Medical Oncology Program

Cancer Treatment Pathways

EFFECTIVE NOVEMBER 1, 2017
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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 November 1, 2017
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.

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 November 1, 2017
# 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>
<tbody>
<tr>
<td>CMV: cisplatin, methotrexate, and vinblastine 3 cycles ², ⁵</td>
<td></td>
</tr>
<tr>
<td>Gemcitabine (Gemzar) and cisplatin 4 cycles ²</td>
<td></td>
</tr>
</tbody>
</table>

<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>BCQ: bacillus calmette-guerin, intravesical ²⁰-²⁴</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>First line therapy (1st line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gemcitabine (Gemzar) and cisplatin ²⁶, ²⁷, ²⁸</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>Second line therapy (2nd line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gemcitabine (Gemzar) ³⁹</td>
<td></td>
</tr>
<tr>
<td>Paclitaxel ¹⁴</td>
<td></td>
</tr>
<tr>
<td>Pembrolizumab (Keytruda) ³⁷ (Added Effective 11/1/2017)</td>
<td></td>
</tr>
</tbody>
</table>

*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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BLADDER CANCER (UROTHELIAL) REFERENCES


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# Breast Cancer Pathways: Neoadjuvant

## Neoadjuvant Therapy | HER2 Negative

**AC → weekly T:** doxorubicin (Adriamycin) and cyclophosphamide (every 3 weeks) followed by weekly paclitaxel\(^8,33,42,60\)

**ddAC → weekly T:** dose dense doxorubicin (Adriamycin) and cyclophosphamide followed by weekly paclitaxel\(^8,11,12,39\)

**TC:** docetaxel (Taxotere) and cyclophosphamide\(^10,43\)

## Neoadjuvant Therapy | HER2 Positive

**AC → TH:** doxorubicin (Adriamycin) and cyclophosphamide followed by paclitaxel and trastuzumab (Herceptin)\(^1,14,23,24,26\)

**TCH:** docetaxel (Taxotere), carboplatin, and trastuzumab (Herceptin)\(^25,49\)

## Neoadjuvant Therapy | HER2 Positive | Hormone receptor (ER/PR) negative

**TCH+P:** docetaxel (Taxotere), carboplatin, trastuzumab (Herceptin), and pertuzumab (Perjeta)\(^50,51,54,55,57\)

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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.


57. Pickart-Gebhart MJ, 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 (L), trastuzumab (T), their sequence (T→L), or their combination (T+L) in the adjuvant treatment of HER2-positive early breast cancer (EOC). J Clin Oncol. 2013; 31;35:1146.


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These Guidelines are a work in progress that may be refined as often as new significant data becomes available.

The NCCN Guidelines® are a statement of consensus of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient’s care or treatment. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

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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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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 2 randomised 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


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Effective November 1, 2017
# Breast Cancer Pathways: Advanced/Metastatic Disease

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

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capecitabine (Xeloda)(^{4,24-26,28,60,65})</td>
</tr>
<tr>
<td>Doxorubicin (Adriamycin)(^{4,5,9,65})</td>
</tr>
<tr>
<td>Gemcitabine (Gemzar)(^{14,60})</td>
</tr>
<tr>
<td>Paclitaxel(^{18,20,65})</td>
</tr>
<tr>
<td>Vinorelbine (Navelbine)(^{15-17,65})</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capecitabine (Xeloda) and trastuzumab (Herceptin)(^{40-43})</td>
</tr>
<tr>
<td>Gemcitabine (Gemzar) and trastuzumab (Herceptin)(^{44,45})</td>
</tr>
<tr>
<td>Paclitaxel and trastuzumab (Herceptin)(^{35,36})</td>
</tr>
<tr>
<td>Pertuzumab (Perjeta), trastuzumab (Herceptin), and docetaxel (Taxotere)(^{32,33,35})</td>
</tr>
<tr>
<td>Pertuzumab (Perjeta), trastuzumab (Herceptin), and paclitaxel(^{34})</td>
</tr>
<tr>
<td>Vinorelbine (Navelbine) and trastuzumab (Herceptin)(^{46,47})</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ado-trastuzumab emtansine (Kadcyla)(^{59,61,62})</td>
</tr>
<tr>
<td>Capecitabine (Xeloda) and lapatinib (Tykerb)(^{51,52})</td>
</tr>
<tr>
<td>Capecitabine (Xeloda) and trastuzumab (Herceptin)(^{40-43})</td>
</tr>
<tr>
<td>Gemcitabine (Gemzar) and trastuzumab (Herceptin)(^{44,45})</td>
</tr>
<tr>
<td>Paclitaxel and trastuzumab (Herceptin)(^{35,36})</td>
</tr>
<tr>
<td>Pertuzumab (Perjeta), trastuzumab (Herceptin), and docetaxel (Taxotere)(^{32,33,35,82})</td>
</tr>
<tr>
<td>Pertuzumab (Perjeta), trastuzumab (Herceptin), and paclitaxel(^{34})</td>
</tr>
<tr>
<td>Trastuzumab (Herceptin) and lapatinib (Tykerb)(^{49,50})</td>
</tr>
<tr>
<td>Trastuzumab (Herceptin) monotherapy(^{37,48})</td>
</tr>
<tr>
<td>Vinorelbine (Navelbine) and trastuzumab (Herceptin)(^{46,47})</td>
</tr>
</tbody>
</table>

