



MEDICAL ONCOLOGY VALUE-BASED PATHWAYS

EviCore Oncology Value-Based Pathways

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EviCore

By ~~EVERNORTH~~

EviCore healthcare Clinical Decision Support Tool Diagnostic Strategies: This tool addresses common symptoms and symptom complexes. Imaging requests for individuals with atypical symptoms or clinical presentations that are not specifically addressed will require physician review. Consultation with the referring physician, specialist, and/or individual's Primary Care Physician (PCP) may provide additional insight.

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Medical Oncology Value-Based Pathways

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EviCore's value-based pathways program was created to promote the use of evidence-based, high value, cancer treatment regimens. Pathway regimens are a subset of regimens recommended by the National Comprehensive Cancer Network[®] (NCCN) that deliver the best clinical outcomes for patients.

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Anal Cancer Pathways

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Localized Disease: To be treated with Chemoradiation
• Mitomycin + fluorouracil (5FU)
• Mitomycin + capecitabine

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

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Unresectable/Metastatic: First Line	Unresectable/Metastatic: Second Line
• Durvalumab + gemcitabine + cisplatin	• FOLFOX (fluorouracil [5FU], leucovorin, and oxaliplatin)
• Gemcitabine + cisplatin	• FOLFIRI (fluorouracil [5FU], leucovorin, and irinotecan)
• Capecitabine	• Capecitabine
• Gemcitabine	• Gemcitabine

Bladder Cancer Pathways

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Locally Advanced Unresectable or Metastatic: First Line, Cisplatin Eligible	Locally Advanced Unresectable or Metastatic: First Line, Cisplatin Ineligible	Locally Advanced/ Unresectable Metastatic: Second Line Post Immunotherapy and Enfortumab	Locally Advanced Unresectable Metastatic: Second Line Post Chemotherapy and Immunotherapy
• Pembrolizumab + enfortumab vedotin	• Pembrolizumab + enfortumab vedotin	• DDMVAC (dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin)	• Enfortumab vedotin
• Nivolumab + gemcitabine + cisplatin followed by nivolumab maintenance	• Pembrolizumab	• Gemcitabine + cisplatin	
• Gemcitabine + cisplatin	• Gemcitabine + carboplatin	• Gemcitabine + carboplatin	
• Avelumab maintenance (if no progression on platinum-based chemotherapy)		• Paclitaxel	
		• Docetaxel	
		• Gemcitabine	

Breast Cancer Pathways

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Neoadjuvant/Adjuvant

HER2 Negative/Hormone Receptor Positive	Triple Negative (HER2-, ER-, and PR-Negative) – 80kg or less patient
• TC (docetaxel and cyclophosphamide)	• NeoPact regimen with pembrolizumab IV weight-based dosing
• Dose Dense AC (doxorubicin and cyclophosphamide) followed by weekly paclitaxel	

Metastatic

HER2 Negative; If Triple Negative then Third Line and beyond	HER2 Positive: First Line	HER2 Positive: Second Line or beyond	HER2 Positive: Third Line or beyond	HER2 Positive: Fourth Line or beyond
• Docetaxel	• Docetaxel + trastuzumab* + pertuzumab [§]	• Fam-trastuzumab deruxtecan	• Ado-trastuzumab emtansine	• Chemo + trastuzumab*
• Paclitaxel	• Paclitaxel + trastuzumab* + pertuzumab [§]		• Tucatinib + capecitabine + trastuzumab*	• Lapatinib + trastuzumab*
• Gemcitabine				
• Vinorelbine				
• Capecitabine				
• Doxorubicin				

* Use of preferred oncology medication products may be required for coverage. Refer to the health plan's coverage policy for additional information.

§ Pertuzumab, trastuzumab, and hyaluronidase-zzxf injection for subcutaneous use may be substituted for intravenous pertuzumab and intravenous trastuzumab.

