



MEDICAL ONCOLOGY VALUE-BASED PATHWAYS

Evicore Oncology Value-Based Pathways

Effective: August 1, 2024

VERSION 1.0.2024



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.

EviCore's Clinical Review Criteria ("CRC") and related content is made available for the limited uses of: reference; and individual use, only limited to facilitating the determination of medically necessary and appropriate clinical treatment by clinicians for specific delegated patients under their care. The CRC and related content is proprietary information of eviCore, and copyrighted to the full extent of the law. Except as expressly permitted, you may not modify, copy, reproduce, republish, upload, post, transmit, hyperlink to or from, or distribute in any way the CRC, nor may you sell, transfer, distribute, assign, lease, reproduce, or otherwise use the CRC in commerce, in a manner that competes with us or infringes upon our rights, or for any public or commercial endeavor without our prior and express written consent.

CPT® (Current Procedural Terminology) is a registered trademark of the American Medical Association (AMA). CPT® five-digit codes, nomenclature and other data are copyright 2024 American Medical Association. All Rights Reserved. No fee schedules, basic units, relative values or related listings are included in the CPT® book. AMA does not directly or indirectly practice medicine or dispense medical services. AMA assumes no liability for the data contained herein or not contained herein.

Table of Contents

Guideline	Page
Medical Oncology Value-Based Pathways - General Information.....	3
Pathways by Cancer Type.....	5
References for Pathways by Cancer Type.....	32

Medical Oncology Value-Based Pathways - General Information

Guideline	Page
Medical Oncology Value-Based Pathways.....	4

Medical Oncology Value-Based Pathways

MEDONC.VBPW.A**v1.0.2024**

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.

Evicore Oncology Value-Based Pathways

Pathways by Cancer Type

Guideline	Page
Anal Cancer Pathways.....	6
Biliary Tract Cancers (Gallbladder/Cholangiocarcinoma) Pathways.....	7
Bladder Cancer Pathways.....	8
Breast Cancer Pathways.....	9
Chronic Myeloid Leukemia Pathways.....	10
Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Pathways.....	11
Colorectal Cancer Pathways.....	12
Diffuse Large B-Cell Lymphoma Pathways.....	13
Endometrial Cancer Pathways.....	14
Esophageal and Esophagogastric Junction Cancer Pathways.....	15
Follicular B-Cell Lymphoma Pathways.....	17
Head and Neck Cancer Pathways.....	18
Hepatocellular Carcinoma Pathways.....	19
Hodgkin's Lymphoma Pathways.....	20
Kidney Cancer Pathways.....	21
Lung Cancer: Non-Small Cell Lung Cancer Pathways.....	22
Lung Cancer: Small Cell Lung Cancer Pathways.....	23
Myelodysplastic Syndrome (MDS) Pathways.....	24
Melanoma Pathways.....	25
Multiple Myeloma Pathways.....	26
Neuroendocrine Cancer Pathways.....	27
Ovarian Cancer Pathways.....	28
Pancreatic Cancer Pathways.....	29
Prostate Cancer Pathways.....	30
Testicular Cancer Pathways.....	31

Anal Cancer Pathways

MEDONC.VBPW.A
v1.0.2024

Localized Disease: Definitive Chemoradiation	Advanced/Metastatic: First Line	Advanced/Metastatic: Subsequent Therapy
• Mitomycin + 5FU (fluorouracil)	• Carboplatin + paclitaxel	• Nivolumab
• Mitomycin + capecitabine		

Biliary Tract Cancers (Gallbladder/Cholangiocarcinoma) Pathways

MEDONC.VBPW.A
v1.0.2024

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

Bladder Cancer Pathways

MEDONC.VBPW.A
v1.0.2024

Neoadjuvant/ Adjuvant Therapy	Advanced/ Metastatic: First Line, Cisplatin eligible	Advanced/ Metastatic: First Line, Cisplatin ineligible	Advanced/ Metastatic: Subsequent Therapy, Post- Platinum
• DDMVAC (dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin)	• Pembrolizumab + enfortumab vedotin	• Pembrolizumab + enfortumab vedotin	• Pembrolizumab (only if no prior CPI)
• Cisplatin + gemcitabine	• Nivolumab + gemcitabine + cisplatin	• Pembrolizumab	• Paclitaxel
	• Gemcitabine + cisplatin	• Gemcitabine + carboplatin	• Docetaxel
	• Avelumab maintenance (if no progression on platinum-based chemotherapy)	• Gemcitabine + paclitaxel	• Gemcitabine
		• Gemcitabine	

Evicore Oncology Value-Based Pathways

Breast Cancer Pathways

MEDONC.VBPW.A
v1.0.2024

Advanced/ Metastatic: HER2 Positive, First Line	Advanced/ Metastatic: HER2 Negative	Neoadjuvant/ Adjuvant: HER2 Negative	Advanced/ Metastatic: HER2 Positive, Second Line and beyond	Advanced/ Metastatic: HER2 Positive, Third Line and beyond
• Docetaxel + Trastuzumab [*] + Pertuzumab [§]	• Docetaxel	• TC (docetaxel and cyclophosphamide)	• Fam- trastuzumab deruxtecan	• Ado- trastuzumab emtansine
• Paclitaxel + Trastuzumab [*] + Pertuzumab [§]	• Paclitaxel	• Dose Dense AC (doxorubicin and cyclophosphamide) followed by weekly paclitaxel		• Chemo + Trastuzumab [*]
	• Gemcitabine			• Lapatinib + Trastuzumab [*]
	• Vinorelbine			
	• Capecitabine			
	• Doxorubicin			
	• Liposomal 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.

Chronic Myeloid Leukemia Pathways

MEDONC.VBPW.A

v1.0.2024

First Line: Low Risk Score Disease

- Imatinib

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Pathways

MEDONC.VBPW.A
v1.0.2024

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.

Colorectal Cancer Pathways

MEDONC.VBPW.A
v1.0.2024

Metastatic disease: First/ second line RAS/RAF wild type	Metastatic disease: RAS/ RAF mutant or unknown subsequent therapy	Advanced/Metastatic: dMMR/MSI-H or POLE/ POLD1 mutation
• FOLFIRI + Panitumumab	• Bevacizumab [*] + FOLFIRI	• Pembrolizumab
• FOLFOX + Panitumumab	• 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

MEDONC.VBPW.A
v1.0.2024

Subsequent Therapy: Transplant-Eligible	Subsequent Therapy: Transplant-Ineligible
• 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*

* 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

MEDONC.VBPW.A
v1.0.2024

Recurrent/Metastatic: First Line and Subsequent Therapy
• Carboplatin + Paclitaxel
• Carboplatin + Paclitaxel + Trastuzumab* (only for HER2 positive serous carcinoma)
• Cisplatin + Doxorubicin
• Paclitaxel
• Doxorubicin
• Topotecan
• Cisplatin
• Carboplatin

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

Esophageal and Esophagogastric Junction Cancer Pathways

MEDONC.VBPW.A

v1.0.2024

Advanced/ Metastatic: First Line, adenocarcinoma, HER2 Negative, MSS	Advanced/Metastatic: First Line, squamous cell, MSS	Advanced/Metastatic: Subsequent Therapy, adenocarcinoma or 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) CPS >5 only	• Pembrolizumab + FOLFOX (fluorouracil [5FU], leucovorin, and oxaliplatin) CPS >10 only	
• Nivolumab + CapeOx (capecitabine and oxaliplatin) CPS >5 only	• Pembrolizumab + CapeOx (capecitabine and oxaliplatin) CPS >10 only	
	• Pembrolizumab + Fluorouracil [5FU] or capecitabine + cisplatin CPS >10 only	
	• Nivolumab + FOLFOX (fluorouracil [5FU], leucovorin, and oxaliplatin)	
	• Nivolumab + CapeOx (capecitabine and oxaliplatin)	

Advanced/ Metastatic: First Line, adenocarcinoma, HER2 Negative, MSS	Advanced/Metastatic: First Line, squamous cell, MSS	Advanced/Metastatic: Subsequent Therapy, adenocarcinoma or squamous cell
	• Nivolumab + Fluorouracil [5FU] or capecitabine + cisplatin	

Follicular B-Cell Lymphoma Pathways

MEDONC.VBPW.A
v1.0.2024

First Line: Grade 1-2
• 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

MEDONC.VBPW.A
v1.0.2024

Advanced Disease: Definitive Chemoradiation
• High dose cisplatin
• Carboplatin + infusional 5FU
• Weekly cisplatin
• Weekly carboplatin + paclitaxel

Hepatocellular Carcinoma Pathways

MEDONC.VBPW.A
v1.0.2024

Metastatic/unresectable disease: First line	Metastatic/unresectable disease: Subsequent therapy
• Lenvatinib	• Regorafenib
• Atezolizumab + Bevacizumab *	• Pembrolizumab
• Tremelimumab + 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’s Lymphoma Pathways

MEDONC.VBPW.A
v1.0.2024

Stage III/IV classical Hodgkin's lymphoma
• ABVD (Doxorubicin, Bleomycin, Vinblastine, and Dacarbazine)

Kidney Cancer Pathways

MEDONC.VBPW.A
v1.0.2024

First line: Good risk
• Sunitinib
• Pazopanib
• Lenvatinib + Pembrolizumab
• Cabozantinib + Nivolumab

Lung Cancer: Non-Small Cell Lung Cancer Pathways

MEDONC.VBPW.A
v1.0.2024

Table 1: Non-small Cell Lung Cancer Pathways: Nonsquamous

Advanced/Metastatic: First line, nonsquamous, PD-L1 ≥ 50%, no actionable mutations	Metastatic: First line, nonsquamous, PD-L1<50%, no driver mutation	Metastatic: Subsequent Therapy, nonsquamous, no actionable mutations
• Pembrolizumab	• Pembrolizumab + pemetrexed + (carboplatin or cisplatin)	• Nivolumab (only if no prior CPI)
• Cemiplimab	• Cemiplimab + pemetrexed + (carboplatin or cisplatin)	• Pembrolizumab (only if no prior CPI)
	• Cemiplimab + paclitaxel + (carboplatin or cisplatin)	• Pemetrexed
		• Gemcitabine
		• Docetaxel

Table 2: Non-small Cell Lung Cancer Pathways: Squamous

Advanced/Metastatic: First line, squamous, PD-L1 ≥ 50%, no actionable mutations	Metastatic: First line, squamous, PD-L1<50%, no driver mutation	Metastatic: Subsequent Therapy, squamous, no actionable mutations
• Pembrolizumab	• Pembrolizumab + paclitaxel + carboplatin	• Nivolumab (only if no prior CPI)
• Cemiplimab	• Cemiplimab + paclitaxel + (carboplatin or cisplatin)	• Pembrolizumab (only if no prior CPI)
		• Gemcitabine
		• Docetaxel

Lung Cancer: Small Cell Lung Cancer Pathways

MEDONC.VBPW.A
v1.0.2024

Limited Stage Disease	Extensive Stage Disease: First Line	Extensive Stage Disease: Subsequent Therapy
• Cisplatin + etoposide +/- radiation	• Atezolizumab + carboplatin + etoposide	• Cisplatin + etoposide (for relapse > 6 months)
• Carboplatin + etoposide +/- radiation	• Carboplatin + etoposide	• Carboplatin + etoposide (for relapse > 6 months)
		• Topotecan

Myelodysplastic Syndrome (MDS) Pathways

MEDONC.VBPW.A

v1.0.2024

IPSS-R: intermediate, high, very high, non-transplant candidate
• Azacitidine

Melanoma Pathways

MEDONC.VBPW.A
v1.0.2024

Metastatic: First line, BRAF mutation (+)	Metastatic: First line, BRAF mutation (-)
• Vemurafenib + Cobimetinib	• Pembrolizumab
• Pembrolizumab	• Nivolumab
• Nivolumab	• Ipilimumab + Nivolumab
• Ipilimumab + Nivolumab	

Multiple Myeloma Pathways

MEDONC.VBPW.A
v1.0.2022

First Line: Transplant Eligible	First Line: Transplant Ineligible
VRD: Bortezomib, Lenalidomide, and Dexamethasone	VRD: Bortezomib, Lenalidomide, and Dexamethasone
CyBorD: Bortezomib, Cyclophosphamide and Dexamethasone	RD: Lenalidomide and Dexamethasone

Neuroendocrine Cancer Pathways

MEDONC.VBPW.A
v1.0.2024

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

Ovarian Cancer Pathways

MEDONC.VBPW.A
v1.0.2024

Primary therapy: Stage II-IV	Recurrent disease, platinum sensitive
• Carboplatin + Taxol	• Carboplatin + Gemzar
	• Cisplatin + Gemzar
	• Carboplatin + Taxol

Pancreatic Cancer Pathways

MEDONC.VBPW.A
v1.0.2024

Neoadjuvant: Adenocarcinoma	Advanced/Metastatic: First line, adenocarcinoma
• Modified FOLFIRINOX (fluorouracil [5FU],leucovorin, irinotecan, and oxaliplatin)	• FOLFIRINOX or modified FOLFIRINOX
	• Gemcitabine + albumin-bound Paclitaxel

Prostate Cancer Pathways

MEDONC.VBPW.A
v1.0.2024

Metastatic: Adenocarcinoma, Castration Resistant
• Abiraterone
• Enzalutamide
• Docetaxel
• Cabazitaxel (prior docetaxel)

