenomegaly (≥6 cm below the costal margin) or massive lymphadenopathy (> 10 cm in longest diameter)
  - Clinically significant progressive or symptomatic anemia or thrombocytopenia
    - Not caused by autoimmune etiology, unless poor response to conventional immunosuppressive therapy
- High risk disease, particularly with progressive cytopenias

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Effective February 5, 2018
NHL: CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) / SMALL LYMPHOCYTIC LYMPHOMA (SLL) REFERENCES

NCCN Practice Guidelines: Chronic Lymphocytic Leukemia / Small Lymphocytic Lymphoma V1.2018


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Effective February 5, 2018
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)\(^1\)-\(^4\)

**First Line of Therapy (1st Line) | Contraindication to Anthracycline**

- **R-CEOP**: cyclophosphamide, etoposide (Toposar), vincristine (Vincasar), prednisone, and rituximab (Rituxan)\(^13\),\(^14\),\(^40\),\(^41\)

**Second and Subsequent Lines of Therapy (2nd Line+) | Transplant Candidates**

- **R-GDP**: gemcitabine (Gemzar), dexamethasone, cisplatin, and rituximab (Rituxan)\(^23\),\(^24\),\(^43\)
- **R-GDP**: gemcitabine (Gemzar), dexamethasone, carboplatin, and rituximab (Rituxan)\(^23\),\(^24\),\(^43\)
- **R-ICE**: ifosfamide (Ifex), carboplatin, etoposide (Toposar), and rituximab (Rituxan)\(^18\),\(^19\),\(^29\)

**Second and Subsequent Lines of Therapy (2nd Line+) | Non-Transplant Candidates**

- **BR**: bendamustine (Bendeka, Treanda) and Rituximab (Rituxan)\(^32\),\(^33\)
- **R-GDP**: gemcitabine (Gemzar), dexamethasone, cisplatin, and rituximab (Rituxan)\(^23\),\(^24\)
- **R-GDP**: gemcitabine (Gemzar), dexamethasone, carboplatin, and rituximab (Rituxan)\(^23\),\(^24\)
- **R-GemOx**: gemcitabine (Gemzar), oxaliplatin, and rituximab (Rituxan)\(^25\),\(^27\)

Rituximab (Rituxan) monotherapy reserved for frail patients or elderly patients

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Effective February 5, 2018
NHL: DIFFUSE LARGE B CELL LYMPHOMA REFERENCES


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Effective February 5, 2018

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Effective February 5, 2018
NHL: Follicular 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\textsuperscript{33,34}

**Splenic Marginal Zone\dagger or Gastric MALT Lymphoma | First Line of Therapy (1st Line)**

Rituximab (Rituxan) monotherapy\textsuperscript{27,29}

**Follicular (Grade I-IIIA) and Other Marginal Zone Lymphomas | First Line of Therapy (1st Line)**

- **BR**: Bendamustine (Bendeka, Treanda) and rituximab (Rituxan)\textsuperscript{5,6}
- **R-CHOP(21)**: Cyclophosphamide, doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, and rituximab (Rituxan)\textsuperscript{1-3,5}
- **R-CVP**: Cyclophosphamide, vincristine (Vincasar), prednisone, and rituximab (Rituxan)\textsuperscript{1,4}
- Rituximab (Rituxan) monotherapy\textsuperscript{7,17}

**Follicular and Other Marginal Zone Lymphomas | First Line of Therapy (1st Line) | Additional options for the elderly or infirm**

- Chlorambucil (Leukeran)\textsuperscript{10}
- Chlorambucil (Leukeran) and rituximab (Rituxan)\textsuperscript{10,11}
- Cyclophosphamide\textsuperscript{11-13}
- Cyclophosphamide and rituximab (Rituxan)

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

- **R-CHOP(21)**: Cyclophosphamide, doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, and rituximab (Rituxan)\textsuperscript{1-5}
- **R-CEOP**: Cyclophosphamide, etoposide (Toposar), vincristine (Vincasar), prednisone, and rituximab (Rituxan)\textsuperscript{13,35-37}

*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.