HER2 Negative; If Triple Negative then Third Line and beyond	HER2 Positive: First Line	HER2 Positive: Second Line or beyond	HER2 Positive: Third Line or beyond	HER2 Positive: Fourth Line or beyond
• Liposomal doxorubicin				

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Pathways

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First Line: WITHOUT del (17P)/TP53 Mutation	First Line: WITH del (17P)/TP53 Mutation
• Ibrutinib	• Ibrutinib
• Acalabrutinib	• Acalabrutinib
• Zanubrutinib	• Zanubrutinib
• Venetoclax + obinutuzumab	• Venetoclax + obinutuzumab
• Bendamustine + rituximab *	

* Use of preferred oncology medication products may be required for coverage. Refer to the health plan's coverage policy for additional information.

Chronic Myeloid Leukemia Pathways

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First Line: Low Risk Score Disease

- Imatinib

Colorectal Cancer Pathways

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Metastatic: First or Second Line Therapy for RAS/RAF Wild Type – EGFR Inhibitor Planned	Metastatic: Subsequent Therapy with a VEGF Inhibitor	Metastatic: dMMR/MSI-H or POLE/POLD1 Mutation
• Panitumumab-based therapy	• Bevacizumab* + FOLFIRI (fluorouracil [5FU], leucovorin, and irinotecan)	• Pembrolizumab
	• Bevacizumab* + irinotecan	

* Use of preferred oncology medication products may be required for coverage. Refer to the health plan's coverage policy for additional information.

Diffuse Large B-Cell Lymphoma Pathways

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Second Line Therapy, Relapsed Disease >12 Months: Intention to Transplant	Second Line Therapy, Relapsed Disease >12 Months: No Intention to Transplant or CAR T
• ICE (ifosfamide, carboplatin and etoposide) +/- rituximab*	• GemOx (gemcitabine and oxaliplatin) +/- rituximab*
• GDP (gemcitabine, dexamethasone and cisplatin) +/- rituximab* or gemcitabine, dexamethasone and carboplatin) +/- rituximab*	• GDP (gemcitabine, dexamethasone and cisplatin) +/- rituximab* or gemcitabine, dexamethasone and carboplatin) +/- rituximab*
• DHAX (dexamethasone, cytarabine and oxaliplatin) +/- rituximab*	• Polatuzumab vedotin +/- bendamustine +/- rituximab*
	• Glofitamab + GemOx (gemcitabine and oxaliplatin)

* Use of preferred oncology medication products may be required for coverage. Refer to the health plan's coverage policy for additional information.

Endometrial Cancer Pathways

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pMMR, Stage IVB, Checkpoint Inhibitor Planned, Recurrent/Metastatic: First Line Therapy

- Carboplatin + paclitaxel + pembrolizumab

Esophageal and Esophagogastric Junction Cancer Pathways

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Unresectable/Recurrent Metastatic: First Line, Adenocarcinoma, HER2 Negative, MSS	Unresectable/Recurrent Metastatic: First Line, Squamous Cell, MSS	Unresectable/Recurrent/ Metastatic: Second-Line or Subsequent, Squamous Cell
• FOLFOX (fluorouracil [5FU], leucovorin, and oxaliplatin)	• FOLFOX (fluorouracil [5FU], leucovorin, and oxaliplatin)	• Paclitaxel
• CapeOx (capecitabine and oxaliplatin)	• CapeOx (capecitabine and oxaliplatin)	• Docetaxel
• Fluorouracil [5FU] or capecitabine + cisplatin	• Fluorouracil [5FU] or capecitabine + cisplatin	• Irinotecan
• Nivolumab + FOLFOX (fluorouracil [5FU], leucovorin, and oxaliplatin) (For CPS ≥ 5 only)	• Nivolumab + (fluorouracil [5FU] or capecitabine) + cisplatin	• Pembrolizumab (For second line, CPS ≥ 10 and no prior CPI only)
• Nivolumab + CapeOx (capecitabine and oxaliplatin) (For CPS ≥ 5 only)	• Nivolumab + FOLFOX (fluorouracil [5FU], leucovorin, and oxaliplatin)	• Nivolumab (For no prior CPI only)
• Pembrolizumab + (fluorouracil [5FU] or capecitabine) + cisplatin (For CPS ≥ 10 only)	• Nivolumab + CapeOx (capecitabine and oxaliplatin)	
• Pembrolizumab + FOLFOX (fluorouracil [5FU], leucovorin, and oxaliplatin) (For CPS ≥ 10 only)	• Pembrolizumab + (fluorouracil [5FU] or capecitabine) + cisplatin (For CPS ≥ 10 only)	