Testicular Cancer Pathways

MEDONC.VBPW.A
v1.0.2024

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

References for Pathways by Cancer Type

Guideline	Page
References – Anal Cancer.....	33
References – Biliary Tract Cancers.....	34
References – Bladder Cancer.....	35
References – Breast Cancer.....	37
References – Chronic Lymphocytic Leukemia (CLL).....	39
References – Chronic Myeloid Leukemia (CML).....	40
References – Colorectal Cancer.....	41
References – Diffuse Large B-Cell Lymphoma (DLCL).....	42
References – Endometrial Cancer.....	43
References – Esophageal and Esophagogastric Junction (GEJ) Cancer.....	45
References – Follicular Lymphoma.....	47
References – Head and Neck Cancer.....	48
References – Hepatocellular Carcinoma.....	49
References – Hodgkin’s Lymphoma.....	50
References – Kidney Cancer.....	51
References – Lung Cancer: NSCLC.....	52
References – Lung Cancer: SCLC.....	54
References – Myelodysplastic Syndrome (MDS).....	56
References – Melanoma.....	57
References – Multiple Myeloma.....	58
References – Neuroendocrine Cancer.....	59
References – Ovarian Cancer.....	60
References – Pancreatic Cancer.....	61
References – Prostate Cancer.....	62
References – Testicular Cancer.....	63

References – Anal Cancer

v1.0.2024

Localized Disease: Definitive Chemoradiation

1. Ajani JA, Winter KA, Gunderson LL, et al. Fluorouracil, mitomycin, and radiotherapy vs fluorouracil, cisplatin, and radiotherapy for carcinoma of the anal canal: a randomized controlled trial. *JAMA*. 2008;299(16):1914-1921. doi:10.1001/jama.299.16.1914.
2. Flam M, John M, Pajak TF, et al. Role of mitomycin in combination with fluorouracil and radiotherapy, and of salvage chemoradiation in the definitive nonsurgical treatment of epidermoid carcinoma of the anal canal: results of a phase III randomized intergroup study. *J Clin Oncol*. 1996;14(9):2527-2539. doi:10.1200/JCO.1996.14.9.2527.
3. Goodman KA, Rothenstein D, Laijhem C, Wu A, Cercek A, Saltz LB. Capecitabine plus mitomycin in patients undergoing definitive chemoradiation for anal squamous cell carcinoma. *Int J Radiat Oncol Phys*. 2014;90(1):S32-S33. doi:10.1016/j.ijrobp.2014.05.141.
4. Thind G, Johal B, Follwell M, Kennecke HF. Chemoradiation with capecitabine and mitomycin-C for stage I-III anal squamous cell carcinoma. *Radiat Oncol*. 2014;9:124. Published 2014 May 29. doi:10.1186/1748-717X-9-124.
5. Gunderson LL, Winter KA, Ajani JA, et al. Long-term update of US GI Intergroup RTOG 98-11 Phase III trial for anal carcinoma: survival, relapse, and colostomy failure with concurrent chemoradiation involving fluorouracil/mitomycin versus fluorouracil/cisplatin. *J Clin Oncol*. 2012;30(35):4344-4351. doi:10.1200/JCO.2012.43.8085.
6. James RD, Glynne-Jones R, Meadows HM, et al. Mitomycin or cisplatin chemoradiation with or without maintenance chemotherapy for treatment of squamous-cell carcinoma of the anus (ACT II): a randomized, phase 3, open-label, 2x2 factorial trial. *Lancet Oncol*. 2013;14(6):516-524. doi:10.1016/S1470-2045(13)70086-X.

Advanced/Metastatic: First Line

1. Rao S, Sclafani F, Eng C, et al. International Rare Cancers Initiative Multicenter Randomized Phase II Trial of Cisplatin and Fluorouracil Versus Carboplatin and Paclitaxel in Advanced Anal Cancer: InterAACT. *J Clin Oncol*. 2020;38(22):2510-2518. doi:10.1200/JCO.19.03266.
2. Mondaca S, Chatila WK, Bates D, et al. FOLFICIS Treatment and Genomic Correlates of Response in Advanced Anal Squamous Cell Cancer. *Clin Colorectal Cancer*. 2019;18(1):e39-e52. doi:10.1016/j.clcc.2018.09.005.
3. Kim S, François E, André T, et al. Docetaxel, cisplatin, and fluorouracil chemotherapy for metastatic or unresectable locally recurrent anal squamous cell carcinoma (Epitopes-HPV02): a multicenter, single-arm, phase 2 study. *Lancet Oncol*. 2018;19(8):1094-1106. doi:10.1016/S1470-2045(18)30321-8.
4. Kim S, Jary M, Mansi L, et al. DCF chemotherapy is a promising treatment for recurrent advanced squamous cell anal carcinoma. *Ann Oncol*. 2013;24(12):3045-3050. doi:10.1093/annonc/mdt396.

Advanced/Metastatic: Subsequent Therapy

1. Morris VK, Salem ME, Nimeiri H, et al. Nivolumab for previously treated unresectable metastatic anal cancer (NCI9673): a multicenter, single-arm, phase 2 study. *Lancet Oncol*. 2017;18(4):446-453. doi:10.1016/S1470-2045(17)30104-3.
2. Ott PA, Piha-Paul SA, Munster P, et al. Safety and antitumor activity of the anti-PD-1 antibody pembrolizumab in patients with recurrent carcinoma of the anal canal. *Ann Oncol*. 2017;28(5):1036-1041. doi:10.1093/annonc/mdx029.

References – Biliary Tract Cancers

v1.0.2024

Advanced/Metastatic: First Line

1. Valle J, Wasan H, Palmer DH, et al. Cisplatin plus gemcitabine versus gemcitabine for biliary tract cancer. *N Eng J Med*. 2010;362(14):1273-1281. doi:10.1056/NEJMoa0908721.
2. Sahai V, Catalano PJ, Zalupski MM, et al. Nap-paclitaxel and gemcitabine as first-line treatment of advanced or metastatic cholangiocarcinoma: a phase 2 clinical trial. *JAMA Oncol*. 2018;4(12):1707-1712. doi:10.1001/jamaoncol.2018.3277.
3. Sharma A, Dwary AD, Mohanti BK, et al. Best supportive care compared with chemotherapy for unresectable gall bladder cancer: a randomized controlled study. *J Clin Oncol*. 2010;28(30):4581-4586. doi:10.1200/JCO.2010.29.3605.
4. Oh D, Ruth He A, Qin S, et al. Durvalumab plus Gemcitabine and Cisplatin in Advanced Biliary Tract Cancer. *NEJM Evidence*. 2022;1(8):EVIDoa2200015. doi:10.1056/EVIDoa220001.
5. Kelley RK, Ueno M, Yoo C, et al. Pembrolizumab in combination with gemcitabine and cisplatin compared with gemcitabine and cisplatin alone for patients with advanced biliary tract cancer (KEYNOTE-966): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2023;401(10391):1853-1865. doi:10.1016/S0140-6736(23)00727-4.

Advanced/Metastatic: Subsequent Therapy

1. Lamarca A, Palmer DH, Wasan HS, et al. Second-line FOLFOX chemotherapy versus active symptom control for advanced biliary tract cancer (ABC-06): a phase 3, open-label, randomized, controlled trial. *Lancet Oncol*. 2021;22(5):690-701. doi:10.1016/S1470-2045(21)00027-9.
2. Demols A, Borbath I, Van den Eynde M, et al. Regorafenib after failure of gemcitabine and platinum-based chemotherapy for locally advanced/metastatic biliary tumors: REACHIN, a randomized, double-blind, phase II trial. *Ann Oncol*. 2020;31(9):1169-1177. doi:10.1016/j.annonc.2020.05.018.
3. Caparica R, Lengelé A, Bekolo W, Hendlisz A. FOLFIRI as second-line treatment of metastatic biliary tract cancer patients. *Autops Case Rep*. 2019;9(2):e2019087. Published 2019 Jun 24. doi:10.4322/acr.2019.087.
4. Yoo C, Kim KP, Jeong JH, et al. Liposomal irinotecan plus fluorouracil and leucovorin versus fluorouracil and leucovorin for metastatic biliary tract cancer after progression on gemcitabine plus cisplatin (NIFTY): a multicentre, open-label, randomised, phase 2b study. *Lancet Oncol*. 2021;22(11):1560-1572. doi:10.1016/S1470-2045(21)00486-1.
5. Kim RD, Chung V, Alese OB, et al. A Phase 2 Multi-institutional Study of Nivolumab for Patients With Advanced Refractory Biliary Tract Cancer. *JAMA Oncol*. 2020;6(6):888-894. doi:10.1001/jamaoncol.2020.0930.

References – Bladder Cancer

v1.0.2024

Neoadjuvant/Adjuvant Therapy

1. Sternberg CN, de Mulder PH, Schornagel JH, et al. Randomized phase III trial of high-dose-intensity methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC) chemotherapy and recombinant human granulocyte colony-stimulating factor versus classic MVAC in advanced urothelial tract tumors: European Organization for Research and Treatment of Cancer Protocol no. 30924. *J Clin Oncol*. 2001;19(10):2638-2646. doi:10.1200/JCO.2001.19.10.2638.
2. Von der Maase H, Hansen SW, Roberts JT, et al. Gemcitabine and cisplatin versus methotrexate, vinblastine, doxorubicin, and cisplatin in advanced or metastatic bladder cancer: results of a large, randomized, multinational, multicenter, phase III study. *J Clin Oncol*. 2000;18(17):3068-3077. doi:10.1200/JCO.2000.18.17.3068.
3. Pfister C, Gravis G, Flechon A, et al. 6520 Dose-dense methotrexate, vinblastine, doxorubicin and cisplatin (dd-MVAC) or gemcitabine and cisplatin (GC) as perioperative chemotherapy for patients with muscle-invasive bladder cancer (MIBC): Results of the GETUG/AFU VESPER V05 phase III trial. *Ann Oncol*. 2021;32(5):S678. doi:10.1016/j.annonc.2021.08.048.
4. Pfister C, Gravis G, Flechon A, et al. Perioperative dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin in muscle-invasive bladder cancer (VESPER): survival endpoints at 5 years in an open-label, randomised, phase 3 study. *Lancet Oncol*. 2024;25(2):255-264. doi:10.1016/S1470-2045(23)00587-9.

Advanced/Metastatic: First Line, Cisplatin Eligible

1. Sternberg CN, de Mulder PH, Schornagel JH, et al. Randomized phase III trial of high-dose-intensity methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC) chemotherapy and recombinant human granulocyte colony-stimulating factor versus classic MVAC in advanced urothelial tract tumors: European Organization for Research and Treatment of Cancer Protocol no. 30924. *J Clin Oncol*. 2001;19(10):2638-2646. doi:10.1200/JCO.2001.19.10.2638.
2. Von der Maase H, Hansen SW, Roberts JT, et al. Gemcitabine and cisplatin versus methotrexate, vinblastine, doxorubicin, and cisplatin in advanced or metastatic bladder cancer: results of a large, randomized, multinational, multicenter, phase III study. *J Clin Oncol*. 2000;18(17):3068-3077. doi:10.1200/JCO.2000.18.17.3068.
3. Powles T, Park SH, Voog E, et al. Avelumab maintenance therapy for advanced or metastatic urothelial carcinoma. *N Eng J Med*. 2020;383(13):1218-1230. doi:10.1056/NEJMoa2002788.
4. Powles T, Valderrama BP, Gupta S, et al. Enfortumab Vedotin and Pembrolizumab in Untreated Advanced Urothelial Cancer. *N Engl J Med*. 2024;390(10):875-888. doi:10.1056/NEJMoa2312117.
5. van der Heijden MS, Sonpavde G, Powles T, et al. Nivolumab plus Gemcitabine-Cisplatin in Advanced Urothelial Carcinoma. *N Engl J Med*. 2023;389(19):1778-1789. doi:10.1056/NEJMoa2309863.

Advanced/Metastatic: First Line, Cisplatin Ineligible

1. Balar AV, Galsky MD, Rosenberg JE, et al. Atezolizumab as first-line treatment in cisplatin-ineligible patients with locally advanced and metastatic urothelial carcinoma: a single-arm multicentre, phase 2 trial. *Lancet*. 2017;389(10064):67-76. doi:10.1016/S0140-6736(16)32455-2.
2. Grande E, Arranz JA, De Santis M, et al. Atezolizumab plus chemotherapy versus placebo plus chemotherapy in untreated locally advanced or metastatic urothelial carcinoma (IMvigor130): final overall survival analysis results from a randomised, controlled, phase 3 study. *Lancet Oncol*. 2024;25(1):29-45. doi:10.1016/S1470-2045(23)00540-5.
3. Balar AV, Castellano D, O'Donnell PH, et al. First-line pembrolizumab in cisplatin-ineligible patients with locally advanced and unresectable or metastatic urothelial cancer (KEYNOTE-052): a multicentre, single-arm, phase 2 study. *Lancet Oncol*. 2017;18(11):1483-1492. doi:10.1016/S1470-2045(17)30616-2.

4. Powles T, Csőszi T, Özgüroğlu M, et al. Pembrolizumab alone or combined with chemotherapy versus chemotherapy as first-line therapy for advanced urothelial carcinoma (KEYNOTE-361): a randomized, open-label, phase 3 trial. *Lancet Oncol.* 2021;22(7):931-945. doi:10.1016/S1470-2045(21)00152-2.
5. De Santis M, Bellmunt J, Mead G, et al. Randomized phase II/III trial assessing gemcitabine/carboplatin and methotrexate/carboplatin/vinblastine in patients with advanced urothelial cancer who are unfit for cisplatin-based chemotherapy: EORTC study 30986. *J Clin Oncol.* 2012;30(2):191-199. doi:10.1200/JCO.2011.37.3571.
6. Stadler WM, Kuzel T, Roth B, Raghavan D, Dorr FA. Phase II study of single-agent gemcitabine in previously untreated patients with metastatic urothelial cancer. *J Clin Oncol.* 1997;15(11):3394-3398. doi:10.1200/JCO.1997.15.11.3394.
7. Albers P, Park SI, Niegisch G, et al. Randomized phase III trial of 2nd line gemcitabine and paclitaxel chemotherapy in patients with advanced bladder cancer: short-term versus prolonged treatment [German Association of Urological Oncology (AUO) trial AB 20/99]. *Ann Oncol.* 2011;22(2):288-294. doi:10.1093/annonc/mdq398.
8. Siefker-Radtke AO, Dinney CP, Shen Y, et al. A phase 2 clinical trial of sequential neoadjuvant chemotherapy with ifosfamide, doxorubicin, and gemcitabine followed by cisplatin, gemcitabine, and ifosfamide in locally advanced urothelial cancer: final results. *Cancer.* 2013;119(3):540-547. doi:10.1002/cncr.27751.