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BREAST CANCER ADVANCED/METASTATIC REFERENCES


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65 Park IH, Lee KS, Im SA, et al. [OT3-1-08] The PROCEED trial KCSG BR11-01: Phase III multicenter randomized open label study of irinotecan plus capcitabine versus bevacizumab in patients previously treated with anthracycline and taxane for HER2 negative metastatic breast cancer. Cancer Res. 2013 December 15; 73: OT3-1-08. Abstract OT3-1-08


73 Tutt A, Ellis P, Kilburn L, et al. [S3-01] TNT: A randomized phase III trial of carboplatin (C) compared with docetaxel (D) for patients with metastatic or recurrent locally advanced triple negative or BRCA1/2 breast cancer (CRUK/07/012). 2014 San Antonio Breast Cancer Symposium. Presented December 11, 2014. Abstract S3-01


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Effective November 1, 2017
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

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Effective November 1, 2017
BREAST CANCER ENDOCRINE THERAPY FOR RECURRENT OR METASTATIC DISEASE REFERENCES


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Effective November 1, 2017
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35 Ellis MJ, Prahladan 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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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


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Effective November 1, 2017
# Chronic Myelogenous Leukemia (CML) Pathways

## First line of therapy (1st line)

- **Dasatinib** *(Sprycel)* for Intermediate or High risk disease\(^{1,2,30,37-39}\
- **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)  
<table>
<thead>
<tr>
<th>Following treatment failure, suboptimal response(^{†}), or intolerance to first line therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bosutinib</strong> <em>(Bosulif)</em>(^{23,33}|</td>
</tr>
<tr>
<td><strong>Dasatinib</strong> <em>(Sprycel)</em>(^{1,2,9,10,12,36}|</td>
</tr>
<tr>
<td><strong>Nilotinib</strong> <em>(Tasigna)</em>(^{16,17,18,31,32}|</td>
</tr>
<tr>
<td><strong>Ponatinib</strong>(^{‡})* <em>(Iclusig)</em>(^{26}|</td>
</tr>
</tbody>
</table>

## Third line of therapy (3rd line)

- **Ponatinib** *(Iclusig)*\(^{26}\|

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* 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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CHRONIC MYELOGENOUS LEUKEMIA (CML) REFERENCES


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NCCN Clinical Practice Guidelines:


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Colorectal Cancer Pathways

**Adjuvant therapy***

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

**FOLFOX**: fluorouracil (5-FU), leucovorin, and oxaliplatin \(^{7,8,50,51,60,69}\).

**FULV**: fluorouracil (5FU) and leucovorin\(^{14,7,49,52,69}\).

**Metastatic disease | RAS Wild Type (WT) or Mutant (MT) \(†\) | First or second lines of therapy (1\textsuperscript{st} or 2\textsuperscript{nd} 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 (1\textsuperscript{st} or 2\textsuperscript{nd} 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)\(^{11,62}\).

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

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

**Metastatic disease | RAS wild type (WT) | Third or subsequent lines of therapy (3\textsuperscript{rd} 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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COLORECTAL CANCER REFERENCES


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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


Venook AP, Niedzwiecki D, Lenz H, et al. CALGB/SWOG 80405: Phase III trial of irinotecan/5-FU/leucovorin (FOLFIRI) 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).