Unresectable/Recurrent Metastatic: First Line, Adenocarcinoma, HER2 Negative, MSS	Unresectable/Recurrent Metastatic: First Line, Squamous Cell, MSS	Unresectable/Recurrent/ Metastatic: Second-Line or Subsequent, Squamous Cell
• Pembrolizumab + CapeOx (capecitabine and oxaliplatin) (<i>For CPS ≥ 10 only</i>)	• Pembrolizumab + FOLFOX (fluorouracil [5FU], leucovorin, and oxaliplatin) (<i>For CPS ≥ 10 only</i>)	
Tislelizumab + (fluorouracil [5FU] or capecitabine) + cisplatin (<i>For CPS ≥ 5 only</i>)	• Pembrolizumab + CapeOx (capecitabine and oxaliplatin) (<i>For CPS ≥ 10 only</i>)	
Tislelizumab + FOLFOX (fluorouracil [5FU], leucovorin, and oxaliplatin) (<i>For CPS ≥ 5 only</i>)	• Tislelizumab + (fluorouracil [5FU] or capecitabine) + cisplatin (<i>For CPS or TAP ≥ 10 only</i>)	
Tislelizumab + CapeOx (capecitabine and oxaliplatin) (<i>For CPS ≥ 5 only</i>)	• Tislelizumab + FOLFOX (fluorouracil [5FU], leucovorin, and oxaliplatin) (<i>For CPS or TAP ≥ 10 only</i>)	
	• Tislelizumab + CapeOx (capecitabine and oxaliplatin) (<i>For CPS or TAP ≥ 10 only</i>)	
	• Tislelizumab + cisplatin + paclitaxel (<i>For CPS or TAP ≥ 10 only</i>)	
	• Tislelizumab + oxaliplatin + paclitaxel (<i>For CPS or TAP ≥ 10 only</i>)	

Follicular B-Cell Lymphoma Pathways

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Grade 1-2 Disease: First Line
• BR (bendamustine and rituximab [*])
• R-CHOP (rituximab [*] , cyclophosphamide, doxorubicin, vincristine and prednisone)
• R-CVP (rituximab [*] , cyclophosphamide, vincristine and prednisone)

^{*} Use of preferred oncology medication products may be required for coverage. Refer to the health plan's coverage policy for additional information.

Head and Neck Cancer Pathways

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Advanced Disease: Definitive Chemoradiation
• High dose cisplatin
• Carboplatin + infusional fluorouracil (5FU)
• Weekly cisplatin (40 mg/m ² weekly)
• Weekly carboplatin + paclitaxel

Hepatocellular Carcinoma Pathways

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Metastatic or Unresectable Disease: First Line
• Lenvatinib
• Atezolizumab + bevacizumab *
• Tremelimumab-actl + durvalumab
• Durvalumab

* Use of preferred oncology medication products may be required for coverage. Refer to the health plan's coverage policy for additional information.

Hodgkin Lymphoma Pathways

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Stage III/IV Classical Hodgkin Lymphoma - Ages 18-60 years old

- Nivolumab-AVD (doxorubicin, vinblastine, and dacarbazine)

Kidney Cancer Pathways

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Clear Cell, First line: Favorable Risk	Clear Cell, First Line: Intermediate or Poor Risk
• Lenvatinib + pembrolizumab	• Ipilimumab (1 mg/kg x 4 doses) + nivolumab IV
• Cabozantinib + nivolumab	
• Ipilimumab (1 mg/kg x 4 doses) + nivolumab IV	
• Sunitinib (<i>if not candidate for CPI</i>)	
• Pazopanib (<i>if not candidate for CPI</i>)	

Lung Cancer: Non-Small Cell Lung Cancer Pathways

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Metastatic, EGFR Exon 19 deletion or Exon 21 L858R Mutations

Metastatic, EGFR Exon 19 deletion or Exon 21 L858R Mutations

First Line

- Osimertinib
- Osimertinib + pemetrexed + (cisplatin or carboplatin) (*For nonsquamous only*)