Advanced/Metastatic: Subsequent Therapy, Post-Cisplatin

1. Bellmunt J, de Wit R, Vaughn DJ, et al. Pembrolizumab as second-line therapy for advanced urothelial carcinoma. *N Eng J Med.* 2017;376(11):1015-1026. doi:10.1056/NEJMoa1613683.
2. Sharma P, Retz M, Siefker-Radtke A, et al. Nivolumab in metastatic urothelial carcinoma after platinum therapy (CheckMate 275): A multicentre, single-arm, phase 2 trial. *Lancet Oncol.* 2017;18(3):312-322. doi:10.1016/S1470-2045(17)30065-7.
3. Patel MR, Ellerton J, Infante JR, et al. Avelumab in metastatic urothelial carcinoma after platinum failure (JAVELIN Solid Tumor): pooled results from two expansion cohorts of an open-label, phase 1 trial. *Lancet Oncol.* 2018;19(1):51-64. doi:10.1016/S1470-2045(17)30900-2.
4. Stadler WM, Kuzel T, Roth B, Raghavan D, Dorr FA. Phase II study of single-agent gemcitabine in previously untreated patients with metastatic urothelial cancer. *J Clin Oncol.* 1997;15(11):3394-3398. doi:10.1200/JCO.1997.15.11.3394.
5. Sideris S, Aoun F, Zanaty M, et al. Efficacy of weekly paclitaxel treatment as a single agent chemotherapy following first-line cisplatin treatment in urothelial bladder cancer. *Mol Clin Oncol.* 2016;4(6):1063-1067. doi:10.3892/mco.2016.821.
6. McCaffrey JA, Hilton S, Mazumdar M, et al. Phase ii trial of docetaxel in patients with advanced or metastatic transitional-cell carcinoma. *J Clin Oncol.* 1997;15(5):1853-1857. doi:10.1200/JCO.1997.15.5.1853.
7. Yu EY, Petrylak DP, O'Donnell PH, et al. Enfortumab vedotin after PD-1 or PD-L1 inhibitors in cisplatin-ineligible patients with advanced urothelial carcinoma (EV#201): a multicentre, single-arm, phase 2 trial. *Lancet Oncol.* 2021;22(6):872-882. doi:10.1016/S1470-2045(21)00094-2.

References – Breast Cancer

v1.0.2024

Neoadjuvant/Adjuvant: HER2 Negative

1. Citron ML, Berry DA, Cirincione C, et al. Randomized trial of dose-dense versus conventionally scheduled and sequential versus concurrent combination chemotherapy as postoperative adjuvant treatment of node-positive primary breast cancer: first report of Intergroup Trial C9741/Cancer and Leukemia Group B Trial 9741. *J Clin Oncol.* 2003;21(8):1431-1439. doi:10.1200/JCO.2003.09.081.
2. Sparano JA, Wang M, Martino S, et al. Weekly paclitaxel in adjuvant treatment of breast cancer. *N Eng J Med.* 2008;358(16):1663-1671. doi:10.1056/NEJMoa0707056.
3. Budd GT, Barlow WE, Moore HC, et al. SWOG S0221: a phase III trial comparing chemotherapy schedules in high-risk early-stage breast cancer. *J Clin Oncol.* 2015;33(1):58-64. doi:10.1200/JCO.2014.56.3296.
4. Jones S, Holmes FA, O'Shaughnessy J, et al. Docetaxel With Cyclophosphamide Is Associated With an Overall Survival Benefit Compared With Doxorubicin and Cyclophosphamide: 7-Year Follow-Up of US Oncology Research Trial 9735. *J Clin Oncol.* 2009;27(8):1177-1183. doi:10.1200/JCO.2008.18.4028.

HER2 Positive Metastatic Disease

1. Swain SM, Miles D, Kim SB, et al. Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA): end-of-study results from a double-blind, randomised, placebo-controlled, phase 3 study. *Lancet Oncol.* 2020;21(4):519-530. doi:10.1016/S1470-2045(19)30863-0.
2. Swain S, Kim S-B, Cortes J, et al. Abstract P5-18-26: Confirmatory overall survival (OS) analysis of CLEOPATRA: a randomized, double-blind, placebo-controlled Phase III study with pertuzumab (P), trastuzumab (T), and docetaxel (D) in patients (pts) with HER2-positive first-line (1L) metastatic breast cancer (MBC). *Cancer Res.* 2012;72(24_Supplement):P5-1826-P518-26.
3. Bachelot T, Ciruelos E, Schneeweiss A, et al. Preliminary safety and efficacy of first-line pertuzumab combined with trastuzumab and taxane therapy for HER2-positive locally recurrent or metastatic breast cancer (PERUSE). *Ann Oncol.* 2019;30(5):766-773. doi:10.1093/annonc/mdz061.
4. Baselga J, Cortés J, Kim SB, et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. *N Eng J Med.* 2012;366(2):109-119. doi:10.1056/NEJMoa1113216.
5. Verma S, Miles D, Gianni L, et al. Trastuzumab emtansine for HER2-positive advanced breast cancer. *N Eng J Med.* 2012;367(19):1783-1791. doi:10.1056/NEJMoa1209124.
6. Modi S, Saura C, Yamashita T, et al. Trastuzumab deruxtecan in previously treated HER2-positive advanced breast cancer. *N Eng J Med.* 2020;382(7):610-621. doi:10.1056/NEJMoa1914510.
7. Cortés J, Kim SB, Chung WP, et al. Trastuzumab Deruxtecan versus Trastuzumab Emtansine for Breast Cancer. *N Engl J Med.* 2022;386(12):1143-1154. doi:10.1056/NEJMoa2115022
8. Murthy RK, Loi S, Okines A, et al. Tucatinib, trastuzumab, and capecitabine for HER-2 positive metastatic breast cancer. *N Eng J Med.* 2020;382(7):597-609. doi:10.1056/NEJMoa1914609.
9. Blackwell KL, Burstein HJ, Storniolo AM, et al. Overall survival benefit with lapatinib in combination with trastuzumab for patients with human epidermal growth factor receptor 2-positive metastatic breast cancer: final results from the EFG104900 study. *J Clin Oncol.* 2012;30(21):2585-2592. doi:10.1200/JCO.2011.35.6725.
10. Geyer CE, Forster J, Lindquist D, et al. Lapatinib plus capecitabine for HER2-Positive advanced breast cancer. *N Eng J Med.* 2006;355(26):2733-2743. doi:10.1056/NEJMoa064320.
11. Saura C, Oliveira M, Feng YH, et al. Neratinib + capecitabine versus lapatinib + capecitabine in patients with HER2+ metastatic breast cancer previously treated with ≥ HER2-directed regimens: Findings from the multinational, randomized, phase III NALA trial. *J Clin Oncol.* 2019;37(15_suppl):1002-1002. doi:10.1200/JCO.2019.37.15_suppl.1002.
12. Rugo HS, Im SA, Cardoso F, et al. Efficacy of margetuximab vs trastuzumab in patients with pretreated ERBB2-positive advanced breast cancer. *JAMA Oncol.* 2021;7(4):573-584. doi:10.1001/jamaoncol.2020.7932.

HER2 Negative Metastatic Disease

1. Seidman AD, Tiersten A, Hudis C, et al. Phase II Trial of Paclitaxel by 3-Hour Infusion as Initial and Salvage Chemotherapy for Metastatic Breast Cancer. *J Clin Oncol*. 1995;13(10):2575-2581. doi:10.1200/JCO.1995.13.10.2575.
2. Perez EA, Vogel CL, Irwin DH, Kirshner JJ, Patel R. Multicenter Phase II Trial of Weekly Paclitaxel in Women with Metastatic Breast Cancer. *J Clin Oncol*. 2001;19(22):4216-4223. doi:10.1200/JCO.2001.19.22.4216.
3. Burris HA 3rd. Single-agent docetaxel (Taxotere) in randomized phase III trials. *Semin Oncol*. 1999;26(3 Suppl 9):1-6. Available at: <https://pubmed.ncbi.nlm.nih.gov/10426452/>.
4. Harvey V, Mouridsen H, Semiglazov V, et al. Phase III trial comparing three doses of docetaxel for second-line treatment of advanced breast cancer. *J Clin Oncol*. 2006;24(31):4963-4970. doi:10.1200/JCO.2005.05.0294.
5. Rivera E, Mejia JA, Arun BK, et al. Phase 3 study comparing the use of docetaxel on an every-3-week versus weekly schedule in the treatment of metastatic breast cancer. *Cancer*. 2008;112(7):1455-1461. doi:10.1002/cncr.23321.
6. Chan S, Friedrichs K, Noel D, et al. Prospective randomized trial of docetaxel versus doxorubicin in patients with metastatic breast cancer. *J Clin Oncol*. 1999;17(8):2341-2354. doi:10.1200/JCO.1999.17.8.2341.
7. Gasparini G, Dal Fior S, Panizzoni GA, Favretto S, Pozza F. Weekly epirubicin versus doxorubicin as second line therapy in advanced breast cancer. A randomized clinical trial. *Am J Clin Oncol*. 1991;14(1):38-44. doi:10.1097/00000421-199102000-00009.
8. O'Brien ME, Wigler N, Inbar M, et al. Reduced cardiotoxicity and comparable efficacy in a phase III trial of pegylated liposomal doxorubicin HCL versus conventional doxorubicin for first-line treatment of metastatic breast cancer. *Ann Oncol*. 2004;15(3):440-449. doi:10.1093/annonc/mdh097.
9. Seidman AD. Gemcitabine as single-agent therapy in the management of advanced breast cancer. *Oncology*. 2001;15(2):11-14. Available at: <https://www.cancernetwork.com/view/gemcitabine-single-agent-therapy-management-advanced-breast-cancer>.
10. Zelek L, Barthier S, Riofrio M, et al. Weekly vinorelbine is an effective palliative regimen after failure with anthracyclines and taxanes in metastatic breast carcinoma. *Cancer*. 2001;92(9):2267-2272. doi:10.1002/1097-0142(20011101)92:9<2267::aid-cncr1572>3.0.co;2-q.
11. Bajetta E, Procopio G, Celio L, et al. Safety and efficacy of two different doses of capecitabine in the treatment of advanced breast cancer in older women. *J Clin Oncol*. 2005;23(10):2155-2161. doi:10.1200/JCO.2005.02.167.
12. Gradishar WJ, Tjulandin S, Davidson N, et al. Phase III trial of nanoparticle albumin-bound paclitaxel compared with polyethylated castor oil-based paclitaxel in women with breast cancer. *J Clin Oncol*. 2005;23(31):7794-7803. doi:10.1200/JCO.2005.04.937.
13. Perez EA, Lerzo G, Pivot X, et al. Efficacy and safety of ixabepilone (BMS-247550) in a phase II study of patients with advanced breast cancer resistant to an anthracycline, a taxane, and capecitabine. *J Clin Oncol*. 2007;25(23):3407-3414. doi:10.1200/JCO.2006.09.3849.
14. Cortes J, O'Shaughnessy J, Loesch D, et al. Eribulin monotherapy versus treatment of physician's choice in patients with metastatic breast cancer (EMBRACE): a phase 3 open-label randomised study. *Lancet*. 2011;377(9769):914-923. doi:10.1016/S0140-6736(11)60070-6.

References – Chronic Lymphocytic Leukemia (CLL)

v1.0.2024

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

1. Burger JA, Tedeschi A, Barr PM, et al. Ibrutinib as initial therapy for patients with chronic lymphocytic leukemia. *N Eng J Med*. 2015;373(25):2425-2437. doi:10.1056/NEJMoa1509388.
2. Burger JA, Barr PM, Robak T, et al. Long-term efficacy and safety of first-line ibrutinib treatment for patients with CLL/SLL: 5 years of follow-up from the phase 3 RESONATE-2 study. *Leukemia*. 2020;34(3):787-798. doi:10.1038/s41375-019-0602-x.
3. Fischer K, Al-Sawaf O, Bahlo J, et al. Venetoclax and obinutuzumab in patients with CLL and coexisting conditions. *N Eng J Med*. 2019;380(23):2225-2236. doi:10.1056/NEJMoa1815281.
4. Al-Sawaf O, Zhang C, Tandon M, et al. Venetoclax plus obinutuzumab versus chlorambucil plus obinutuzumab for previously untreated chronic lymphocytic leukaemia (CLL14): follow-up results from a multicentre, open-label, randomised, phase 3 trial. *Lancet Oncol*. 2020;21(9):1188-1200. doi:10.1016/S1470-2045(20)30443-5.
5. Awan FT, Schuh A, Brown JR, et al. Acalabrutinib monotherapy in patients with chronic lymphocytic leukemia who are intolerant to ibrutinib. *Blood Adv*. 2019;3(9):1553-1562. doi:10.1182/bloodadvances.2018030007.
6. Sharman JP, Egyed M, Jurczak W, et al. Acalabrutinib with or without obinutuzumab versus chlorambucil and obinutuzumab for treatment-naïve chronic lymphocytic leukaemia (ELEVATE TN): a randomised, controlled, phase 3 trial. *Lancet*. 2020;395(10232):1278-1291. doi:10.1016/S0140-6736(20)30262-2.
7. Tam C, et al. Zanubrutinib versus bendamustine and rituximab in untreated chronic lymphocytic leukaemia and small lymphocytic lymphoma (SEQUOIA): a randomised, controlled, phase 3 trial. *Lancet Oncol*. 2022;23(8):1031-1043. doi:10.1016/S1470-2045(22)00293-5.
8. Sharman JP, Burke JM, Yimer HA, et al. Phase 2, multicenter GIBB study of obinutuzumab plus bendamustine in previously untreated patients with chronic lymphocytic leukemia. *Leuk Lymphoma*. 2021;62(4):791-800. doi:10.1080/10428194.2020.1850719.
9. Michallet AS, Aktan M, Hiddemann W, et al. Rituximab plus bendamustine or chlorambucil for chronic lymphocytic leukemia: primary analysis of the randomized, open-label MABLE study. *Haematologica*. 2018;103(4):698-706. doi:10.3324/haematol.2017.170480.
10. Moreno C, Greil R, Demirkan F, et al. Ibrutinib plus obinutuzumab versus chlorambucil plus obinutuzumab in first-line treatment of chronic lymphocytic leukaemia (iLLUMINATE): a multicentre, randomised, open-label, phase 3 trial. *Lancet Oncol*. 2019;20(1):43-56. doi:10.1016/S1470-2045(18)30788-5.
11. Shanafelt TD, Wang XV, Kay NE, et al. Ibrutinib-Rituximab or Chemoimmunotherapy for Chronic Lymphocytic Leukemia. *N Engl J Med*. 2019;381(5):432-443. doi:10.1056/NEJMoa1817073.
12. Wierda WG, Allan JN, Siddiqi T, et al. Ibrutinib Plus Venetoclax for First-Line Treatment of Chronic Lymphocytic Leukemia: Primary Analysis Results From the Minimal Residual Disease Cohort of the Randomized Phase II CAPTIVATE Study. *J Clin Oncol*. 2021;39(34):3853-3865. doi:10.1200/JCO.21.00807.