Tabernero J, Yoshino T, RAISE Study Investigators, et al. Ramucirumab versus placebo in combination with second-line FOLFIRI in patients with metastatic colorectal carcinoma that progressed during or after first-line therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine (RAISE); a randomised, double-blind, multicentre, phase 3 study. Lancet Oncol. 2015 May;16(5):499-508. PMID: 25677855


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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)\(^35\)
- Paclitaxel and carboplatin with concurrent RT\(^3\)

**Post-operative treatment**

- Fluorouracil (5FU) and leucovorin with concurrent RT\(^38\)

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

- Cisplatin and fluorouracil (5FU)\(^15,19,21,26\)
- Fluorouracil (5FU) and irinotecan (Camptosar)\(^25,26\)
- **FLO / FOLFOX**: fluorouracil (5FU), leucovorin, and oxaliplatin\(^27\)
- **FLP**: fluorouracil (5FU), leucovorin, and cisplatin\(^27\)

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

- Cisplatin, fluorouracil (5FU), and trastuzumab (Herceptin)\(^15\)

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

- Irinotecan (Camptosar)\(^24,29\)
- Paclitaxel\(^33\)

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GASTRIC, ESOPHAGEAL, AND GASTROESOPHAGEAL JUNCTION (ADENOCARCINOMA) CANCERS REFERENCES


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# Head and Neck Cancer Pathways

<table>
<thead>
<tr>
<th>Hypopharynx and larynx: candidate for local therapy (M0)</th>
<th>Primary systemic therapy &amp; concurrent radiation therapy (RT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dose cisplatin* with concurrent RT</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hypopharynx and larynx: candidate for local therapy (M0)</th>
<th>Post-operative systemic therapy &amp; concurrent radiation therapy (RT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dose cisplatin* with concurrent RT</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lip, oral cavity, oropharynx, ethmoid sinus, maxillary sinus, occult primary: candidate for local therapy (M0)</th>
<th>Primary systemic therapy &amp; concurrent radiation therapy (RT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dose cisplatin* with concurrent RT</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lip, oral cavity, oropharynx, ethmoid sinus, maxillary sinus, occult primary: candidate for local therapy (M0)</th>
<th>Post-operative systemic therapy &amp; concurrent radiation therapy (RT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dose cisplatin* with concurrent RT</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nasopharynx: candidate for local therapy (M0)</th>
<th>Primary systemic therapy &amp; concurrent radiation therapy (RT) followed by adjuvant therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dose cisplatin* with concurrent RT, followed by adjuvant cisplatin and fluorouracil (5FU)</td>
<td></td>
</tr>
</tbody>
</table>

### Nasopharynx | Metastatic and recurrent disease | First and subsequent lines of therapy (1st line +) | Performance Status 0, 1, 2

- Carboplatin
- Cisplatin
- Cisplatin† and gemcitabine (Gemzar)
- Cisplatin† and paclitaxel
- Fluorouracil (5FU)
- Gemcitabine (Gemzar)
- Gemcitabine (Gemzar) and vinorelbine (Navelbine)
- Methotrexate
- Paclitaxel

### Non-Nasopharyngeal (Squamous cell) | Metastatic and recurrent disease | First line of therapy (1st 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 and subsequent lines of therapy (2nd line +) | Performance Status 0, 1, 2

- 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

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HEAD AND NECK CANCER REFERENCES


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Effective November 1, 2017
Hodgkin Lymphoma Pathways

### Classical Hodgkin Lymphoma | Early Stage (Stage I-IIA, favorable and unfavorable risk)

**ABVD**: doxorubicin (Adriamycin), bleomycin, vinblastine, and dacarbazine (DTIC) ± ISRT*1,3,4,5,30

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

**ABVD**: doxorubicin (Adriamycin), bleomycin, vinblastine, and dacarbazine (DTIC) ± ISRT*7,8,9,10,32

* ISRT – Involved Site Radiation Therapy

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HODGKIN LYMPHOMA REFERENCES


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Effective November 1, 2017 45
Kidney Cancer (Renal Cell Carcinoma)

Pathways

**Metastatic disease | First line of therapy (1st line)**

- High dose intravenous (IV) interleukin-2 (IL2, Proleukin)\(^ {17,18}\) *(clear cell only)*
- Pazopanib (Votrient)\(^ {4,5,7}\)

**Metastatic disease | First line of therapy (1st line) | Poor prognosis* or Non-clear cell histology**

- Temsirolimus (Torisel)\(^ {23}\)