\dagger Splenectomy is also a recommended option for Splenic Marginal Zone Lymphoma (NCCN 2A).

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Effective February 5, 2018
Effective February 5, 2018

NHL: FOLLICULAR AND MARGINAL ZONE LYMPHOMA REFERENCES


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References


18. Forstpointner R, Dreyling M, Repp R, et al. The addition of rituximab to a combination of fludarabine, cyclophosphamide, mitoxantrone (FCM) significantly increases the response rate and prolongs survival as compared with FCM alone in patients with relapsed and refractory follicular and

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Effective February 5, 2018
NHL: Mantle Cell Lymphoma Pathways

<table>
<thead>
<tr>
<th>First Line of Therapy (1st Line)</th>
<th>ASCT Candidates</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alternating R-CHOP/R-DHAP:</strong></td>
<td>cyclophosphamide (Cytoxan), doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, rituximab (Rituxan) alternating with dexamethasone, cisplatin, cytarabine (Ara-C), and rituximab (Rituxan)⁴,⁵,²⁸,³⁰,³¹</td>
</tr>
<tr>
<td><strong>Nordic Regimen:</strong></td>
<td>dose intensified rituximab (Rituxan), cyclophosphamide, vincristine (Vincasar), doxorubicin (Adriamycin), prednisone alternating with rituximab (Rituxan) and high dose cytarabine (Ara-C)³</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>First Line of Therapy (1st Line)</th>
<th>Not an ASCT Candidate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BR:</strong> bendamustine (Bendeka, Treanda) and rituximab (Rituxan)⁹,¹⁰</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Second and Subsequent Lines of Therapy (2nd Line+)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BR:</strong> bendamustine (Bendeka, Treanda) and rituximab (Rituxan)</td>
</tr>
<tr>
<td>Bortezomib (Velcade)¹⁷</td>
</tr>
<tr>
<td>Ibrutinib (Imbruvica)¹⁸,²⁰</td>
</tr>
<tr>
<td>Lenalidomide (Revlimid)²⁰-²³</td>
</tr>
</tbody>
</table>

*Note: Pathway lists are solely for the purpose of eligibility for enhanced reimbursement and are independent of specific health plan medical policy coverage criteria. Health plan medical policy/clinical guidelines should be consulted to determine whether proposed services will be covered.*

Effective February 5, 2018
NHL: MANTLE CELL LYMPHOMA REFERENCES


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References


13. Forstpointner R, Dreyling M, German Low-Grade Lymphoma Study Group, et al. The addition of rituximab to a combination of fludarabine, cyclophosphamide, mitoxantrone (FCM) significantly increases the response rate and prolongs survival as compared with FCM alone in patients with relapsed and refractory follicular and mantle cell lymphomas: results of a prospective randomized study of the German Low-Grade Lymphoma Study Group. Blood. 2004 Nov 15;104(10):3064-3071. PMID: 15284112


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Ovarian Cancer (Epithelial) Pathways

<table>
<thead>
<tr>
<th>Adjuvant Therapy</th>
<th>Stage IA/B (Grade 2 or 3) or IC (Grade 1-3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin and dose dense paclitaxel(^6-8)</td>
<td></td>
</tr>
<tr>
<td>Carboplatin and paclitaxel(^2,5,7)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adjuvant or Primary Therapy</th>
<th>Stage II, III, IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin and dose dense paclitaxel(^6-8,45) (\text{No Longer Effective 2/5/2018})</td>
<td></td>
</tr>
<tr>
<td>Carboplatin and paclitaxel(^6-8,45) (\text{(Administered weekly or every 3 weeks) (\text{Added Effective 2/5/2018}}\text{ (Stage III only)})</td>
<td></td>
</tr>
</tbody>
</table>

| Intravenous (IV) paclitaxel and Intraperitoneal (IP) cisplatin and IP paclitaxel\(^1-49\) |