References – Chronic Myeloid Leukemia (CML)

v1.0.2024

First Line: Low Risk Score Disease

1. O'Brien SG, Guilhot F, Larson RA, et al. Imatinib compared with interferon and low-dose cytarabine for newly diagnosed chronic-phase chronic myeloid leukemia. *N Eng J Med*. 2003;348(11):994-1004. doi:10.1056/NEJMoa022457.
2. Jabbour E, Kantarjian HM, Jones D, et al. Imatinib mesylate dose escalation is associated with durable responses in patients with chronic myeloid leukemia after cytogenetic failure on standard-dose imatinib therapy. *Blood*. 2009;113(10):2154-2160. doi:10.1182/blood-2008-04-154344.
3. Cortes JE, Saglio G, Kantarjian HM, et al. Final 5-year study results of DASISION: the dasatinib versus imatinib study in treatment-naïve chronic myeloid leukemia patients trial. *J Clin Oncol*. 2016;34(20):2333-2340. doi:10.1200/JCO.2015.64.8899.
4. Hochhaus A, Saglio G, Hughes TP, et al. Long-term benefits and risks of frontline nilotinib vs imatinib for chronic myeloid leukemia in chronic phase: 5-year update of the randomized ENESTnd trial. *Leukemia*. 2016;30(5):1044-1054. doi:10.1038/leu.2016.5.
5. Cortes JE, Gambacorti-Passerini C, Deininger MW, et al. Bosutinib versus imatinib for newly diagnosed chronic myeloid leukemia: results from the randomized BFORE trial. *J Clin Oncol*. 2018;36(3):231-237. doi:10.1200/JCO.2017.74.7162.

References – Colorectal Cancer

v1.0.2024

Metastatic Disease: First/Second Line RAS/RAF Wild Type

1. Qin S, Li J, Wang L, et al. Efficacy and Tolerability of First-Line Cetuximab Plus Leucovorin, Fluorouracil, and Oxaliplatin (FOLFOX-4) Versus FOLFOX-4 in Patients With RAS Wild-Type Metastatic Colorectal Cancer: The Open-Label, Randomized, Phase III TAILOR Trial. *J Clin Oncol*. 2018;36(30):3031-3039. doi:10.1200/JCO.2018.78.3183.
2. Douillard JY, Siena S, Cassidy J, et al. Final results from PRIME: randomized phase III study of panitumumab with FOLFOX4 for first-line treatment of metastatic colorectal cancer. *Ann Oncol*. 2014;25(7):1346-1355. doi:10.1093/annonc/mdu141.
3. Bylsma L, Dean R, Lowe K, Sangaré L, Alexander DD, Fryzek JP. The incidence of infusion reactions associated with monoclonal antibody drugs targeting the epidermal growth factor receptor in metastatic colorectal cancer patients: A systematic literature review and meta-analysis of patient and study characteristics. *Cancer Med*. 2019;8(12):5800-5809. doi:10.1002/cam4.2413.

Metastatic Disease: RAS/RAF Mutant or Unknown Subsequent Therapy

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.
2. Tabernero J, Yoshino T, Cohn AL, 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;16(5):499-508. doi:10.1016/S1470-2045(15)70127-0.
3. Tabernero J, Van Cutsem E, Lakomý R, et al. Aflibercept versus placebo in combination with fluorouracil, leucovorin and irinotecan in the treatment of previously treated metastatic colorectal cancer: prespecified subgroup analyses from the VELOUR trial. *Eur J Cancer*. 2014;50(2):320-331. doi:10.1016/j.ejca.2013.09.013.

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.
2. Lenz HJ, Van Cutsem E, Luisa Limon M, et al. First-Line Nivolumab Plus Low-Dose Ipilimumab for Microsatellite Instability-High/Mismatch Repair-Deficient Metastatic Colorectal Cancer: The Phase II CheckMate 142 Study. *J Clin Oncol*. 2022;40(2):161-170. doi:10.1200/JCO.21.01015.

References – Diffuse Large B-Cell Lymphoma (DBCL)

v1.0.2024

Subsequent Therapy: No Intention to Proceed to Transplant

1. López A, Gutiérrez A, Palacios A, et al. GEMOX-R regimen is a highly effective salvage regimen in patients with refractory/relapsing diffuse large-cell lymphoma: a phase II study. *Eur J Haematol*. 2008;80(2):127-132. doi:10.1111/j.1600-0609.2007.00996.x
2. Gopal AK, Press OW, Shustov AR, et al. Efficacy and safety of gemcitabine, carboplatin, dexamethasone, and rituximab in patients with relapsed/refractory lymphoma: a prospective multi-center phase II study by the Puget Sound Oncology Consortium. *Leuk Lymphoma*. 2010;51(8):1523-1529. doi:10.3109/10428194.2010.491137.
3. Sehn LH, Herrera AF, Flowers CR, et al. Polatuzumab vedotin in relapsed or refractory diffuse large B-cell lymphoma. *J Clin Oncol*. 2020;38(2):155-165. doi:10.1200/JCO.19.00172.
4. Salles G, Duell J, González Barca E, et al. Tafasitamab plus lenalidomide in relapsed or refractory diffuse large B-cell lymphoma (L-MIND): a multicentre, prospective, single-arm, phase 2 study. *Lancet Oncol*. 2020;21(7):978-988. doi:10.1016/S1470-2045(20)30225-4.

Subsequent Therapy: Intention to Proceed 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.
2. Crump M, Kuruvilla J, Couban S, et al. Randomized comparison of gemcitabine, dexamethasone, and cisplatin versus dexamethasone, cytarabine, and cisplatin chemotherapy before autologous stem-cell transplantation for relapsed and refractory aggressive lymphomas: NCIC-CTG LY.12. *J Clin Oncol*. 2014;32(31):3490-3496. doi:10.1200/JCO.2013.53.9593.
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>.
4. Velasquez WS, McLaughlin P, Tucker S, et al. ESHAP--an effective chemotherapy regimen in refractory and relapsing lymphoma: a 4-year follow-up study. *J Clin Oncol*. 1994;12(6):1169-1176. doi:10.1200/JCO.1994.12.6.1169.
5. Lignon J, Sibon D, Madelaine I, et al. Rituximab, dexamethasone, cytarabine, and oxaliplatin (R-DHAX) is an effective and safe salvage regimen in relapsed/refractory B-cell non-Hodgkin lymphoma. *Clin Lymphoma Myeloma Leuk*. 2010;10(4):262-269. doi:10.3816/CLML.2010.n.055.
6. Rigacci L, Fabbri A, Puccini B, et al. Oxaliplatin-based chemotherapy (dexamethasone, high-dose cytarabine, and oxaliplatin)+/-rituximab is an effective salvage regimen in patients with relapsed or refractory lymphoma. *Cancer*. 2010;116(19):4573-4579. doi:10.1002/cncr.25216.

References – Endometrial Cancer

v1.0.2024

Recurrent/Metastatic: First Line and Subsequent Therapy

1. Miller DS, Filiaci VL, Mannel RS, et al. Carboplatin and paclitaxel for advanced endometrial cancer: final overall survival and adverse event analysis of a phase III trial (NRG Oncology/GOG0209). *J Clin Oncol*. 2020;38(33):3841-3850. doi:10.1200/JCO.20.01076.
2. Secord AA, Havrilesky LJ, Carney ME, et al. Weekly low-dose paclitaxel and carboplatin in the treatment of advanced or recurrent cervical and endometrial cancer. *Int J Clin Oncol*. 2007;12(1):31-36. doi:10.1007/s10147-006-0619-9.
3. Fleming GF, Brunetto VL, Cella D, et al. Phase III trial of doxorubicin plus cisplatin with or without paclitaxel plus filgrastim in advanced endometrial carcinoma: a Gynecologic Oncology Group study. *J Clin Oncol*. 2004;22(11):2159-2166. doi:10.1200/JCO.2004.07.184.
4. Cella D, Huang H, Homesley HD, et al. Patient-reported peripheral neuropathy of doxorubicin and cisplatin with and without paclitaxel in the treatment of advanced endometrial cancer: results from GOG 184. *Gynecol Oncol*. 2010;119(3):538-542. doi:10.1016/j.ygyno.2010.08.022.
5. Fader AN, Roque DM, Siegel E, et al. Randomized phase II trial of carboplatin-paclitaxel versus carboplatin-paclitaxel-trastuzumab in uterine serous carcinomas that overexpress human epidermal growth factor receptor 2/neu. *J Clin Oncol*. 2018;36(20):2044-2051. doi:10.1200/JCO.2017.76.5966.
6. Lorusso D, Ferrandina G, Colombo N, et al. Carboplatin-paclitaxel compared to carboplatin-paclitaxel-bevacizumab in advanced or recurrent endometrial cancer: MITO END-2 - a randomized phase II trial. *Gynecol Oncol*. 2019;155(3):406-412. doi:10.1016/j.ygyno.2019.10.013.
7. Nomura H, Aoki D, Takahashi F, et al. Randomized phase II study comparing docetaxel plus cisplatin, docetaxel plus carboplatin, and paclitaxel plus carboplatin in patients with advanced or recurrent endometrial carcinoma: a Japanese Gynecologic Oncology Group study (JGOG2041). *Ann Oncol*. 2011;22(3):636-642. doi:10.1093/annonc/mdl401.
8. Lissoni A, Zanetta G, Losa G, Gabriele A, Parma G, Mangioni C. Phase II study of paclitaxel as salvage treatment in advanced endometrial cancer. *Ann Oncol*. 1996;7(8):861-863. doi:10.1093/oxfordjournals.annonc.a010768.
9. Thigpen JT, Blessing JA, DiSaia PJ, Yordan E, Carson LF, Evers C. A randomized comparison of doxorubicin alone versus doxorubicin plus cyclophosphamide in the management of advanced or recurrent endometrial carcinoma: a Gynecologic Oncology Group study. *J Clin Oncol*. 1994;12(7):1408-1414. doi:10.1200/JCO.1994.12.7.1408.
10. Wadler S, Levy DE, Lincoln ST, Soori GS, Schink JC, Goldberg G. Topotecan is an active agent in the first-line treatment of metastatic or recurrent endometrial carcinoma: Eastern Cooperative Oncology Group study E3E93. *J Clin Oncol*. 2003;21(11):2110-2114. doi:10.1200/JCO.2003.12.093.
11. Seski JC, Edwards CL, Herson J, Rutledge FN. Cisplatin chemotherapy for disseminated endometrial cancer. *Obstet Gynecol*. 1982;59(2):225-228. Available at: <https://pubmed.ncbi.nlm.nih.gov/7043339/>.
12. Van Wijk FH, Lhomme C, Bolis G, et al. Phase II study of carboplatin in patients with advanced or recurrent endometrial carcinoma. a trial of the EORTC Gynaecological Cancer Group. *Eur J Cancer*. 2003;39(1):78-85. doi:10.1016/s0959-8049(02)00504-x.
13. Aghajanian, Sill MW, Darcy KM, et al. Phase II trial of bevacizumab in recurrent or persistent endometrial cancer: a Gynecologic Oncology Group study. *J Clin Oncol*. 2011;29(16):2259-2265. doi:10.1200/JCO.2010.32.6397.
14. Muggia FM, Blessing JA, Sorosky J, Reid GC. Phase II trial of the pegylated liposomal doxorubicin in previously treated metastatic endometrial cancer: a Gynecologic Oncology Group study. *J Clin Oncol*. 2002;20(9):2360-2364. doi:10.1200/JCO.2002.08.171.
15. Oza AM, Elit L, Tsao MS, et al. Phase II study of temsirolimus in women with recurrent or metastatic endometrial cancer: a trial of the NCIC Clinical Trials group. *J Clin Oncol*. 2011;29(24):3278-3285. doi:10.1200/JCO.2010.34.1578.

16. Katsumata N, Noda K, Nozawa S, et al. Phase II trial of docetaxel in advanced or metastatic endometrial cancer: a Japanese Cooperative study. *Br J Cancer*. 2005;93(9):999-1004. doi:10.1038/sj.bjc.6602817.