**Metastatic disease | Second or subsequent lines of therapy (2nd line+) | Clear cell carcinoma**

- Nivolumab (Opdivo)\(^ {29}\)

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* 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 ≤ 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 November 1, 2017


7 Garnick MB. How to Interpret patient preferences in selecting the best drug: are the current measurements up to the job? J Clin Oncol. 2014; 32(14):1392-3. PMID: 24687838


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

## Adjuvant

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin and paclitaxel</td>
</tr>
<tr>
<td>Cisplatin and gemcitabine (Gemzar)</td>
</tr>
<tr>
<td>Cisplatin and vinorelbine (Navelbine)</td>
</tr>
</tbody>
</table>

## Primary therapy | Locally advanced / Unresectable disease | Stage III

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin and etoposide (Toposar) with concurrent XRT</td>
</tr>
<tr>
<td>Paclitaxel and carboplatin with concurrent XRT</td>
</tr>
</tbody>
</table>

## Metastatic disease | ALK positive or ROS1 positive | First line of therapy (1st line)

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crizotinib (Xalkori)</td>
</tr>
</tbody>
</table>

## Metastatic disease | EGFR positive | First line of therapy (1st line)

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erlotinib (Tarceva)</td>
</tr>
</tbody>
</table>

## Metastatic disease | PD-L1 Expression High (≥50%) | EGFR and ALK negative | First line of therapy (1st line) | ECOG Performance Status = 0, 1, 2

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembrolizumab (Keytruda)*105,106</td>
</tr>
</tbody>
</table>

## Metastatic disease | Non-squamous | First line of therapy (1st line) | ECOG Performance Status = 0, 1, 2

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin* and paclitaxel</td>
</tr>
<tr>
<td>Carboplatin, paclitaxel, and bevacizumab (Avastin)</td>
</tr>
<tr>
<td>Cisplatin* and gemcitabine (Gemzar)</td>
</tr>
<tr>
<td>Cisplatin* and pemetrexed (Alimta)</td>
</tr>
</tbody>
</table>

## Metastatic disease | Squamous | First line of therapy (1st line) | PD-L1 Expression <50% | ECOG Performance Status = 0, 1, 2

<table>
<thead>
<tr>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin* and paclitaxel</td>
</tr>
<tr>
<td>Cisplatin* and gemcitabine (Gemzar)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Metastatic disease</th>
<th>Non-squamous</th>
<th>Maintenance</th>
<th>ECOG Performance Status = 0, 1, 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continuation bevacizumab (Avastin)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continuation pemetrexed (Alimta)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Switch pemetrexed (Alimta)</td>
<td></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>Osimertinib (Tagrisso)†</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic disease</th>
<th>ALK positive or EGFR positive</th>
<th>Second or subsequent lines of therapy (2nd line +)</th>
<th>ECOG Performance Status = 0, 1, 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin* and paclitaxel</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cisplatin* and gemcitabine (Gemzar)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cisplatin* and pemetrexed (Alimta)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic disease</th>
<th>Second or subsequent lines of therapy (2nd line+)</th>
<th>ECOG Performance Status = 0, 1, 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atezolizumab (Tecentriq)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nivolumab (Opdivo) (any histology/pathology)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pemetrexed (Alimta) (Non-Squamous histology/pathology)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic disease</th>
<th>EGFR positive</th>
<th>ECOG Performance Status = 3, 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erlotinib (Tarceva)</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

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Effective November 1, 2017
LUNG CANCER: NON-SMALL CELL LUNG CANCER (NSCLC)

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 Therapy (1st line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin and etoposide (Toposar) ± XRT³</td>
<td></td>
</tr>
<tr>
<td>Cisplatin and etoposide (Toposar) ± XRT¹,²</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Extensive Stage</th>
<th>First line of therapy (1st line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin and etoposide (Toposar)⁹</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Second and subsequent lines of therapy (2nd line +)</th>
<th>Relapse greater than 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin and etoposide (Toposar)⁹</td>
<td></td>
</tr>
</tbody>
</table>

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LUNG CANCER: SMALL CELL LUNG CANCER REFERENCES


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# Melanoma Pathways: Metastatic Melanoma

<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) *(^{35,45,55,56})</td>
<td></td>
<td></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)(^{26,40-42})</td>
<td></td>
<td></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)(^{26,40-42})</td>
<td></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>Any BRAF status</th>
<th>ECOG PS: 0, 1, 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipilimumab (Yervoy)(^{1,14,15,35,36})</td>
<td></td>
<td></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.