<table>
<thead>
<tr>
<th>Recurrent Disease</th>
<th>First and Subsequent Lines of Therapy (1st Line+)</th>
<th>Platinum-Sensitive*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin(^8,9,12)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carboplatin and gemcitabine (Gemzar)(^12,13)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carboplatin and paclitaxel(^8,9,15)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carboplatin and weekly paclitaxel</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recurrent Disease</th>
<th>Maintenance Therapy</th>
<th>Platinum-Sensitive*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Niraparib (Zejula)(^54)</td>
<td></td>
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<table>
<thead>
<tr>
<th>Recurrent Disease</th>
<th>Second and Subsequent Lines of Therapy (2nd Line+)</th>
<th>Platinum Resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bevacizumab (Avastin) monotherapy(^42)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Docetaxel (Taxotere)(^17)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gemcitabine (Gemzar)(^19,20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liposomal doxorubicin (Doxil or Lipodox)(^19,20,21)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paclitaxel (weekly)(^22,23)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paclitaxel and bevacizumab (Avastin)(^36-38)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tamoxifen(^56)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topotecan (Hycamtin)(^21,24)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topotecan (Hycamtin) and bevacizumab (Avastin)(^36,37)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vinorelbine (Navelbine)(^34,35)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Platinum sensitive disease is defined as recurrence of greater than 6 months after prior platinum-based therapy

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Effective February 5, 2018
OVARIAN CANCER (EPITHELIAL) REFERENCES

NCCN Clinical Practice Guidelines: Ovarian Cancer, Including Fallopian Tube Cancer and Primary Peritoneal Cancer V2.2017


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41. Tillmanns TD, Lowe MP, Walker MS, Stepanski EJ, and Schwartzberg LS. Phase II clinical trial of bevacizumab with albumin-bound paclitaxel in patients with platinum-resistant primary epithelial ovarian or primary peritoneal carcinoma. Gynecol Oncol. 2013 Feb;128(2):221-8. PMID: 22960352


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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 of Therapy (1\(^{st}\) Line) | ECOG PS: 0, 1, 2

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

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PANCREATIC CANCER (ADENOCARCINOMA) REFERENCES

NCCN Clinical Practice Guidelines: Pancreatic Adenocarcinoma V3.2017


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Effective February 5, 2018
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 (RT)

- Goserelin* (Zoladex)\(^4\)
- Goserelin* (Zoladex) with abiraterone (Zytiga)\(^4,1\)
- Leuprolide* (Eligard/Lupron)\(^4\)
- Leuprolide* (Eligard/Lupron) with abiraterone (Zytiga)\(^4,1\)
- Triptorelin* (Trelstar)\(^4\)
- Triptorelin* (Trelstar) with abiraterone (Zytiga)\(^4,1\)

Recurrent and Metastatic Disease | Hormone Sensitive

- Abiraterone (Zytiga) and prednisone with Androgen Deprivation Therapy** (ADT)\(^3,9,41\)
- Docetaxel (Taxotere) (every 3 weeks) with Androgen Deprivation Therapy** (ADT)\(^1,9\)
- Goserelin (Zoladex)\(^6\)
- Leuprolide (Eligard/Lupron)\(^6\)
- Triptorelin (Trelstar)\(^6\)

Bilateral orchiectomy (surgical castration) is an equally effective alternative to medical castration

*May be coadministered with bicalutamide (Casodex) or flutamide (Eulexin) for up to 30-60 days in patients who are at risk of developing symptoms associated with testosterone flare

**ADT Pathway options, when given as listed above: goserelin (Zoladex), leuprolide (Eligard/Lupron), triptorelin (Trelstar) or history of orchiectomy

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Effective February 5, 2018
### Recurrent and Metastatic Disease | Hormone Resistant | First Line of Therapy (1st Line)