References – Esophageal and Esophagogastric Junction (GEJ) Cancer

v1.0.2024

Advanced/Metastatic: First Line, Adenocarcinoma, HER2 Negative, MSS

1. Al-Batran SE, Hartmann JT, Probst S, et al. Phase III trial in metastatic gastroesophageal adenocarcinoma with fluorouracil, leucovorin plus either oxaliplatin or cisplatin: a study of the Arbeitsgemeinschaft Internistische Onkologie. *J Clin Oncol*. 2008;26(9):1435-1442. doi:10.1200/JCO.2007.13.9378.
2. Van Meerten E, Eskens FA, van Gameren EC, Doorn L, van der Gaast A. First-line treatment with oxaliplatin and capecitabine in patients with advanced or metastatic oesophageal cancer: a phase II study. *Br J Cancer*. 2007;96(9):1348-1352. doi:10.1038/sj.bjc.6603750.
3. Cunningham D, Starling N, Rao S, et al. Capecitabine and oxaliplatin for advanced esophagogastric cancer. *N Eng J Med*. 2008;358(1):36-46. doi:10.1056/NEJMoa073149.
4. Kim GM, Jeung HC, Rha SY, et al. A randomized phase II trial of S-1-oxaliplatin versus capecitabine-oxaliplatin in advanced gastric cancer. *Eur J Cancer*. 2012;48(4):518-526. doi:10.1016/j.ejca.2011.12.017.
5. Dank M, Zaluski J, Barone C, et al. Randomized phase III study comparing irinotecan combined with 5-fluorouracil and folinic acid to cisplatin combined with 5-fluorouracil in chemotherapy naive patients with advanced adenocarcinoma of the stomach or esophagogastric junction. *Ann Oncol*. 2008;19(8):1450-1457. doi:10.1093/annonc/mdn166.
6. Janjigian YY, Shitara K, Moehler M, et al. First-line nivolumab plus chemotherapy versus chemotherapy alone for advanced gastric, gastroesophageal junction, and oesophageal adenocarcinoma (CheckMate 649): a randomised, open-label, phase 3 trial. *Lancet*. 2021;398(10294):27-40. doi:10.1016/S0140-6736(21)00797-2.
7. Sun JM, Shen L, Shah MA, et al. Pembrolizumab plus chemotherapy versus chemotherapy alone for first-line treatment of advanced oesophageal cancer (KEYNOTE-590): a randomised, placebo-controlled, phase 3 study. *Lancet*. 2021;398(10302):759-771. doi:10.1016/S0140-6736(21)01234-4.

Advanced/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.
2. Lee SJ, Kim S, Kim M, et al. Capecitabine in combination with either cisplatin or weekly paclitaxel as a first-line treatment for metastatic esophageal squamous cell carcinoma: a randomized phase II study. *BMC Cancer*. 2015;15:693. doi:10.1186/s12885-015-1716-9.
3. Sun JM, Shen L, Shah MA, et al. Pembrolizumab plus chemotherapy versus chemotherapy alone for first-line treatment of advanced oesophageal cancer (KEYNOTE-590): a randomised, placebo-controlled, phase 3 study. *Lancet*. 2021;398(10302):759-771. doi:10.1016/S0140-6736(21)01234-4.
4. Doki Y, Ajani JA, Kato K, et al. Nivolumab Combination Therapy in Advanced Esophageal Squamous-Cell Carcinoma. *N Engl J Med*. 2022;386(5):449-462. doi:10.1056/NEJMoa2111380.

Advanced/Metastatic: Subsequent Therapy, Adenocarcinoma Or 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.
2. Ilson DH, Wadleigh RG, Leichman LP, Kelsen DP. Paclitaxel given by a weekly 1-h infusion in advanced esophageal cancer. *Ann Oncol*. 2007;18(5):898-902. doi:10.1093/annonc/mdm004.

3. Muro K, Hamaguchi T, Ohtsu A, et al. A phase II study of single-agent docetaxel in patients with metastatic esophageal cancer. *Ann Oncol*. 2004;15(6):955-959. doi:10.1093/annonc/mdh231.
4. Ford HE, Marshall A, Bridgewater JA, et al. Docetaxel versus active symptom control for refractory oesophagogastric adenocarcinoma (COUGAR-02): an open-label, phase 3 randomised controlled trial. *Lancet Oncol*. 2014;15(1):78-86. doi:10.1016/S1470-2045(13)70549-7.
5. Mizota A, Shitara K, Kondo C, et al. A retrospective comparison of docetaxel and paclitaxel for patients with advanced or recurrent esophageal cancer who previously received platinum-based chemotherapy. *Oncology*. 2011;81(3-4):237-242. doi:10.1159/000334057.
6. Thuss-Patience PC, Kretzschmar A, Bichev D, et al. Survival advantage for irinotecan versus best supportive care as second-line chemotherapy in gastric cancer--a randomised phase III study of the Arbeitsgemeinschaft Internistische Onkologie (AIO). *Eur J Cancer*. 2011;47(15):2306-2314. doi:10.1016/j.ejca.2011.06.002.
7. Wilke H, Muro K, Van Cutsem E, et al. Ramucirumab plus paclitaxel versus placebo plus paclitaxel in patients with previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (RAINBOW): a double-blind, randomised phase 3 trial. *Lancet Oncol*. 2014;15(11):1224-1235. doi:10.1016/S1470-2045(14)70420-6.
8. Marabelle A, Le DT, Ascierto PA, et al. Efficacy of Pembrolizumab in Patients with Noncolorectal High Microsatellite Instability/Mismatch Repair-Deficient Cancer: Results From the Phase II KEYNOTE-158 Study. *J Clin Oncol*. 2020;38(1):1-10. doi:10.1200/JCO.19.02105.
9. Shitara K, Doi T, Dvorkin M, et al. Trifluridine/tipiracil versus placebo in patients with heavily pretreated metastatic gastric cancer (TAGS): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol*. 2018;19(11):1437-1448. doi:10.1016/S1470-2045(18)30739-3.
10. Fuchs CS, Tomasek J, Yong CJ, et al. Ramucirumab monotherapy for previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (REGARD): an international, randomised, multicentre, placebo-controlled, phase 3 trial. *Lancet*. 2014;383(9911):31-39. doi:10.1016/S0140-6736(13)61719-5.
11. Kojima T, Shah MA, Muro K, et al. Randomized phase III KEYNOTE-181 study of pembrolizumab versus chemotherapy in advanced esophageal cancer. *J Clin Oncol*. 2020;38(35):4138-418. doi:10.1200/JCO.20.01888.
12. Kato K, Cho BC, Takahashi M, et al. Nivolumab versus chemotherapy in patients with advanced oesophageal squamous cell carcinoma refractory or intolerant to previous chemotherapy (ATTRACTION-3): a multicentre, randomised, open-label, phase 3 trial. *Lancet Oncol*. 2019;20(11):1506-1517. doi:10.1016/S1470-2045(19)30626-6.

References – Follicular Lymphoma

v1.0.2024

First Line: Grade 1-2

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.
2. Czuczman MS, Grillo-López AJ, White CA, et al. Treatment of patients with low-grade B-cell lymphoma with the combination of chimeric anti-CD20 monoclonal antibody and CHOP chemotherapy. *J Clin Oncol*. 1999;17(1):268-276. doi:10.1200/JCO.1999.17.1.268.
3. Hiddemann W, Kneba M, Dreyling M, et al. Frontline therapy with rituximab added to the combination of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) significantly improves the outcome for patients with advanced-stage follicular lymphoma compared with therapy with CHOP alone: results of a prospective randomized study of the German Low-Grade Lymphoma Study Group. *Blood*. 2005;106(12):3725-3732. doi:10.1182/blood-2005-01-0016.
4. Rummel MJ, Niederle N, Maschmeyer G, et al. Bendamustine plus rituximab versus CHOP plus rituximab as first-line treatment for patients with indolent and mantle-cell lymphomas: an open-label, multicentre, randomised, phase 3 non-inferiority trial. *Lancet*. 2013;381(9873):1203-1210. doi:10.1016/S0140-6736(12)61763-2.
5. Flinn IW, van der Jagt R, Kahl BS, et al. Randomized trial of bendamustine-rituximab or R-CHOP/R-CVP in first-line treatment of indolent NHL or MCL: the BRIGHT study. *Blood*. 2014;123(19):2944-2952. doi:10.1182/blood-2013-11-531327.
6. Marcus R, Imrie K, Solal-Celigny P, et al. Phase III study of R-CVP compared with cyclophosphamide, vincristine, and prednisone alone in patients with previously untreated advanced follicular lymphoma. *J Clin Oncol*. 2008;26(28):4579-4586. doi:10.1200/JCO.2007.13.5376.
7. Morschhauser F, Fowler NH, Feugier P, et al. Rituximab plus Lenalidomide in Advanced Untreated Follicular Lymphoma. *N Engl J Med*. 2018;379(10):934-947. doi:10.1056/NEJMoa1805104.
8. Morschhauser F, Nastoupil L, Feugier P, et al. Six-Year Results From RELEVANCE: Lenalidomide Plus Rituximab (R2) Versus Rituximab-Chemotherapy Followed by Rituximab Maintenance in Untreated Advanced Follicular Lymphoma. *J Clin Oncol*. 2022;40(28):3239-3245. doi:10.1200/JCO.22.00843.
9. Bachy E, Houot R, Feugier P, et al. Obinutuzumab plus lenalidomide in advanced, previously untreated follicular lymphoma in need of systemic therapy: a LYSA study. *Blood*. 2022;139(15):2338-2346. doi:10.1182/blood.2021013526.

References – Head and Neck Cancer

v1.0.2024

Advanced Disease: Definitive Chemoradiation

1. Bernier J, Dommene 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.
2. Chitapanarux I, Lorvidhaya V, Kamnerdsupaphon P, et al. Chemoradiation comparing cisplatin versus carboplatin in locally advanced nasopharyngeal cancer: randomised, non-inferiority, open trial. *Eur J Cancer*. 2007;43(9):1399-1406. doi:10.1016/j.ejca.2007.03.022.
3. Kiyota N, Tahara M, Fujii H, et al. Phase II/III trial of post-operative chemoradiotherapy comparing 3-weekly cisplatin with weekly cisplatin in high-risk patients with squamous cell carcinoma of head and neck (JCOG1008). *J Clin Oncol*. 2020;38(15_suppl):abstract 6502. doi:10.1200/JCO.2020.38.15_suppl.6502.
4. Clark JI, Hofmeister C, Choudhury A, et al. Phase II evaluation of paclitaxel in combination with carboplatin in advanced head and neck carcinoma. *Cancer*. 2001;92(9):2334-2340. doi:10.1002/1097-0142(20011101)92:9<2334::aid-cncr1580>3.0.co;2-3.
5. Gebre-Medhin M, Brun E, Engström P, et al. ARTSCAN III: A Randomized Phase III Study Comparing Chemoradiotherapy With Cisplatin Versus Cetuximab in Patients With Locoregionally Advanced Head and Neck Squamous Cell Cancer. *J Clin Oncol*. 2021;39(1):38-47. doi:10.1200/JCO.20.02072.

References – Hepatocellular Carcinoma

v1.0.2024

Metastatic 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.
2. Kudo M, Finn RS, Qin S, et al. Lenvatinib versus sorafenib in first-line treatment of patients with unresectable hepatocellular carcinoma: a randomised phase 3 non-inferiority trial. *Lancet*. 2018;391(10126):1163-1173. doi:10.1016/S0140-6736(18)30207-1.
3. Finn RS, Qin S, Ikeda M, et al. Atezolizumab plus bevacizumab in unresectable hepatocellular carcinoma. *N Eng J Med*. 2020;382(20):1894-1905. doi:10.1056/NEJMoa1915745.
4. Yau T, Park JW, Finn RS, et al. LBA38_PR - CheckMate 459: A randomized, multi-center phase III study of nivolumab (NIVO) vs sorafenib (SOR) as first-line treatment in patients with advanced hepatocellular carcinoma (aHCC). *Ann Oncol*. 2019;30(5_Suppl):v874-v875. doi:10.1093/annonc/mdz394.029.
5. Abou-Alfa GK, Lau G, Kudo M, et al. Tremelimumab plus Durvalumab in Unresectable Hepatocellular Carcinoma. *NEJM Evid*. 2022;1(8):EVIDoa2100070. doi:10.1056/EVIDoa2100070.
6. Zhu AX, Finn RS, Edeline J, et al. Pembrolizumab in patients with advanced hepatocellular carcinoma previously treated with sorafenib (KEYNOTE-224): a non-randomised, open-label phase 2 trial. *Lancet Oncol*. 2018;19(7):940-952. doi:10.1016/S1470-2045(18)30351-6.

Metastatic Disease: Subsequent Therapy

1. Bruix J, Qin S, Merle P, et al. Regorafenib for patients with hepatocellular carcinoma who progressed on sorafenib treatment (RESORCE): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2017;389(10064):56-66. doi:10.1016/S0140-6736(16)32453-9.
2. Abou-Alfa GK, Meyer T, Cheng AL, et al. Cabozantinib in patients with advanced and progressing hepatocellular carcinoma. *N Eng J Med*. 2018;379(1):54-63. doi:10.1056/NEJMoa1717002.
3. Zhu AX, Kang YK, Yen CJ, et al. REACH-2: a randomized, double-blind, placebo-controlled phase 3 study of ramucirumab versus placebo as second-line treatment in patients with advanced hepatocellular carcinoma (HCC) and elevated baseline alpha-fetoprotein (AFP) following firstline sorafenib. *J Clin Oncol*. 2018;36(15_suppl):4003-4003. doi:10.1200/jco.2018.36.15_suppl.4003.
4. Crocenzi TS, El-Khoueiry AB, Yau TC, et al. Nivolumab (nivo) in sorafenib (sor)-naive and-experienced pts with advanced hepatocellular carcinoma (HCC): CheckMate 040 study. *J Clin Oncol*. 2017;35(15_suppl):4013-4013. doi:10.1200/jco.2017.35.15_suppl.4013.
5. Qin S, Chen Z, Fang W, et al. Pembrolizumab plus best supportive care versus placebo plus best supportive care as second-line therapy in patients in Asia with advanced hepatocellular carcinoma (HCC): Phase 3 KEYNOTE-394 study. *J Clin Oncol*. 2022;40(4_suppl):383-383. doi:10.1200/jco.2022.40.4_suppl.383.