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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**

<table>
<thead>
<tr>
<th>Pathway</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>VRD/VDR</td>
<td>bortezomib (Velcade), lenalidomide (Revlimid), and dexamethasone^{10,12,79}</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Pathway</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CyBorD or VDC</td>
<td>bortezomib (Velcade), cyclophosphamide, and dexamethasone^{9,10,84}</td>
</tr>
<tr>
<td>R-dex</td>
<td>lenalidomide (Revlimid) and low-dose dexamethasone^{10,11,13,73}</td>
</tr>
<tr>
<td>VRD/VDR</td>
<td>bortezomib (Velcade), lenalidomide (Revlimid), and dexamethasone^{10,12,79}</td>
</tr>
<tr>
<td>VD</td>
<td>bortezomib (Velcade) and dexamethasone^{1,3,12,24,89}</td>
</tr>
</tbody>
</table>

**Maintenance therapy | Post-transplant**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lenalidomide (Revlimid)</td>
<td>^{26,27,83,92}</td>
</tr>
</tbody>
</table>

**Relapsed disease | Second and subsequent lines of therapy (2nd line +)**

<table>
<thead>
<tr>
<th>Pathway</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRd or KRd</td>
<td>carfilzomib (Kyprolis), lenalidomide (Revlimid), and dexamethasone^{82}</td>
</tr>
<tr>
<td>DRD</td>
<td>daratumumab (Darzalex), lenalidomide (Revlimid), and dexamethasone^{100}</td>
</tr>
<tr>
<td>DVD</td>
<td>daratumumab (Darzalex), bortezomib (Velcade), and dexamethasone^{103}</td>
</tr>
</tbody>
</table>

**Relapsed disease | Third and subsequent lines of therapy (3rd line +)**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daratumumab (Darzalex)</td>
<td>^{95}</td>
</tr>
<tr>
<td>Elotuzumab (Empliciti), lenalidomide (Revlimid), and dexamethasone</td>
<td>^{97}</td>
</tr>
</tbody>
</table>

---

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MYELOMA: MULTIPLE MYELOMA REFERENCES


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

<table>
<thead>
<tr>
<th>First line of therapy (1st line)</th>
<th>With 17p Deletion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibrutinib (Imbruvica)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>First line of therapy (1st line)</th>
<th>Without 17p Deletion</th>
</tr>
</thead>
<tbody>
<tr>
<td>BR: bendamustine (Bendeka, Treanda) and rituximab (Rituxan)</td>
<td></td>
</tr>
<tr>
<td>FCR: fludarabine (Fludara), cyclophosphamide, and rituximab (Rituxan)</td>
<td></td>
</tr>
<tr>
<td>Ibrutinib (Imbruvica)</td>
<td></td>
</tr>
<tr>
<td>Obinutuzumab (Gazyva) (Monotherapy)</td>
<td>(Added Effective11/1/2017)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Second and subsequent lines of therapy (2nd line +)</th>
<th>With 17p Deletion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibrutinib (Imbruvica)</td>
<td></td>
</tr>
<tr>
<td>Idelalisib (Zydelig) (Added Effective11/1/2017)</td>
<td></td>
</tr>
<tr>
<td>Idelalisib (Zydelig) and rituximab (Rituxan) (Added Effective11/1/2017)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Second and subsequent lines of therapy (2nd line +)</th>
<th>Without 17p Deletion</th>
</tr>
</thead>
<tbody>
<tr>
<td>BR: bendamustine (Bendeka, Treanda) and rituximab (Rituxan)</td>
<td></td>
</tr>
<tr>
<td>Ibrutinib (Imbruvica)</td>
<td></td>
</tr>
<tr>
<td>Idelalisib (Zydelig) (Added Effective11/1/2017)</td>
<td></td>
</tr>
<tr>
<td>Idelalisib (Zydelig) and rituximab (Rituxan) (Added Effective11/1/2017)</td>
<td></td>
</tr>
</tbody>
</table>

Indications to initiate treatment may include (not limited to):

1. WBC elevation above 200-300 x 10^9
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

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NHL: CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) / SMALL LYMPHOCYTIC LYMPHOMA (SLL) REFERENCES


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Munir T, Howard DR, McParland L, et al. Results of the randomized phase IIB ADMIRE trial of FCR with or without mitoxantrone in previously untreated CLL. *Leukemia.* 2017:e-publication. PMID: 28216660.