Nonsquamous, Metastatic

First Line, PD-L1 $\geq$ 50%, No Actionable Mutations	First line, PD-L1 < 50%, No Driver Mutations	Subsequent Therapy, No Actionable Mutations
• Pembrolizumab	• Pembrolizumab + pemetrexed + (carboplatin or cisplatin)	• Nivolumab (<i>only if no prior CPI</i>)
• Cemiplimab-rwlc	• Cemiplimab-rwlc + pemetrexed + (carboplatin or cisplatin)	• Pembrolizumab (<i>only if no prior CPI</i>)
• Atezolizumab	• Cemiplimab-rwlc + paclitaxel + (carboplatin or cisplatin)	• Atezolizumab (<i>only if no prior CPI</i>)
		• Pemetrexed
		• Gemcitabine
		• Docetaxel

Squamous, Metastatic

First Line, PD-L1 $\geq$ 50%, No Actionable Mutations	First line, PD-L1<50%, No Driver Mutations	Subsequent Therapy, No Actionable Mutations
• Pembrolizumab	• Pembrolizumab + paclitaxel + carboplatin	• Nivolumab (<i>only if no prior CPI</i>)
• Cemiplimab-rwlc	• Cemiplimab-rwlc + paclitaxel + (carboplatin or cisplatin)	• Pembrolizumab (<i>only if no prior CPI</i>)
• Atezolizumab		• Atezolizumab (<i>only if no prior CPI</i>)
		• Gemcitabine
		• Docetaxel

Lung Cancer: Small Cell Lung Cancer Pathways

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Limited Stage Disease	Extensive Stage Disease: First Line	Extensive Stage Disease: Subsequent Therapy
• Cisplatin + etoposide +/- radiation	• Atezolizumab + carboplatin + etoposide	• Cisplatin + etoposide (<i>for prolonged disease-free interval</i>)
• Carboplatin + etoposide +/- radiation (<i>only if cisplatin ineligible or intolerant</i>)	• Carboplatin + etoposide	• Carboplatin + etoposide (<i>for prolonged disease-free interval</i>)
		• Topotecan

Myelodysplastic Syndrome (MDS) Pathways

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IPSS-R: Intermediate, High, Very High, Non-Transplant Candidate
• Azacitidine

Melanoma Pathways

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Stage III, Clinical Node Positive, Resectable Disease, Neoadjuvant/Adjuvant	Metastatic: First Line, BRAF Mutation Positive	Metastatic: First Line, BRAF Mutation Negative
• Nivolumab IV + ipilimumab followed by observation (<i>if major pathological response</i>)	• Vemurafenib + cobimetinib	• Pembrolizumab
	• Pembrolizumab	• Nivolumab
	• Nivolumab	• Ipilimumab + nivolumab IV
	• Ipilimumab + nivolumab IV	

Multiple Myeloma Pathways

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First Line: Transplant Eligible	First Line: Transplant Deferred or Not Indicated
• Bortezomib + lenalidomide + dexamethasone	• Bortezomib + lenalidomide + dexamethasone
• Daratumumab + lenalidomide + bortezomib + dexamethasone	• Lenalidomide + dexamethasone
• Isatuximab-irfc + lenalidomide + bortezomib + dexamethasone	• Daratumumab + lenalidomide + dexamethasone
	• Daratumumab + lenalidomide + bortezomib + dexamethasone
	• Isatuximab-irfc + lenalidomide + dexamethasone
	• Isatuximab-irfc + lenalidomide + bortezomib + dexamethasone

Neuroendocrine Cancer Pathways

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Metastatic, Poorly-Differentiated, Large or Small Cell (Extrapulmonary)
• Cisplatin + etoposide
• Carboplatin + etoposide
• FOLFOX (fluorouracil [5FU], leucovorin, and oxaliplatin) (<i>following progression on platinum + etoposide</i>)
• FOLFIRI (fluorouracil [5FU], leucovorin, and irinotecan) (<i>following progression on platinum + etoposide</i>)

Ovarian Cancer Pathways

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Primary Therapy: Stage II-IV	Recurrent Disease, Platinum Sensitive
• Carboplatin + paclitaxel	• Carboplatin + gemcitabine
	• Cisplatin + gemcitabine
	• Carboplatin + paclitaxel