References – Hodgkin's Lymphoma

v1.0.2024

Stage III/IV Classical Hodgkin's Lymphoma

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.
2. Johnson P, Federico M, Kirkwood A, et al. Adapted treatment guided by interim PET-CT scan in advanced Hodgkin's lymphoma. *N Eng J Med*. 2016;374(25):2419-2429. doi:10.1056/nejmoa1510093.
3. Straus DJ, Długosz-Danecka M, Alekseev S, et al. Brentuximab vedotin with chemotherapy for stage III/IV classical Hodgkin lymphoma: 3-year update of the ECHELON-1 study. *Blood*. 2020;13(10):5:735-742. doi:10.1182/blood.2019003127.

References – Kidney Cancer

v1.0.2024

First Line: Good Risk

1. Motzer RJ, Hutson TE, Cella D, et al. Pazopanib versus sunitinib in metastatic renal-cell carcinoma. *N Eng J Med*. 2013;369(8):722-731. doi:10.1056/NEJMoa1303989.
2. Motzer RJ, Tannir NM, McDermott DF, et al. Nivolumab plus ipilimumab versus sunitinib in advanced renal-cell carcinoma. *N Eng J Med*. 2018;378(14):1277-1290. doi:10.1056/NEJMoa1712126.
3. Motzer RJ, Penkov K, Haanen J, et al. Avelumab plus axitinib versus sunitinib for advanced renal-cell carcinoma. *N Eng J Med*. 2019;380(12):1103-1115. doi:10.1056/NEJMoa1816047.
4. Motzer RJ, Alekseev B, Rha SY, et al. Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma. *N Eng J Med*. 2021;384(14):1289-1300. doi:10.1056/NEJMoa2035716.
5. Choueiri TK, Powles T, Burotto M, et al. 6960_PR Nivolumab + cabozantinib vs sunitinib in first-line treatment for advanced renal cell carcinoma: First results from the randomized phase III CheckMate 9ER trial. *Ann Oncol*. 2020;31:S1159. doi:10.1016/j.annonc.2020.08.2257.
6. Rini BI, Plimack ER, Stus V, et al. Pembrolizumab plus axitinib versus sunitinib for advanced renal-cell carcinoma. *N Eng J Med*. 2019;380(12):1116-1127. doi:10.1056/NEJMoa1816714.

First Line: Intermediate/Poor Risk

1. Motzer RJ, Tannir NM, McDermott DF, et al. Nivolumab plus ipilimumab versus sunitinib in advanced renal-cell carcinoma. *N Eng J Med*. 2018;378(14):1277-1290. doi:10.1056/NEJMoa1712126.
2. Motzer RJ, Alekseev B, Rha SY, et al. Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma. *N Eng J Med*. 2021;384(14):1289-1300. doi:10.1056/NEJMoa2035716.
3. Choueiri TK, Powles T, Burotto M, et al. 696O_PR Nivolumab + cabozantinib vs sunitinib in first-line treatment for advanced renal cell carcinoma: First results from the randomized phase III CheckMate 9ER trial. *Ann Oncol*. 2020;31:S1159. doi:10.1016/j.annonc.2020.08.2257.
4. Rini BI, Plimack ER, Stus V, et al. Pembrolizumab plus axitinib versus sunitinib for advanced renal-cell carcinoma. *N Eng J Med*. 2019;380(12):1116-1127. doi:10.1056/NEJMoa1816714.
5. Choueiri TK, Halabi S, Sanford BL, et al. Cabozantinib versus sunitinib as initial targeted therapy for patients with metastatic renal cell carcinoma of poor or intermediate risk: the Alliance A031203 CABOSUN trial. *J Clin Oncol*. 2017;35(6):591-597. doi:10.1200/JCO.2016.70.7398.

References – Lung Cancer: NSCLC

v1.0.2024

Advanced/Metastatic: First Line, Squamous or Nonsquamous, PD-L1 # 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.
2. Reck M, Rodríguez-Abreu D, Robinson AG, et al. Five-year outcomes with pembrolizumab versus chemotherapy for metastatic non-small-cell lung cancer with PD-L1 tumor proportion score $\geq$ 50. *J Clin Oncol*. 2021;39(21):2339-2349. doi:10.1200/JCO.21.00174.
3. Herbst RS, Giaccone G, de Marinis F, et al. Atezolizumab for First-Line Treatment of PD-L1-Selected Patients with NSCLC. *N Eng J Med*. 2020;383(14):1328-1339. doi:10.1056/NEJMoa1917346.
4. Spigel D, de Marinis F, Giaccone G, et al. IMpower110: interim overall survival (OS) analysis of a phase III study of atezolizumab (atezo) vs platinum-based chemotherapy (chemo) as first-line (1L) treatment (tx) in PD-L1-selected NSCLC. *Ann Oncol*. 2019;30(Suppl 5):v915. doi:10.1093/annonc/mdz293.
5. Sezer A, Kilickap S, Gümüş M, et al. Cemiplimab monotherapy for first-line treatment of advanced non-small-cell lung cancer with PD-L1 of at least 50%: a multicentre, open-label, global, phase 3, randomised, controlled trial. *Lancet*. 2021;397(10274):592-604. doi:10.1016/S0140-6736(21)00228-2.
6. Gogishvili M, Melkadze T, Makharadze T, et al. Cemiplimab plus chemotherapy versus chemotherapy alone in non-small cell lung cancer: a randomized, controlled, double-blind phase 3 trial. *Nat Med*. 2022;28(11):2374-2380. doi:10.1038/s41591-022-01977-y.
7. Johnson ML, Cho BC, Luft A, et al. Durvalumab With or Without Tremelimumab in Combination With Chemotherapy as First-Line Therapy for Metastatic Non-Small-Cell Lung Cancer: The Phase III POSEIDON Study. *J Clin Oncol*. 2023;41(6):1213-1227. doi:10.1200/JCO.22.00975.

Metastatic: First Line, Squamous or Nonsquamous, PD-L1 <50%, No Driver Mutation

1. Gandhi L, Rodríguez-Abreu D, Gadgeel S, et al. Pembrolizumab plus Chemotherapy in Metastatic Non-Small-Cell Lung Cancer. *N Eng J Med*. 2018;378(22):2078-2092. doi:10.1056/NEJMoa1801005.
2. Gadgeel S, Rodríguez-Abreu D, Speranza G, et al. Updated Analysis From KEYNOTE-189: Pembrolizumab or Placebo Plus Pemetrexed and Platinum for Previously Untreated Metastatic Nonsquamous Non-Small-Cell Lung Cancer. *J Clin Oncol*. 2020;38(14):1505-1517. doi:10.1200/JCO.19.03136.
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.
4. Socinski M, otte RM, Cappuzzo F, et al. Atezolizumab for First-Line Treatment of Metastatic Nonsquamous NSCLC. *N Eng J Med*. 2018;378(24):2288-2301. doi:10.1056/NEJMoa1716948.
5. West H, McCleod M, Hussein M, et al. Atezolizumab in combination with carboplatin plus nab-paclitaxel chemotherapy compared with chemotherapy alone as first-line treatment for metastatic non-squamous non-small-cell lung cancer (IMpower130): a multicentre, randomised, open-label, phase 3 trial. *Lancet Oncol*. 2019;20(7):924-937. doi:10.1016/S1470-2045(19)30167-6.
6. Hellmann MD, Paz-Ares L, Bernabe Caro R, et al. Nivolumab plus ipilimumab in advanced non-small-cell lung cancer. *N Eng J Med*. 2019;381(21):2020-2031. doi:10.1056/NEJMoa1910231.
7. Paz-Ares L, Ciuleanu TE, Cobo M, et al. First-line nivolumab plus ipilimumab combined with two cycles of chemotherapy in patients with non-small-cell lung cancer (CheckMate 9LA): an international, randomised, open-label, phase 3 trial. *Lancet Oncol*. 2021;22(2):198-211. doi:10.1016/S1470-2045(20)30641-0.
8. Jotte R, Cappuzzo F, Vynnychenko I, et al. Atezolizumab in Combination with Carboplatin and Nab-Paclitaxel in Advanced Squamous NSCLC (IMpower131): Results From a Randomized Phase III Trial. *J Thorac Oncol*. 2020;15(8):1351-1360. doi:10.1016/j.jtho.2020.03.028.

9. Gogishvili M, Melkadze T, Makharadze T, et al. Cemiplimab plus chemotherapy versus chemotherapy alone in non-small cell lung cancer: a randomized, controlled, double-blind phase 3 trial. *Nat Med*. 2022;28(11):2374-2380. doi:10.1038/s41591-022-01977-y.
10. Johnson ML, Cho BC, Luft A, et al. Durvalumab With or Without Tremelimumab in Combination With Chemotherapy as First-Line Therapy for Metastatic Non-Small-Cell Lung Cancer: The Phase III POSEIDON Study. *J Clin Oncol*. 2023;41(6):1213-1227. doi:10.1200/JCO.22.00975.

Metastatic: Subsequent Therapy, Squamous or Nonsquamous, No Actionable Mutation

1. Herbst RS, Baas P, Kim DW, et al. Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small-cell lung cancer (KEYNOTE-010): a randomised controlled trial. *Lancet*. 2016;387(10027):1540-1550. doi:10.1016/S0140-6736(15)01281-7.
2. Herbst RS, Garon EB, Kim DW, et al. Long-term outcomes and retreatment among patients with previously treated, programmed death-ligand 1-positive, advanced non-small-cell lung cancer in the KEYNOTE-010 study. *J Clin Oncol*. 2020;38(14):1580-1590. doi:10.1200/JCO.19.02446.
3. Borghaei H, Paz-Ares L, Horn L, et al. Nivolumab versus docetaxel in advanced nonsquamous non-small-cell lung cancer. *N Eng J Med*. 2015;373(17):1627-1639. doi:10.1056/NEJMoa1507643.
4. Vokes EE, Ready N, Felip E, et al. Nivolumab versus docetaxel in previously treated advanced non-small-cell lung cancer (CheckMate 017 and CheckMate 057): 3-year update and outcomes in patients with liver metastases. *Ann Oncol*. 2018;29(4):959-965. doi:10.1093/annonc/mdy041.
5. Brahmer J, Reckamp KL, Baas P, et al. Nivolumab versus docetaxel in advanced squamous-cell non-small-cell lung cancer. *N Eng J Med*. 2015;373(2):123-135. doi:10.1056/NEJMoa1504627.
6. Rittmeyer A, Barlesi F, Waterkamp D, et al. Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a phase 3, open-label, multicentre randomised controlled trial. *Lancet*. 2017;389(10066):255-265. doi:10.1016/S0140-6736(16)32517-X.
7. Hanna N, Shepherd FA, Fossella FV, et al. Randomized phase III trial of pemetrexed versus docetaxel in patients with non-small-cell lung cancer previously treated with chemotherapy. *J Clin Oncol*. 2004;22(9):1589-1597. doi:10.1200/JCO.2004.08.163.
8. Fossella FV, DeVore R, Kerr RN, et al. Randomized phase III trial of docetaxel versus vinorelbine or ifosfamide in patients with advanced non-small-cell lung cancer previously treated with platinum-containing chemotherapy regimens. The TAX 320 Non-Small Cell Lung Cancer Study Group. *J Clin Oncol*. 2000;18(12):2354-2362. doi:10.1200/JCO.2000.18.12.2354.
9. Anderson H, Hopwood P, Stephens RJ, et al. Gemcitabine plus best supportive care (BSC) vs BSC in inoperable non-small cell lung cancer--a randomized trial with quality of life as the primary outcome. UK NSCLC Gemcitabine Group. Non-Small Cell Lung Cancer. *Br J Cancer*. 2000;83(4):447-453. doi:10.1054/bjoc.2000.1307.
10. Garon EB, Ciuleanu TE, Arrieta O, et al. Ramucirumab plus docetaxel versus placebo plus docetaxel for second-line treatment of stage IV non-small-cell lung cancer after disease progression on platinum-based therapy (REVEL): a multicentre, doubleblind, randomised phase 3 trial. *Lancet*. 2014;384(9944):665-673. doi:10.1016/S0140-6736(14)60845-X.
11. Morgensztern D, Cobo M, Ponce Aix S, et al. ABOUN2L+: A randomized phase 2 study of nanoparticle albumin-bound paclitaxel with or without CC-486 as second-line treatment for advanced nonsquamous non-small cell lung cancer (NSCLC). *Cancer*. 2018;124(24):4667-4675. doi:10.1002/cnrc.31779.

References – Lung Cancer: SCLC

v1.0.2024

Limited Stage Disease

1. Turrisi AT 3rd, Kim K, Blum R, et al. Twice-daily compared with once-daily thoracic radiotherapy in limited small-cell lung cancer treated concurrently with cisplatin and etoposide. *N Engl J Med*. 1999;340(4):265-271. doi:10.1056/NEJM199901283400403.
2. Faivre-Finn C, Snee M, Ashcroft L, et al. Concurrent once-daily versus twice-daily chemoradiotherapy in patients with limited-stage small-cell lung cancer (CONVERT): an open-label, phase 3, randomised, superiority trial. *Lancet Oncol*. 2017;18(8):1116-1125. doi:10.1016/S1470-2045(17)30318-2.
3. Okamoto H, Watanabe K, Nishiwaki Y, et al. Phase II study of area under the plasma-concentration-versus-time curve-based carboplatin plus standarddose intravenous etoposide in elderly patients with small-cell lung cancer. *J Clin Oncol*. 1999;17(11):3540-3545. doi:10.1200/JCO.1999.17.11.3540.
4. Skarlos DV, Samantas E, Briassoulis E, et al. Randomized comparison of early versus late hyperfractionated thoracic irradiation concurrently with chemotherapy in limited disease small-cell lung cancer: a randomized phase II study of the Hellenic Cooperative Oncology Group (HeCOG). *Ann Oncol*. 2001;12(9):1231-1238. doi:10.1023/a:1012295131640.