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These Guidelines are a work in progress that may be refined as often as new significant data becomes available.

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Effective November 1, 2017
# NHL: Diffuse Large B-Cell Lymphoma Pathways

## First line of therapy (1st line)

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>R-CHOP (21)</td>
<td>cyclophosphamide, doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, and rituximab (Rituxan)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>R-CEOP</td>
<td>cyclophosphamide, etoposide (Toposar), vincristine (Vincasar), prednisone, and rituximab (Rituxan)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>R-GDP</td>
<td>gemcitabine (Gemzar), dexamethasone, cisplatin, and rituximab (Rituxan) OR gemcitabine (Gemzar), dexamethasone, carboplatin, and rituximab (Rituxan)</td>
</tr>
<tr>
<td>R-ICE</td>
<td>ifosfamide (Ifex), carboplatin, etoposide (Toposar), and rituximab (Rituxan)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>BR</td>
<td>bendamustine (Bendeka, Treanda) and Rituximab (Rituxan)</td>
</tr>
<tr>
<td>R-GDP</td>
<td>gemcitabine (Gemzar), dexamethasone, cisplatin, and rituximab (Rituxan) OR gemcitabine (Gemzar), dexamethasone, carboplatin, and rituximab (Rituxan)</td>
</tr>
<tr>
<td>R-GemOx</td>
<td>gemcitabine (Gemzar), oxaliplatin, and rituximab (Rituxan)</td>
</tr>
</tbody>
</table>

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

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Effective November 1, 2017
NHL: DIFFUSE LARGE B CELL LYMPHOMA REFERENCES


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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* eradication33,34

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

Rituximab (Rituxan) monotherapy27-29

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) monotherapy7,17

Follicular 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

Cyclophosphamide11-13

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)1-5

R-CEOP: Cyclophosphamide, etoposide (Toposar), vincristine (Vincasar), prednisone, and rituximab (Rituxan)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.

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

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NHL: FOLLICULAR AND MARGINAL ZONE LYMPHOMA REFERENCES


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# NHL: Mantle Cell Lymphoma Pathways

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

**Alternating R-CHOP/R-DHAP:** cyclophosphamide (Cytoxan), doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, rituximab (Rituxan) alternating with dexamethasone, cisplatin, cytarabine (Ara-C), and rituximab (Rituxan)\(^4,5,28,30,31\) (Added Effective 11/1/2017)

**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)\(^{17}\)
- Ibrutinib (Imbruvica)\(^{19,20}\)
- Lenalidomide (Revlimid)\(^{20,23}\) (Added Effective 11/1/2017)

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Effective November 1, 2017
NHL: MANTLE CELL LYMPHOMA REFERENCES


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# Ovarian Cancer (Epithelial) Pathways

<table>
<thead>
<tr>
<th>Pathway</th>
<th>Stage</th>
<th>Therapy Details</th>
</tr>
</thead>
</table>
| **Adjuvant Therapy | Stage IA/B (Grade 2 or 3) or IC (Grade 1-3)** | Carboplatin and dose dense (weekly) paclitaxel<sup>6,7,8</sup>  
Carboplatin and paclitaxel<sup>2-5,7</sup> |
| **Adjuvant or Primary Therapy | Stage II, III, IV** | Carboplatin and dose dense (weekly) paclitaxel (Taxol)<sup>6,8,45</sup>  
Intravenous (IV) paclitaxel and Intraperitoneal (IP) cisplatin and IP paclitaxel<sup>1,49</sup> (Stage III only) |
| **Recurrent Disease | First and subsequent lines of therapy (1st line +) | Platinum-sensitive* | Carboplatin<sup>8,9,12</sup>  
Carboplatin and gemcitabine (Gemzar)<sup>12,13</sup>  
Carboplatin and paclitaxel<sup>8,9,15</sup>  
Carboplatin and weekly paclitaxel |
| **Recurrent Disease | Maintenance Therapy | Platinum-sensitive (Added Effective 11/1/2017) | Niraparib (Zejula)<sup>54</sup> (Added Effective11/1/2017) |
| **Recurrent Disease | Second and subsequent lines of therapy (2nd line +) | Platinum resistant | Bevacizumab (Avastin) monotherapy<sup>42</sup>  
Docetaxel (Taxotere)<sup>17</sup>  
Gemcitabine (Gemzar)<sup>19,20</sup>  
Liposomal doxorubicin (Doxil or Lipodox)<sup>19,20,21</sup>  
Paclitaxel (weekly)<sup>22,23</sup>  
Paclitaxel and bevacizumab (Avastin)<sup>36,38</sup>  
Tamoxifen<sup>56</sup> (Added Effective11/1/2017)  
Topotecan (Hycamtin)<sup>21,24</sup>  
Topotecan (Hycamtin) and bevacizumab (Avastin)<sup>36,37</sup>  
Vinorelbine (Navelbine)<sup>34,35</sup> |