Pancreatic Cancer Pathways

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Adenocarcinoma: Neoadjuvant Therapy	Adenocarcinoma, Advanced/Metastatic: First Line Therapy
Modified FOLFIRINOX (fluorouracil [5FU], leucovorin, irinotecan, and oxaliplatin)	FOLFIRINOX or modified FOLFIRINOX
Gemcitabine + cisplatin (<i>for BRCA1/2 or PALB2 mutations only</i>)	Gemcitabine + albumin-bound paclitaxel

Prostate Cancer Pathways

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Metastatic: Adenocarcinoma, Castration Resistant	Abiraterone Dosing – All indications
• Abiraterone 250 mg/day (with a low-fat meal)	• Abiraterone 250 mg/day (with a low-fat meal)
• Enzalutamide	
• Docetaxel	
• Cabazitaxel (post docetaxel)	

Testicular Cancer Pathways

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First Line: Good Risk	First Line: Intermediate/Poor Risk
• BEP (bleomycin, etoposide, and cisplatin) x 3 cycles	• BEP (bleomycin, etoposide, and cisplatin) x 4 cycles

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References – Anal Cancer

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Localized Disease: To be treated with Chemoradiation

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Unresectable/Metastatic: First Line

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References – Bladder Cancer

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Locally Advanced/Unresectable or Metastatic: First Line, Cisplatin Eligible

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Locally Advanced Unresectable or Metastatic: First Line, Cisplatin Ineligible

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Locally Advanced Unresectable or Metastatic: Second Line Post Chemotherapy and Immunotherapy

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References – Breast Cancer

v1.0.2026

Neoadjuvant/Adjuvant: HER2 Negative/Hormone Receptor Positive

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HER2 Positive Metastatic Disease

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HER2 Negative Metastatic Disease; If Triple Negative then Third Line and Beyond

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References – Chronic Lymphocytic Leukemia (CLL)

v1.0.2026

First Line, with or without del (17p)/TP53 Mutation

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References – Chronic Myeloid Leukemia (CML)

v1.0.2026

First Line: Low Risk Score Disease

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References – Colorectal Cancer

v1.0.2026

Metastatic Disease: Subsequent Therapy with a VEGF Inhibitor

1. Bennouna J, Sastre J, Arnold D, et al. Continuation of bevacizumab after first progression in metastatic colorectal cancer (ML18147): a randomised phase 3 trial. *Lancet Oncol*. 2013;14(1):29-37. doi:10.1016/S1470-2045(12)70477-1.
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Metastatic Disease: dMMR/MSI-H or POLE/POLD1 Mutation

1. André T, Shiu KK, Kim TW, et al. Pembrolizumab in microsatellite-instability-high advanced colorectal cancer. *N Engl J Med*. 2020;383(23):2207-2218. doi:10.1056/NEJMoa2017699.
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Metastatic Disease: First Line or Second Line Therapy for RAS/RAF Wild Type – EGFR Inhibitor Planned

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References – Diffuse Large B-Cell Lymphoma (DBCL)

v1.0.2026

Second Line Therapy, Relapsed Disease >12 months, No Intention to Transplant or CART

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Second Line Therapy, Relapsed Disease >12 months, Intention to Transplant

1. Kewalramani T, Zelenetz AD, Nimer SD, et al. Rituximab and ICE as second-line therapy before autologous stem cell transplantation for relapsed or primary refractory diffuse large B-cell lymphoma. *Blood*. 2004;103(10):3684-3688. doi:10.1182/blood-2003-11-3911.
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3. Velasquez WS, Cabanillas F, Salvador P, et al. Effective salvage therapy for lymphoma with cisplatin in combination with high-dose Ara-C and dexamethasone (DHAP). *Blood*. 1988;71(1):117-122. Available at: <https://www.sciencedirect.com/science/article/pii/S0006497120782327?via%3Dihub>.
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References – Endometrial Cancer

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pMMR, Stage IVB, Checkpoint Inhibitor Planned, Recurrent/Metastatic: First Line Therapy

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References – Esophageal and Esophagogastric Junction (GEJ) Cancer

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Unresectable/Recurrent/Metastatic: First Line, Adenocarcinoma, HER2 Negative, MSS

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Unresectable/Recurrent/Metastatic: First Line, Squamous Cell, MSS