Extensive Stage Disease: First Line

1. Hanna N, Bunn PA Jr, Langer C, et al. Randomized phase III trial comparing irinotecan/cisplatin with etoposide/cisplatin in patients with previously untreated extensive-stage disease small-cell lung cancer. *J Clin Oncol*. 2006;24(13):2038-2043. doi:10.1200/JCO.2005.04.8595.
2. Noda K, Nishiwaki Y, Kawahara M, et al. Irinotecan plus cisplatin compared with etoposide plus cisplatin for extensive small-cell lung cancer. *N Engl J Med*. 2002;346(2):85-91. doi:10.1056/NEJMoa003034.
3. Niell HB, Herndon JE 2nd, Miller AA, et al. Randomized phase III intergroup trial of etoposide and cisplatin with or without paclitaxel and granulocyte colony-stimulating factor in patients with extensive-stage small-cell lung cancer: Cancer and Leukemia Group B Trial 9732. *J Clin Oncol*. 2005;23(16):3752-3759. doi:10.1200/JCO.2005.09.071.
4. Paz-Ares L, Dvorkin M, Chen Y, et al. Durvalumab plus platinum-etoposide versus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): a randomised, controlled, open-label, phase 3 trial. *Lancet*. 2019;394(10212):1929-1939. doi:10.1016/S0140-6736(19)32222-6.
5. Horn L, Mansfield AS, Szczesna A, et al. First-line atezolizumab plus chemotherapy in extensive-stage small-cell lung cancer. *N Engl J Med*. 2018;379(23):2220-2229. doi:10.1056/NEJMoa1809064.
6. Schmittel A, Fischer von Weikersthal L, Sebastian M, et al. A randomized phase II trial of irinotecan plus carboplatin versus etoposide plus carboplatin treatment in patients with extended disease small-cell lung cancer. *Ann Oncol*. 2006;17(4):663-667. doi:10.1093/annonc/mdj137.
7. Schmittel A, Sebastian M, Fischer von Weikersthal L, et al. A German multicenter, randomized phase III trial comparing irinotecan-carboplatin with etoposide-carboplatin as first-line therapy for extensive-disease small-cell lung cancer. *Ann Oncol*. 2011;22(8):1798-1804. doi:10.1093/annonc/mdq652.

Extensive Stage Disease: Subsequent Therapy

1. Von Pawel J, Schiller JH, Shepherd FA, et al. Topotecan versus cyclophosphamide, doxorubicin, and vincristine for the treatment of recurrent small-cell lung cancer. *J Clin Oncol*. 1999;17(2):658-667. doi:10.1200/JCO.1999.17.2.658.
2. O'Brien ME, Ciuleanu TE, Tsekov H, et al. Phase III trial comparing supportive care alone with supportive care with oral topotecan in patients with relapsed small-cell lung cancer. *J Clin Oncol*. 2006;24(34):5441-5447. doi:10.1200/JCO.2006.06.5821.

3. Eckardt JR, von Pawel J, Pujol JL, et al. Phase III study of oral compared with intravenous topotecan as second-line therapy in small-cell lung cancer. *J Clin Oncol*. 2007;25(15):2086-2092. doi:10.1200/JCO.2006.08.3998.
4. Trigo J, Subbiah V, Besse B, et al. Lurbinectedin as second-line treatment for patients with small-cell lung cancer: a single-arm, open-label, phase 2 basket trial. *Lancet Oncol*. 2020;21(5):645-654. doi:10.1016/S1470-2045(20)30068-1.
5. Antonia SJ, López-Martin JA, Bendell J, et al. Nivolumab alone and nivolumab plus ipilimumab in recurrent small-cell lung cancer (CheckMate 032): a multicentre, open-label, phase 1/2 trial. *Lancet Oncol*. 2016;17(7):883-895. doi:10.1016/S1470-2045(16)30098-5.
6. Ready NE, Ott PA, Hellmann MD, et al. Nivolumab monotherapy and nivolumab plus ipilimumab in recurrent small cell lung cancer: results from the CheckMate 032 randomized cohort. *J Thorac Oncol*. 2020;15(3):426-435. doi:10.1016/j.jtho.2019.10.004.
7. Owonikoko TK, Kim HR, Govindan R, et al. Nivolumab (nivo) plus ipilimumab (ipi), nivo, or placebo (pbo) as maintenance therapy in patients (pts) with extensive disease small cell lung cancer (ED-SCLC) after first-line (1L) platinum-based chemotherapy (chemo): Results from the double-blind, randomized phase III CheckMate 451 study. *Ann Oncol*. 2019;30(Supplement_2):1177. doi:10.1093/annonc/mdz094.
8. Rudin CM, Awad MM, Navarro A, et al. Pembrolizumab or placebo plus etoposide and platinum as first-line therapy for extensive-stage small-cell lung cancer: randomized, double-blind, phase III KEYNOTE-604 study. *J Clin Oncol*. 2020;38(21):2369-2379. doi:10.1200/JCO.20.00793.

References – Myelodysplastic Syndrome (MDS)

v1.0.2024

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

1. Fenaux P, Mufti GJ, Hellstrom-Lindberg E, et al. Efficacy of azacitidine compared with that of conventional care regimens in the treatment of higher-risk myelodysplastic syndromes: a randomised, open-label, phase III study. *Lancet Oncol.* 2009;10(3):223-232. doi:10.1016/S1470-2045(09)70003-8.
2. Lübbert M, Suciu S, Baila L, et al. Low-dose decitabine versus best supportive care in elderly patients with intermediate- or high-risk myelodysplastic syndrome (MDS) ineligible for intensive chemotherapy: final results of the randomized phase III study of the European Organisation for Research and Treatment of Cancer Leukemia Group and the German MDS Study Group. *J Clin Oncol.* 2011;29(15):1987-1996. doi:10.1200/JCO.2010.30.9245.
3. Garcia-Manero G, Griffiths EA, Steensma DP et al. Oral cedazuridine/decitabine for MDS and CMML: a phase 2 pharmacokinetic/pharmacodynamic randomized crossover study. *Blood.* 2020;136(6):674-683. doi:10.1182/blood.2019004143.

References – Melanoma

v1.0.2024

Metastatic: First Line Therapy BRAF Mutated

1. Larkin J, Ascierto PA, Dreno B, et al. Combined vemurafenib and cobimetinib in BRAF-mutated melanoma. *N Engl J Med*. 2014;371(20):1867-1876. doi:10.1056/NEJMoa1408868.
2. Ascierto PA, McArthur GA, Dreno B, et al. Cobimetinib combined with vemurafenib in advanced BRAF(V600)-mutant melanoma (coBRIM): updated efficacy results from a randomised, double-blind, phase 3 trial. *Lancet Oncol*. 2016;17(9):1248-1260. doi:10.1016/S1470-2045(16)30122-X.
3. Long GV, Stroyakovskiy D, Gogas H, et al. Dabrafenib and trametinib versus dabrafenib and placebo for Val600 BRAF-mutant melanoma: a multicentre, double-blind, phase 3 randomised controlled trial. *Lancet*. 2015;386(9992):444-451. doi:10.1016/S0140-6736(15)60898-4.
4. Long GV, Flaherty KT, Stroyakovskiy D, et al. Dabrafenib plus trametinib versus dabrafenib monotherapy in patients with metastatic BRAF V600E/Kmutant melanoma: long-term survival and safety analysis of a phase 3 study. *Ann Oncol*. 2017;2828(7):1631-1639. doi:10.1093/annonc/mdx176.
5. Robert C, Karaszewska B, Schachter J, et al. Improved overall survival in melanoma with combined dabrafenib and trametinib. *N Engl J Med*. 2015;372(1):30-39. doi:10.1056/NEJMoa1412690.
6. Dummer R, Ascierto PA, Gogas HJ, et al. Encorafenib plus binimetinib versus vemurafenib or encorafenib in patients with BRAF-mutant melanoma (COLUMBUS): a multicentre, open-label, randomised phase 3 trial. *Lancet Oncol*. 2018;19(5):603-615. doi:10.1016/S1470-2045(18)30142-6.

Metastatic: No Prior Immunotherapy

1. Robert C, Schachter J, Long GV, et al. Pembrolizumab versus ipilimumab in advanced melanoma. *N Engl J Med*. 2015;372(26):2521-2532. doi:10.1056/NEJMoa1503093.
2. Schachter J, Ribas A, Long GV, et al. Pembrolizumab versus ipilimumab for advanced melanoma: final overall survival results of a multicentre, randomised, open-label phase 3 study (KEYNOTE-006). *Lancet*. 2017;390(10105):1853-1862. doi:10.1016/S0140-6736(17)31601-X.
3. Robert C, Ribas A, Schachter J, et al. Pembrolizumab versus ipilimumab in advanced melanoma (KEYNOTE-006): post-hoc 5-year results from an openlabel, multicentre, randomised, controlled, phase 3 study. *Lancet Oncol*. 2019;20(9):1239-1251. doi:10.1016/S1470-2045(19)30388-2.
4. Larkin J, Chiarion-Sileni V, Gonzalez R, et al. Combined nivolumab and ipilimumab or monotherapy in untreated melanoma. *N Engl J Med*. 2015;373(1):23-34. doi:10.1056/NEJMoa1504030.
5. Hodi FS, Chiarion-Sileni V, Gonzalez R, et al. Nivolumab plus ipilimumab or nivolumab alone versus ipilimumab alone in advanced melanoma (CheckMate 067): 4-year outcomes of a multicentre, randomised, phase 3 trial. *Lancet Oncol*. 2018;19(11):1480-1492. doi:10.1016/S1470-2045(18)30700-9.
6. Larkin J, Chiarion-Sileni V, Gonzalez R, et al. Five-year survival with combined nivolumab and ipilimumab in advanced melanoma. *N Engl J Med*. 2019;381(16):1535-1546. doi:10.1056/NEJMoa1910836.
7. Tawbi H, Schadendorf D, Lipson EJ, et al. Relatlimab and Nivolumab versus Nivolumab in Untreated Advanced Melanoma. *N Eng J Med*. 2022;386(1):24-34. doi:10.1056/NEJMoa2109970.

References – Multiple Myeloma

v1.0.2022

First Line: Transplant Eligible

1. Roussel M, Lauwers-Cances V, Robillard N, et al. Front-line transplantation program with lenalidomide, bortezomib, and dexamethasone combination as induction and consolidation followed by lenalidomide maintenance in patients with multiple myeloma: a phase II study by the Intergroupe Francophone du Myelome. *J Clin Oncol*. 2014;32(25):2712-2717. doi:10.1200/JCO.2013.54.8164.
2. Voorhees PM, Kaufman JL, Laubach J, et al. Daratumumab, lenalidomide, bortezomib, and dexamethasone for transplant-eligible newly diagnosed multiple myeloma: the GRIFFIN trial. *Blood*. 2020;136(8):936-945. doi:10.1182/blood.2020005288.
3. Kumar S, Flinn I, Richardson PG, et al. Randomized, multicenter, phase 2 study (EVOLUTION) of combinations of bortezomib, dexamethasone, cyclophosphamide, and lenalidomide in previously untreated multiple myeloma. *Blood*. 2012;119(19):4375-4382. doi:10.1182/blood-2011-11-395749.

First Line: Transplant Ineligible

1. Durie BG, Hoering A, Abidi MH, et al. Bortezomib with lenalidomide and dexamethasone versus lenalidomide and dexamethasone alone in patients with newly diagnosed myeloma without intent for immediate autologous stem-cell transplant (SWOG S0777): a randomised, open-label, phase 3 trial. *Lancet*. 2017;389(10068):519-527. doi:10.1016/S0140-6736(16)31594-X.
2. Facon T, Kumar S, Plesner T, et al. Daratumumab plus lenalidomide and dexamethasone for untreated myeloma. *N Engl J Med*. 2019;380(22):2104-2115. doi:10.1056/NEJMoa1817249.
3. Kumar SK, Jacobus SJ, Cohen AD, et al. Carfilzomib or bortezomib in combination with lenalidomide and dexamethasone for patients with newly diagnosed multiple myeloma without intention for immediate autologous stem-cell transplantation (ENDURANCE): a multicentre, open-label, phase 3, randomised, controlled trial. *Lancet Oncol*. 2020;21(10):1317-1330. doi:10.1016/S1470-2045(20)30452-6.
4. Mateos MV, Dimopoulos MA, Cavo M, et al. Daratumumab plus bortezomib, melphalan, and prednisone for untreated myeloma. *N Engl J Med*. 2018;378(6):518-528. doi:10.1056/NEJMoa1714678.
5. Mateos MV, Cavo M, Blade J, et al. Overall survival with daratumumab, bortezomib, melphalan, and prednisone in newly diagnosed multiple myeloma (ALCYONE): a randomised, open-label, phase 3 trial. *Lancet*. 2020;395(10218):132-141. doi:10.1016/S0140-6736(19)32956-3.