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

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OVARIAN CANCER (EPITHELIAL) REFERENCES


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23 Gynecologic Oncology Group1, Markman M, Blessing J, et al. Phase II trial of weekly paclitaxel (80 mg/m2) in platinum and paclitaxel-resistant ovarian and primary peritoneal cancers: a Gynecologic Oncology Group study. Gynecol Oncol. 2006 Jun;101(3):436-40. PMID: 16325893


38 O’Malley DM, Richardson DL, Rheumse PS, et al. Addition of bevacizumab to weekly paclitaxel significantly improves progression-free survival in heavily pretreated recurrent epithelial ovarian cancer. Gynecol Oncol. 2011 May 1;121(2):269-72. PMID: 21315428


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 recurrent, platinum-resistant primary ovarian or primary peritoneal carcinoma. Gynecol Oncol. 2013 Feb;128(2):211-8. PMID: 22963362


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## Pancreatic Cancer (Adenocarcinoma) Pathways

### Adjuvant Therapy

<table>
<thead>
<tr>
<th>Therapy Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capecitabine (Xeloda) and gemcitabine (Gemzar)(^{36,40})</td>
</tr>
<tr>
<td><strong>FULV</strong>: fluorouracil (5FU) and leucovorin(^{4,6,9})</td>
</tr>
<tr>
<td>Gemcitabine (Gemzar) monotherapy(^{1,3-7})</td>
</tr>
</tbody>
</table>

### Locally Advanced/Unresectable and Metastatic Disease | First line of therapy (1st line) | ECOG PS: 0, 1, 2

<table>
<thead>
<tr>
<th>Therapy Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FOLFIRINOX</strong>: fluorouracil (5FU), leucovorin, irinotecan (Camptosar), and oxaliplatin(^{5,21})</td>
</tr>
<tr>
<td>Gemcitabine (Gemzar)(^{5,15-21})</td>
</tr>
<tr>
<td>Gemcitabine (Gemzar) and nab-paclitaxel (Abraxane)(^{5,15,33})</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Therapy Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OFF</strong>: Fluorouracil (5FU), leucovorin, and oxaliplatin(^{32})</td>
</tr>
<tr>
<td>Gemcitabine (Gemzar) monotherapy(^{21})</td>
</tr>
</tbody>
</table>

---

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PANCREATIC CANCER (ADENOCARCINOMA) REFERENCES


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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)\(^4\)
- Goserelin* (Zoladex) with abiraterone (Zytiga)\(^41\) (Added Effective 11/1/2017)
- Goserelin* (Zoladex) with docetaxel (Taxotere) (every 3 weeks) No Longer Effective 11/1/2017
- Leuprolide* (Eligard/Lupron)\(^4\)
- Leuprolide* (Eligard/Lupron) with abiraterone (Zytiga)\(^41\) (Added Effective 11/1/2017)
- Leuprolide* (Eligard/Lupron) with docetaxel (Taxotere) (every 3 weeks) No Longer Effective 11/1/2017
- Triptorelin* (Trelstar)\(^4\)
- Triptorelin* (Trelstar) with abiraterone (Zytiga)\(^41\) (Added Effective 11/1/2017)
- Triptorelin* (Trelstar) with docetaxel (Taxotere) (every 3 weeks) No Longer Effective 11/1/2017

**Recurrent and Metastatic disease | Hormone Sensitive**
- Abiraterone (Zytiga) and prednisone with Androgen Deprivation Therapy (ADT)\(^39,41\) (Added Effective 11/1/2017)
- Docetaxel (Taxotere) (every 3 weeks) with Androgen Deprivation Therapy (ADT)\(^119\)
- 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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# Prostate Cancer (Adenocarcinoma) Pathways (continued)