1. Lorenzen S, Schuster T, Porschen R, et al. Cetuximab plus cisplatin-5-fluorouracil versus cisplatin-5-fluorouracil alone in first-line metastatic squamous cell carcinoma of the esophagus: a randomized phase II study of the Arbeitsgemeinschaft Internistische Onkologie. *Ann Oncol*. 2009;20(10):1667-1673. doi:10.1093/annonc/mdp069.
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a global, randomised, placebo-controlled, phase 3 study. *Lancet Oncol.* 2023;24(5):483-495. doi:10.1016/S1470-2045(23)00108-0. Erratum in: *Lancet Oncol.* 2024;25(3):e102. doi:10.1016/S1470-2045(24)00018-4.

Unresectable/Recurrent/Metastatic: Second Line or Subsequent Therapy, Squamous Cell

1. Hironaka S, Ueda S, Yasui H, et al. Randomized, open-label, phase III study comparing irinotecan with paclitaxel in patients with advanced gastric cancer without severe peritoneal metastasis after failure of prior combination chemotherapy using fluoropyrimidine plus platinum: WJOG 4007 trial. *J Clin Oncol.* 2013;31(35):4438-4444. doi:10.1200/JCO.2012.48.5805.
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References – Follicular B-Cell Lymphoma

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Grade 1-2 Disease: First Line

1. Hiddemann W, Barbui AM, Canales MA, et al. Immunochemotherapy with obinutuzumab or rituximab for previously untreated follicular lymphoma in the GALLIUM study: influence of chemotherapy on efficacy and safety. *J Clin Oncol*. 2018;36(23):2395-2404. doi:10.1200/JCO.2017.76.8960.
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References – Head and Neck Cancer

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Advanced Disease: Definitive Chemoradiation

1. Bernier J, Domette C, Ozsahin M, et al. Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. *N Engl J Med*. 2004;350(19):1945-1952. doi:10.1056/NEJMoa032641.
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References – Hepatocellular Carcinoma

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Metastatic or Unresectable Disease: First Line

1. Llovet JM, Ricci S, Mazzaferro V, et al. Sorafenib in advanced hepatocellular carcinoma. *N Eng J Med*. 2008;359(4):378-390. doi:10.1056/NEJMoa0708857.
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References – Hodgkin Lymphoma

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Stage III/IV Classical Hodgkin Lymphoma – Ages 18-60 years old

1. Gordon LI, Hong F, Fisher RI, et al. Randomized phase III trial of ABVD versus Stanford V with or without radiation therapy in locally extensive and advanced-stage Hodgkin lymphoma: an intergroup study coordinated by the Eastern Cooperative Oncology Group (E2496). *J Clin Oncol*. 2013;31(6):684-691. doi:10.1200/JCO.2012.43.4803.
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References – Kidney Cancer

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Clear Cell, First Line: Favorable Risk

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Clear Cell, First Line: Intermediate/Poor Risk

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References – Lung Cancer: NSCLC

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Metastatic: First Line, Squamous or Nonsquamous, PD-L1 $\geq$ 50%, No Actionable Mutations

1. Reck M, Rodríguez-Abreu D, Robinson AG, et al. Pembrolizumab versus chemotherapy for PD-L1-positive non-small-cell lung cancer. *N Eng J Med*. 2016;375(19):1823-1833. doi:10.1056/NEJMoa1606774.
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Metastatic: First Line, Squamous or Nonsquamous, PD-L1 TPS <50%, No Driver Mutation

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3. Paz-Ares L, Luft A, Vicente D, et al. Pembrolizumab plus chemotherapy for squamous non-small-cell lung cancer. *N Engl J Med*. 2018;379(21):2040-2051. doi:10.1056/NEJMoa1810865.
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Metastatic: Subsequent Therapy, Squamous or Nonsquamous, No Actionable Mutation

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References – Melanoma

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References – Multiple Myeloma

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First Line: Transplant Eligible

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First Line: Transplant Deferred or Not Indicated

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References – Neuroendocrine Cancer

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Metastatic, Poorly-Differentiated, Large or Small Cell (Extrapulmonary)

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References – Ovarian Cancer

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Primary Therapy: Stage II-IV

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Recurrent Disease, Platinum Sensitive

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