References – Neuroendocrine Cancer

v1.0.2024

Well-Differentiated Grade 1/2, GI Tract, Lung, and Thymus

1. Rinke A, Müller HH, Schade-Brittinger C, et al. Placebo-controlled, double-blind, prospective, randomized study on the effect of octreotide LAR in the control of tumor growth in patients with metastatic neuroendocrine midgut tumors: a report from the PROMID Study Group. *J Clin Oncol*. 2009;27(28):4656-4663. doi:10.1200/JCO.2009.22.8510.
2. Caplin ME, Pavel M, Cwikla JB, et al. Lanreotide in Metastatic Enteropancreatic Neuroendocrine Tumors. *N Engl J Med*. 2014;371:224-233. doi:10.1056/NEJMoa1316158.
3. Pavel ME, Baudin E, Öberg KE, et al. Efficacy of everolimus plus octreotide LAR in patients with advanced neuroendocrine tumor and carcinoid syndrome: final overall survival from the randomized, placebo-controlled phase 3 RADIANT-2 study. *Ann Oncol*. 2017;28(7):1569-1575. doi:10.1093/annonc/mdx193.
4. O'Toole D, Ducreux M, Bommelaer G, et al. Treatment of carcinoid syndrome: a prospective crossover evaluation of lanreotide versus octreotide in terms of efficacy, patient acceptability, and tolerance. *Cancer*. 2000;88(4):770-776. doi:10.1002/(sici)1097-0142(20000215)88:4<770::aid-cnrcr6>3.0.co;2-0.

Poorly-Differentiated, Large or Small Cell (Extrapulmonary)

1. Iwasa S, Morizane C, Okusaka T, et al. Cisplatin and etoposide as first-line chemotherapy for poorly differentiated neuroendocrine carcinoma of the hepatobiliary tract and pancreas. *Jpn J Clin Oncol*. 2010;40(4):313-318. doi:10.1093/jjco/hyp173.
2. Frizziero M, Spada F, Lamarca A, et al. Carboplatin in Combination with Oral or Intravenous Etoposide for Extra-Pulmonary, Poorly-Differentiated Neuroendocrine Carcinomas. *Neuroendocrinology*. 2019;109(2):100-112. doi:10.1159/000497336.
3. Hanna N, Bunn PA Jr, Langer C, et al. Randomized phase III trial comparing irinotecan/cisplatin with etoposide/cisplatin in patients with previously untreated extensive-stage disease small-cell lung cancer. *J Clin Oncol*. 2006;24:2038-2043. doi:10.1200/JCO.2005.04.8595.
4. Schmittl A, Sebastian M, Fischer von Weikersthal L, et al. A German multicenter, randomized phase III trial comparing irinotecan–carboplatin with etoposide–carboplatin as first-line therapy for extensive-disease small-cell lung cancer. *Ann Oncol*. 2011;22:1798-1804. doi:10.1093/annonc/mdq652.
5. Hadoux J, Malka D, Planchard D, et al. Post-first-line FOLFOX chemotherapy for grade 3 neuroendocrine carcinoma. *Endocr Relat Cancer*. 2015; 22(3):289-298. doi:10.1530/ERC-15-0075.
6. Hentic O, Hammel P, Couvelard A, et al. FOLFIRI regimen: an effective second-line chemotherapy after failure of etoposide-platinum combination in patients with neuroendocrine carcinomas grade 3. *Endocr Relat Cancer*. 2012;19(6):751-757. doi:10.1530/ERC-12-0002.
7. Zhu J, Strosberg JR, Dropkin E, et al. Treatment of High-Grade Metastatic Pancreatic Neuroendocrine Carcinoma with FOLFIRINOX. *J Gastrointest Cancer*. 2015;46(2):166-169. doi:10.1007/s12029-015-9689-0.
8. Rogowski W, Wachuła E, Gorzelak A, et al. Capecitabine and temozolomide combination for treatment of high-grade, well-differentiated neuroendocrine tumour and poorly-differentiated neuroendocrine carcinoma - retrospective analysis. *Endokrynol Pol*. 2019;70(4):313-317. doi:10.5603/EP.a2019.0010.
9. Klein O, Kee D, Markman B, et al. Immunotherapy of Ipilimumab and Nivolumab in Patients with Advanced Neuroendocrine Tumors: A Subgroup Analysis of the CA209-538 Clinical Trial for Rare Cancers. *Clin Cancer Res*. 2020;26(17):4454-4459. doi:10.1158/1078-0432.CCR-20-0621.
10. Marabelle A, Fakih M, Lopez J, et al. Association of tumour mutational burden with outcomes in patients with advanced solid tumours treated with pembrolizumab: prospective biomarker analysis of the multicohort, open-label, phase 2 KEYNOTE-158 study. *Lancet Oncol*. 2020;21(10):1353-1365. doi:10.1016/S1470-2045(20)30445-9.

References – Ovarian Cancer

v1.0.2024

Primary Therapy: Stage II-IV

1. du Bois A, Lück HJ, Meier W, et al. A randomized clinical trial of cisplatin/paclitaxel versus carboplatin/paclitaxel as first-line treatment of ovarian cancer. *J Natl Cancer Inst.* 2003;95(17):1320–1330. doi:10.1093/jnci/djg036.
2. Bookman MA, Brady MF, McGuire WP, et al. Evaluation of new platinum-based treatment regimens in advanced-stage ovarian cancer: a phase III Trial of the Gynecologic Cancer Intergroup. *J Clin Oncol.* 2009;27(9):1419-1425. doi:10.1200/JCO.2008.19.1684.
3. Perren T, Swart AM, Pfisterer J, et al. A Phase 3 Trial of Bevacizumab in Ovarian Cancer. *N Eng J Med.* 2011;365(26):2484-2496. doi:10.1056/NEJMoa1103799
4. Oza AM, Cook AD, Pfisterer J, et al. Standard chemotherapy with or without bevacizumab for women with newly diagnosed ovarian cancer (ICON7): overall survival results of a phase 3 randomised trial. *Lancet Oncol.* 2015;16(8):928-936. doi:10.1016/S1470-2045(15)00086-8.
5. Burger RA, Brady MF, Bookman MA, et al. Incorporation of Bevacizumab in the Primary Treatment of Ovarian Cancer. *N Eng J Med.* 2011;365(26):2473-2483. doi:10.1056/NEJMoa1104390.
6. Tewari KS, Burger RA, Enserro D, et al. Final Overall Survival of a Randomized Trial of Bevacizumab for Primary Treatment of Ovarian Cancer. *J Clin Oncol.* 2019;37(26):2317-2328. doi:10.1200/JCO.19.01009.

Recurrent Disease, Platinum Sensitive

1. Pfisterer J, Plante M, Vergote I, et al. Gemcitabine plus carboplatin compared with carboplatin in patients with platinum-sensitive recurrent ovarian cancer: an intergroup trial of the AGO-OVAR, the NCIC CTG, and the EORTC GCG. *J Clin Oncol.* 2006;24(29):4699-707. doi:10.1200/JCO.2006.06.0913.
2. Aghajanian C, Blank SV, Goff BA, et al. OCEANS: a randomized, double-blind, placebo-controlled phase III trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer. *J Clin Oncol.* 2012;30(17):2039-45. doi:10.1200/JCO.2012.42.0505.
3. Aghajanian C, Goff B, Nycum LR, et al. Final overall survival and safety analysis of OCEANS, a phase 3 trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent ovarian cancer. *Gynecol Oncol.* 2015;139(1):10-16. doi:10.1016/j.ygyno.2015.08.004.
4. Wagner U, Marth C, Largillier R, et al. Final overall survival results of phase III GCIG CALYPSO trial of pegylated liposomal doxorubicin and carboplatin vs paclitaxel and carboplatin in platinum-sensitive ovarian cancer patients. *Br J Cancer.* 2012;107(4):588-591. doi:10.1038/bjc.2012.307.
5. Coleman RL, Brady MF, Herzog TJ, et al. Bevacizumab and paclitaxel-carboplatin chemotherapy and secondary cytoreduction in recurrent, platinum-sensitive ovarian cancer (NRG Oncology/Gynecologic Oncology Group study GOG-0213): a multicentre, open-label, randomised, phase 3 trial. *Lancet Oncol.* 2017;18(6):779-791. doi:10.1016/S1470-2045(17)30279-6.
6. Pfisterer J, Shannon CM, Baumann K, et al. Bevacizumab and platinum-based combinations for recurrent ovarian cancer: a randomised, open-label, phase 3 trial. *Lancet Oncol.* 2020;21(5):699-709. doi:10.1016/S1470-2045(20)30142-X.

References – Pancreatic Cancer

v1.0.2024

Neoadjuvant: Adenocarcinoma

1. Katz MH, Shi Q, Ahmad SA, Herman JM, et al. Preoperative Modified FOLFIRINOX Treatment Followed by Capecitabine-Based Chemoradiation for Borderline Resectable Pancreatic Cancer: Alliance for Clinical Trials in Oncology Trial A021101. *JAMA Surg.* 2016;151(8):e161137. doi:10.1001/jamasurg.2016.1137.
2. Murphy JE, Wo JY, Ryan DP, et al. Total Neoadjuvant Therapy With FOLFIRINOX Followed by Individualized Chemoradiotherapy for Borderline Resectable Pancreatic Adenocarcinoma: A Phase 2 Clinical Trial. *JAMA Oncol.* 2018;4(7):963–969. doi:10.1001/jamaoncol.2018.0329.
3. O'Reilly EM, Lee JW, Zalupski M, et al. Randomized, multicenter, phase II trial of gemcitabine and cisplatin with or without veliparib in patients with pancreas adenocarcinoma and a germline BRCA/PALB2 mutation. *J Clin Oncol.* 2020;38(13):1378-1388. doi:10.1200/JCO.19.02931.
4. Sohal DPS, Duong M, Ahmad SA, et al. Efficacy of Perioperative Chemotherapy for Resectable Pancreatic Adenocarcinoma: A Phase 2 Randomized Clinical Trial. *JAMA Oncol.* 2021;7(3):421–427. doi:10.1001/jamaoncol.2020.7328.

Advanced/Metastatic: First Line, Adenocarcinoma

1. Conroy T, Desseigne F, Ychou M, et al. FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. *N Engl J Med.* 2011;364(19):1817-1825. doi:10.1056/NEJMoa1011923.
2. Von Hoff DD, Ervin T, Arena FP, et al. Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. *N Engl J Med.* 2013;369(18):1691-1703. doi:10.1056/NEJMoa1304369.
3. Wainberg ZA, Melisi D, Macarulla T, et al. NALIRIFOX versus nab-paclitaxel and gemcitabine in treatment-naïve patients with metastatic pancreatic ductal adenocarcinoma (NAPOLI 3): a randomised, open-label, phase 3 trial. *Lancet.* 2023;402(10409):1272-1281. doi:10.1016/S0140-6736(23)01366-1.

References – Prostate Cancer

v1.0.2024

Metastatic: Adenocarcinoma, Castration Resistant

1. Ryan CJ, Smith MR, de Bono JS, et al. Abiraterone in metastatic prostate cancer without previous chemotherapy. *N Engl J Med*. 2013;368(2):138-148. doi:10.1056/NEJMoa1209096.
2. Beer TM, Armstrong AJ, Rathkopf DE, et al. Enzalutamide in metastatic prostate cancer before chemotherapy. *N Engl J Med*. 2014;371(5):424-433. doi:10.1056/NEJMoa1405095.
3. Tannock IF, de Wit R, Berry WR, et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. *N Engl J Med*. 2004;351(15):1502-1512. doi:10.1056/NEJMoa040720.
4. De Bono JS, Oudard S, Ozguroglu M, et al. Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial. *Lancet*. 2010;376(9747):1147-1154. doi:10.1016/S0140-6736(10)61389-X.
5. Kantoff PW, Higano CS, Shore ND, et al. Sipuleucel-T immunotherapy for castration-resistant prostate cancer. *N Engl J Med*. 2010;363(5):411-422. doi:10.1056/NEJMoa1001294.

References – Testicular Cancer

v1.0.2024

First Line: Good Risk

1. Saxman SB, Finch D, Gonin R, et al. Long-term follow-up of a phase III study of three versus four cycles of bleomycin, etoposide, and cisplatin in favorable-prognosis germ-cell tumors: the Indian University experience. *J Clin Oncol*. 1998;16(2):702-706. doi:10.1200/JCO.1998.16.2.702.
2. Culine S, Kerbrat P, Kramar A, et al. Refining the optimal chemotherapy regimen for good-risk metastatic nonseminomatous germ-cell tumors: a randomized trial of the Genito-Urinary Group of the French Federation of Cancer Centers (GETUG T93BP). *Ann Oncol*. 2007;18(5):917-924. doi:10.1093/annonc/mdm062.

First Line: Intermediate/Poor Risk

1. de Wit R, Stoter G, Sleijfer DT, et al. Four cycles of BEP vs four cycles of VIP in patients with intermediate-prognosis metastatic testicular non-seminoma: a randomized study of the EORTC Genitourinary Tract Cancer Cooperative Group. European Organization for Research and Treatment of Cancer. *Br J Cancer*. 1998;78(6):828-832. doi:10.1038/bjc.1998.587.
2. Culine S, Kramar A, Théodore C, et al. Randomized trial comparing bleomycin/etoposide/cisplatin with alternating cisplatin/cyclophosphamide/doxorubicin and vinblastine/bleomycin regimens of chemotherapy for patients with intermediate- and poor-risk metastatic nonseminomatous germ cell tumors: Genito-Urinary Group of the French Federation of Cancer Centers Trial T93MP. *J Clin Oncol*. 2008;26(3):421-427. doi:10.1200/JCO.2007.13.8461.
3. Nichols CR, Catalano PJ, Crawford ED, et al. Randomized comparison of cisplatin and etoposide and either bleomycin or ifosfamide in treatment of advanced disseminated germ cell tumors: an Eastern Cooperative Oncology Group, Southwest Oncology Group, and Cancer and Leukemia Group B Study. *J Clin Oncol*. 1998;16(4):1287-1293. doi:10.1200/JCO.1998.16.4.1287.