## Recurrent and Metastatic Disease | Hormone Resistant | First line of therapy (1st line)

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abiraterone** (Zytiga) and prednisone with continued ADT**</td>
<td>[^8,12,25,26,27]\</td>
</tr>
<tr>
<td>Docetaxel** (Taxotere) (every 3 weeks) with continued ADT**</td>
<td>[^9,10,19]\</td>
</tr>
<tr>
<td>Enzalutamide (Xtandi)</td>
<td></td>
</tr>
<tr>
<td>Enzalutamide (Xtandi) with goserelin (Zoladex)</td>
<td></td>
</tr>
<tr>
<td>Enzalutamide (Xtandi) with leuprolide (Eligard/Lupron)</td>
<td></td>
</tr>
<tr>
<td>Enzalutamide (Xtandi) with triptorelin (Trelstar)</td>
<td></td>
</tr>
<tr>
<td>Goserelin (Zoladex) with bicalutamide (Casodex)</td>
<td>[^6,7]\</td>
</tr>
<tr>
<td>Leuprolide (Eligard/Lupron) with bicalutamide (Casodex)</td>
<td>[^6,7]\</td>
</tr>
<tr>
<td>Triptorelin (Trelstar) with bicalutamide (Casodex)</td>
<td>[^6,7]\</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abiraterone (Zytiga)** and prednisone with continued ADT**</td>
<td>[^8,12,25,26,27]\</td>
</tr>
<tr>
<td>Cabazitaxel (Jevtana) with ADT**</td>
<td>[^11]\</td>
</tr>
<tr>
<td>Docetaxel** (Taxotere) (every 3 weeks) with continued ADT**</td>
<td>[^9,10,19]\</td>
</tr>
<tr>
<td>Docetaxel (Taxotere) rechallenge with ADT**</td>
<td>[^21,22]\</td>
</tr>
<tr>
<td>Goserelin (Zoladex) with bicalutamide (Casodex)</td>
<td>[^6,7]\</td>
</tr>
<tr>
<td>Leuprolide (Eligard/Lupron) with bicalutamide (Casodex)</td>
<td>[^6,7]\</td>
</tr>
<tr>
<td>Triptorelin (Trelstar) with bicalutamide (Casodex)</td>
<td>[^6,7]\</td>
</tr>
<tr>
<td>Continued ADT** with supportive care ± dexamethasone</td>
<td>[^13,14,15,16,24]\</td>
</tr>
</tbody>
</table>

**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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PROSTATE CANCER (ADENOCARCINOMA) REFERENCES


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Effective November 1, 2017
## Testicular (Germ Cell Tumors) Cancer Pathways

<table>
<thead>
<tr>
<th>Pathway</th>
<th>Stage</th>
<th>Risk</th>
<th>Therapy</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>**Seminoma</td>
<td>Stage II-IIIA</td>
<td>Primary Therapy**</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>BEP:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bleomycin, etoposide (Toposar), and cisplatin⁵</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>EP:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>etoposide (Toposar) and cisplatin⁴</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>**Seminoma</td>
<td>Stage IIIB-C</td>
<td>Good and Intermediate Risk</td>
<td>and Metastatic Disease**</td>
<td></td>
</tr>
<tr>
<td><strong>BEP:</strong></td>
<td></td>
<td></td>
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<td>Stage II-IIIA</td>
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<td></td>
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<tr>
<td>**Nonseminoma</td>
<td>Adjuvant Therapy after RPLND*</td>
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<td></td>
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<tr>
<td><strong>EP:</strong></td>
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<td></td>
<td></td>
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<tr>
<td>etoposide (Toposar) and cisplatin⁸,⁹,²⁶</td>
<td></td>
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</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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TESTICULAR (GERM CELL TUMORS) CANCER REFERENCES


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Uterine (Endometrial) Cancer Pathways

<table>
<thead>
<tr>
<th>Adjuvant Therapy</th>
<th>Stage III-IV or High Risk Histologies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin and paclitaxel⁶,⁶</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recurrent / Metastatic</th>
<th>First and Subsequent Lines of Therapy (1st line +)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin and paclitaxel⁵,²⁷-²⁹</td>
<td></td>
</tr>
<tr>
<td>Cisplatin and doxorubicin (Adriamycin)²⁴,²⁵</td>
<td></td>
</tr>
</tbody>
</table>

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Effective November 1, 2017
UTERINE (ENDOMETRIAL) CANCER REFERENCES


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**NCCN Practice Guidelines**: Uterine Neoplasms V2.2017


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