- Abiraterone (Zytiga) and prednisone with continued ADT**8,12,25,26,27
- Docetaxel (Taxotere) (every 3 weeks) with continued ADT**9,10,19
- Enzalutamide (Xtandi)
- Enzalutamide (Xtandi) with goserelin (Zoladex)
- Enzalutamide (Xtandi) with leuprolide (Eligard/Lupron)
- Enzalutamide (Xtandi) with triptorelin (Trelstar)
- 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+)

- Abiraterone (Zytiga) and prednisone with continued ADT**†8,12,25,26,27
- Cabazitaxel (Jevtana) with ADT **11
- Docetaxel (Taxotere) (every 3 weeks) with continued ADT**‡9,10,19
- Docetaxel (Taxotere) rechallenge with ADT**21,22
- Goserelin (Zoladex) with bicalutamide (Casodex)‡6,7
- Leuprolide (Eligard/Lupron) with bicalutamide (Casodex)‡6,7
- Triptorelin (Trelstar) with bicalutamide (Casodex)‡6,7
- Continued ADT** with supportive care ± dexamethasone13,14,15,16,24

---

Bilateral orchiectomy (surgical castration) is an equally effective alternative to medical castration

*May be coadministered with bicalutamide (Casodex) or flutamide (Eulexin) for up to 30-60 days in patients who are at risk of developing symptoms associated with testosterone flare.

**ADT Pathway options, when given as listed above: goserelin (Zoladex), leuprolide (Eligard/Lupron), triptorelin (Trelstar), or history of orchiectomy

†If neither abiraterone nor enzalutamide have been previously used

‡If not previously used in the first line (1st Line) setting

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Effective February 5, 2018
PROSTATE CANCER (ADENOCARCINOMA) REFERENCES

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References


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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


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Effective February 5, 2018
# Testicular (Germ Cell Tumors) Cancer Pathways

<table>
<thead>
<tr>
<th>Seminoma</th>
<th>Stage II-IIIA</th>
<th>Primary Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BEP:</strong> bleomycin, etoposide (Toposar), and cisplatin⁵</td>
<td><strong>EP:</strong> etoposide (Toposar) and cisplatin⁴</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Seminoma</th>
<th>Stage IIIB-C</th>
<th>Good and Intermediate Risk</th>
<th>and Metastatic Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BEP:</strong> bleomycin, etoposide (Toposar), and cisplatin⁵,⁶ †</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nonseminoma</th>
<th>Stage II-IIIA</th>
<th>Primary Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BEP:</strong> bleomycin, etoposide (Toposar), and cisplatin⁵,⁶</td>
<td><strong>EP:</strong> etoposide (Toposar) and cisplatin⁴</td>
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<tr>
<th>Nonseminoma</th>
<th>Adjuvant Therapy after RPLND*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EP:</strong> etoposide (Toposar) and cisplatin⁸,⁹,²⁶</td>
<td></td>
</tr>
</tbody>
</table>

†BEP is typically given for 3 cycles in good risk seminoma, and 4 cycles in intermediate risk

*RPLND: Retroperitoneal Lymph Node Dissection

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Effective February 5, 2018
TESTICULAR (GERM CELL TUMORS) CANCER REFERENCES


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Effective February 5, 2018
Uterine (Endometrial) Cancer Pathways

**Adjuvant Therapy | Stage III-IV or High Risk Histologies**

- Carboplatin and paclitaxel[^6]

**Recurrent /Metastatic | First and Subsequent Lines of Therapy (1st Line+)**

- Carboplatin and paclitaxel[^6,^27-^29]
- Cisplatin and doxorubicin (Adriamycin)[^24,^25]

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UTERINE (ENDOMETRIAL) CANCER REFERENCES


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References

1. Wolfson AH, Brady MF, Rocereto T, et al. A gynecological oncology group randomized phase III trial of whole abdominal irradiation (WAI) vs. cisplatin-ifosfamide and mesna (CIM) as post-surgical therapy in stage IV carcinosarcoma (CS) of the uterus. Gynecol Oncol. 2007; 107:177-85. PMID: 17822748

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